

# **Physical activity behaviors, associated parameters, and the feasibility of an online physical exercise intervention in individuals with diabetes**

PhD thesis by

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## **Preface**

The overall purpose of this thesis was to study the physical activity behaviors and feasibility of an intervention aiming to increase and maintain physical activity in individuals with diabetes. The work described in this thesis was mainly conducted in the period from 2021 to 2024 at the Research Unit Exercise Epidemiology, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, and the Research and Implementation Unit PROgrez, Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals.

My work in this PhD has consisted of several elements. First of all, different data sources have been used in the included papers of this PhD. Working with different datasets and different measurements of physical activity have been educational and contributed to view physical activity from different perspectives. The feasibility study was conducted in close collaboration with the Centre for Physical Activity Research, Rigshospitalet and the Danish Diabetes Association. We developed the intervention in close collaboration with individuals with type 2 diabetes from September 2021 to March 2022, and conducted the feasibility study from March 2022 to May 2022. As part of my PhD program, I visited the Department of Public Health and Nursing, Norwegian University of Science and Technology. The main focus of my research visit was a collaboration with Professor Paul Jarle Mork and Postdoc Eivind Schjelderup Skarpsno on sleep behaviors and physical activity in individuals with diabetes using data from the Norwegian Trøndelag Health Study (HUNT4).

I hope that this thesis can shed light on different perspectives of physical activity behaviors in individuals with diabetes and contribute to future research and decision-making within this field.

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## List of included papers

### *Paper I*

Mortensen, S. R., Kristensen, P. L., Grøntved, A., Ried-Larsen, M., Lau, C., & Skou, S.

**T. Determinants of physical activity among 6856 individuals with diabetes: a nationwide cross-sectional study.**

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### *Paper II*

Mortensen, S. R., Skou, S. T., Brønd, J. C., Ried-Larsen, M., Petersen, T. L., Jørgensen, L. B., Jepsen, R., Tang, L. H., Bruun-Rasmussen, N. E., & Grøntved, A. **Detailed descriptions of physical activity patterns among individuals with diabetes and prediabetes: the Lolland-Falster Health Study.**

*BMJ Open Diabetes Research & Care, Sep 2023*

### *Paper III*

Mortensen, S. R., Grøntved, A., Brønd, J. C., Ried-Larsen, M., Petersen, T. L., Jørgensen, L. B., Jepsen, R., Tang, L. H., & Skou, S. T. **Sedentary activity, sedentary bouts, and patterns of total daily sedentary activity, and their relationship with stress and well-being in individuals with diabetes and prediabetes: The Lolland-Falster Health Study.**

*Mental Health and Physical Activity, Mar 2024*

### *Paper IV*

Mortensen, S. R., Pedersen, M. E., Skou, S. T., & Ried-Larsen, M. **Online Physical Exercise and Group Sessions to Increase and Maintain Physical Activity in Individuals with Type 2 Diabetes: A Single-Arm Feasibility Study.**

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## Additional papers during the PhD – not included in the thesis

### Published papers

Pedersen, J., Rasmussen, M. G. B., Sørensen, S. O., **Mortensen, S. R.**, Olesen, L. G., Brønd, J. C., Brage, S., Kristensen, P. L., & Grøntved, A. (2022). Effects of Limiting Recreational Screen Media Use on Physical Activity and Sleep in Families With Children: A Cluster Randomized Clinical Trial. *JAMA Pediatrics*, 176(8), 741-749. <https://doi.org/10.1001/jamapediatrics.2022.1519>

Pedersen, J., Rasmussen, M. G. B., Sørensen, S. O., **Mortensen, S. R.**, Olesen, L. G., Brage, S., Kristensen, P. L., Puterman, E., & Grøntved, A. (2022). Effects of limiting digital screen use on well-being, mood, and biomarkers of stress in adults. *npj Mental Health Research*, Article 14. <https://doi.org/10.1038/s44184-022-00015-6>

Jørgensen, L. B., Bricca, A., Bernhardt, A., Juhl, C. B., Tang, L. H., **Mortensen, S. R.**, Eriksen, J. A., Walløe, S., & Skou, S. T. (2022). Objectively measured physical activity levels and adherence to physical activity guidelines in people with multimorbidity—A systematic review and meta-analysis. *PLOS ONE*, 17(10), Article e0274846. <https://doi.org/10.1371/journal.pone.0274846>

**Mortensen, S. R.**, Schmidt-Persson, J., Olesen, L. G., Egebæk, H. K., Boye, H., Bilenberg, N., & Grøntved, A. (2023). Parental recreational screen media practices and behavioral difficulties among Danish 7-year-old children. *Academic Pediatrics*, 23(3), 667-674. <https://doi.org/10.1016/j.acap.2023.01.004>

Zangger, G., Bricca, A., Liaghat, B., Juhl, C. B., **Mortensen, S. R.**, Andersen, R. M., Damsted, C., Hamborg, T. G., Ried-Larsen, M., Tang, L. H., Thygesen, L. C., & Skou, S. T. (2023). Benefits and Harms of Digital Health Interventions Promoting Physical Activity in People With Chronic Conditions: Systematic Review and Meta-Analysis. *Journal of Medical Internet Research*, 25, Article e46439. <https://doi.org/10.2196/preprints.46439>, <https://doi.org/10.2196/46439>

Zangger, G., **Mortensen, S. R.**, Tang, L. H., Thygesen, L. C., & Skou, S. T. (2024). Association between digital health literacy and physical activity levels among individuals with and without long-term health conditions: Data from a cross-sectional survey of 19,231 individuals. *Digital Health*, 10, Article 20552076241233158. <https://doi.org/10.1177/20552076241233158>

## **Selected papers submitted or in preparation for submission**

**Mortensen, S. R.**, Mork, P. J., Skou, S. T., Kongsvold, A., Åsvold, B. O., Nielsen, T. I. L., & Skarpsno, E. S. Insomnia and its association with device-measured physical activity among 1,354 individuals with diabetes: The HUNT Study.

*Manuscript in preparation for International Journal of Behavioral Nutrition and Physical Activity*

Pérez, J. P., **Mortensen, S. R.**, Gírbés, E. L., Grønne, D. T., Thorlund, J. B., Roos, E. M., & Skou, S. T. Association between widespread pain and psychosocial factors in people with knee osteoarthritis: A cross-sectional study of patients from primary care in Denmark.

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Luijk, A., **Mortensen, S. R.**, Hamborg, T. G., Zangger, G., Eriksen, J. R., Christensen, J., Skou, S. T., & Tang, L. H. The effectiveness of digital health interventions for maintenance of physical activity following cardiac rehabilitation: a systematic review and meta-analysis.

*Manuscript in preparation for Archives of Physical Medicine and Rehabilitation*

Jørgensen, L. B., **Mortensen, S. R.**, Tang, L. H., Grøntved, A., Brønd, J. C., Jepsen, R., Petersen, T. L., & Skou, S. T. Associations between number and type of conditions and physical activity levels in adults with multimorbidity – a cross-sectional study from the Danish Lolland-Falster Health Study.

*In revision for Journal of Multimorbidity and Comorbidity*

## Summary in English

### *Introduction*

Diabetes has become one of the fastest growing public health challenges of the 21<sup>st</sup> century. The incidence of disability and morbidity caused by diabetes has increased significantly in the last decades. Engagement in regular physical activity is a cornerstone of diabetes management, not only to prevent long-term complications and premature mortality, but also to improve overall well-being and health. While the evidence and recommendations are clear on providing physical activity in prevention and treatment of diabetes, increasing and maintaining physical activity in individuals with diabetes remains challenging. Understanding physical activity behaviors and how to improve it in individuals with diabetes needs to be investigated from different perspectives to understand why regular engagement in physical activity can be a major challenge.

### *Aim*

The overall aim of this thesis is to provide detailed descriptions of physical activity characteristics, determinants, and patterns among Danish individuals with diabetes sampled from recent population-based studies and to evaluate the feasibility, fidelity, and acceptability of an online physical exercise intervention combined with group sessions to increase and maintain physical activity in individuals with type 2 diabetes.

### *Methods*

Paper I was performed as a nationwide cross-sectional study using data from the Danish National Health Survey from 2017. The primary outcome measure was weekly moderate to vigorous physical activity (MVPA). Exposures included self-reported number of chronic conditions, body mass index (BMI), perceived stress, and health-related quality of life (HRQoL). Mean differences in MVPA across exposures were estimated by multiple linear regression analyses.

Paper II and III were performed as cross-sectional studies, both using data from the Danish household-based, mixed rural-provincial population study, The Lolland-Falster Health Study from 2016-2020. Participants were categorized into diabetes, prediabetes, and no diabetes based on their HbA1c level and self-reported use of diabetes medication. For Paper II, the outcome was physical activity in terms of intensities and timing of engagement in activity assessed with a lower-back worn accelerometer, and exposure was diabetes status (diabetes, prediabetes, no diabetes). The outcomes in Paper III were total daily sedentary activity, sedentary bouts, and breaks in sedentary

activity assessed with thigh-worn and lower back-worn accelerometers, and exposures were well-being and stress. Finally, Paper IV was designed as a one-armed feasibility study and the intervention was developed using a co-creation approach. Individuals with type 2 diabetes were recruited for eight weeks of 30-minute online physical exercise intervention followed by 30-minute online group meetings in smaller groups once a week. Outcomes included pre-defined research progression criteria, secondary measurements of health parameters, and participant feedback.

### *Results*

Paper I: Among individuals with diabetes, 40% were insufficiently physically active. Having three or more comorbidities were associated with lower weekly MVPA (-0.48 h/week, 95% CI -0.88; -0.07) compared with participants with no comorbidities. Furthermore, overweight or obese individuals engaged in less weekly MVPA (obese class III vs. normal weight: -1.98 h/week, 95% CI -2.49; -1.47). Higher perceived stress was associated with lower weekly MVPA (-1.76 h/week, 95% CI -2.18; -1.34) vs. low perceived stress. An association between low HRQoL and lower weekly MVPA was found when compared to those with moderate or high HRQoL (physical HRQoL: -0.93 h/week, 95% CI -1.19; -0.66 and mental HRQoL: -0.39 h/week, 95% CI -0.71; -0.08).

Paper II and III: Of participants with diabetes, 63% did not adhere to the WHO recommendations of weekly MVPA, while numbers of participants with prediabetes and no diabetes were 60% and 50%, respectively. Around a third of those with diabetes were highly inactive (<5 min/day of MVPA) daily and had >2 consecutive days of inactivity. Mean time spent physically active daily at any intensity was lowest among participants with diabetes. Higher well-being was associated with lower total sedentary activity in participants with diabetes (-1.1 min/day, 95% CI -2.0; -0.2) and participants with prediabetes (-0.6 min/day, 95% CI -1.1; -0.05). No association was found between stress and sedentary activity.

Paper IV: Most research progression criteria reached a level of acceptance, with exception of participant recruitment, burden of objectively measured physical activity, and adverse events related to the intervention, where changes are needed before continuing to an RCT.

### *Conclusion*

Our findings showed that on a nationwide level, 40% of individuals with diabetes do not meet the WHO recommendations of physical activity. The objectively measured physical activity findings

showed that 63% of individuals with did not adhere to the WHO recommendations. The associations analyses revealed that the prevalence of comorbidities, higher BMI, higher perceived stress, and lower HRQoL were significantly associated with lower engagement in weekly MVPA in individuals with diabetes. Further, higher well-being contributed to lower daily sedentary activity. This underscores the necessity for tailored interventions that recognize these factors to enhance physical activity engagement. Thus, an intervention combining online physical exercise and group sessions may be a feasible approach to accommodate some of these factors and other barriers to participating in physical activity. Altogether, the findings of this thesis emphasize the importance of acknowledging differences in physical activity and sedentary behaviors among individuals with diabetes and how these differences could be accounted for and integrated into future tailored interventions to enhance physical activity engagement in this population.

## **Dansk resumé (summary in Danish)**

### *Introduktion*

Diabetes er én af de hurtigst voksende sundhedsudfordringer i det 21. århundrede. Incidensen af funktionsnedsættelse og sygelighed forårsaget af diabetes er steget signifikant i de seneste årtier. Fysisk aktivitet spiller en central rolle i håndteringen af diabetes, ikke kun for at forebygge længerevarende komplikationer og tidlig død, men også for at øge personers velvære og helbred. Selvom der eksisterer stærke og klare anbefalinger for at behandle og forebygge diabetes, er det fortsat en udfordring for personer med diabetes at øge og forblive fysisk aktive. For at forstå hvorfor det kan være en udfordring for personer med diabetes at være regelmæssigt fysisk aktive, er det vigtigt at undersøge fysisk aktivitet fra forskellige perspektiver.

### *Formål*

Det overordnede formål for denne afhandling er at levere detaljerede beskrivelser af fysiske aktivitets karakteristika, determinanter og mønstre blandt danske personer med diabetes via nylige populationsbaserede studier, samt at evaluere feasibilitet, fidelitet og acceptabilitet af en online fysisk træningsintervention kombineret med gruppesessioner med henblik på at øge og vedligeholde fysisk aktivitet blandt personer med type 2 diabetes.

### *Metode*

Studie I blev udført som et tværsnitstudie via data fra Den Nationale Sundhedsprofil fra 2017. Det primære udfaldsmål var ugentlig moderat til hård fysisk aktivitet (MVPA). Eksponeringsvariable inkluderede selvrapporeret antal kroniske sygdomme, body mass index (BMI), stress og helbredsrelateret livskvalitet (HRQoL). Den gennemsnitlige forskel i MVPA på tværs af eksponeringsvariable blev estimeret via multiple lineær regressionsanalyse.

Studie II og III blev udført som tværsnitstudier, begge med brug af data fra den danske, husholdningsbaserede, blandet land-provins befolkningsundersøgelse, "Lolland Falster-Undersøgelsen" fra 2016-2020. Deltagere blev kategoriseret som diabetes, prædiabetes og ingen diabetes baseret på deres HbA1c niveau og selvrapporeret brug af diabetesmedicin. Udfaldsvariablen i studie II var fysisk aktivitet i relation til intensitetstyper og timing af aktivitet bestemt via et accelerometer placeret på lænden, og eksponeringsvariablen var diabetesstatus (diabetes, prædiabetes, ingen diabetes). Udfaldsvariable for studie III var total daglig stillesiddende aktivitet og stillesiddende omgange/intervaller bestemt via to accelerometere placeret på henholdsvis lår og lænd, og



eksponeringsvariablerne var trivsel og stress.

Studie IV var designet som et en-armet feasibility studie og interventionen blev udviklet via en fællesskabende tilgang. Individuer med type 2 diabetes blev rekrutteret til en otte ugers intervention bestående af en ugentlig 30 minutters online fysisk træning efterfulgt af 30 minutters online gruppemøder. Udfaldsvariable inkluderede prædefinerede forskningsprogressionskriterier, sekundære mål af helbredsparametre og deltagerfeedback.

### *Resultater*

Studie I: Blandt personer med diabetes var 40% utilstrækkeligt fysisk aktive. At have tre eller flere komorbiditeter var associeret med lavere ugentlig MVPA (-0.48 t/ugen 95% CI -0.88; -0.07) sammenlignet med individer med ingen komorbiditeter. Ydermere, havde overvægtige eller svært overvægtige deltagere lavere ugentlig MVPA (overvægtklasse III vs. normalvægtig: -1.98 t/ugen, 95% CI -2.49; -1.47). Højere selvopfattet stress var associeret med lavere ugentlig MVPA (-1.76 t/ugen, 95% CI -2.18; -1.34) vs. lav selvopfattet stress. Ligeledes fandt vi en association mellem lav HRQoL og lav ugentlig MVPA sammenlignet med dem, der havde moderat til høj HRQoL (fysisk HRQoL: -0.93 t/ugen, 95 % CI -1.19; -0.66 and mental HRQoL: -0.39 t/ugen, 95% CI -0.71; -0.08)

Studie II og III: Blandt deltagere med diabetes levede 63% ikke op til minimumsanbefalingerne for ugentlig MVPA, hvorimod tallene for deltagere med prædiabetes eller ingen diabetes var henholdsvis 60% og 50%. Omkring en tredjedel af dem med diabetes var meget inaktive (<5 min/dag af MVPA) dagligt og havde >2 sammenhængende inaktive dage. Den gennemsnitlige tid brugt på at være fysisk aktiv uanset intensitet i løbet af en dag var lavest blandt deltagere med diabetes. Højere trivsel var associeret med lavere total stillesiddende aktivitet blandt deltagere med diabetes (-1.1 min/dag, 95 % CI -2.0; -0.2) og deltagere med prædiabetes (-0.6 min/dag, 95 % CI -1.1; -0.05). Ingen association blev fundet mellem stress og stillesiddende aktivitet.

Studie IV: De fleste af forskningsprogressionskriterierne opnåede et acceptabelt niveau med undtagelse af deltagerrekruttering, byrden af objektivt målt fysisk aktivitet og bivirkninger relateret til interventionen. Før der arbejdes videre med et RCT-studie, skal der foretages ændringer ved disse forskningsprogressionskriterier.

### *Konklusion*

Vores fund viste at på et landsdækkende niveau lever hele 40% af individer med diabetes ikke op til WHO's anbefalinger for fysisk aktivitet. Fundene for den objektivt målt fysiske aktivitet viste, at

63% af individer med diabetes ikke overholdte minimumsanbefalinger. Associationsanalyserne afslørede, at prævalensen af komorbiditeter, højere BMI, højere selvopfattet stress og lavere HRQoL var signifikant associeret med lavere ugentlig MVPA blandt individer med diabetes. Derudover fandt vi, at højere trivsel bidrog til lavere total daglig stillesiddende aktivitet. Dette understreger behovet for skræddersyede interventioner, som anerkender disse faktorer for at forøge deltagelse i fysisk aktivitet. Således kan en intervention, der kombinerer online træning og gruppesessioner, være en mulig måde at imødekomme nogle af disse faktorer og andre barrierer for deltagelse i fysisk aktivitet. Samlet set fremhæver fundene fra denne afhandling vigtigheden af at anerkende forskelle i fysisk aktivitet og stillesiddende aktivitetsadfærd blandt personer med diabetes, samt hvordan disse forskelle kan tages i betragtning og integreres i fremtidige skræddersyede interventioner for at øge deltagelse i fysisk aktivitet blandt denne population.

## Abbreviations

ADA	American Diabetes Association
BMI	Body Mass Index
CFAS	Centre for Physical Activity Research
CI	Confidence interval
CPR	Danish Civil Registration System
DAG	Directed acyclic graph
DDA	Danish Diabetes Association
DNHS	Danish National Health Survey
EASD	European Association for the Study of Diabetes
GP	General practitioner
HbA1c	Glycated hemoglobin levels
HRQoL	Health-related quality of life
IQR	Interquartile range
LOFUS	Lolland-Falster Health Study
LPA	Light physical activity
MET	Metabolic equivalent of task
MPA	Moderate physical activity
MVPA	Moderate-to-vigorous physical activity
OSF	Open Science Framework
OR	Odds ratio
PSS	Perceived Stress Scale
RCT	Randomized controlled trial
SAP	Statistical analysis plan
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
T2D	Type 2 diabetes
VPA	Vigorous physical activity
WHO	World Health Organization

## Definitions

Physical activity	Definition from WHO: “ <i>Any bodily movement produced by skeletal muscles that requires energy expenditure and can be performed at a variety of intensities, as part of work, domestic chores, transportation or during leisure time, or when participating in exercise or sports activities.</i> ”
Physical exercise	Planned, structured, and repetitive bodily activities that are purposeful, intentional, and often performed at a moderate to high intensity level.
Physical inactivity	Not adhering to the recommended levels of weekly MVPA from the WHO.
Sedentary behavior	Time spent sedentary related to specific sedentary behaviors such as TV-viewing, eating, social events, or working.
Sedentary activity	Time spent in a sedentary position (sitting, reclined, or lying).
Sedentary time	In this PhD thesis, sedentary time will be used as a general term, including both time spent on sedentary behaviors and time spent on sedentary activity, as the definitions above.

## List of appendices

Appendix I	Paper I + Supplements
Appendix II	Paper II + Supplements
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Appendix V	Statistical analysis plan for Paper I
Appendix VI	Statistical analysis plan for Paper II
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# 1. Background

## 1.1. Diabetes – a growing public health challenge

Diabetes is a chronic, metabolic condition characterized by elevated levels of blood glucose (1). Diabetes has become one of the fastest growing public health challenges of the 21<sup>st</sup> century and around 537 million adults worldwide are currently living with diabetes, in which type 2 diabetes (T2D) accounts for more than 90% of these cases (1, 2). Further, it is estimated that almost 45% adults (between 20-79 years old) are living with diabetes but are unaware of their diabetes status (2). The incidence of disability and morbidity caused by diabetes has increased significantly in the last decades (3), and with an increase by 70% in deaths caused by type 1 and 2 diabetes from 2000 to 2019, diabetes entered the top ten causes of death and disability worldwide (4).

Diabetes is one of the most prevalent chronic conditions, and the prevalence is predicted to increase rapidly (1). Economic development, growing urbanization, population ageing, and changing lifestyles such as reduced levels of physical activity and unhealthy eating habits are believed to be contributing factors to the increased prevalence of particularly T2D (1, 5, 6). Such factors have contributed to a high prevalence of individuals with impaired fasting glucose or impaired glucose tolerance, also known as prediabetes (7), which can progress to T2D (1, 8, 9). Also, the rates of early-onset T2D ( $\leq 40$  years of age) are increasing and thereby introducing a new public health and societal challenge (10).

Around 11.5% of the total health expenditure worldwide is spent on diabetes-related health, and among the ten countries with the highest diabetes-related health expenditure per person, nine countries are from Europe (1). Diabetes is an expensive chronic condition because it requires ongoing medical care and management to maintain optimal health and prevent complications. The direct costs associated with diabetes includes various components such as hospitalization, medication, outpatient visits, costs associated with treating and managing diabetes-related complications, as well as costs related to diabetes self-management education and lifestyle interventions. Also, the indirect costs of diabetes are many and includes productivity loss while at work, absence from work, inability to work because of disease-related disability and lost productive capacity due to early mortality (11).

As diabetes is a chronic condition that comes with several disease-related complications and challenges, the individual's life can be significantly affected both physically and mentally. Most individuals with diabetes are overweight or obese and suffers from other chronic conditions (12). In addition to this, living with diabetes can be stressful and affect the individual's health-related quality of life (HRQoL) and overall well-being (13, 14), because they may worry about existing and future complications, as well as feeling ashamed of not adhering to lifestyle recommendations, e.g. in terms of diet, weight, and physical activity (15).

Due to the enormous consequences related to public health, economy, and the individual, it is highly relevant to focus on this population.

## **1.2. Recommendations on physical activity and sedentary behavior in individuals with diabetes**

Engagement in regular physical activity is a cornerstone of T2D management, not only to prevent long-term diabetes complications and premature mortality, but also to improve the overall health in individuals with diabetes (16-20). Physical activity is defined by the World Health Organization (WHO) as:

*“Any bodily movement produced by skeletal muscles that requires energy expenditure and can be performed at a variety of intensities, as part of work, domestic chores, transportation or during leisure time, or when participating in exercise or sports activities.”* (21)

Adults living with diabetes are recommended to engage in at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity aerobic physical activity weekly spread over at least three days, or at least have no more than two consecutive days of inactivity (21, 22). This refers to a minimum threshold for achieving significant health outcomes, including improved insulin sensitivity, weight management, and cardiovascular health (22). However, focusing solely on meeting the recommended levels of physical activity may overlook the importance of other physical activity behaviors throughout the day.

In 2022, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published a consensus report stressing out the importance of 24-hour physical

activity behaviors in individuals with T2D. An individual's 24-hour physical activity behaviors encompass not only structured exercise sessions but also activities of daily living, occupational tasks, and leisure activities, sedentary behaviors, and time spent sleeping which contribute cumulatively health-related benefits (23). While the recommended levels of weekly physical activity remain a cornerstone of physical activity guidelines for individuals with diabetes, considering 24-hour physical activity behaviors provide a more holistic perspective on the role of physical activity in managing the condition and promoting overall health and well-being (23).

Being physically inactive is defined as not adhering to the recommended levels of weekly physical activity (21). Physical inactivity is the fourth leading cause of death worldwide (24), and it is recognized as an independent risk factor of the development of T2D (25). Meeting the recommendations of physical activity is a major challenge among individuals with diabetes, and some studies report that about 50-65% of individuals with diabetes are inactive (26-28).

In recent years, reductions in sedentary behavior have become an increased focus in diabetes management instead of only increasing physical activity, because evidence indicates that higher levels of sedentary behavior are associated with the development of T2D, cardiovascular diseases, and all-cause mortality (29-31). Sedentary behavior is defined by the WHO as:

*“Any waking behavior characterized by an energy expenditure of 1.5 METs or lower while sitting, reclining, or lying.”* (21)

Adults with T2D are recommended to reduce the amount of time spent sedentary, and prolonged sitting should be interrupted every 30 minutes with small “doses” of light activity to improve glycemic control (22, 32). Since individuals with diabetes are highly sedentary and spent a limited amount of time on physical activity compared to individuals without diabetes (33, 34), targeting reductions in time spent sedentary instead of reaching 150 minutes of moderate to vigorous physical activity (MVPA) could be a more feasible strategy to improve health in individuals with diabetes. However, the recommendations emphasize that reducing sedentary behavior should be an addition to the recommendations of physical activity and not replace the increase in MVPA (22).

Despite strong and clear recommendations to treat and prevent diabetes-related complications, increasing physical activity in individuals with diabetes remains challenging (26, 27). Given that physical activity is an effective and, in many ways, a simple approach for the individual, family,



peers, and healthcare system to enhance diabetes self-management, it becomes increasingly vital to investigate and understand various facets of physical activity and time spent sedentary in individuals with diabetes. To grasp why consistent participation in physical activity can pose a significant challenge for individuals with diabetes and to explore avenues for improvement, it is imperative to expand and consider various perspectives in understanding physical activity among this population.

### **1.3. Determinants of physical activity and time spent sedentary**

As physical activity plays a crucial role in the management of individuals with diabetes, understanding the determinants of physical activity in this population is important for developing effective interventions to improve physical activity behaviors and reduce time spent sedentary. Among these determinants, obesity stands as a significant consideration, given its high prevalence in diabetes and its impact on mobility (12). Another important determinant to consider is multimorbidity, the coexistence of multiple chronic conditions, which may challenge the individual even further in several ways, both physically and mentally (35).

Well-being emerges as a critical determinant, encompassing emotional, physical, and social aspects (36) that can either facilitate or hinder engagement in physical activity. Studies within the field of diabetes suggest that low well-being could significantly impede diabetic control and self-care practices related to the condition (37-39). Therefore, improving well-being is emphasized as an important focus as part of the ADA recommendations on diabetes self-management education and support, as well-being is foundational for achieving diabetes treatment goals and maximize quality of life (22). Stress reflects an emotional burden when demands exceed an individual's perceived resources which may occur by the demands of diabetes management (40), affecting the individual's motivation and ability to participate in regular physical activity as well as time spent sedentary. Conversely, a positive HRQoL can serve as an essential motivator, as this term specifically evaluates the impact of health on the individual's quality of life, which may drive the individual to prioritize physical activity.

As all these determinants are associated with lower physical activity levels in the general population (41-44), it is likely to believe that this is also the case in individuals with diabetes since these factors are more prevalent in this population when compared to the general population (13, 14, 45-

48). Living with diabetes and simultaneously struggling with other factors could potentially affect the individual's ability to engage in regular physical activity and reduce time spent sedentary. Hence, it is important to consider if the treatment of individuals with diabetes should not necessarily revolve around increasing physical activity. Moreover, understanding these determinants could be useful to consider if physical activity should be promoted differently depending on potential factors that the individual might struggle with. By addressing obesity, multimorbidity, well-being, stress and HRQoL, healthcare professionals can empower individuals to adopt and maintain healthy lifestyles and thereby optimizing diabetes management.

#### **1.4. Perspectives of physical activity and time spent sedentary**

Most studies reporting engagement in physical activity only report proportions of individuals adhering or not adhering to the recommendations based on self-reported information (26, 28). There are several reasons why this is a problematic approach to investigate physical activity behavior. First, relying on self-reported instruments to assess physical activity only may introduce inaccurate estimates e.g., due to social desirability and recall bias. Therefore, studies measuring physical activity with accelerometer-based devices are needed to obtain more accurate estimates (49). Second, reporting physical activity only as adhering or not adhering to the recommendations does not truly reflect the individual's actual daily engagement in physical activity and health. An individual can adhere to the recommendations of physical activity and yet still engage in excessive amounts of sedentary time which may lead to an increased disease risk, because sedentary behavior is an independent risk factor (50, 51). Therefore, it is important to distinguish between physical activity, physical inactivity, and time spent sedentary when describing and investigating physical activity behaviors. Finally, considering that physical activity is strongly recommended to be an integrated part of the individual with diabetes' daily life to manage the disease (22, 32), there should be an increased focus on incorporating physical activity through a whole-day approach, including activities of daily living and leisure time activities (23). Instead of solely increasing structured physical activity such as going to fitness or playing football, it is important to prioritize reducing time spent sedentary and promoting daily unstructured physical activity, such as active transport, garden work, or household chores. Such a strategy could be more feasible in populations that are unable to increase structured physical activity due to factors such as obesity or comorbidities (52).

Previous physical activity recommendations did not recognize the benefits of activity bouts of less than 10 minutes, making the value of physical activity primarily concentrating on structured physical activity (53). However, the newest recommendations from WHO have emphasized that all activity counts as beneficial for the individual's health regardless of bout duration (21). Therefore, studies should cover a broader spectrum of engagement in physical activity and sedentary behavior, including levels, patterns, timing of engagement during a weekday and a weekend day, particularly among individuals with chronic conditions such as diabetes where physical activity is a cornerstone of the treatment and prevention (18).

Recent developments of technological wearable devices for use in research provide new possibilities to describe detailed patterns of physical activity, sedentary behavior, sleep characteristics, and other physiological factors over long time periods (54). The second-by-second continuous assessment offer many opportunities to advance research in physical activity and sedentary behaviors among individuals with chronic conditions that are expected to have different behaviors compared to the general population (55, 56). Such knowledge is important to strengthen the opportunities within personalized medicine approach, which is an approach that focuses on optimization of diagnosis, prediction, prevention, and treatment of diabetes by integrating multidimensional data that accounts for individual differences (57). This approach uses complex data obtained from devices and behavioral monitors to characterize the individual's health status to improve for instance individually tailored treatment, because some patients do not require treatment even though they have a diagnosis, whereas other patients may need additional treatment. Thereby, a personalized medicine approach can be considered as using patient characteristics to guide the choice of treatment which is important to better utilize resources in diabetes treatment and prevention (57). Hence, wearable accelerometer-based devices could be used as a screening tool to identify and stratify individuals with diabetes into subgroups based on their physical activity levels and patterns (58).

### **1.5. Supporting maintenance of a physically active lifestyle**

Although lifelong physical activity is a crucial prevention strategy for individuals with diabetes (22), many individuals struggle maintaining a physically active lifestyle (59, 60). Despite awareness of the health-related benefits and good intentions of engagement in physical activity, individuals with diabetes may find it challenging due to expected physical discomfort, absence of easily

accessible long-term programs or digital possibilities to facilitate social support (61, 62). Existing physical activity interventions often fail to align with their needs concerning content, timing, and accessibility, making it difficult for them to integrate physical activity into their daily routines while increasing physical activity (61). In addition, the transfer from community-based supervised exercise to home can be experienced as a confrontation with the real world, and the individual may find it difficult to transfer the obtained physical activity habits to a home-based setting (61, 63, 64). This scenario may occur in individuals with diabetes in a Danish context, as most are offered supervised exercise in the municipality due to their diabetes disease or in relation to other comorbidities. To enhance long-term physical activity behaviors, interventions should evolve around individual preferences and local societal opportunities. Being a part of an exercise community can be essential for some people with chronic conditions to feel supported in managing efforts of daily physical activity engagement (61). However, these communities often require facilitation by peers or healthcare professionals (61, 65) e.g., group-based exercise organized by clinicians, patient and sports associations.

Digital-based health solutions such as activity wearables and internet-based interventions have been highlighted and recommended as potential tools to promote physical activity and increase self-management in adults with T2D (18, 66). Particularly smartwatches and activity wearables tracking step counts are effective tools to support behavior change through goal setting and feedback (67). Physical activity interventions delivered online (online physical exercise) have been developed for several chronic conditions because it enables the individual to attend the intervention despite lack of resources, time, or geographical distances (61, 68). Although online physical exercise might meet the individuals' needs in many ways, attending an online physical exercise could reduce relational and mental effects and lower adherence due to a feeling of social distancing behind the screen (68, 69). Therefore, it is relevant to investigate whether it is feasible to obtain a sense of social support through online group-based exercise as this may solve the challenges related to online physical exercise.

Physical activity interventions in diabetes treatment that have showed the most promising results in terms of glycemetic outcomes encompassed multifactorial exercise programs that were structured, flexible, individually tailored and supervised with behavioral support, and included digital technology (12). Thus, these elements are relevant to consider in addition to involvement of

individuals with diabetes when developing physical activity interventions aiming for long-term adherence and effectiveness. Developing such interventions requires the involvement of end-users in a co-creation approach, as this has been proposed as a more efficient way to achieve positive societal changes (70), instead of one-size-fits all interventions and top-down approaches (71). The purpose of the co-creation approach is to enhance the feeling of ownership among end-users and thereby improve adherence, satisfaction, and effectiveness (70, 72). Particularly in disadvantaged groups such as individuals with diabetes, the co-creation approach has proven to be beneficial (73).

To address the challenges individuals with diabetes face in maintaining a physically active lifestyle, incorporating digital health solutions and social support, while involving end-users in a co-creation approach, holds promise for enhancing long-term adherence and effectiveness in physical activity interventions aimed at diabetes management.

#### **1.6. The rationale behind this PhD thesis**

The rationale for undertaking this PhD thesis lies in addressing the urgent and multifaceted challenges posed by diabetes, as presented in the introduction. Understanding the determinants and patterns of physical activity and time spent sedentary among individuals with diabetes is essential for developing tailored interventions that promote and maintain physical activity engagement. Furthermore, the development of tailored interventions requires involvement of end-users to account for diverse needs and preferences in individuals with diabetes of which digital solutions offer promising avenues for supporting a physically active lifestyle.

## 2. Aims

The overall aim of this thesis is to provide detailed descriptions of physical activity characteristics, determinants, and patterns among Danish individuals with diabetes sampled from recent population-based studies and to evaluate the feasibility, fidelity, and acceptability of an online physical exercise intervention combined with group sessions to increase and maintain physical activity in individuals with T2D.

The overall aim was pursued in studies which were written into four separate research papers (Appendix I-IV), hereafter referred to as Paper I, II, III, and IV. The aims of each Paper were:

### *Paper I*

- To describe habitual physical activity, adherence to WHO recommendations, and investigate the associations of comorbidity, obesity, stress, and HRQoL with MVPA among individuals with diabetes.

### *Paper II*

- To describe objectively measured physical activity patterns, including daily activity according to day type (weekdays and weekend days) and the four seasons, frequency, distribution, and timing of engagement in activity during the day in individuals with diabetes and prediabetes and compared to individuals with no diabetes while adjusting for determinants of physical activity.

### *Paper III*

- To investigate the associations of stress and well-being with the total amount of sedentary activity, characterized by sitting, reclined, and lying during waking hours, and durations of continuous sedentary bouts in individuals with diabetes and prediabetes. A secondary aim was to explore the daily sedentary activity pattern during a day in individuals with diabetes and prediabetes.

### *Paper IV*

- To evaluate the feasibility, fidelity, and acceptability of 8-week high intensity online training combined with online group meetings in individuals with T2D.

### **3. Paper I: Determinants of physical activity among 6,856 individuals with diabetes: a nationwide cross-sectional study**

The following part of the thesis includes the methods and results section for Paper I. These sections include some information, which was previously described in the published version of Paper I (Appendix I).

Paper I is a cross-sectional study aiming to 1) describe habitual physical activity and adherence to WHO recommendations, and 2) investigate the association of comorbidity, obesity, stress, and HRQoL with MVPA among individuals with diabetes based on data from a large nationwide Danish survey.

#### **3.1. Methods**

##### *3.1.1. Setting and data sources*

Paper I used data from the Danish National Health Survey (DNHS) from 2017. The DNHS is a nationwide survey based on six mutually exclusive random subsamples from each of the five Danish administrative regions and one national sample. The DNHS is conducted every third to fourth year and aims to monitor the status and trends in physical and mental health in the adult Danish population ( $\geq 16$  years of age). The DNHS has a webpage with detailed descriptions about the DNHS design (<https://www.danskernessundhed.dk/>).

The Danish Civil Registration System (CPR in Danish) was utilized to randomly select individuals from the population, who were then invited to participate in the survey through either a secure electronic mail service (Digital Post) or regular postal service (74, 75).

In 2017, 312,349 individuals were invited to participate, and the questionnaire was fully or partially completed (meaning that questions regarding age, sex, and at least one other question were answered) by 183,372 respondents corresponding to a response rate of 58.7% (75).

Reporting of Paper I followed the “Strengthening the Reporting of Observational Studies in Epidemiology” (STROBE) checklist (76). Data storage and management for Paper I was approved by the Danish Data Protection Agency through the University of Southern Denmark (Journal nr.: 11.397).

### 3.1.2. Participants

Respondents with information regarding diabetes status were included in Paper I. Respondents were asked if they have diabetes or have had diabetes, and if they suffered from sequela due to the diabetes. This information was used to categorize respondents into “Have diabetes” and “No known diabetes”. Respondents were categorized as “Have diabetes” if they had answered “I have diabetes now” or “I have had diabetes” and “I suffer from sequela due to the diabetes”.

Out of 183,372 respondents, 10,216 had diabetes. Respondents were considered eligible for Paper I, if they had complete data on outcome, exposure, and confounder variables.

### 3.1.3. Exposure variables

*Comorbidity (excluding diabetes).* Respondents reported information about whether they had or have had selected long-term conditions, and whether they were suffering from sequelae due to the specific long-term condition. The selected long-term conditions were organized in ten groups of body systems according to Willadsen et al. (77). Due to lack of information on long-term conditions in all body systems, and since diabetes was the only endocrine condition in the DNHS survey, only seven body system groups were used to define the comorbidity-variable. The seven groups of conditions were: 1) Lung, 2) Musculoskeletal, 3) Mental, 4) Cancer, 5) Neurological, 6) Cardiovascular, and 7) Sensory organs.

A variable that counted the number of conditions from zero to three or more from different body systems including diabetes was developed. The variable was categorized into 1) Have diabetes and no comorbidities, 2) Have diabetes and one comorbidity, 3) Have diabetes and two comorbidities, and 4) Have diabetes and three or more comorbidities. If a respondent reported several long-term conditions within the same body system, e.g., hypertension and myocardial infarction, it would still only count as one comorbidity. Studies have found a lower engagement in physical activity in individuals with comorbidities and decreased mental health compared to individuals with solely somatic comorbidities (78, 79). Therefore, a variable that differentiated between comorbidities with and without a mental health condition was developed to take these differences into account.

*Obesity.* Respondents reported their height and weight, which were used to calculate their body mass index (BMI) ( $\text{kg}/\text{m}^2$ ). We followed the WHO’s classification of obesity and categorized BMI



into five: underweight/normal weight (BMI<25.0), overweight (BMI  $\geq$ 25.0 to <30.0), obese class I (BMI  $\geq$ 30.0 to <35.0), obese class II (BMI  $\geq$ 35.0 to <40.0), and obese class III (BMI  $\geq$ 40) (80).

*Stress.* Self-reported psychological stress was assessed using the Danish version of Cohen's 10-item Perceived Stress Scale (PSS) (81, 82). The stress variable was categorized into three: 1) Low perceived stress (scores ranging from 0-13), 2) Moderate perceived stress (scores ranging from 14-26), and 3) High perceived stress (scores ranging from 27-40).

*Health-related quality of life.* The 12-item Short-Form Health Survey (SF-12) was used to assess HRQoL (physical and mental) among respondents. A physical health variable and a mental health variable differentiating between low HRQoL and moderate to high HRQoL were developed. A physical score of 50 or less was categorized as "Low physical HRQoL", and a mental score of 42 or less was categorized as "Low mental HRQoL" (83).

#### 3.1.4. Outcome variables

The outcomes of interest in Paper I were self-reported MVPA h/week, adherence to WHO recommendations of physical activity and sedentary behavior, total sedentary behavior h/day, and motivation for physical activity.

*Moderate to vigorous physical activity (h/week).* The outcome MVPA was assessed with the following question: "During a regular week, how much time do you spend on moderate and vigorous physical activities, where you can feel your pulse and your breathing increase (e.g., walking, cycling as transport or recreational activity, hard gardening, running or exercise sports)? Indicate only activities lasting at least 10 minutes". Respondents replied in hours and minutes the amount of engagement in weekly MVPA. MVPA was assessed in h/week.

*Adherence to WHO recommendations.* The question regarding weekly MVPA and the following question were used to assess adherence to WHO recommendations: "How much time of the above-mentioned physical activities do you spend in a regular week on vigorous physical activities? These are activities where your pulse is substantially increased, you sweat, and which cause you to be out of breath and to find it hard to talk (e.g., swimming, running, cycling at high speed, strength training or ball games)". Respondents were categorized as "Following WHO recommendations" if they reported at least 150 mins/week of moderate intensity, or 75 mins/week of vigorous intensity,

or an equivalent combination (21).

Additionally, self-reported MVPA was used to categorize respondents into four levels of habitual physical activity based on the WHO recommendations: 1) Inactive: 0 h/week, 2) Inadequate: participants do not meet 150-300 mins/week of moderate intensity or 75-150 mins/week of vigorous intensity, 3) Adequate: Participants meet recommendations, but no more than 300 mins/week of moderate intensity or 150 mins/week of vigorous intensity, and 4) Optimal: Participants with more than 300 mins/week of moderate intensity or 150 mins/week of vigorous intensity.

*Total sedentary behavior (h/day).* The following question was used to assess total sedentary behavior: “On a typical weekday/workday, how much time do you spend on sitting down in each of the following situations? Please consider your total sitting time and distribute it in each of the following categories”. Respondents reported minutes and hours spent daily on 1) Transport (e.g., in car, bus or train. Not cycling), 2) Work/school/education (e.g., sitting by desk or at meeting), 3) Leisure time: by screen (e.g., TV, computer, tablet, smartphone), 4) Leisure time: other (e.g., meals, reading, social gatherings). Total sedentary behavior was assessed in h/day. Questions regarding total sedentary behavior have previously been validated (84).

*Motivation for physical activity.* After reporting engagement in physical activity and sedentary behavior, respondents were asked if they were motivated for being more physically active with the response categories Yes and No.

### 3.1.5. Covariates

In Paper I, the following covariates were suggested a priori to be potential independent risk factors of the four exposures (comorbidity, obesity, stress, and HRQoL) and the outcome (physical activity): Age, sex, ethnicity, marital status, educational level, alcohol consumption, smoking, and diet. Directed Acyclic Graphs (DAGs) (85) of the assumed causal relations between exposures and outcome of the primary analysis are provided in Appendix V.

Age, sex, and ethnicity were obtained from the Danish CPR-register. Ethnicity was categorized into three groups: Danish background, other Western background. Self-reported information about respondents’ marital status was dichotomized into “Married or living with partner” or “Living alone”. Respondents’ highest level of education was used to assess educational level with three categories: 1) Primary or lower secondary education, 2) Upper secondary (shorter length education

(2-3 years) or vocational education, and 3) Higher education (medium (3-4 years) and longer (>4 years) length education). Smoking status was categorized into 1) Smoker, 2) Ex-smoker, and 3) Never smoked. Respondent's weekly alcohol consumption was measured by the number of drinks of beer, wine, and spirits consumed in a typical week and categorized in accordance with the national recommendations from the Danish Health Authority: 1) No alcohol (0 drinks), 2) Below low risk (men >0 to <14 drinks, women >0 to <7 drinks), 3) Above low risk (men  $\geq 14$  to  $\leq 21$  drinks, women  $\geq 7$  to  $\leq 14$  drinks), and 4) High risk (men >21 drinks, women >14 drinks). Diet habits were used to measure a diet-score that divided the respondents into three health levels based on their diet: 1) Healthy diet, 2) Medium healthy diet, and 3) Unhealthy diet (86).

### *3.1.6. Statistical methods*

A statistical analysis plan (SAP) was developed (Appendix V) and registered in the Open Science Framework (OSF) (<https://osf.io/25u4g/>) before commencing the analyses. The text in the following paragraph is very similar to the SAP as well as the description of the analyses section described in the published version of Paper I (Appendix I). All statistical analyses were conducted in STATA/BE 17.0 using an  $\alpha$ -level of 0.05 two-sided.

We conducted cross-tabulations to describe characteristics among participants with and without diabetes to display potential subgroup differences. Further, cross-tabulations were conducted to describe characteristics among participants with diabetes stratified into four levels of habitual physical activity. The descriptive statistics were presented as numbers and percentages, means or standard deviations (SD), or medians and interquartile range (25<sup>th</sup> and 75<sup>th</sup>) (IQR).

Four separate multiple linear regression analyses were performed to examine the relationships between the exposures (comorbidity, obesity, stress, and HRQoL) and the outcome measure MVPA. The results of these regression analyses were presented as mean differences with 95% confidence intervals (CI) across various exposure levels, using the categories of no comorbidities, underweight/normal weight, low perceived stress, and moderate to high HRQoL as reference groups.

In order to investigate the association between the same four exposures and adherence to WHO recommendations for physical activity, four multiple logistic regression analyses were conducted. The results of these logistic regressions were presented as odds ratios (OR) with 95% CI.

Additionally, we conducted four multiple linear regression analyses with total daily sedentary behavior as the outcome variable.

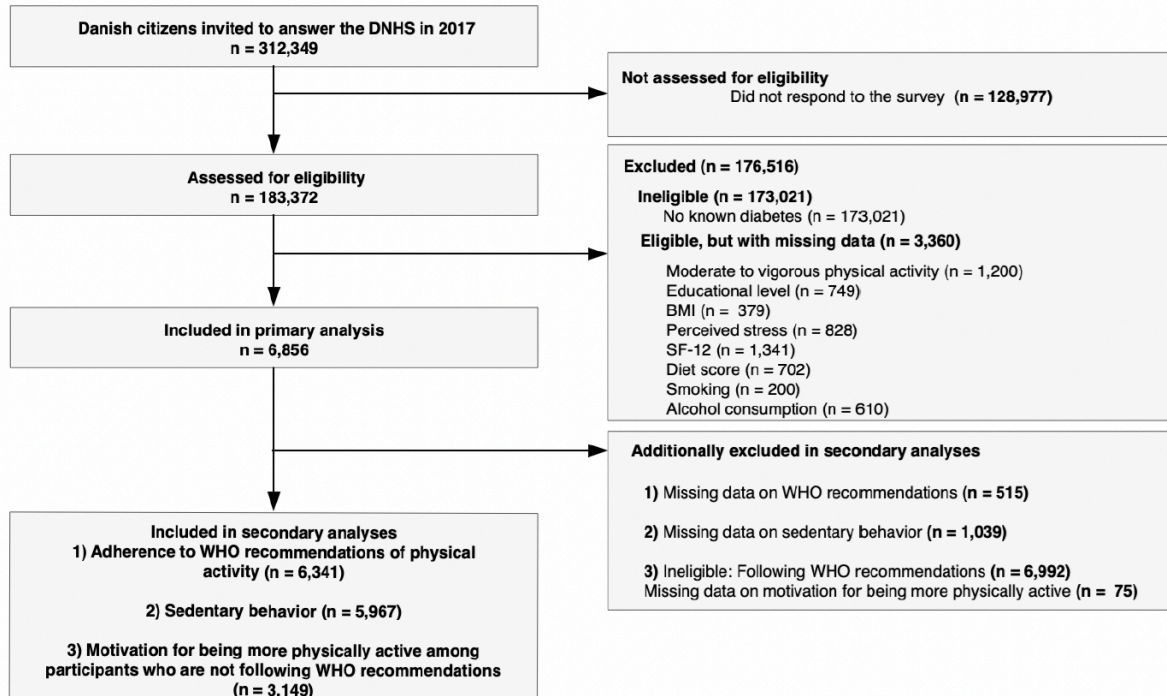
All models were reported both crude and adjusted for age, sex, ethnicity, marital status, educational level, alcohol consumption, smoking, and diet. Furthermore, since the four exposures were considered to be potential independent risk factors in the individual model, these variables were included as confounders in the respective model. Because obesity is a strong determinant of a wide range of morbidities, we conducted post hoc analyses of comorbidities and MVPA that excluded the adjustment of BMI. This analysis was performed to investigate the size of difference in MVPA between numbers of comorbidities allowing for adiposity levels to differ across comorbidities. Lastly, we performed cross-tabulations to describe the proportions and characteristics of participants with diabetes who did not adhere to the WHO recommendations for physical activity and their motivation for increasing their level of physical activity.

In all models, statistically weighted data from the DNHS were incorporated to account for non-response among certain populations groups. These weights were computed by Statistics Denmark and consider various factors including age, sex, educational level, income, socioeconomic group, municipality of residence, marital status, ethnic background, healthcare utilization, and research protection, thereby accounting for relevant differences (87).

### **3.2. Results**

183,372 respondents had complete or partial responses to the DNHS, and among those 10,216 were categorized as “Have diabetes”. Of these, 6,856 participants had complete data on outcome, exposures, and covariates in the primary analysis (Fig. 1).

## Flowchart of included participants



**Fig. 1.** Flowchart of all included participants in the primary analysis and the three secondary analyses in Paper I from the Danish National Health Survey (DNHS) 2017.

### 3.2.1. Participant characteristics

Table 1 represents the characteristics of participants with diabetes, including those with and without complete data, and participants with no known diabetes. Given the disparities in age and sex between diabetes status, direct standardization was conducted on participants with no known diabetes to adjust for the age- and sex-specific distribution observed among participants with diabetes.

Among those with diabetes, only 60% adhered to the WHO recommendations, whereas 70% of those with no diabetes adhered to the recommended levels of physical activity. Furthermore, participants with diabetes exhibited higher BMI, a greater number of comorbidities, higher perceived stress, and lower levels of HRQoL compared to those with no known diabetes.

**Table 1.** Characteristics of participants with diabetes with and without complete responses and no known diabetes

	Diabetes (Complete data)	Diabetes (Incomplete data)	No known diabetes
<i>n</i> (%)	6,856 (8.4)*	10,216 (8.8)*	173,021 (91.2)
Marital status			
Married/ living with partner	4,928 (63.7)	6,977 (61.1)	119,029 (66.8)
Living alone	1,928 (36.3)	3,239 (38.9)	53,992 (33.2)
Educational level			
Primary	1,113 (19.8)	1,848 (22.6)	18,478 (16.0)
Upper secondary	4,071 (58.9)	5,563 (58.3)	86,947 (55.3)
Higher	1,672 (21.3)	2,056 (19.1)	53,911 (28.7)
Ethnic background			
Danish	6,320 (88.1)	9,387 (87.0)	159,429 (91.6)
Western	187 (3.9)	273 (4.0)	5,847 (4.3)
Non-Western	349 (7.9)	556 (9.0)	7,745 (4.1)
Alcohol consumption (drinks consumed weekly)			
No alcohol	2,161 (35.5)	3,372 (39.4)	35,883 (22.0)
Below low risk	3,440 (47.3)	4,551 (44.4)	88,587 (54.0)
Above low risk	753 (10.4)	1,027 (9.8)	24,361 (16.1)
High risk	502 (6.8)	656 (6.4)	10,967 (7.8)
Smoking			
Smoker	1,309 (19.8)	1,935 (20.8)	33,017 (19.3)
Ex-smoker	3,023 (42.9)	4,388 (41.9)	52,149 (39.2)
Never smoked	2,524 (37.3)	3,693 (37.3)	79,529 (41.5)
Diet score			
Unhealthy	997 (14.9)	1,522 (16.6)	23,609 (16.5)
Medium healthy	4,669 (68.2)	6,325 (66.3)	105,169 (65.5)
Healthy	1,190 (16.9)	1,667 (17.1)	29,405 (17.9)
Obesity			
Underweight /Normal	1,492 (23.1)	2,170 (23.2)	78,160 (43.9)
Overweight	2,584 (37.2)	3,740 (36.9)	57,078 (39.5)
Obese class I	1,725 (24.6)	2,436 (24.3)	18,805 (12.6)
Obese class II	691 (9.5)	980 (9.8)	4,980 (2.9)
Obese class III	364 (5.6)	511 (5.8)	2,146 (1.1)
Comorbidities including mental health conditions			
No comorbidities	839 (11.6)	1,205 (11.9)	59,297 (27.3)
One comorbidity	1,813 (25.1)	2,653 (25.0)	53,182 (30.2)
Two comorbidities	1,989 (28.6)	2,980 (28.4)	35,944 (23.9)
Three or more comorbidities	2,215 (34.5)	3,378 (34.7)	24,598 (18.6)
Perceived stress			
Low perceived stress	3,739 (50.1)	4,771 (46.5)	96,095 (61.2)
Moderate perceived stress	2,826 (44.9)	4,207 (48.2)	57,962 (36.1)
High perceived stress	291 (5.0)	410 (5.3)	5,217 (2.7)
HRQoL			
Low physical HRQoL	4,715 (71.8)	6,335 (73.7)	60,680 (50.6)
Low mental HRQoL	1,845 (30.6)	2,567 (32.8)	36,103 (20.8)
Adherence to WHO recommendations of physical activity			
Following recommendations	2,457 (59.1)	4,902 (58.4)	102,881 (68.9)
Not following recommendations	3,884 (40.9)	3,224 (41.6)	40,578 (31.1)

Data are presented as number (%)

*n* is different due to variations in complete responses in each variable.

\*Proportion of individuals with diabetes compared with proportion of individuals with no known diabetes.

### *3.2.2. Characteristics of participants with diabetes by level of habitual physical activity*

Table 2 represents characteristics of participants with diabetes stratified by their level of habitual physical activity in accordance with the WHO recommendations. Of 6,341 participants with information about their level of habitual physical activity, 2,530 (38.8%) participants had optimal amount of habitual physical activity whereas 955 (16.4%) were defined as inactive. Inactive participants with diabetes were lower educated, had higher BMI, higher perceived stress, more comorbidities, and lower physical and mental HRQoL compared to participants with inadequate, adequate, and optimal habitual physical activity.

**Table 2.** Characteristics of participants with diabetes stratified by level of habitual physical activity

	Level of habitual physical activity <sup>1</sup>			
	Inactive	Inadequate	Adequate	Optimal
<i>n</i> (%)	955 (16.4)	1,502 (23.5)	1,354 (21.3)	2,530 (38.8)
Sex				
Male	547 (57.8)	912 (60.1)	785 (57.8)	1,558 (62.2)
Female	408 (42.2)	590 (39.9)	569 (42.2)	942 (37.8)
Age (years)	64 (53; 74)	64 (54; 72)	62 (53; 71)	63 (52; 71)
Marital status				
Married/ living with partner	640 (59.8)	1,097 (66.6)	981 (65.6)	1,841 (66.1)
Living alone	315 (40.2)	405 (33.4)	373 (34.4)	689 (33.9)
Educational level				
Primary	211 (24.8)	229 (17.2)	191 (16.2)	365 (16.3)
Upper secondary	577 (59.6)	887 (60.0)	794 (60.4)	1,488 (58.9)
High	167 (15.6)	386 (22.7)	369 (23.4)	677 (24.8)
Ethnic background				
Danish	877 (86.4)	1,394 (88.7)	1,256 (87.8)	2,347 (88.9)
Western	33 (5.7)	45 (3.9)	27 (2.9)	67 (3.7)
Non-Western	45 (7.8)	63 (7.4)	71 (9.3)	116 (7.3)
Smoking				
Smoker	231 (24.5)	315 (22.8)	253 (19.9)	420 (18.8)
Ex-smoker	431 (43.4)	666 (42.6)	579 (40.0)	1,117 (42.1)
Never smoked	293 (32.1)	521 (34.6)	522 (40.1)	993 (37.1)
Diet score				
Unhealthy	255 (26.3)	274 (20.1)	139 (10.5)	255 (10.0)
Medium healthy	594 (62.5)	1,044 (68.8)	971 (70.9)	1,702 (68.1)
Healthy	106 (11.2)	184 (11.1)	244 (18.7)	573 (21.9)
Alcohol consumption (drinks consumed weekly)				
No alcohol	415 (45.6)	453 (33.8)	369 (31.3)	716 (31.9)
Below low risk	380 (38.0)	736 (46.8)	758 (53.8)	1,336 (50.1)
Above low risk	78 (7.7)	168 (10.7)	144 (9.3)	317 (11.9)
High risk	82 (8.7)	145 (8.8)	83 (5.6)	161 (6.1)
MVPA in leisure time (h/week)	0 (0; 0)	1 (0.5; 1.5)	2.5 (2; 3.25)	6 (4.5; 9)
Total sedentary behavior (h/day)	9 (6.5; 12)	8.5 (6; 12)	8.25 (6; 11.6)	8.2 (6; 11.7)
Obesity				
Underweight /Normal	150 (16.5)	270 (18.4)	271 (21.3)	686 (28.9)
Overweight	331 (33.9)	536 (35.0)	514 (37.4)	1,017 (38.6)
Obese class I	238 (24.2)	430 (28.2)	365 (26.1)	548 (21.4)
Obese class II	142 (14.4)	168 (11.0)	133 (9.5)	199 (7.6)
Obese class III	94 (11.0)	98 (7.4)	71 (5.7)	80 (3.5)
Comorbidities including mental health conditions				
No comorbidities	76 (8.3)	140 (8.8)	171 (13.5)	391 (16.3)
One comorbidity	191 (19.3)	373 (24.3)	381 (25.9)	738 (28.2)
Two comorbidities	272 (27.9)	461 (30.2)	420 (29.5)	689 (26.7)
Three or more comorbidities	416 (44.5)	528 (36.7)	382 (31.1)	712 (28.8)
Perceived stress				
Low perceived stress	411 (40.2)	778 (46.3)	759 (50.6)	1,566 (58.9)
Moderate perceived stress	455 (50.0)	657 (47.8)	546 (44.9)	897 (37.7)
High perceived stress	89 (9.8)	67 (5.9)	49 (4.5)	67 (3.3)
HRQoL				
Low physical HRQoL	820 (86.3)	1,137 (76.8)	930 (70.0)	1,450 (58.8)
Low mental HRQoL	955 (43.6)	1,502 (34.1)	1,354 (28.1)	2,530 (23.4)

n = 6,341

Data are presented as number and proportion (%) except from Age, MVPA and Sedentary Behavior, which is presented as median and interquartile range (IQR)

<sup>1</sup>Level of habitual physical activity was categorized in accordance with the “WHO Guidelines of Physical Activity and Sedentary Behavior”: 1) Inactive = 0 h/week, 2) Inadequate = Participants do not meet recommendations (150-300 mins/week of moderate intensity or 75-150 mins/week of vigorous intensity), 3) Adequate = Participants meet recommendations, but not more than 300 mins/week of moderate intensity or 150 mins/week of vigorous intensity, and 4) Optimal = Participants with more than 300 mins/week of moderate intensity or 150 mins/week of vigorous intensity of physically activity



### 3.2.3. Associations between comorbidity, obesity, perceived stress, and HRQoL and MVPA

The results from the primary analyses regarding associations between exposures and engagement in MVPA (h/week) in participants with diabetes are represented in Table 3.

Compared to participants without comorbidities, participants with diabetes with three or more comorbidities including mental health conditions had significantly lower weekly MVPA after adjustments (-0.48 h/week, 95% CI -0.88; -0.07). However, the association between three or more comorbidities excluding mental health conditions and MVPA was non-significant after adjustments (-0.54 h/week, 95% CI -0.76; 0.04) when compared to those without comorbidities.

When excluding the adjustment of BMI in our post hoc analyses, having two comorbidities and three or more comorbidities with mental health conditions were significantly associated with lower weekly MVPA (two comorbidities: -0.58 h/week, 95% CI -0.98; -0.18, and three or more comorbidities: -0.85 h/week, 95% CI -1.25; -0.45) compared to having no comorbidities.

Furthermore, significant results were also found between comorbidities excluding mental health conditions and MVPA without adjusting for BMI (two comorbidities: -0.51 h/week, 95% -0.89; -0.12, and three or more comorbidities: -0.72 h/week, 95% -1.12; -0.32).

Being overweight or obese class I-III were significantly associated with lower weekly MVPA after adjustments (overweight: -0.61 h/week, 95% CI -0.94; -0.29, obese class I: -1.08 h/week, 95% CI -1.43; -0.74, obese class II: -1.43 h/week, 95% CI -1.85; -1.01, obese class III: -1.98 h/week, 95% CI -2.49; -1.47) when compared to underweight/normal weight participants with diabetes.

Suffering from moderate and high perceived stress were significantly associated with lower weekly MVPA after adjustments (moderate perceived stress: -0.59 h/week, 95% CI -0.83; -0.34, and high perceived stress: -1.76 h/week, 95% CI -2.18; -1.34) when comparing to those with low perceived stress.

Lastly, the analyses between HRQoL and MVPA showed that low physical and mental HRQoL were associated with lower weekly MVPA after adjustments (low physical HRQoL: -0.93 h/week, 95% CI -1.19; -0.66 and low mental HRQoL: -0.39 h/week, 95% CI -0.71; -0.08) when comparing to participants with moderate to high HRQoL.

Overall, the pattern of association of comorbidity, obesity, and stress with MVPA appeared consistent with an inverse graded relationship.

**Table 3.** Linear regressions on the associations of determinants with MVPA in participants with diabetes

	MVPA h/week					
	Crude		Multivariable adjusted		Multivariable adjusted (excluding BMI) <sup>b</sup>	
	$\beta^a$ [95% CI]	<i>p</i> value	$\beta$ [95% CI]	<i>p</i> value	$\beta$ [95% CI]	<i>p</i> value
<b>Comorbidities including mental health conditions<sup>1</sup></b>						
No comorbidities	(Reference)		(Reference)		(Reference)	
One comorbidity	-0.38 [-0.79; 0.02]	0.064	-0.08 [-0.48; 0.34]	0.688	-0.29 [-0.69; 0.11]	0.161
Two comorbidities	-0.73 [-1.13; -0.34]	0.001*	-0.31 [-0.70; 0.09]	0.135	-0.58 [-0.98; -0.18]	0.004*
Three or more comorbidities	-1.04 [-1.44; -0.65]	0.001*	-0.48 [-0.88; -0.07]	0.021*	-0.85 [-1.25; -0.45]	0.001*
<b>Comorbidities excluding mental health conditions<sup>1</sup></b>						
No comorbidities	(Reference)		(Reference)		(Reference)	
One comorbidity	-0.27 [-0.66; 0.12]	0.0175	-0.04 [-0.34; 0.43]	0.823	-0.16 [-0.55; 0.23]	0.417
Two comorbidities	-0.65 [-1.03; -0.27]	0.001*	-0.23 [-0.61; 0.16]	0.243	-0.51 [-0.89; -0.12]	0.010*
Three or more comorbidities	-0.91 [-1.29; -0.53]	0.001*	-0.54 [-0.76; 0.04]	0.081	-0.72 [-1.12; -0.32]	0.001*
<b>Obesity<sup>2</sup></b>						
Underweight /Normal	(Reference)		(Reference)			
Overweight	-0.61 [-0.93; -0.29]	0.001*	-0.61 [-0.94; -0.29]	0.001*		
Obese class I	-1.12 [-1.47; -0.77]	0.001*	-1.08 [-1.43; -0.74]	0.001*		
Obese class II	-1.49 [-1.92; -1.07]	0.001*	-1.43 [-1.85; -1.01]	0.001*		
Obese class III	-2.05 [-2.58; -1.52]	0.001*	-1.98 [-2.49; -1.47]	0.001*		
<b>Stress<sup>3</sup></b>						
Low perceived stress	(Reference)		(Reference)			
Moderate perceived stress	-0.68 [-0.92; -0.44]	0.001*	-0.59 [-0.83; -0.34]	0.001*		
High perceived stress	-1.90 [-2.29; -1.51]	0.001*	-1.76 [-2.18; -1.34]	0.001*		
<b>HRQoL<sup>4</sup></b>						
<i>Physical score</i>						
Moderate to high physical HRQoL	(Reference)		(Reference)			
Low physical HRQoL	-1.35 [-1.59; -1.09]	0.001*	-0.93 [-1.19; -0.66]	0.001*		
<i>Mental score</i>						
Moderate to high mental HRQoL	(Reference)		(Reference)			
Low mental HRQoL	-0.90 [-1.15; -0.65]	0.001*	-0.39 [-0.71; -0.08]	0.015*		

n = 6,856

<sup>a</sup>  $\beta$  coefficients and 95% confidence intervals (95% CI) represent mean difference in MVPA (h/week) compared with the reference. Significant results ( $p < 0.05$ ) are marked with \*<sup>b</sup> Post hoc analyses of comorbidities and MVPA excluding adjustment of BMI

Crude and adjusted models were weighted for non-response. Each multivariable model was adjusted as follows:

<sup>1</sup> Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, BMI. <sup>2</sup> Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, comorbidity. <sup>3</sup> Age, sex, educational level, marital status, smoking, BMI, comorbidity. <sup>4</sup> Age, sex, educational level, marital status, smoking, BMI, comorbidity, stress.

### 3.2.4. Adherence to WHO recommendations and association with daily sedentary behavior

The logistic regression models' estimated associations between exposures and adherence to WHO recommendations closely resembled those of the linear models (Appendix I, Supplement S1).

The results of the association between comorbidity, obesity, perceived stress, and HRQoL and daily sedentary behavior revealed significant associations indicating that participants classified as obese class II and III exhibited higher levels of daily sedentary behavior compared to underweight/normal-weight participants with diabetes (Appendix I, Supplement S2).

### 3.2.5. Motivation for being more physically active

Characteristics of insufficiently physically active participants with diabetes and their motivation for being more physically active are represented in Table 4. Participants of younger age were more motivated for increasing habitual physical activity compared to participants of older age. Further, most participants with a BMI corresponding to obese class II and III were motivated to increase their habitual physical activity.

Information regarding the distribution and characteristics of participants with diabetes adhering to the WHO recommendations for physical activity, as well as their motivation for increased physical activity, can be found in Appendix I, Supplement S3.

**Table 4.** Distribution of insufficiently physically active participants and their motivation for being more physically active

	Motivated	Not motivated	Don't know
<i>n</i> (%)	1,914 (59.8)	604 (19.2)	631 (21.0)
Sex			
Male	1,089 (59.6)	389 (20.3)	360 (20.1)
Female	825 (60.1)	215 (17.7)	271 (22.2)
Age (categories)			
16-34 years	59 (72.5)	6 (9.2)	13 (18.3)
35-54 years	414 (77.1)	47 (9.4)	72 (13.6)
55-64 years	545 (65.6)	131 (14.9)	147 (19.4)
65-74 years	592 (56.1)	211 (21.6)	206 (22.3)
≥75 years	304 (41.4)	209 (30.8)	193 (27.8)
Obesity			
Underweight /Normal	285 (52.3)	138 (26.7)	106 (21.0)
Overweight	642 (57.6)	244 (22.6)	214 (19.8)
Obese class I	489 (58.4)	141 (16.6)	192 (25.0)
Obese class II	289 (71.2)	44 (11.2)	65 (17.6)
Obese class III	177 (72.6)	27 (9.6)	41 (18.9)
Comorbidities including mental health conditions			
No comorbidities	162 (61.5)	64 (23.0)	43 (15.5)
One comorbidity	412 (59.7)	141 (18.9)	151 (21.3)
Two comorbidities	556 (57.5)	184 (20.2)	193 (22.3)
Three or more comorbidities	784 (61.0)	215 (18.0)	244 (21.0)
Stress			
Low perceived stress	820 (59.5)	296 (21.5)	258 (19.0)
Moderate perceived stress	871 (60.6)	248 (18.1)	281 (21.0)
High perceived stress	121 (62.0)	22 (11.9)	47 (26.1)
HRQoL			
Physical score			
Moderate to high physical HRQoL	359 (66.9)	107 (18.9)	83 (14.2)
Low physical HRQoL	1,395 (59.8)	415 (18.2)	473 (22.0)
Mental score			
Moderate to high mental HRQoL	1,103 (59.3)	373 (20.5)	353 (20.2)
Low mental HRQoL	651 (63.8)	149 (15.1)	203 (21.1)

*n* = 3,149 (*n* differs due to variations in complete responses in each variable)

Data are presented as number (%)

## **4. Paper II: Detailed descriptions of physical activity patterns among individuals with diabetes and prediabetes: The Lolland-Falster Health Study & Paper III: Sedentary activity, sedentary bouts, and patterns of total daily sedentary activity, and their relationship with stress and well-being in individuals with diabetes and prediabetes: The Lolland-Falster Health Study**

This part of the thesis includes the methods and results sections for Paper II and III. These sections include some information that has been previously described in the published versions of Paper II and Paper III (Appendix II and III).

The study design of both papers was cross-sectional. The aims of Paper II were to describe objectively measured physical activity patterns, including daily activity according to day type (weekdays and weekend days) and the four seasons, frequency, distribution, and timing of engagement in activity during the day among individuals with diabetes and individuals with prediabetes and compare these patterns to those without diabetes. Additionally, Paper II aimed to investigate whether there were any distinct differences in physical activity patterns across diabetes status, while considering other important diabetes-related determinants of activity such as obesity, comorbidities, and mental well-being.

The primary aim of Paper III was to investigate the associations of stress and well-being with the total amount of sedentary activity, characterized by sitting, reclined, and lying during waking hours, and durations of continuous sedentary bouts in individuals with diabetes and prediabetes. A secondary aim was to explore the daily sedentary activity pattern during a day in individuals with diabetes and prediabetes.

### **4.1. Methods**

#### *4.1.1. Setting and data sources*

Paper II and III were based on data from the Danish household-based prospective cohort study, the Lolland-Falster Health Study (LOFUS). The LOFUS study enrolled 19,000 participants aged 0-96 years between 8<sup>th</sup> of February 2016 and 13<sup>th</sup> of February 2020. Inhabitants  $\geq 18$  years were

randomly selected from the Danish CPR-register and invited to participate with their household members of all ages. LOFUS is conducted in a mixed rural-provincial area of Southeastern Denmark (Guldborgsund and Lolland). This area is generally considered disadvantaged because of the relatively high prevalence of low educational level, unemployment, and low income among inhabitants (88, 89).

Questionnaires, a site visit including physical examinations, and collection of biological samples were part of the data collection in the LOFUS study. The questionnaires developed for the adult population ( $\geq 18$  years) contained 299 items on a wide range of topics, such as self-reported medical conditions, well-being, and health behaviors. The questionnaire development has been described in a previous study by Egholm et al. (90). Following the physical examinations, a subsample was asked to wear accelerometers (91). The collection of accelerometer data was initiated as a part of a PhD project investigating the resemblance in physical activity behaviors within families with children (92). Therefore, between February 2017 and November 2018, families were included if at least one adult and one child agreed to accelerometer assessment, and from December 2018 to February 2020, all participants were eligible for inclusion in the accelerometer assessment (93). Detailed information about the LOFUS study protocol is described in Jepsen et al. (94).

Both papers were reported in accordance with the STROBE checklist (76). Data used in Paper II-III were approved by Region Zealand's Ethical Committee on Health Research (SJ-421) and the Danish Protection Agency (REG-024-2015) and registered in Clinical Trials (NCT02482896). Data storage and management for both papers were approved by the Danish Data Protection Agency through the University of Southern Denmark (Journal nr.: 11.396). Written informed consent from participants was obtained at the site visit (94).

#### *4.1.2. Participants*

In Paper II and III, 7,208 adults ( $\geq 18$  years) participating in the LOFUS were eligible to wear accelerometers. Paper II included LOFUS participants with valid accelerometer data from the lower back and information about their diabetes status. Paper III included participants if they had provided valid accelerometer data from the lower back and the right thigh and information regarding their diabetes status, stress, and well-being.

Participants' diabetes status was defined using information about their glycosylated hemoglobin levels (HbA1c) measured from the biological samples and self-reported use of antidiabetic medication (insulin and other diabetes medication). Participants were defined as "Have diabetes" if one of the following criteria were met: 1) HbA1c  $\geq$ 48 mmol/mol, or 2) HbA1c  $<$ 48 mmol/mol and self-reported use of antidiabetic medication. Participants were defined as "Have prediabetes" if their HbA1c were between  $<$ 48 mmol/mol and  $\geq$ 39 mmol/mol according to ADA and no self-reported use of antidiabetic medication (22). If participants' HbA1c were  $<$ 39 mmol/mol and there was no self-reported use of antidiabetic medication, they were defined as "No known diabetes".

#### 4.1.3. Exposure variables

Some of the included variables are similar to the variables described in Paper I, therefore, parts of the following text will be a repetition.

In Paper II, the exposure variable was the participants' diabetes status, as defined above categorized into diabetes, prediabetes, and no diabetes.

In Paper III, the exposure variables were stress and well-being, categorized as below:

*Stress.* Self-reported psychological stress was obtained with Cohen's 10-item PSS (82) from the questionnaire. All items were summed into a total score ranging from 0-40, and a higher score indicates higher perceived stress (82). A variable that distinguished between the prevalence of low (scores below  $<$ 18) and moderate to high stress (scores  $\geq$ 18) was developed, because this cut-off corresponds to the upper quintile of PSS levels in Denmark and is associated with higher mortality (95).

*Well-being.* Self-reported mental well-being was obtained with the WHO-5 Well-Being Index (96). Each question was scored from 0 (none of the time) to 5 (all the time). Following the recommendations, the raw scores were afterwards multiplied by 4 to obtain a percentage score ranging from 0-100 (97). A higher score indicates a better perceived well-being. A variable distinguishing between the prevalence of low (scores  $\leq$ 50) and moderate to high well-being was developed based on previous research (97).

#### 4.1.4. Outcome variables

In Paper II, physical activity was the outcome of interest, while Paper III focused on sedentary activity.

In both papers, physical activity and sedentary activity were objectively measured using Axivity AX3 (Axivity, Newcastle UK) accelerometers. Participants were instructed to wear two accelerometers attached to the skin using adhesive tape (91) (one was placed on the right thigh, and the other on the lower back) consecutively for seven days, including during sleep and water activities.

By evaluating acceleration and temperature data from the accelerometer, raw valid wear periods were identified. The intensity cut-points for adults ( $\geq 18$  years) were as follows: Sedentary:  $< 100$ , Light: 100, Moderate: 3522, Vigorous: 6016 counts (93). Time spent in different physical activity intensities was determined by generating ActiGraph counts using 10 seconds-epochs from the raw acceleration (98). The method described by Skotte et al. (99) using both the thigh and the back-worn accelerometer was used to determine time spent sedentary, as this was based on activity types. This method has been validated (100) and demonstrated a very high degree of sensitivity and specificity with the identification of several activity types in adults (99).

Paper II used data from the lower back-worn accelerometer as this paper focused on physical activity intensities, while Paper III used data from both accelerometers to determine time spent in a sitting, reclined, or lying position. For both papers, data from the thigh-worn accelerometer was used to determine time spent sleeping by an algorithm detecting continuous time spent lying down. In addition, a restricted time-frame from 6:00 am to 11:59:59 pm was added to ensure that awake time did not exceed 18 hours. This restricted time-frame was used in Paper II, while Paper III had a restricted time-frame of 7:00 am to 10:00 pm to ensure that time spent sedentary (sitting, reclined, or lying) primarily determined during waking hours.

For both papers, a minimum of 22 hours of wear time out of 24 hours was the criteria for valid data for a day, and a measurement period was considered valid if participants had at least three valid weekdays and one valid weekend day. Detailed information about data processing is described in Petersen et al. (93).

For Paper III, an additional criterion of minimum 10 hours of awake time during a day was added to

ensure participants had provided sufficient data regarding time spent sedentary during waking hours.

In Paper II, the following outcomes were included:

- Sedentary behavior: Hours spent on sedentary behavior (counts below light intensity) (93).
- Light physical activity (LPA): Minutes spent on light intensity activity.
- Moderate physical activity (MPA): Minutes spent on moderate intensity activity.
- MVPA: Minutes spent on moderate to vigorous intensity activity.
- Vigorous physical activity (VPA): Minutes spent on vigorous intensity activity.
- Total time spent physically active: LPA + MPA + VPA.

#### *Adherence to the recommendations of physical activity*

Adherence to the WHO recommendations of weekly physical activity was assessed with MPA and VPA. Based on the WHO recommendations (150 min/week MPA and 75 min/week VPA) (21), we developed a variable that ‘double-counted’ VPA and accounted for varying number of valid measurement days among participants. Therefore, total daily MVPA were derived as follows:  $MVPA = MPA + (VPA * 2)$ .  $MVPA < (150 \text{ min}/7 \text{ days})$  was categorized as “Not following recommendations” and  $MVPA \geq (150 \text{ min}/7 \text{ days})$  as “Following recommendations”.

Adherence to the ADA recommendations of daily physical activity (engagement in  $\geq 30$  min/day MVPA) was calculated by summarizing daily MVPA and categorized into: 1) Sufficient physical activity ( $\geq 30$  min/day MVPA), 2) Some physical activity ( $\geq 5$  min/day and  $< 30$  min/day MVPA), and 3) Highly inactivity ( $< 5$  min/day MVPA) (22, 101). The threshold distinguishing between high inactivity and some physical activity was applied as it has been suggested to provide the minimum clinical important difference in inactive adults (102).

In Paper III, the following outcomes were included:

- Total sedentary activity (h/day and min/day): Total time spent in a sitting, reclined, or lying position during waking hours (between 7:00 am and 10:00 pm during).
- Sedentary bouts (n/day): A sedentary bout was classified if the individual had been in a sitting or lying position for at least 10 seconds duration.



- Categories of sedentary bouts in terms of duration on a given day: <1 min,  $\geq 1$  min to <3 min,  $\geq 3$  min to <10 min,  $\geq 10$  min to <30 min, and  $\geq 30$  min.
- Prolonged sedentary bouts (n/day): Sedentary bouts of >30 min during a given day.
- Breaks in sedentary activity in terms of duration on a given day: A break in sedentary activity during waking hours was defined as a transition from a sitting, reclined, or lying position of at least 10 seconds duration to any of the following positions/activities of at least 10 seconds duration during waking hours: Stand, move, walk, and run. The following categories of breaks in sedentary activity were made based on the distribution: <1 min,  $\geq 1$  min to <3 min,  $\geq 3$  min to <10 min, and  $\geq 10$  min.
- MVPA: Minutes spent on moderate to vigorous intensity activity from the lower back-worn accelerometer.

#### *Differences in time spent sedentary between Paper II and III*

It is important to mention that Paper II and III view time spent sedentary differently. In Paper II we use the term ‘sedentary behavior’ as this variable was assessed using the lower back-worn accelerometer and was based on activity counts <3522 with no criteria of the number of waking hours. Whereas Paper III used the term ‘sedentary activity’ as this variable was assessed using both accelerometers to determine time spent sedentary through positions (sitting, reclined, or lying) to capture all time spent sedentary.

#### *4.1.5. Covariates and variables to describe the population*

Information about age and sex of the participants were derived from the CPR-register and other background information stemmed from the LOFUS questionnaire (90).

#### *Self-reported measurements*

*Marital status.* Participants’ marital status was dichotomized into: “Married or living with partner” or “Living alone”.

*Educational level.* Highest completed level of education was categorized into 1) Primary or lower secondary education, 2) Upper secondary (shorter length education (2-3 years) or vocational education, and 3) Higher education (medium (3-4 years) and longer (>4 years) length education).

*Occupational status.* Participants reported their occupational status with the following categories: 1) Employed, 2) Unemployed, 3) Absent due to sick leave, 4) Retired, 5) Student, and 6) Other. In Paper II and Paper III, the categories were collapsed into three in the analyses: 1) Employed, student, or other, 2) Unemployed or absent due to sick leave, and 3) Retired.

*Comorbidity.* The prevalence of comorbidities was developed using the same method as in Paper I. In Paper II and III, the following body systems according to Willadsen et al. (77) was included: 1) Lung, 2) Musculoskeletal, 3) Endocrine, 4) Mental, 5) Cancer, 6) Neurological, 7) Gastrointestinal, 8) Cardiovascular, 9) Kidney, and 10) Sensory organs. In addition to predefined selected conditions, participants were asked to add if they had any other condition(s) that was not already included in the response categories. All “other” conditions were coded into the ten groups of body systems by two researchers (SRM and LBJ) independently following the classification by Tang et al. (103). The classification in this differed from Tang et al. by including hypertension, however, all other risk factors (e.g., increased cholesterol) were excluded. Disagreements were discussed until consensus was reached.

In the predefined response categories of selected conditions, diabetes was the only one in the endocrine group. Therefore, the endocrine comorbidity group included all other endocrine conditions obtained from the “other” category.

In Paper II, the comorbidity variable was categorized as follows: 1) No comorbidities, 2) One comorbidity from one body system, 3) Two comorbidities from different body systems, and 4) Three or more comorbidities from different body systems. In Paper III, category 2) and 3) were collapsed into one variable due to low numbers in some categories. The category was then labelled “Two or more comorbidities”. Suffering from several long-term conditions within the same body system, e.g., hypertension and angina pectoris, would still only count as one comorbidity.

*Stress.* In Paper II, self-reported psychological stress was included as a covariate and classified as: 1) Low perceived stress (scores from 0-13), 2) Moderate perceived stress (scores from 14-26), and 3) High perceived stress (scores from 27-40) (82).

*Chronic pain.* A binary variable distinguishing whether participants had long-lasting pain (6 months or more) or not was developed.

*Medication use.* Information about participants' use of insulin, other diabetes medication, cholesterol-lowering medication, and diuretics were reported.

#### *Objective measurements*

*BMI.* Participants' height and weight were obtained at the health examinations to calculate BMI (kg/m<sup>2</sup>). Height was measured with SECA 216 Wall-mounted height measure, and weight was measured with Tanita Body Composition Analyzer (BC-420MA III or Electronic scale Tanita WB 150 SMA) (94).

In Paper II, BMI was categorized into: Underweight/normal weight (BMI <25), overweight (BMI ≥25 to <30), obese class I (BMI ≥30 to <35), obese class II (BMI ≥35 to <40), and obese class III (BMI ≥40), as defined by WHO (80).

In Paper III, the obese class categories were collapsed into one (obese: BMI ≥30).

*Glycemic level.* Data on participants' HbA1c-level from blood samples were used to classify controlled glycemic level (for adults) following the ADA recommendations (22) and categorized into: Controlled glycemic level (HbA1c <53 mmol/mol); Uncontrolled glycemic level (HbA1c ≥53 mmol/mol).

Covariates in the analyses of Paper II were the following: Age, sex, BMI, comorbidities, stress, well-being, and chronic pain.

Covariates in the analyses of Paper III were the following: Age, sex, educational level, occupational status, marital status, BMI, comorbidities, and chronic pain.

#### *4.1.6. Statistical analyses*

For both Paper II and III, SAPs were developed and stored openly available at OSF (Paper II: <https://osf.io/34t2c/> (Appendix VI), Paper III: <https://osf.io/7bnyp/> (Appendix VII)).

In both papers, all statistical analyses were performed using the software STATA/BE 17.0 and R statistical (R Core Team, Vienna, Austria) software version 2023.06.0+421. RStudio (RStudio Inc., Boston, MA, USA) version 2022.07.2 using an  $\alpha$ -level of 0.05 two-sided.

#### *Descriptive statistics*

In Paper II and III, the *dstat* function in STATA (104) was used to describe statistical distributions

by diabetes status (Paper III including groups of stress and well-being) with standardization of age and sex.

In Paper II, characteristics of participants with diabetes, prediabetes, and no diabetes were summarized as numbers and proportions or means and standard errors. The distribution and comparison of daily sedentary behavior, LPA, MPA, VPA, and MVPA in total, during weekdays, and weekend days by diabetes status were estimated with median and IQR. MVPA percentile differences across diabetes status by weekdays, weekend days, and season of the year were estimated with coefficients and 95% CI. Further, adherence to physical activity recommendations by WHO was distributed and displayed with numbers and proportions. Differences across diabetes status were investigated using Wald test within regression models (which varied based on outcome distribution) to adjust for age and sex by testing the null hypothesis that all coefficients are jointly zero.

In Paper III, descriptive statistics of participants with diabetes and prediabetes with and without moderate to high levels of stress or well-being were summarized as numbers and proportions. The distribution of total sedentary activity across diabetes status and categories of stress and well-being was estimated with mean and SD. Number of sedentary bouts, categories of sedentary bouts, and breaks in activity in terms of duration, and MVPA were estimated with median and IQR.

#### *Inactive days in Paper II*

The distribution of 0, 1, 2, 3, 4, 5, 6, and  $\geq 7$  highly inactive days ( $< 5$  min/day MVPA) and the prevalence of  $> 2$  consecutive highly inactive days were estimated by diabetes status with adjustment for age, sex, and number of days with valid accelerometer data (104). We used zero-inflated Poisson regression models to predict number of days with highly inactivity during a 7-days period of measurement by diabetes status adjusted for age and sex with number of valid days with accelerometer data as exposure time.

#### *Daily activity profiles*

Both papers used mixed linear regression models with adjustment for age and sex to estimate and display the daily activity and sedentary profile (mean time spent physically active at any intensity or time spent sedentary over the waking hours (per 15 min)) by diabetes status. We used a Savitzky-Golay smoothing filter with an order of 3 and length of 15 to generate a smoothed trend based on

the point estimates for every 15-min obtained from the mixed model. The order of 3 was chosen to reflect the expected pattern in physical activity and sedentary activity data with the length of 15 determined iteratively to best describe the general trend in the data.

Based on visual inspection of the activity profile in Paper II, we conducted post hoc analyses with additional adjustments of occupational status, BMI, and stress to investigate if differences in daily activity profile could be explained by other major determinants of physical inactivity.

In Paper III, three models were performed to investigate the extent to which differences in the sedentary pattern between participants with diabetes and prediabetes were explained by stress or well-being. The first model was adjusted for age and sex, the second model for age, sex, and stress, and the third model for age, sex, and well-being.

#### *Association analyses*

Paper II used multiple quantile regression models with additional adjustments to investigate if any differences in physical activity intensities by diabetes status were explained by other factors.

Therefore, Model 1 was adjusted for age and sex; Model 2 was adjusted for age, sex, and BMI; and Model 3 was adjusted for age, sex, BMI, comorbidities, stress, well-being, and chronic pain.

In Paper III, multiple linear regression models were performed to investigate the association between the exposures stress and well-being and the outcome total sedentary activity in participants with diabetes and participants with prediabetes. Additionally, multiple quantile regression models were performed to investigate the association between stress and well-being (exposures) and sedentary bouts and prolonged sedentary bouts in participants with diabetes and prediabetes.

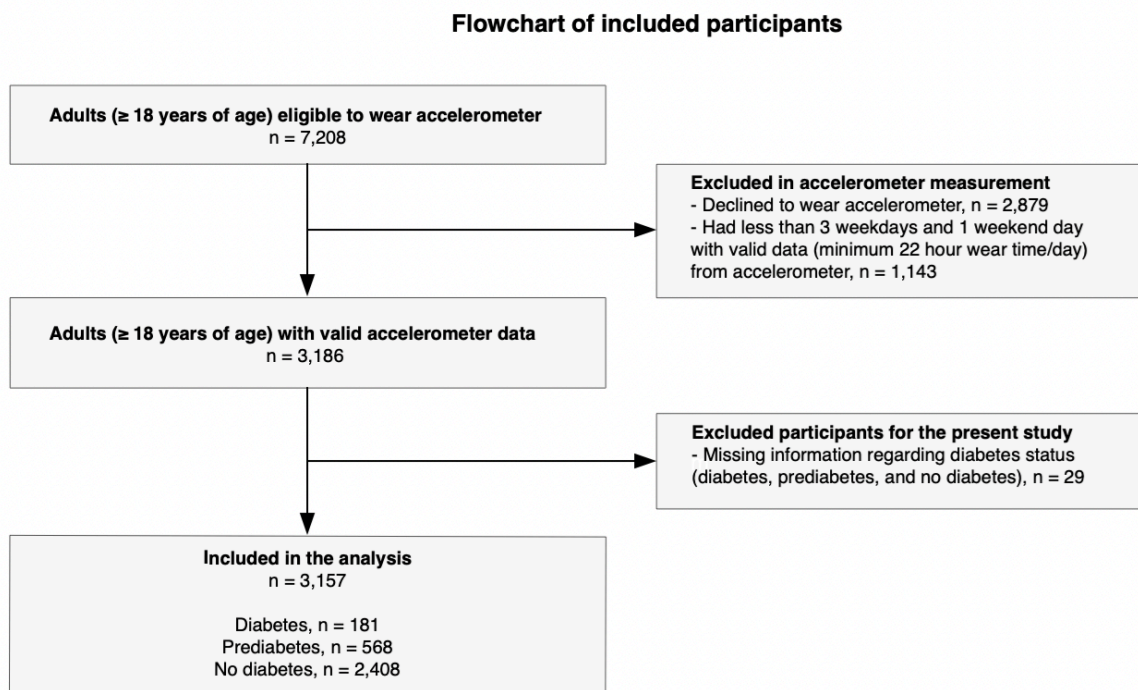
Models with stress were adjusted for age and sex in the first model, and additionally, for educational level, occupational status, marital status, BMI, and comorbidities in the second model. Similarly, the well-being models were adjusted for the same covariates, with addition of chronic pain in the second model.

## **4.2. Results of Paper II**

Among 3,157 participants with valid accelerometer data and information on diabetes status, 181 (6%) participants had diabetes, 568 (18%) participants had prediabetes, and 2,408 (76%)

participants had no diabetes (Fig. 2).

Participants with diabetes had a median (IQR) age of 67.8 (60.7–73.8) years, while those with prediabetes were 65.1 (54.5–72.2) and those with no diabetes were 51.1 (40.1–65.4) years. The proportion of men was higher among participants with diabetes (59.1%) compared to participants with prediabetes (46.1%) or no diabetes (44.7%).



**Fig. 2.** Flowchart of included participants in Paper II.

Table 5 represents characteristics of participants with diabetes, prediabetes, and no diabetes with standardization of age and sex. A larger proportion of participants with diabetes were on sick leave or retired, had higher BMI, suffered from chronic pain, and had more comorbidities compared to participants with prediabetes or no diabetes. Further, participants with prediabetes had higher BMI and more comorbidities compared to participants with no diabetes.

**Table 5.** Characteristics of participants with diabetes, prediabetes, and no diabetes

	Diabetes	Prediabetes	No diabetes	<i>p</i> -value
<i>n</i> (%)	181 (6%)	568 (18%)	2,408 (76%)	
Marital status				0.294
Married/ living with partner	136 (79.1)	421 (78.2)	1,853 (81.4)	
Living alone	36 (20.9)	118 (21.8)	423 (18.6)	
Educational level				0.060
Primary or lower secondary	31 (17.8)	42 (7.9)	182 (8.0)	
Upper secondary or vocational	105 (60.7)	331 (61.6)	1,286 (56.3)	
Higher	33 (19.2)	144 (26.7)	701 (30.7)	
Other	4 (2.3)	20 (3.8)	114 (5.0)	
Occupational status				<0.001*
Employed	74 (43.9)	326 (62.1)	1,313 (58.4)	
Unemployed	2 (1.1)	9 (1.7)	29 (1.3)	
Absent (sick leave)	25 (14.6)	34 (6.4)	90 (4.0)	
Retired	56 (33.2)	145 (27.5)	724 (32.2)	
Student	12 (7.3)	1 (0.1)	74 (3.3)	
Other	0 (0)	11 (2.1)	17 (0.7)	
BMI categories				<0.001*
Underweight /Normal	35 (20.2)	143 (26.0)	961 (40.6)	
Overweight	49 (28.2)	189 (34.3)	919 (38.8)	
Obese class I (BMI ≥30-<35)	59 (34.4)	148 (26.8)	351 (14.8)	
Obese class II (BMI ≥35-<40)	23 (13.4)	50 (9.1)	103 (4.4)	
Obese class III (BMI ≥40)	7 (3.8)	21 (3.8)	34 (1.4)	
Comorbidities				<0.001*
No comorbidities	55 (30.2)	181 (31.9)	818 (34.0)	
One comorbidity	51 (28.2)	160 (28.1)	789 (32.8)	
Two comorbidities	38 (21.0)	131 (23.1)	509 (21.1)	
Three or more comorbidities	37 (20.6)	96 (16.8)	292 (12.1)	
Perceived stress				0.696
Low perceived stress	15 (9.1)	42 (8.2)	163 (7.4)	
Moderate perceived stress	147 (89.5)	463 (90.2)	1,994 (90.6)	
High perceived stress	2 (1.4)	8 (1.6)	44 (2.0)	
Mental well-being				0.001*
Moderate to high mental well-being	135 (81.8)	415 (80.2)	1,927 (86.0)	
Low mental well-being	30 (18.2)	102 (19.8)	313 (14.0)	
Suffers from chronic pain	65 (37.5)	185 (34.5)	648 (28.4)	<0.001*
Use of medication				
Insulin	58 (33.8)	-	-	-
Other diabetes medication	81 (47.4)	-	-	-
Cholesterol-lowering medication	74 (43.1)	99 (18.9)	225 (10.0)	<0.001*
Diuretics	40 (23.6)	40 (7.8)	150 (6.7)	<0.001*
HbA1c-level	54.1 (1.45)	40.7 (0.08)	34.3 (0.05)	<0.001*
Controlled glycemic level (HbA1c-level <53 mmol/mol)	102 (56.6)	-	-	-
Median number of valid days with accelerometer measurement	6 (6–7)	6 (6–7)	6 (6–7)	0.074

Categorical data are presented as *n* and proportion (%) with standardization on age and sex. Continuous data are presented with mean and standard error due to standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference). Wald test was used to joint test coefficients for categories of diabetes. The null hypothesis for the Wald test in this context is that all coefficients associated with diabetes status are simultaneously zero, implying no effect of diabetes status on the outcome of interest after adjusting for age and sex. Significant results ( $p < 0.05$ ) are marked with \*.

*n* varies due to variations in complete responses for each variable.

Among participants with diabetes, 63% did not adhere to the WHO recommendations of weekly MVPA, while 60% of participants with prediabetes and 50% of participants with no diabetes did not follow the recommendations. The proportion of highly inactive (<5 min/day MVPA) participants was 33% among those with diabetes, 18% with prediabetes, and 13% with no diabetes (Table 6 and Fig. 3a). The percentage point difference in highly inactive participants with diabetes (reference) compared to prediabetes and no diabetes was -14.7% (95% CI -18.2; -11.4) and -20.1% (95% CI -25.9; -15.1), respectively (Fig. 3b).

Among participants with no diabetes, the 25<sup>th</sup>, 50<sup>th</sup>, and 75<sup>th</sup> percentile of MVPA were significantly higher compared to participants with diabetes. The difference in 25<sup>th</sup> percentile was 6.1 min/day, 95% CI 4.9; 7.3, and the difference in the 50<sup>th</sup> percentile was 11.9 min/day, 95% CI 9.9; 14.0, and lastly, the difference in the 75<sup>th</sup> percentile was 10.0 min/day, 95% CI 4.2; 15.9 (Appendix II, Supplement S1). Daily MVPA between weekdays and weekends was significantly different in participants with diabetes, prediabetes, and no diabetes (Appendix II, Supplement S2). We found no variations in seasonal distribution of daily MVPA across diabetes status (Appendix II, Supplement S3).

After adjustment for sex, there was no age-related differences in MVPA (min/day) between participants with diabetes and no diabetes except for a difference in the lowest percentile (p25) of MVPA (4.2 min/day difference among participants  $\geq 65$  years and 7.9 min/day difference among participants  $< 65$  years,  $p=0.02$  for interaction (for more information see Appendix II, Supplement S4)).



**Table 6.** Distribution of daily sedentary behavior, LPA, MPA, VPA, and MVPA and adherence to recommendations among participants with diabetes, prediabetes, and no diabetes

	Diabetes n = 181	Prediabetes n = 568	No diabetes n = 2,408	p-value
<i>Total</i>				
Sedentary behavior	11.6 (10.0 – 12.6)	11.0 (9.9 – 12.1)	10.8 (9.7 – 11.9)	<0.001*
LPA	156.4 (123.4 – 214.8)	197.8 (158.2 – 230.4)	194.2 (156.7 – 234.0)	<0.001*
MPA	8.5 (2.8 – 18.4)	12.5 (5.9 – 23.8)	15.8 (8.1 – 26.1)	<0.001*
VPA	0.6 (0.1 – 2.3)	1.2 (0.4 – 3.2)	1.6 (0.5 – 4.4)	<0.001*
MVPA	9.3 (3.5 – 22.9)	14.3 (6.6 – 27.8)	18.9 (9.6 – 32.1)	<0.001*
<i>Weekdays</i>				
Sedentary behavior	11.6 (10.2 – 12.8)	11.1 (9.9 – 12.2)	11.0 (9.9 – 12.1)	<0.001*
LPA	151.6 (122.7 – 214.8)	195.4 (155.8 – 235.2)	192.0 (154.5 – 237.9)	<0.001*
MPA	7.5 (2.8 – 19.0)	13.2 (5.7 – 23.8)	15.8 (7.8 – 27.0)	<0.001*
VPA	0.5 (0.2 – 2.5)	1.2 (0.3 – 3.0)	1.5 (0.5 – 4.2)	<0.001*
MVPA	8.8 (3.2 – 22.1)	14.6 (6.5 – 26.9)	18.4 (9.2 – 31.8)	<0.001*
<i>Weekend days</i>				
Sedentary behavior	10.7 (9.7 – 12.3)	10.9 (9.6 – 12.1)	10.4 (9.2 – 11.7)	<0.001*
LPA	175.5 (118.0 – 225.8)	187.2 (137.9 – 238.8)	190.7 (146.2 – 237.4)	<0.001*
MPA	7.8 (2.3 – 17.2)	8.3 (3.7 – 19.7)	12.9 (5.3 – 26.7)	<0.001*
VPA	0.5 (0.1 – 2.0)	0.9 (0.3 – 2.5)	1.3 (0.3 – 3.8)	<0.001*
MVPA	9.3 (2.5 – 24.9)	9.7 (4.2 – 23.3)	15.7 (6.2 – 31.7)	<0.001*
<i>Adherence to WHO recommendations<sup>a</sup></i>				
Following recommendations	67 (36.8)	230 (40.5)	1,214 (50.4)	
Not following recommendations	114 (63.2)	338 (59.5)	1,194 (49.6)	
<i>Adherence to ADA recommendations<sup>b</sup></i>				
Highly inactivity	60 (33.0)	104 (18.3)	308 (12.8)	<0.001*
Some physical activity	90 (49.8)	350 (61.6)	1,430 (59.4)	
Sufficient physical activity	31 (17.2)	114 (20.1)	670 (27.8)	

Data are standardized on age and sex and presented as medians (IQR) or n and proportion (%). Wald test was used to joint test coefficients for categories of diabetes. The null hypothesis for the Wald test in this context is that all coefficients associated with diabetes status are simultaneously zero, implying no effect of diabetes status on the outcome of interest after adjusting for age and sex. Significant results ( $p < 0.05$ ) are marked with \*.

Abbreviations: LPA; Light physical activity (min/day), MPA; Moderate physical activity (min/day), VPA; Vigorous physical activity (min/day), MVPA; Moderate to vigorous physical activity (min/day).

<sup>a</sup>Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity:  $\geq 150$  minutes MVPA or  $\geq 75$  minutes VPA weekly or an equivalent combination.

<sup>b</sup>Distribution of adherence to recommendations on daily physical activity according to ADA Highly inactivity:  $< 5$  min/day of MVPA, Some activity:  $\geq 5$  min/day and  $< 30$  min/day MVPA, Sufficient activity:  $\geq 30$  min/day MVPA.

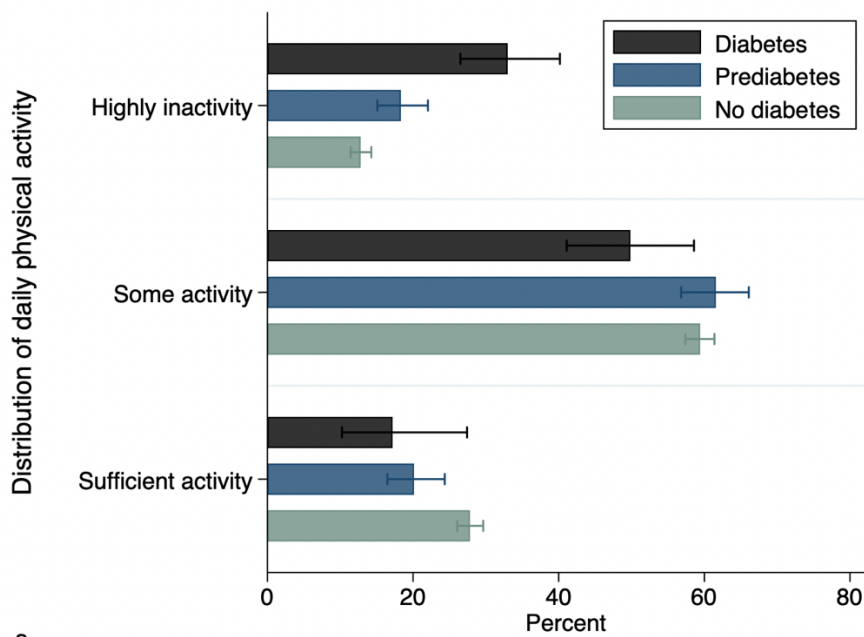


Fig. 3a

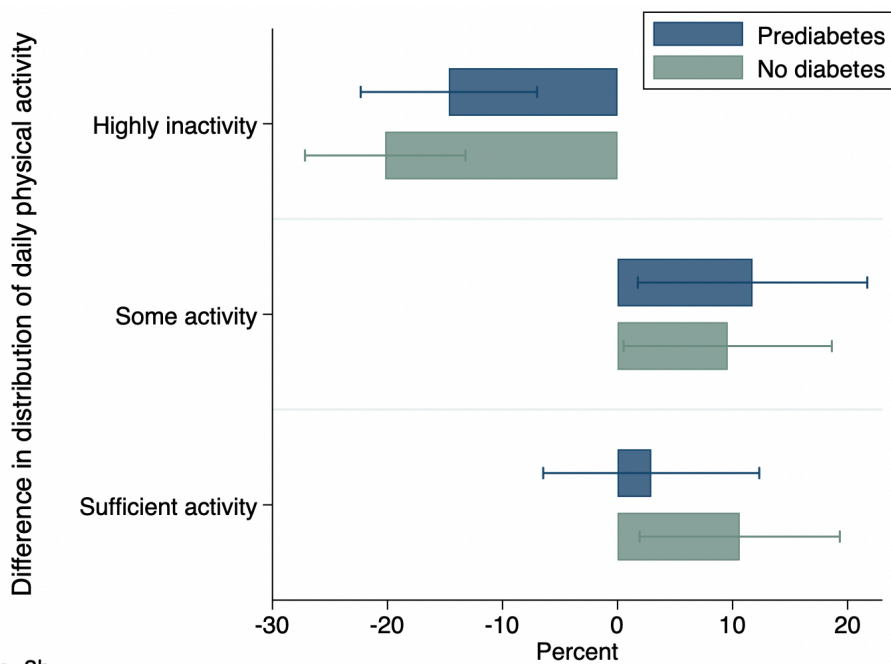


Fig. 3b

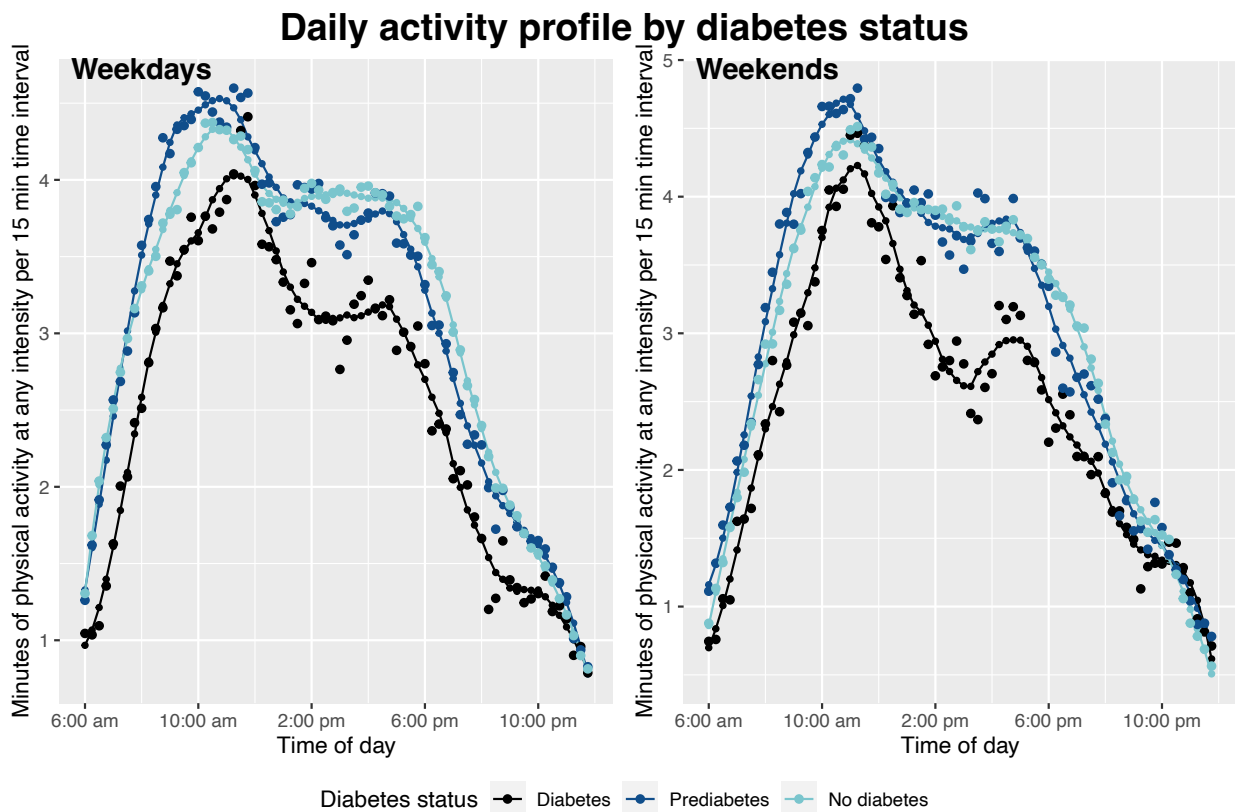
**Fig. 3a.** Distribution of proportion (%) of daily physical activity according to the recommendations by diabetes status.

**Fig. 3b.** Percentage point difference in daily physical activity according to the recommendations in percent by diabetes status with diabetes as reference.

Definitions: Highly inactivity: <5 min/day of MVPA, Some activity:  $\geq 5$  min/day and <30 min/day MVPA, Sufficient activity:  $\geq 30$  min/day MVPA.

Both figures are standardized on age and sex (entropy balancing with the distribution of age- and sex in the total sample as the reference). Error bars are 95% CI.

Mean time spent physically active at any intensity during a weekday and a weekend day was lower among participants with diabetes compared to participants with prediabetes and no diabetes (Fig. 4). In the early afternoon (from 12:00 pm to 15:00 pm), participants with diabetes were significantly less physically active compared to participants with no diabetes (-6.3 min, 95% CI -10.2; -2.4,  $p=0.001$ ). After additional adjustments for BMI, stress, and occupational status, the daily activity profile between diabetes groups were similar to the activity profile with only adjustments of age and sex (Appendix II, Supplement S4-7).



**Fig. 4.** Daily activity profiles by diabetes status are presented as mean time (minutes per 15 min interval) spent physically active at any intensity (light physical activity was the threshold for detection of physical activity at any intensity) during a weekday and a weekend day adjusted for age and sex. The points represent the raw age- and sex adjusted estimates, and the fitted line represents a smoothing trend based on the point estimates.

Among participants with diabetes, 33% had more than two consecutive days with highly inactivity (<5 min/day MVPA) during a seven-days period, whereas the proportion was 20% among participants with prediabetes and 15% among those with no diabetes, respectively (Table 7). After adjusting for age and sex, this is at a rate that is 2.30 (95% CI 1.80; 2.94) and 1.36 (95% CI 1.12; 1.66) times higher compared to participants with prediabetes and participants with no diabetes, respectively. Further, the predicted number of days with highly inactivity during a seven-days period were higher among participants with diabetes (2.2 days, 95% CI 1.98; 2.37) compared to participants with prediabetes (1.75 days, 95% CI 1.63; 1.87) and no diabetes (1.47 days, 95% CI 1.40; 1.54) (Appendix II, Supplement S8).

**Table 7.** The prevalence for accumulating 0, 1, 2, 3, 4, 5, 6, and 7 days of with highly inactivity (<5 min/day of MVPA) among participants with diabetes, prediabetes, and no diabetes

	Diabetes n = 181	Prediabetes n = 568	No diabetes n = 2,408
<i>Inactive days during a week</i>	%	%	%
0 days	33.6	44.0	52.9
1 days	13.6	17.4	17.0
2 days	10.3	10.3	8.4
3 days	9.2	7.3	7.1
4 days	4.4	5.9	4.4
5 days	11.3	4.9	4.2
6 days	11.6	7.7	4.3
≥7 days	6.0	2.4	1.7
<i>Consecutive days with highly inactivity</i>			
>2 days	33.2	19.9	15.1

Data are presented as proportion (%) with standardization on age, sex, and number of valid days with accelerometer measurement.

Table 8 represents the results of the multiple quantile regression analyses. Participants with diabetes had significantly lower median LPA, MPA, MVPA, and higher median sedentary behavior after adjustments for BMI and other major determinants compared to participants with no diabetes. Additionally, participants with prediabetes had significantly lower median MPA, MVPA, and higher sedentary behavior compared to participants with no diabetes when adjusting for age and sex.

After adjusting for BMI, the differences between participants with prediabetes and no diabetes were no longer significant. Furthermore, in the fully adjusted model, participants with prediabetes had significantly higher median LPA and lower sedentary behavior compared to participants with diabetes (Appendix II, Supplement S9).

**Table 8.** Quantile regression models on daily LPA, MPA, VPA, MVPA and sedentary behavior by diabetes status with additional adjustment for other major determinants of physical activity

	Model 1 <sup>a</sup> n = 2,746		Model 2 <sup>b</sup> n = 2,746		Model 3 <sup>c</sup> n = 2,746	
	β [95% CI]	p-value	β [95% CI]	p-value	β [95% CI]	p-value
<i>Total LPA (min/day)</i>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	1.6 [-5.2; 8.4]	0.649	3.4 [-4.0; -10.7]	0.371	4.0 [-3.1; 11.2]	0.269
Diabetes	-42.9 [-54.1; -31.7]	<0.001*	-30.0 [-42.2; -17.7]	<0.001*	-35.3 [-47.2; -23.3]	<0.001*
<i>Total MPA (min/day)</i>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	-3.7 [-5.5; -1.9]	<0.001*	-1.5 [-3.3; 0.3]	0.107	-1.5 [-3.3; 0.3]	0.103
Diabetes	-10.0 [-12.9; -7.0]	<0.001*	-5.1 [-8.2; -2.1]	0.001*	-4.8 [-7.8; -1.7]	0.002*
<i>Total VPA (min/day)</i>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	-0.4 [-0.7; 0.004]	0.053	-0.1 [-0.4; 0.2]	0.444	-0.2 [-0.5; 0.3]	0.242
Diabetes	-0.7 [-1.2; -0.2]	0.011*	-0.3 [-0.8; 0.2]	0.294	-0.2 [-0.8; 0.3]	0.368
<i>Total MVPA (min/day)</i>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	-4.7 [-6.8; -2.6]	<0.001*	-1.1 [-3.3; 1.0]	0.307	-2.1 [-4.1; 0.03]	0.054
Diabetes	-11.6 [-6.8; -2.6]	<0.001*	-5.5 [-9.1; -1.9]	0.003*	-5.5 [-9.0; -2.0]	0.002*
<i>Total sedentary behavior (h/day)</i>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	0.1 [-0.1; 0.3]	0.219	0.04 [-0.1; 0.2]	0.663	0.05 [-0.1; 0.2]	0.608
Diabetes	0.7 [0.4; 1.0]	<0.001*	0.4 [0.1; 0.7]	0.007*	0.5 [0.2; 0.8]	0.001*

β coefficients and 95% confidence intervals (95% CI) represent median difference in LPA, MPA, VPA, MVPA (min/day) and sedentary behavior (h/day) compared with participants with no diabetes as the reference. Significant results (p<0.05) are marked with \*.

<sup>a</sup>Model 1: Multivariable regression model adjusted for age and sex

<sup>b</sup>Model 2: Multivariable regression model adjusted for age, sex, and BMI

<sup>c</sup>Model 3: Multivariable regression model adjusted for age, sex, BMI, comorbidities, stress, mental well-being, and chronic pain

### 4.3. Results of Paper III

In Paper III, we included 562 participants, 144 (26%) had diabetes, and 418 had prediabetes (74%) (Fig. 5). Among all participants, 65% had moderate to high stress and 15% had low well-being. Further, among those with diabetes, 65% had moderate to high stress and 19% had low well-being, while numbers were 66% and 14% among those with prediabetes.

Characteristics of participants with diabetes and prediabetes across categories of stress and well-being are presented in Table 9 and 10.

The proportion of participants suffering from obesity was highest among those with low stress (diabetes: 63% and prediabetes: 38%). Also, participants with moderate to high stress had more comorbidities (diabetes: 65% and prediabetes: 54%) compared with participants with low stress, and a higher proportion reported that they suffered from chronic pain (diabetes: 51% and prediabetes: 37%) (Table 9).

Participants with low well-being had more comorbidities (diabetes: 81% and prediabetes: 73%), and the majority suffered from chronic pain (diabetes: 75% and prediabetes: 69%) compared with participants with moderate to high well-being. Also, participants with diabetes and low well-being were more obese (73%) compared with participants with diabetes and moderate to high well-being (56%), however, no major differences in BMI categories were observed among participants with prediabetes (Table 10).

### Flowchart of included participants

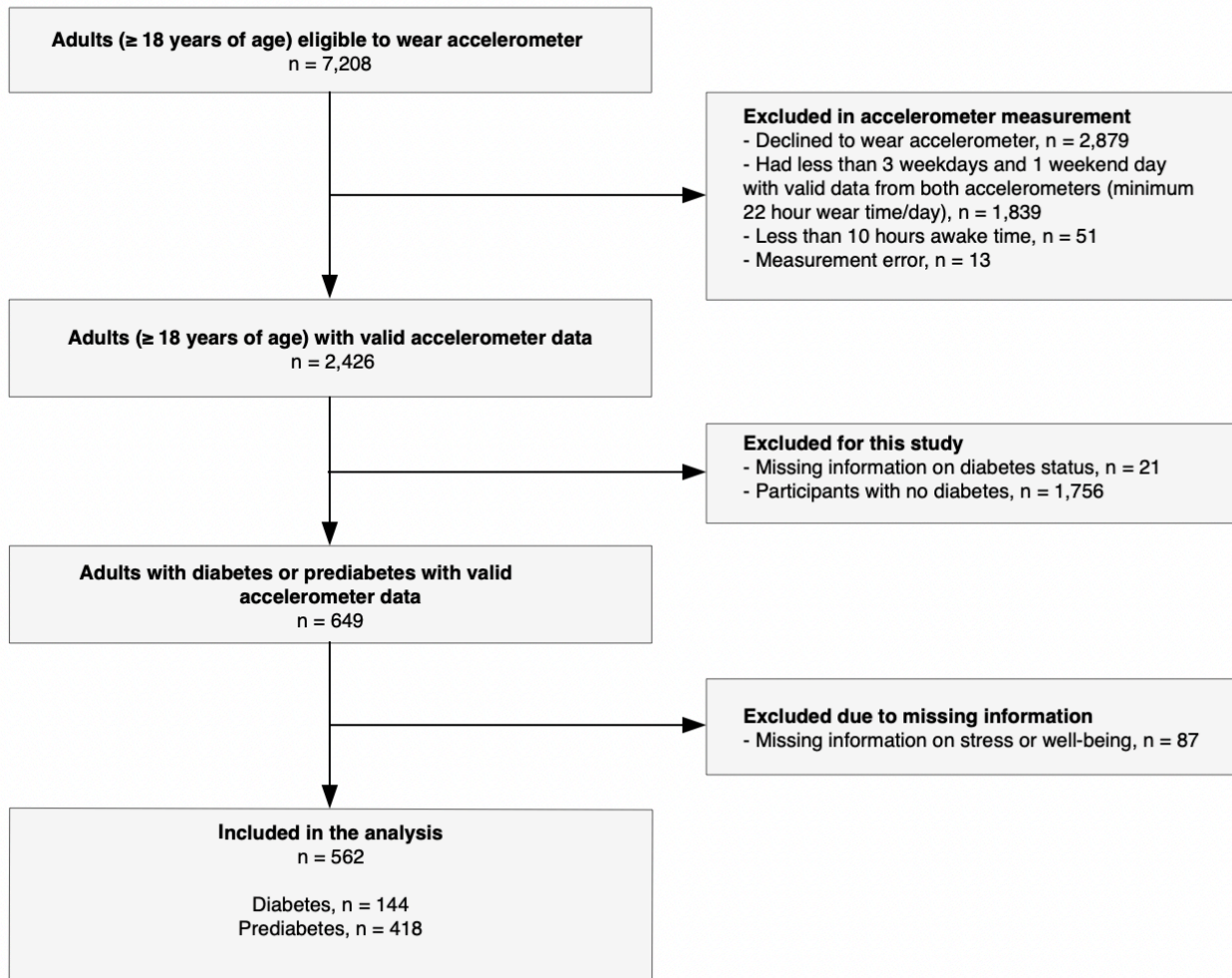


Fig. 5. Flowchart of included participants in the Paper III.

**Table 9.** Age- and sex standardized characteristics of participants with diabetes and prediabetes with low and moderate to high levels of stress

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low stress	Moderate/high stress	Low stress	Moderate/high stress	Low stress	Moderate/high stress
<i>n</i> (%)	50 (34%)	94 (65%)	144 (34%)	274 (66%)	194 (34%)	368 (65%)
Married/Living with partner	38 (76.2)	78 (83.0)	108 (75.3)	223 (81.9)	146 (75.6)	300 (81.8)
Educational level						
Primary, lower secondary or other education	15 (30.5)	9 (10.0)	16 (11.4)	40 (14.8)	31 (16.0)	47 (12.8)
Upper secondary or vocational education	29 (58.1)	60 (63.4)	99 (69.6)	159 (58.3)	128 (66.8)	219 (59.9)
Higher education	6 (11.5)	25 (26.6)	27 (19.0)	73 (26.9)	33 (17.2)	100 (27.3)
Occupational status						
Employed, student, other	19 (39.0)	24 (25.9)	65 (46.0)	101 (38.7)	85 (44.2)	127 (35.9)
Unemployed, absent due to sick leave	4 (7.4)	13 (14.6)	2 (1.2)	19 (7.1)	6 (2.9)	31 (8.7)
Retired	27 (53.6)	54 (59.5)	75 (52.8)	142 (54.2)	102 (52.9)	196 (55.4)
BMI categories <sup>a</sup>						
Underweight/normal weight	8 (16.4)	9 (10.4)	32 (22.7)	71 (26.6)	40 (18.1)	81 (23.0)
Overweight	10 (20.6)	30 (33.8)	55 (39.6)	111 (41.7)	65 (32.3)	140 (39.4)
Obese	30 (63.0)	50 (55.8)	52 (37.6)	84 (31.7)	82 (49.7)	134 (37.8)
Suffers from chronic pain	21 (42.3)	48 (51.6)	40 (28.4)	102 (37.4)	60 (31.6)	150 (41.0)
Comorbidities						
No comorbidities	9 (18.6)	11 (11.4)	33 (22.8)	47 (17.2)	42 (21.9)	57 (15.5)
1 comorbidity	18 (36.6)	21 (22.8)	51 (35.7)	78 (28.6)	70 (36.1)	102 (27.7)
≥2 comorbidities	22 (44.8)	62 (65.8)	60 (41.5)	148 (54.1)	82 (42.1)	209 (56.8)

*n* varies due to variations in complete responses within each variable.

Categorical data are presented as *n* and proportion (%) with standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference).

<sup>a</sup>BMI categories: Underweight/normal weight (<25.0), Overweight (BMI ≥25-<30), and obese (BMI ≥30).

**Table 10.** Age- and sex standardized characteristics of participants with diabetes and prediabetes with low and moderate to high levels of well-being

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being
<i>n</i> (%)	28 (19%)	116 (81%)	57 (14%)	361 (86%)	85 (15%)	477 (85%)
Married/Living with partner	19 (67.1)	97 (83.2)	40 (71.3)	292 (81.2)	59 (70.2)	388 (81.6)
Educational level						
Primary, lower secondary or other education	3 (11.4)	22 (18.6)	10 (18.1)	47 (13.1)	13 (14.7)	67 (14.1)
Upper secondary or vocational education	19 (68.8)	68 (58.7)	33 (57.1)	225 (63.1)	52 (61.4)	295 (62.3)
Higher education	6 (19.8)	26 (22.7)	14 (24.8)	85 (23.8)	20 (23.9)	112 (23.6)
Occupational status						
Employed, student, other	9 (30.9)	35 (30.9)	19 (34.8)	152 (43.3)	27 (33.0)	187 (40.5)
Unemployed, absent due to sick leave	7 (26.0)	9 (8.4)	7 (13.2)	13 (3.7)	15 (17.8)	22 (4.8)
Retired	12 (43.1)	69 (60.7)	28 (52.0)	185 (53.0)	40 (49.3)	253 (54.7)
BMI categories <sup>a</sup>						
Underweight/normal weight	2 (8.8)	16 (15.0)	12 (21.4)	89 (25.5)	14 (16.7)	107 (23.2)
Overweight	5 (18.7)	32 (28.8)	23 (40.3)	144 (41.3)	27 (32.3)	176 (38.4)
Obese	20 (72.5)	62 (56.1)	21 (38.3)	116 (33.2)	43 (51.0)	176 (38.4)
Suffers from chronic pain	21 (75.1)	47 (40.9)	39 (68.9)	105 (29.5)	60 (71.0)	153 (32.3)
Comorbidities						
No comorbidities	0 (0)	19 (16.4)	4 (7.7)	74 (20.4)	5 (5.8)	92 (19.3)
1 comorbidity	5 (19.5)	34 (29.4)	11 (19.2)	123 (34.0)	16 (18.9)	160 (33.5)
≥2 comorbidities	23 (80.5)	63 (54.2)	42 (73.1)	164 (45.5)	64 (75.3)	225 (47.2)

*n* varies due to variations in complete responses within each variable.

Categorical data are presented as *n* and proportion (%) with standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference).

<sup>a</sup>BMI categories: Underweight/normal weight (<25.0), Overweight (BMI ≥25-<30), and obese (BMI ≥30).



Among participants with diabetes and prediabetes, time spent on total sedentary activity, number of sedentary bouts, durations of sedentary bouts, and breaks in sedentary activity showed minimal differences between those reporting moderate to high stress and those reporting low stress. The median of daily MVPA for participants with diabetes and moderate to high stress was 4.8 min/day (IQR: 1.5-12.4), whereas those reporting low stress had a median of 8.0 min/day MVPA (IQR: 1.9-17.7) (Table 11).

**Table 11.** Distribution of age- and sex standardized total sedentary activity, sedentary bouts, duration of breaks in sedentary activity, and MVPA among participants with diabetes, prediabetes, and total sample with low and moderate to high levels of stress

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low stress	Moderate/high stress	Low stress	Moderate/high stress	Low stress	Moderate/high stress
n (%)	50 (35%)	94 (65%)	144 (34%)	274 (66%)	194 (35%)	368 (65%)
Total sedentary activity (h/day)	10.1 ± 1.8	10.3 ± 1.8	9.4 ± 1.7	9.5 ± 1.6	9.6 ± 1.8	9.7 ± 1.7
Sedentary bouts (n/day)	49 (42-59)	49 (40-59)	50 (43-62)	53 (43-67)	50 (43-62)	51 (43-65)
Prolonged sedentary bouts (>30 min) (n/day)	5 (5-7)	6 (5-7)	5 (4-6)	5 (4-6)	5 (4-6)	5 (4-6)
Sedentary bout duration (n/day)						
<1 min.	13 (10-19)	13 (9-18)	15 (11-20)	16 (11-24)	15 (10-20)	15 (11-22)
≥1 to <3 min.	8 (7-12)	9 (6-11)	9 (7-12)	9 (7-13)	9 (7-12)	9 (7-12)
≥3 to <10 min.	11 (8-15)	11 (9-14)	12 (9-16)	12 (9-16)	12 (9-16)	12 (9-16)
≥10 min. to <30 min	10 (9-12)	10 (8-12)	10 (8-12)	10 (9-12)	8 (10-12)	10 (8-12)
Breaks in sedentary activity duration (n/day)						
<1 min.	18 (13-27)	16 (12-24)	19 (13-25)	20 (14-29)	19 (13-25)	19 (14-27)
≥1 to <3 min	12 (9-16)	12 (9-16)	12 (10-16)	12 (9-16)	12 (10-16)	12 (9-16)
≥3 to <10 min.	10 (8-12)	11 (9-13)	12 (9-14)	12 (9-14)	11 (9-14)	12 (9-14)
≥10 min.	7 (6-9)	7 (5-9)	9 (7-10)	9 (7-10)	8 (6-10)	8 (6-10)
MVPA (min/day)	8.0 (1.9-17.7)	4.8 (1.5-12.4)	10.6 (4.6-23.7)	12.1 (5.1-26.6)	9.3 (3.9-22.0)	9.9 (3.6-24.7)

Data are standardized on age and sex. Continuous data are presented as means with standard deviations or medians and interquartile range (25<sup>th</sup> and 75<sup>th</sup> quartile).

In participants with low well-being and diabetes, the average total daily sedentary activity was 11.0 h/day ± 1.8, while participants with prediabetes spent 10.1 h/day ± 1.9 on sedentary activities. Moreover, the median for MVPA for participants with diabetes and low well-being was 4.8 min/day (IQR: 0.8-9.0), while those with moderate to high well-being had a median MVPA of 5.4 min/day (IQR: 1.8-18.1) (Table 12).

**Table 12.** Distribution of age- and sex standardized total sedentary activity, sedentary bouts, duration of breaks in sedentary activity, and MVPA among participants with diabetes, prediabetes, and total sample with low and moderate to high levels of well-being

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being
<i>n</i> (%)	28 (19%)	116 (81%)	57 (14%)	361 (86%)	85 (15%)	477 (85%)
Total sedentary activity (h/day)	11.0 ± 1.8	10.1 ± 1.7	10.2 ± 1.9	9.4 ± 1.6	10.5 ± 1.9	9.6 ± 1.6
Sedentary bouts (n/day)	51 (38-68)	48 (40-58)	57 (47-75)	51 (43-66)	57 (43-72)	51 (43-64)
Prolonged sedentary bouts (>30 min) (n/day)	6 (5-8)	6 (5-7)	5 (4-7)	5 (4-6)	6 (4-7)	5 (4-6)
Sedentary bout duration (n/day)						
<1 min.	13 (10-17)	13 (9-19)	18 (10-24)	15 (11-22)	17 (10-23)	15 (10-22)
≥1 to <3 min.	8 (6-12)	8 (6-11)	9 (7-13)	9 (7-13)	9 (7-13)	9 (6-12)
≥3 to <10 min.	11 (8-15)	11 (8-14)	12 (10-17)	12 (9-16)	12 (9-16)	12 (9-16)
≥10 min. to <30 min	10 (9-12)	10 (8-12)	10 (8-12)	10 (8-12)	10 (8-12)	10 (8-12)
Breaks in sedentary activity (n/day)						
<1 min.	16 (13-24)	17 (12-25)	23 (18-31)	19 (14-26)	22 (15-31)	19 (13-26)
≥1 to <3 min	12 (10-15)	12 (9-16)	13 (11-17)	12 (9-16)	13 (10-17)	12 (9-16)
≥3 to <10 min.	10 (8-14)	11 (9-13)	11 (9-13)	12 (9-14)	11 (8-13)	12 (9-14)
≥10 min.	6 (4-7)	8 (6-10)	7 (5-10)	9 (7-10)	6 (4-9)	9 (7-10)
MVPA (min/day)	4.8 (0.8-9.0)	5.4 (1.8-18.1)	9.4 (1.9-17.5)	12.2 (5.0-26.3)	6.3 (1.8-13.3)	10.7 (4.0-25.3)

Data are standardized on age and sex. Continuous data are presented as means with standard deviations or medians and interquartile range (25<sup>th</sup> and 75<sup>th</sup> quartile).

Table 13 represents the results from the primary analyses. Among participants with diabetes or prediabetes, no associations were observed between stress (PSS) and total sedentary activity, sedentary bouts, and prolonged sedentary bouts. Higher levels of well-being (WHO-5) were significantly associated with lower total sedentary activity after adjustments in participants with diabetes (-1.0 min/day, 95% CI -1.9; -0.1, for every 1-point increase in WHO-5) and participants with prediabetes (-0.6 min/day, 95% CI -1.1; -0.05, for every 1-point increase in WHO-5). Moreover, in participants with diabetes, higher well-being was significantly associated with a lower number of prolonged sedentary bouts after adjusting for age and sex, however, this association became insignificant in the fully adjusted model. In participants with prediabetes, higher well-being was significantly associated with a lower number of sedentary bouts after adjustments (-0.2 bouts/day, 95% CI -1.1; -0.05, for every 1-point increase in WHO-5).

**Table 13.** Cross-sectional association between stress and well-being and total sedentary activity, sedentary bouts, and prolonged sedentary bouts among participants with diabetes and prediabetes.

	<b>Diabetes</b>			
	Model 1 <sup>a</sup> n = 141		Model 2 <sup>b</sup> n = 141	
	$\beta$ [95% CI]	<i>p</i> -value	$\beta$ [95% CI]	<i>p</i> -value
<i>Stress (PSS)</i>				
Total sedentary activity (min/day) <sup>c</sup>	0.7 [-2.7; 4.0]	0.683	-0.9 [-4.5; 2.7]	0.632
Sedentary bouts (n/day) <sup>d</sup>	-0.5 [-1.1; 0.2]	0.153	-0.4 [-1.1; 0.4]	0.327
Prolonged sedentary bouts (n/day) <sup>d</sup>	0.04 [-0.03; 0.1]	0.216	-0.02 [-0.1; 0.05]	0.551
<i>Well-being (WHO-5)</i>				
Total sedentary activity (min/day) <sup>c</sup>	-1.2 [-2.0; -0.4]	0.003*	-1.1 [-2.0; -0.2]	0.023*
Sedentary bouts (n/day) <sup>d</sup>	0.02 [-0.1; 0.2]	0.767	-0.05 [-0.2; 0.1]	0.605
Prolonged sedentary bouts (n/day) <sup>d</sup>	-0.02 [-0.03; -0.01]	0.002*	-0.01 [-0.03; 0.002]	0.100
	<b>Prediabetes</b>			
	Model 1 n = 403		Model 2 n = 403	
	$\beta$ [95% CI]	<i>p</i> -value	$\beta$ [95% CI]	<i>p</i> -value
<i>Stress (PSS)</i>				
Total sedentary activity (min/day) <sup>c</sup>	0.7 [-1.6; 3.0]	0.528	0.3 [-1.8; 2.4]	0.795
Sedentary bouts (n/day) <sup>d</sup>	0.33 [-0.2; 0.8]	0.195	0.22 [-0.2; 0.7]	0.333
Prolonged sedentary bouts (n/day) <sup>d</sup>	0.003 [-0.03; 0.04]	0.834	-0.02 [-0.06; 0.02]	0.383
<i>Well-being (WHO-5)</i>				
Total sedentary activity (min/day) <sup>c</sup>	-1.0 [-1.5; -0.5]	<0.001*	-0.6 [-1.1; -0.05]	0.034*
Sedentary bouts (n/day) <sup>d</sup>	-0.1 [-0.2; 0.04]	0.191	-0.2 [-0.3; -0.06]	0.004*
Prolonged sedentary bouts (n/day) <sup>d</sup>	-0.01 [-0.02; 0.001]	0.076	0.001 [-0.01; 0.01]	0.886

<sup>a</sup>Stress: Model 1: Multivariable regression model adjusted for age and sex.

Well-being: Model 1: Multivariable regression model adjusted for age and sex.

<sup>b</sup>Stress: Model 2: Multivariable regression model adjusted for age, sex, educational level, occupational status, marital status, BMI, and comorbidities.

Well-being: Model 2: Multivariable regression model adjusted for age, sex, educational level, occupational status, marital status, BMI, comorbidities, and chronic pain.

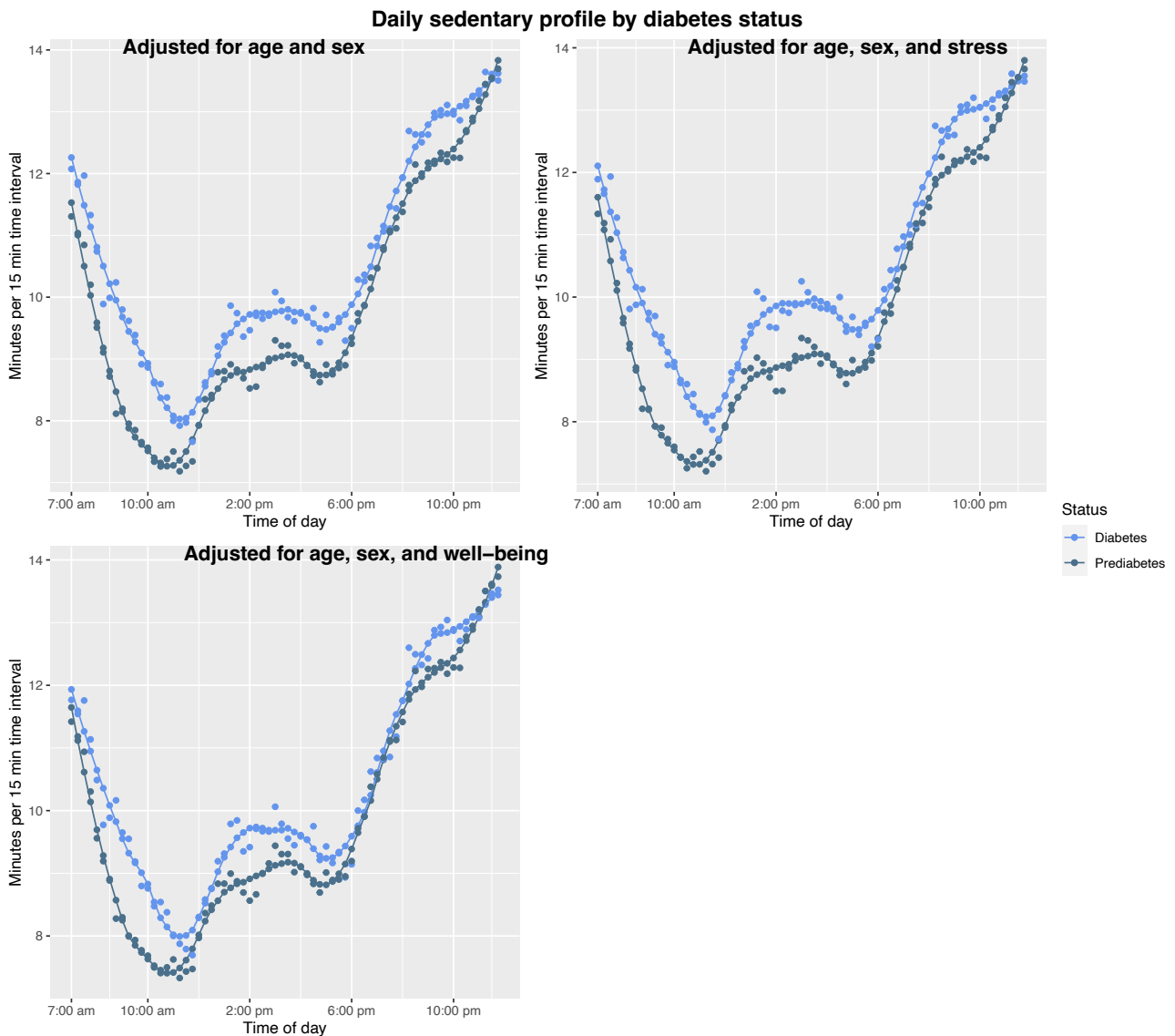
<sup>c</sup>Linear regression.  $\beta$  coefficients and 95% confidence intervals (95% CI) represent mean difference in total sedentary activity (min/day) per 1 point increase in PSS or WHO-5.

<sup>d</sup>Quantile regression.  $\beta$  coefficients and 95% confidence intervals (95% CI) represent difference in the median of sedentary bouts (n/day) and prolonged sedentary bouts (n/day) per 1 point increase in PSS or WHO-5.

Significant results ( $p < 0.05$ ) are marked with \*.

After adjusting for age and sex, participants with diabetes spent more time on sedentary activity during the whole day when compared to those with prediabetes. In both groups, sedentary activity declined from 7:00 am to 10:00 am, followed by an increase in sedentary activity which was stabilized until 6:00 pm, and then a steep rise occurred until night. Mean difference in total daily sedentary activity between participants with diabetes and those with prediabetes was -0.7 h/day

(95% CI -1.1; -0.4) when adjusting for age and sex. This difference remained similar at -0.7 h/day (95% CI -1.1; -0.4) when stress was included in the analysis. However, when adjusting for well-being in addition to age and sex, the differences between groups in total sedentary activity during a day were attenuated, with a mean difference of -0.6 h/day (95% CI -1.0; -0.4) (Fig. 6).



**Fig. 6.** Daily sedentary profiles by diabetes status are presented as mean time (minutes per 15 min interval) spent on sedentary activity during a day adjusted for age and sex, stress, and well-being, respectively. The points represent the raw age- and sex adjusted estimates, and the fitted line represents a smoothing trend based on the point estimates.

## **5. Paper IV: Online physical exercise and group sessions to increase and maintain physical activity in individuals with type 2 diabetes: A single-arm feasibility study**

This part of the thesis includes the method and result sections for Paper IV. The Paper is based on data collected in the feasibility study: *Online Physical Exercise and Group Sessions to Increase and Maintain Physical Activity in Individuals with Type 2 Diabetes: A Single-Arm Feasibility Study*. Parts of the following sections will include some information that has been described previously in the published version of Paper IV (Appendix IV).

The aim of Paper IV was to evaluate the feasibility, fidelity, and acceptability of an 8-week high intensity online physical exercise combined with online group meetings and supported with an activity watch in individuals with T2D.

### **5.1. Methods**

#### *5.1.1. Study design*

Paper IV was designed as a one-armed feasibility study. The one-armed design was chosen because most progression criteria were related to the received intervention. Further, no blinding was applied in the study. The intervention of the feasibility study was carried out from 16<sup>th</sup> of March to 18<sup>th</sup> of May 2022 on the Centre for Physical Activity Research (CFAS), Rigshospitalet, Copenhagen, Denmark. Reporting of the study followed the CONSORT extension to randomized pilot and feasibility trials (105). We conducted the study in accordance with the guidelines of the Declaration of Helsinki, and the study was approved by the Ethics Committee of the Capital Region of Denmark (Protocol code: H-2106295 and date of approval: 13<sup>th</sup> January 2022) and retrospectively registered in [clinicaltrials.gov](https://clinicaltrials.gov) (NCT05668442).

#### *5.1.2. Participants*

Participants were eligible for participation in the study if they were above 18 years of age, diagnosed with T2D by their general practitioner (GP), and if they had access to a computer, smartphone, or tablet. Participants were excluded if they participated in another intervention study

simultaneously or within the last three months, and if the participants were advised against participation in exercise by their GP (106).

Participants were recruited from January to March 2022 from the Capital Region of Denmark and Region Zealand. The following recruitment strategies were used to recruit participants: Posters on the website of the Danish Diabetes Association (DDA), contacts from local organizations within the DDA, posters and flyers in the local Diabetes Centre in Copenhagen, and lastly, individuals with T2D who had previously participated in an exercise trial at CFAS were informed about the project through a social media forum. To determine eligibility for participation, potential participants underwent a telephone screening conducted by one of the project coordinators (MEP). The screening questions were developed in collaboration with a diabetes physician, and in cases where there was uncertainty regarding eligibility, the diabetes physician was consulted for clarification.

### *5.1.3. Study intervention*

The study intervention was developed from April 2021 to January 2022 using a co-creation approach. The framework of the development and design of the intervention, and how the intervention was conducted is described in this section. Initially, the rationale behind selecting the co-creation approach, drawing on insights from Thorsen et al. (61) is described. Subsequently, it elucidates the implementation of the co-creation approach and how this methodology led to a prototyping phase in practice. Lastly, after the co-creation process and the prototyping phase, the final intervention was developed.

#### *Development of the intervention*

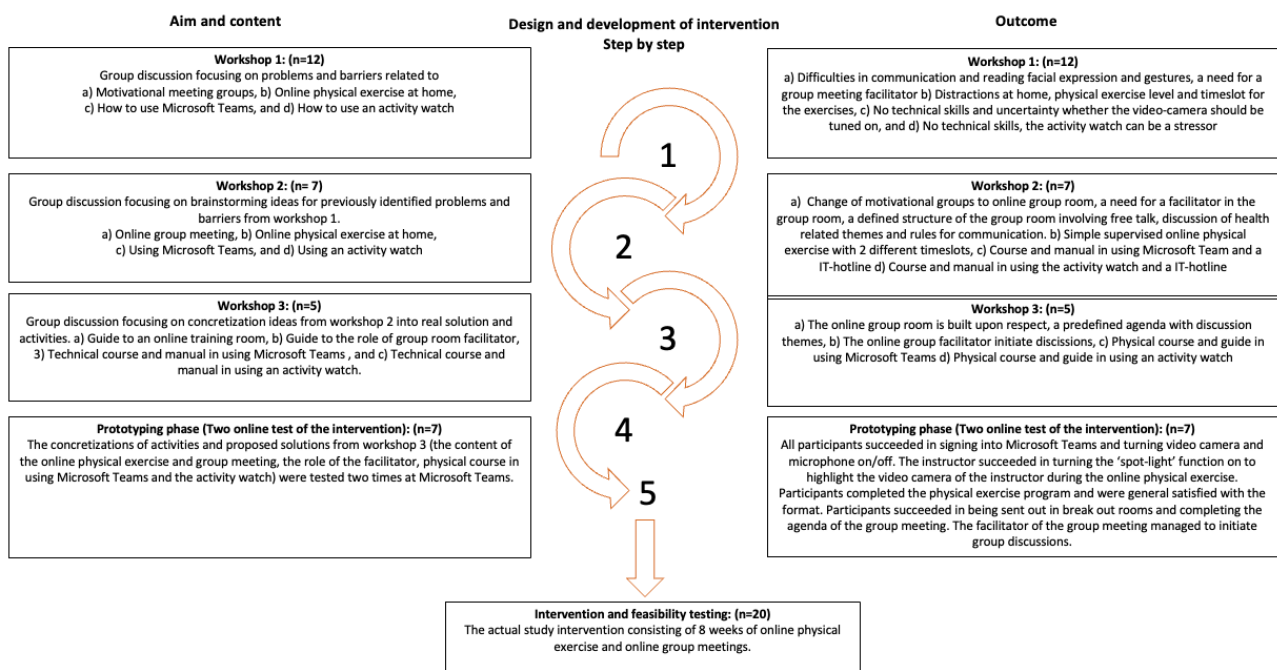
The findings from Thorsen et al. (61) led to the inspiration and rationale of developing an intervention that focused on physical activity engagement among individuals with T2D with the use of a practice theory and user-involvement (107). Thorsen et al. found three central themes as barriers to engage in physical activity among individuals with T2D: 1) Physical activity conflicts with other activities and tasks in everyday life, 2) Lack of physical activity opportunities that they can attend, however, the participants saw a potential in using technology to increase their engagement in physical activity, 3) Lack of community and social support was the general experience when trying to increase and maintain physical activity habits (61). Together with the co-creation approach, these three themes created the framework for the intervention in Paper IV.

The framework for the proposed intervention involved a physical exercise that participants easily could access from home on their own digital device in different timeslots on a weekday, which will from now be referred to as the ‘online physical exercise’. Following each online physical exercise session, it was proposed that participants were distributed into small online groups. The intention with the small online groups was to create a confident online room where participants could internally build relationships and achieve social support to engage in physical activity as well as other diabetes-related challenges. In addition, the use of an activity watch was included in the intervention as a tool for the participants to set and reach activity goals by themselves. The Garmin Vivofit 4 activity watch was suggested for the intervention due to its utility: small size, one year battery life, price, and widget. Lastly, participants were endeavored to decide the content and agenda of the small online groups together.

The co-creation approach was applied to develop and decide the content of the online physical exercise intervention and intending to improve participant satisfaction and long-term adherence. Co-creation entails collaborative efforts among three key groups: end-users (the target population), stakeholders (individuals with interest or involvement in the intervention), and academic researchers (university researchers or health-related practitioners). The three key groups join forces to achieve a shared understanding and work together towards a common goal (72).

From September 2021 to January 2022 we conducted three co-workshops and a prototyping phase. Prior to initiating the co-creation process, we identified stakeholders using a stakeholder analysis that focused on mapping local stakeholders (108). The identified stakeholders included individuals diagnosed with T2D (n=12), health science researchers (n=4), physiotherapists and professionals from sports science (n=3), and consultants from the DDA (n=2). Following identification of stakeholders, the partnership between stakeholders was established. The framework of the intervention was presented for the stakeholders with the purpose to engage them to work towards a common goal. Afterwards, all stakeholders were invited to participate in three face-to-face co-workshops that aimed to develop and decide the content of the online physical exercise intervention. The first co-workshop focused on problem exploration, including identifying key challenges and barriers associated with the online physical exercise and the small online group format. The participants of the co-workshop identified barriers in smaller groups, and then they identified the four key barriers related to the intervention in plenum. The following two co-workshops were inspired by “the future workshop model”. The purpose of “the future workshop

model” is to focus on generating ideas and propose realistic solutions and actions that can accommodate the barriers and challenges identified from the first co-workshop (109). After the three co-workshops were conducted, the specific solutions and actions were integrated in the intervention and then tested in the prototyping phase to identify early potential challenges (72). A small sample of end-users (n=6) who also participated in the co-workshops, participated in the prototyping phase through two intervention sessions to test the delivery and content of the intervention. During the test sessions, observations and feedback were provided from the participants and project group. The intervention was refined based on the feedback and then retested. The result of the prototyping phase was the final intervention. An overview of the co-creation process and how the intervention was designed and developed is shown in Fig. 7.



**Fig. 7.** Design and development of the intervention using a co-creation approach. The development consisted of five steps: 1-3) three co-workshops, 4) a prototyping phase, and 5) the final intervention.

### *The intervention*

The intervention in Paper IV was standardized and described in accordance with the template for intervention description and replication checklist developed for telehealth-interventions (TIDieR-Telehealth) (110).



An introduction course was integrated as a part of the intervention and carried out before baseline measurements. Participants attended the introduction course physically and they were educated in how to use Microsoft Teams, Garmin activity watches, how to wear accelerometers, and other details of the intervention. Participants also received a detailed manual about Microsoft Teams, Garmin activity watches, and accelerometer application, and a calendar with an overview of essential dates from baseline to postintervention.

Participants were invited to attend in an 8-week intervention consisting of one weekly online physical exercise, lasting 30-minutes, accompanied by 30-minutes online group meetings in smaller groups. The intervention took place from March to May 2022. Participants attended the online intervention through the platform Microsoft Teams from their own device (e.g., computer, smartphone, or tablet). The intervention was scheduled on Wednesdays; one session from 10:00 am to 11:00 am, and the other from 5:00 pm to 6:00 pm. Before the intervention was commenced, participants were assigned to one of the scheduled sessions based on their preferences, allowing them to accommodate other activities in their daily life.

The two project coordinators (SRM (MSc Physiotherapy) and MEP (MSc Sports science and clinical biomechanics)) delivered the 30-minutes online physical exercise program. The program consisted of a short warm-up, followed by an interval-typed circuit physical exercise program consisting of bodyweight aerobic and strength exercises targeting individuals with T2D to benefit in relation to glycemic control (18, 111, 112) (detailed information about the physical exercise program is available in Appendix IV, Supplement S1). The Borg-scale was used to evaluate the intensity of the physical exercise program, and we intended to reach an intensity level corresponding to 16 on the Borg-scale (113). At the introduction course, participants were instructed to use the Borg-scale. Right after the online physical exercises, the participants were encouraged to reflect and evaluate on their reached intensity level using the Borg-scale.

After the online physical exercise, the participants were then divided into predefined groups of three to five participants by using the break-out room function in Microsoft Teams. The participants stayed in the same group during the whole intervention period to increase the relations between participants and ensure a feeling of obligation to attend the online group meetings. The project coordinators did not attend the online group meetings. The online group meeting served as a confident room for discussion and evaluation of the online physical exercise, diabetes-related

challenges, and other aspects that the participants found important to discuss. In each group, a participant had volunteered to be a facilitator prior to the intervention. The facilitators were chosen by the project coordinators based on their technology skills. The facilitator's role was to facilitate a group discussion and ensure all group members felt included. At the introduction course, the facilitators received information about how to facilitate a group discussion online and inspiration to topics they could bring up in the group meetings. Furthermore, the facilitators were telephoned by the project coordinator (MEP) after the first three online group meetings to evaluate the group discussions. Afterwards, the facilitators were encouraged to call the project coordinators if needed. In all other aspects, the facilitators participated in the study on equal terms like all other participants.

During the whole intervention period, participants were encouraged to set personal weekly activity goals following the SMART goals structure (114) in order to increase self-management of habitual physical activity. In addition, participants were encouraged to evaluate their activity goals during the small group meetings, so they could receive feedback and support from the group to reach their activity goals.

As a part of the intervention, participants were provided with a Garmin Vivofit 4 activity watch, which they were encouraged to wear throughout all 8 weeks of the intervention. These Garmin activity watches were incorporated into the intervention to help facilitate weekly activity goals and enable continuous evaluation of their daily physical activity, which could then be discussed in the online group meetings. The Garmin Vivofit 4 watches were chosen because of their long battery life and the simple design to increase adherence. However, four participants volunteered to wear the Garmin Forerunner 245 to compare heart rate with self-reported intensity from the Borg scale during the online physical exercise sessions.

#### *5.1.4. Outcomes*

The included outcomes in Paper IV were the following: pre-defined research progression criteria, objectively measured physical activity, self-reported outcomes of a range of health parameters, and participant feedback obtained from questionnaires. Furthermore, the following information was obtained from the baseline questionnaire: general demographic information, including age, sex, marital status, educational level, and ethnicity, and information regarding the participants' severity

of diabetes, including time of diagnosis, complications, medication, and their last measured HbA1c at the GP.

### *Primary outcomes*

The primary outcomes of interest in Paper IV were pre-defined research progression criteria. The research progression criteria are used as a preparation of a definitive randomized controlled trial (RCT) based on a traffic light system of green (continue without changes), amber (changes needed to improve study design and feasibility), and red (major changes are needed) and are represented in Table 14 (115).

Recruitment of participants was evaluated by calculating number of participants recruited within three months. To evaluate retention, the percentage of participants who provided both baseline and postintervention data was calculated in relation to the total number of participants at baseline. Adherence to online physical exercise and group meetings was evaluated with a questionnaire. Participants received a short web-based questionnaire every week right after the online physical exercise and group meeting to respond whether they attended the sessions or not. Adherence was then calculated by counting the number of completed online physical exercises and group meetings separately and then divided by the eight planned sessions. In addition to responding weekly questions about their adherence to online physical exercise and group meetings, participants also wrote down their activity goal for the forthcoming week and whether they had achieved the activity goal from the previous week.

Improvement of habitual physical activity was evaluated with Axivity AX3 (Axivity, Newcastle, UK) accelerometers. All participants were instructed to wear two accelerometers for seven consecutive days, including during sleep and water activities, before, during, and after the intervention (116). One accelerometer was placed on the right thigh and the other one on the lower back. The project coordinators (SRM and MEP) applied the accelerometers on the participants before baseline measurements, and afterwards, participants received the accelerometers by post and were instructed to apply the accelerometers by themselves and reapply them if they fell off. Any improvement in habitual physical activity (measured in daily counts per min) from baseline to postintervention was considered as a positive advancement in terms of the research progression criteria, as even engaging in some physical activity is beneficial for one's health according to the WHO (21). To evaluate the experienced burden of objectively measured physical activity,

participants received a questionnaire at postintervention regarding their satisfaction with applying accelerometers by themselves and wearing them for at least one week at baseline, midway, and postintervention.

Adverse events were evaluated with a questionnaire at postintervention. Participants scored their experienced severity of adverse events following the structure of the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®) (117). In the questionnaire, minor adverse events covered dizziness, acute and prolonged musculoskeletal pain, and minor falls, while serious adverse events covered life-threatening events, disability, permanent damage, or hospitalization (118). Also, participants were informed to contact the project coordinators (SRM and MEP) if they experienced any adverse events during the intervention.

**Table 14.** Research progression criteria for continuing to definitive RCT

<b>Outcome</b>	<b>Green</b>	<b>Amber</b>	<b>Red</b>
<b>Participant recruitment</b>	24 participants recruited within 3 months	Fewer than 24 participants recruited within 3 months	Fewer than 12 participants recruited within 3 months
<b>Completion of intervention</b>	Minimum 75% of the participants complete postintervention	Minimum 50% of the participants complete postintervention	Fewer than 50% of the participants complete postintervention
<b>Adherence to online physical exercise sessions<sup>1</sup></b>	Minimum 75% of the participants complete more than half of the online physical exercise sessions	Minimum 50% of the participants complete more than half of the physical exercise sessions	Fewer than 50% of the participants complete more than half of the physical exercise sessions
<b>Adherence to online group meetings<sup>2</sup></b>	Minimum 75% of the participants complete more than half of the group meeting sessions	Minimum 50% of the participants complete more than half of the group meeting sessions	Fewer than 50% of the participants complete more than half of the group meeting sessions
<b>Adherence to activity goals<sup>3</sup></b>	Minimum 75% of the participants set goals	Minimum 50% of the participants set goals	Fewer than 50% of the participants set goals
<b>Burden of objectively measured physical activity</b>	Minimum 80% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Minimum 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Fewer than 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again
<b>Improvement of physical activity<sup>4</sup></b>	Minimum 50% of the participants have achieved improvements in physical activity at postintervention	Minimum 25% of the participants have achieved improvements in physical activity at postintervention	Fewer than 25% of the participants have achieved improvements in physical activity at postintervention
<b>Adverse events</b>	No or minor adverse events related to the intervention at postintervention	Fewer than five serious adverse events related to the intervention at postintervention	Five or more serious adverse events related to the intervention at postintervention

Research progression criteria based on traffic light system: Green (continue), amber (changes to protocol must be discussed before continuing), and red (do not proceed unless the issue can be solved) (115).

<sup>1</sup>At the beginning and end of the online physical exercise sessions all the participants note if they were participating.

<sup>2</sup>At the beginning and end of each of the group meetings all the participants note if they were participating.

<sup>3</sup>Activity goals assessed during the group meetings.

<sup>4</sup>Any improvement in objectively measured physical activity (count per minute for the day).

## *Secondary outcomes*

*Objective measurements.* Besides any improvement in habitual physical activity (from the research progression criteria), we used data obtained from the accelerometers to include other aspects of physical activity among participants as secondary outcomes. Accelerometer data were processed as in Paper II. Likewise, the criteria for valid accelerometer data were similar to the ones from Paper II. The following physical activity variables were included in Paper IV: LPA, MPA, VPA, MVPA, sedentary behavior, adherence to WHO recommendations, and adherence to recommendations on daily physical activity according to the ADA and the Danish Health Authority (categorized similarly to Paper II) (21, 22). Further, we included total daily step counts which was determined by an algorithm by Godfrey et al. (119).

*Self-reported measurements.* Questionnaires from baseline and postintervention were used to obtain secondary self-reported outcomes. Many of the self-reported measures used in Paper I, II and III were also used in Paper IV as secondary outcomes. Therefore, these measurements will not be elaborated in this section.

Self-reported height and weight was calculated into BMI ( $\text{kg}/\text{m}^2$ ). Cohen's 10-item PSS was used to assess participants' perceived stress (82), and mental well-being was assessed using the WHO5-Well-Being Index (96). The Bayliss Burden of Illness Measure was used to obtain information about participants' number of chronic conditions and the level of interference these conditions caused in their daily life activities. Participants rated their condition's impact on a 5-point Likert scale, ranging from 1 (not at all) to 5 (a lot). The cumulative scores were then used to calculate the total morbidities and the total burden score (120). The Self-Efficacy for Managing Chronic Disease 6-Item Scale was used to measure participants' self-perceived beliefs about their own abilities related to performing an activity. A higher score reflects a greater self-efficacy (121). At last, participants' self-rated feeling of loneliness was assessed using the UCLA 3-Item Loneliness Scale. Each item was scored with points from "hardly ever or never" (1 point) to "often" (3 points), and a higher score indicates a higher level of perceived loneliness (122).

*Participant feedback.* All participants (both facilitators and regular participants) received a questionnaire at postintervention about their satisfaction with selected topics related to the study:

- The communication between the project coordinators and participants

- The introduction course held before baseline measurements
- Online physical exercise sessions
- Online group meetings
- Setting weekly activity goals and prioritization of them along with their usual activities
- Use of Microsoft Teams and Garmin watches
- Burden of tasks in the project
- The experience of a facilitator in online group meetings (facilitators received questions about being a facilitator, and regular participants received questions about their satisfaction with the facilitator role)

Participants responded to what extent they agreed/disagreed with a list of statements within the abovementioned topics. At the end of the study, a voluntary evaluation day was held, where participants were encouraged to suggest potential improvements of the study design, intervention, and procedures.

#### *5.1.5. Sample size*

No sample size calculation was performed, however, according to the rationale for a feasibility study, regulatory and statistical considerations, at least 12 participants should be included to obtain a precise and representable mean and variance (123). Therefore, we aimed to include a minimum of 12 participants in this feasibility study.

#### *5.1.6. Statistical analysis*

Before the analyses were commenced, a SAP (Appendix VIII) was developed and openly available at OSF (<https://osf.io/3nphj/>). The content within the following paragraph bears strong resemblance to both the SAP as well as the description of the statistical analysis section outlined in the published version of Paper IV (Appendix IV).

All statistical analyses were performed using Stata, version 17, (StataCorp) and R statistical (R Core Team, Vienna, Austria) software version 4.2.2 (10<sup>th</sup> of November 2022), RStudio (RStudio Inc., Boston, MA, USA) version 2022.07.2.

We conducted cross-tabulations to describe participant characteristics. Research progression criteria were presented with descriptive statistics in accordance with the traffic light system on the per

protocol population. Continuous data were presented as mean and SD or as median and IQR, and categorical data were presented as number and proportion. Further, changes in secondary outcomes from baseline to postintervention were reported with median and IQR or as number and proportions. No hypothesis-testing was carried out in this feasibility study in accordance with the CONSORT extension to randomized pilot and feasibility trials (105).

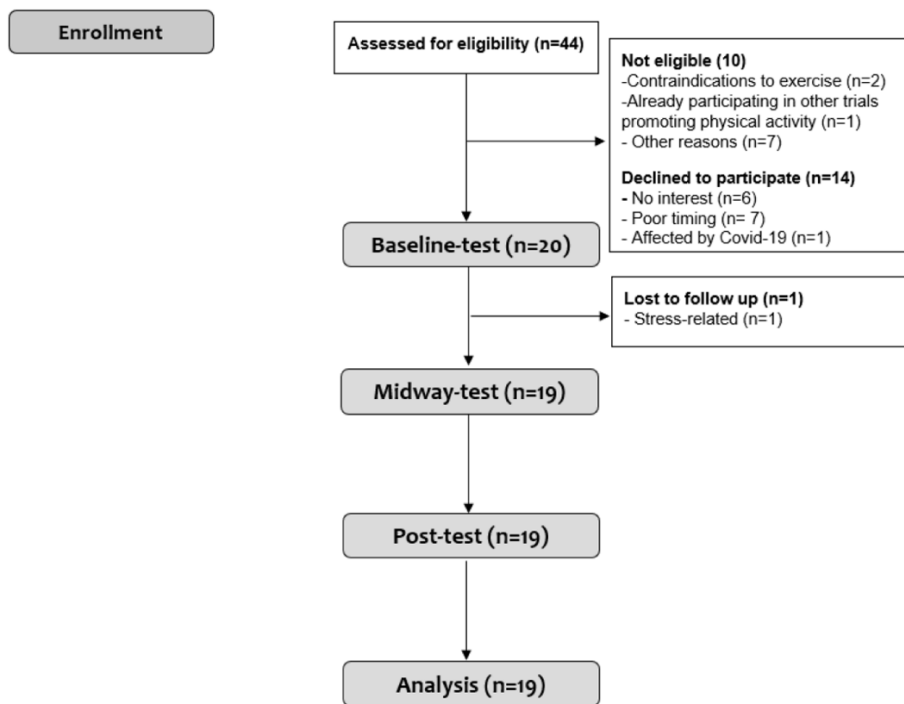
#### *5.1.7. Deviations from the protocol*

Initially, we had intended to gather data on adverse events at the end of every week throughout the intervention. However, considering that participants were already responding multiple weekly questionnaires, we made a modification to the plan. We chose to collect comprehensive information about adverse events at postintervention and informed participants that they should contact the project coordinators (SRM and MEP) if they encountered any adverse events during the intervention. Furthermore, due to the limited sample size, we decided not to perform a sensitivity analysis on differences in measuring daily steps between Garmin watches and accelerometers.

## **5.2. Results**

A total of 44 individuals with T2D were assessed for eligibility from 14<sup>th</sup> of February to 10<sup>th</sup> of March 2022. Twenty participants were allocated to the intervention, and 19 participants were included in the analysis (Fig. 8).

Of the allocated participants, eight were females and 12 were males with a mean age of  $60.4 \pm 8.7$ . Most participants were higher educated and reported moderate or high perceived stress. Further, all participants were overweight or obese and reported a median of 4 comorbidities, and 75 % of participants did not adhere to the WHO recommendations of physical activity at baseline (Table 15).



**Fig. 8.** Flowchart of participant enrolment, follow-up, and analysis. Other reasons for declining to participate were stress and other mental disorders (n=3), personal reasons (n=1), residing abroad (n=1), and loss of spouse (n=1).



**Table 15.** Baseline characteristics of participants

Age, years	60.4 ± 8.7
Women, <i>n</i> (%)	8 (40.0)
Ethnicity, <i>n</i> (%)	18 (90.0)
Living alone, <i>n</i> (%)	6 (30.0)
Educational level, <i>n</i> (%)	
Primary education	3 (15.0)
Upper secondary or vocational	7 (35.0)
Higher education	10 (50.0)
BMI, <i>n</i> (%)	
Underweight/Normal	0
Overweight	8 (40.0)
Obese class I	8 (40.0)
Obese class II	3 (15.0)
Obese class III	1 (5.0)
Diet score (healthy/medium healthy/unhealthy) <sup>a</sup>	7/10/3
Alcohol consumption (no alcohol/below risk group/above risk group) <sup>b</sup>	7/12/1
Smoking status (smoker/ex-smoker/never smoked)	1/10/9
Adherence to WHO recommendations on weekly physical activity <sup>c</sup> , <i>n</i> (%)	
Following recommendations	5 (25.0)
Not following recommendations	15 (75.0)
Adherence to recommendations on daily physical activity <sup>d</sup> , <i>n</i> (%)	
Inactivity	3 (15.0)
Some physical activity	13 (65.0)
Sufficient physical activity	4 (20.0)
WHO-5-Well-Being Index total score, (0-100)	78 (72-80)
Bayliss Burden of Illness Measure	
Median number of comorbidities reported	4 (2.5-6)
Median disease burden reported	5.5 (1.5-9)
SEMCD6, (0-10)	8 (5.7-8.7)
PSS total score, <i>n</i> (%)	
Low perceived stress	1 (5.0)
Moderate perceived stress	16 (80.0)
High perceived stress	3 (15.0)
Loneliness scale, (3-9)	3 (3-5)
Self-reported HbA1c (mmol/mol)*	47 (38-48)

*n* = 20. Data are presented as number (%), means with ± SD, or median (IQR).

Abbreviations: BMI; Body Mass Index, WHO; World Health Organization, SEMCD6; Self-Efficacy for Managing Chronic Disease 6-Item Scale, PSS; Perceived Stress Scale.

<sup>a</sup>Self-reported dietary habits categorized into three based on a diet score.

<sup>b</sup>Self-reported alcohol consumption categorized in accordance with the recommendations from the Danish Health Authority.

<sup>c</sup>Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity: ≥150 min MVPA or ≥75 min VPA weekly or an equivalent combination.

<sup>d</sup>Distribution of adherence to recommendations on daily physical activity according to ADA and the Danish Health Authority. Complete inactivity: <5 min/day of MVPA, Some activity: ≥5 min/day and <30 min/day MVPA, Sufficient activity: ≥30 min/day MVPA.

\**n*=14 due to missing data.

### 5.2.1. Primary outcomes

Table 16 shows the primary results of the feasibility study. Most research progression criteria reached an evaluation with acceptance (i.e., green evaluation, continue to an RCT without changes). However, three specific criteria related to participant recruitment, burden of objectively measured physical activity, and adverse events were categorized as amber (i.e., changes are needed to

improve study design and feasibility). We targeted to recruit 24 participants within three months, but the acceptance of the study protocol from the Ethics Committee delayed the beginning of recruitment, and therefore we only had two months to recruit participants before baseline measurements. Among the 19 participants who completed the intervention, 15 (79.0 %) reported that the number of days they wore the accelerometers was suitable, falling just one percent short of meeting the green criterion. One serious adverse event was reported, because one participant cancelled one online physical exercise due to hospitalization with Benign Paroxymal Positional Vertigo. The participant attended the online physical exercise the following week. Seventeen (89.5%) participants completed half or more of the online physical exercise sessions, while 16 (84.2%) participants completed half or more of the group meetings. Median (IQR) self-reported intensity (Borg-scale) during the online physical exercise sessions was 15.4 (14.4-16.8) and median (IQR) measured heart rate with Garmin Forerunner 245 watches was 115 (111-121). Among participants with valid accelerometer data, more than half had improved their habitual physical activity (daily counts per min) from baseline to postintervention. At last, nine participants reported minor adverse events, such as muscle pain and dizziness.

**Table 16.** Research progression criteria results to evaluate whether to progress with a definitive RCT

Research progression criteria		Evaluation
Participant recruitment, actual <i>n</i> /desired <i>n</i>	20/24	Amber
Participants who completed the intervention, <i>n</i> (%) <sup>*</sup>	19/20 (95.0)	Green
Adherence to online physical exercise sessions		
Participants who completed half of the online physical exercise sessions, <i>n</i> (%)	17/19 (89.5)	Green
Adherence to online group meetings		
Participants who completed half of the online group meetings, <i>n</i> (%)	16/19 (84.2)	Green
Adherence to goalsetting		
Participants who set activity goals, <i>n</i> (%)	19/19 (100.0)	Green
Burden of objectively measured physical activity		
Participants who <u>did not</u> find the attachment and shipping too time-consuming, <i>n</i> (%)	17/19 (89.5)	Green
Participants who found the numbers of days wearing the accelerometer appropriate, <i>n</i> (%)	15/19 (79.0)	Amber
Improvement of physical activity		
Participants who improved physical activity from baseline to postintervention, <i>n</i> (%) <sup>**</sup>	10/19 (62.5)	Green
Adverse events		
Participants who experienced minor adverse events, <i>n</i> (%)	9/19	Green
Participants who experienced serious adverse events, <i>n</i> (%)	1/19	Amber

*n*=19. The research progression criteria were based on the traffic light system (115).

<sup>\*</sup>19/20 participants followed the intervention and had complete data on baseline and postintervention measurements.

<sup>\*\*</sup>16 participants had valid accelerometer data from baseline and postintervention.

### 5.2.2. Secondary outcomes

From baseline to postintervention, an increase in median total daily MPA, MVPA, and steps was observed among participants (Fig. 9-10 and Table 17). Based on Fig. 9, large individual differences in total MVPA were present among participants at baseline, however, these differences were to some degree equalized at postintervention. Median daily steps in weekends were doubled from baseline (4468 steps/day, IQR: 1820-9216) to postintervention (9786 steps/day, IQR: 4326-14252). In general, large differences in daily steps were observed among participants at all three time points (Fig. 10 and Table 17). Median total daily sedentary behavior decreased from baseline (10.7 hours, IQR: 9.4-11.6) to postintervention (10.3 hours, IQR: 9.0-10.8) in participants. The median number of days with sufficient physical activity during a week, as per the recommendations from the ADA and the Danish Health Authority, increased from baseline (0.5 day, IQR: 0-3) to postintervention (1.5 days, IQR: 0-3) (Table 17).

**Table 17.** Secondary outcomes on objectively measured habitual physical activity

	Baseline (before week 1)	Midway (after week 4)	Postintervention (after week 8)
<i>Total</i>			
Sedentary behavior	10.7 (9.4-11.6)	10.2 (8.9-10.5)	10.3 (9.0-10.8)
LPA	136.8 (111.7-155.4)	133.9 (109.5-162.6)	129.2 (113.7-149.7)
MPA	9.2 (5.7-18.9)	11.7 (4.7-16.5)	12.6 (4.6-29.5)
VPA	0.3 (0.1-1.2)	0.3 (0.1-0.9)	0.3 (0.1-0.6)
MVPA	11.8 [5.8-22.2)	14.3 (7.2-19.8)	15.5 (6.2-30.5)
Daily steps	6292 (4044-9336)	8519 (5197-12068)	7478,7 (4569-12780)
<i>Weekdays</i>			
Sedentary behavior	11.4 (9.4-12.9)	10.6 (7.8-12.0)	10.9 (7.3-12.6)
LPA	136.8 (108.6-165.5)	131.0 (109.0-168.7)	112.3 (76.4-165.5)
MPA	7.9 (3.1-21.4)	4.8 (1.7-20.5)	7.0 (1.4-21.5)
VPA	0.2 (0-0.6)	0.2 (0-0.5)	0.2 (0-0.4)
MVPA	8.3 (3.5-23.4)	5.7 (1.8-21.7)	7.6 (1.8-22.7)
Daily steps	6621 (3775-9844)	7298 (3508-12273)	5910 (2709-13243)
<i>Weekends</i>			
Sedentary behavior	9.7 (6.1-11.2)	10.7 (9.3-11.6)	10.8 (9.2-11.8)
LPA	113.2 (70.7-172.3)	155.6 (118.5-195.2)	152.8 (93.7-189.3)
MPA	5.7 (0.8-11.7)	10.2 (1.8-19.8)	7.0 (3.3-33.2)
VPA	0.2 (0-0.3)	0.2 (0-0.5)	0.2 (0-0.7)
MVPA	6.0 (1.2-12.3)	11.8 (2.0-23.3)	9.3 (3.3-37.2)
Daily steps	4468 (1820-9216)	9405 (5237-14784)	9786 (4326-14252)
<i>Adherence to WHO recommendations on weekly physical activity<sup>a</sup></i>			
Following recommendations	4 (25.0)	4 (25.0)	6 (37.5)
Not following recommendations	12 (75.0)	12 (75.0)	10 (62.5)
<i>Adherence to recommendations on daily physical activity during a week<sup>b</sup></i>			
Days with inactivity	2.5 (1-6.5)	3 (1-5.5)	2.5 (1-5.5)
Days with some physical activity	5.5 (2.5-7.5)	3 (1-5)	2.5 (1-4)
Days with sufficient physical activity	0.5 (0-3)	0.5 (0-1.5)	1.5 (0-3)

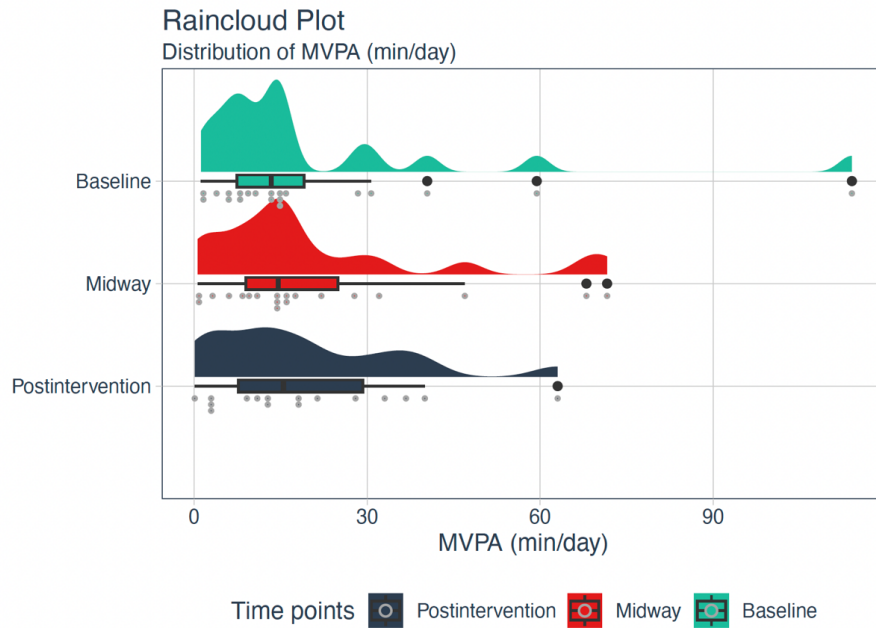
*n*=16 (participants with valid accelerometer data from baseline to postintervention).

Data are presented as medians and interquartile range (IQR) (25<sup>th</sup> and 75<sup>th</sup> quartile) or *n* and proportion (%).

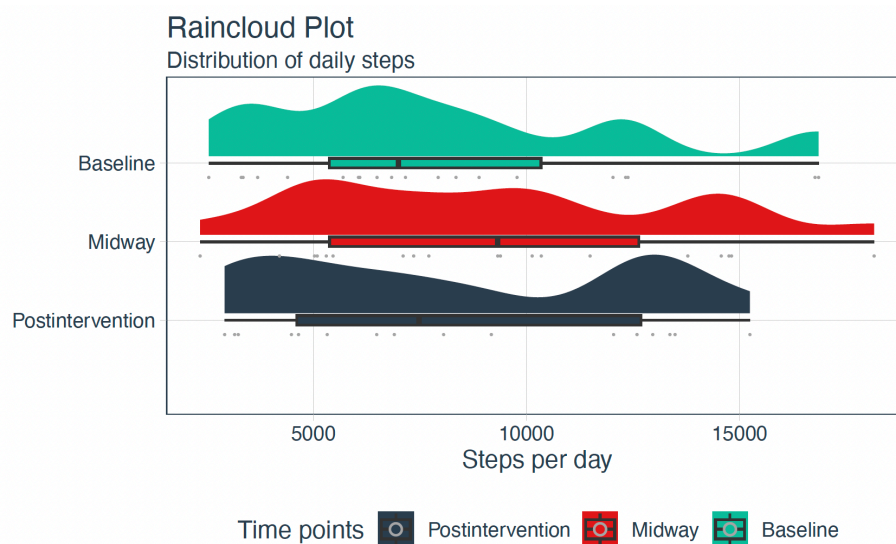
Abbreviations: LPA; Light physical activity (min/day), MPA; Moderate physical activity (min/day), VPA; Vigorous physical activity (min/day), MVPA; Moderate to vigorous physical activity (min/day).

<sup>a</sup>Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity: ≥150 min MVPA or ≥75 min VPA weekly or an equivalent combination.

<sup>b</sup>Median [IQR] number of days during a week with inactivity (<5 min/day of MVPA), some activity (Some activity: ≥5 min/day and <30 min/day MVPA), and sufficient activity (Sufficient activity: ≥30 min/day MVPA) in accordance with recommendations on daily physical activity according to ADA and the Danish Health Authority.



**Fig. 9.** Raincloud plot representing an illustration of data in a half-density distribution (the ‘cloud’) with individual raw data (the ‘rain’), including a boxplot of total daily moderate to vigorous physical activity (MVPA) in minutes at baseline, midway, and postintervention.



**Fig. 10.** Raincloud plot representing an illustration of data in a half-density distribution (the ‘cloud’) with individual raw data (the ‘rain’), including a boxplot of total daily steps at baseline, midway, and postintervention.

Table 18 represents the results of the self-reported secondary outcomes from baseline to postintervention. Median PSS total score decreased with one point from baseline to postintervention. The median reported number of comorbidities decreased at postintervention, while the median disease burden reported increased. No other changes were observed in the secondary outcomes.

**Table 18.** Secondary self-reported outcomes

	Baseline (before week 1)	Postintervention (after week 8)
BMI	31.2 (28.7-33.7)	31.2 (28.2-32.7)
PSS total score, (0-40)	20 (18-23)	19 (17-22)
Loneliness scale, (3-9)	3 (3-5)	3 (3-5)
SEMCD6, (0-10)	8 (4.8-8.8)	8.3 (6.7-9.0)
WHO-5-Well-Being Index total score, (0-100)	80 (72-80)	80 (72-84)
Bayliss Burden of Illness Measure		
Median number of comorbidities	4 (3-7)	3 (2-6)
Median disease burden reported	6 (1-9)	7 (2-14)

*n*=19 (participants with complete data on self-reported secondary outcomes from baseline to postintervention).

Data are presented as medians and quantiles (25<sup>th</sup> and 75<sup>th</sup> percentile).

Abbreviations: BMI; Body Mass Index, WHO; World Health Organization, SEMCD6; Self-Efficacy for Managing Chronic Disease 6-Item Scale, PSS; Perceived Stress Scale.

### 5.2.3. Participant feedback

The majority of participants (89.5%) reported that the project met their expectations, and 94.7% of participants reported that the online physical exercise sessions met their expectations. Most participants (84.2%) felt motivated by doing physical exercises with others even though the physical exercises were conducted online. Also, 68.4% reported that they felt a sense of solidarity in their smaller exercise groups. The measurement of steps by Garmin activity watches was a motivational factor for most participants (73.7%), and they found the Garmin activity watch useful to set and reach their weekly activity goals. Some participants (26.3%) experienced that they needed to prioritize study activities over their daily routines to achieve their weekly activity goal (Appendix IV, Supplement S2).

## 6. Discussion

### 6.1. Key findings

This PhD thesis aimed to provide detailed descriptions of physical activity characteristics, determinants, and patterns among Danish individuals with diabetes and to evaluate the feasibility, fidelity, and acceptability of an online physical exercise intervention to increase and maintain physical activity in individuals with T2D.

Four papers were conducted to individually and combined contribute to answer the overall aim of the PhD thesis.

The nationwide cross-sectional study (Paper I) revealed that the prevalence of comorbidities, higher BMI, higher perceived stress, and lower HRQoL were significantly associated with lower engagement in weekly MVPA. Moreover, this study revealed that 40% of individuals with diabetes do not adhere to the WHO recommendations for physical activity and 60% of those expressed motivation to become more physically active.

The population-based cross-sectional studies (Paper II and III) revealed that individuals with diabetes engaged significantly less in physical activity during weekdays and weekend days and had a higher frequency of highly inactive days compared to individuals with prediabetes or no diabetes. These differences were evident even after adjustment for other major determinants of physical activity, such as BMI and prevalent comorbidities. Moreover, higher well-being scores were associated with lower total daily sedentary activity in individuals with diabetes and prediabetes, while no association was found between stress and sedentary outcomes. Further, individuals with diabetes and prediabetes had a highly sedentary lifestyle, but particularly those with low well-being were more sedentary and less physically active compared with those with moderate to high well-being.

Lastly, Paper IV showed that an online physical exercise and group session intervention supported with an activity watch was feasible and acceptable in terms of completion of the intervention, adherence to the intervention, and improvement of physical activity. This was observed among individuals with T2D with higher educational levels when compared to the general population with T2D. However, the data suggest amendments regarding participant recruitment, burden of

objectively measured physical activity, and adverse events related to the intervention before investigating effectiveness in a future RCT.

## **6.2. Discussion of key findings**

*In the following section, the key findings of Paper I-IV will be discussed combined to provide different perspectives on adherence to physical activity recommendations, determinants of physical activity and sedentary activity, the balance between physical activity and sedentary activity engagement, personalized medicine, and the feasibility of an online physical exercise intervention.*

### **6.2.1. Adherence to physical activity recommendations**

In Paper I, we found that 40% of individuals with diabetes did not adhere to WHO recommendations for physical activity measured by self-report, which is lower when compared with two previous cross-sectional studies outside Denmark. A study by Martinez-Harvell et al. (27) from 2020 found that 54% out of 25,980 adults with diabetes from the US did not meet the recommendations of physical activity (150 min/week of MVPA, or 75 min/week of VPA at least 3 times/week). Additionally, Salman et al. (28) from 2019 found that 66% out of 1,259 adults with diabetes from Scotland did not meet the recommended levels of physical activity (150 min/week MPA or 75 min/week VPA or equivalent combination). These diverse results could reflect differences in diabetes prevalence and characteristics, as well as cultural differences that may affect physical activity behaviors. Importantly, our results were standardized on age and sex to account for age and sex-related differences between individuals with diabetes and those without diabetes.

On the other hand, Paper II revealed that 63% of individuals with diabetes were non-adheres to the WHO recommendations when measuring physical activity using accelerometry. Another Danish study by Domazet et al. (34) investigating adherence to physical activity recommendations with accelerometers in newly diagnosed individuals with T2D (median age of 61.8 years) found that 38% did not meet the recommendations. Further, a Swedish population-based study by Hult et al. (124) found that 57% of 70-year-old adults with diabetes did not adhere to the recommendations. Our study participants in Paper II had a median age of 67.8 years, however, we conducted our analyses with standardization of age and sex to outline age- and sex-related differences in physical activity across diabetes status. Yet, we still found a larger proportion of insufficient physically



active individuals with diabetes compared with the results from Domazet et al. (34) and Hult et al. (124).

Obviously, we found a larger prevalence of non-adherers in Paper II with objective assessment of physical activity when compared with the prevalence from Paper I with self-reported assessment. Information about physical activity behaviors collected through self-reported questionnaires may introduce information bias due to social desirability bias and recall bias (125). Thus, the absolute prevalence of non-adherers in Paper I may be underestimated. Although Paper I has this limitation, it is also important to mention that data from Paper II was collected in a socio-economically disadvantaged area of Denmark (88), which could explain the differences in results between the studies, as physical activity is typically lower in individuals with low socio-economic status (126, 127).

Questions about physical activity behaviors in Paper I were estimated on a general weekly basis, whereas physical activity measured with accelerometers in Paper II was estimated daily and calculated as a mean based on the number of valid measurement days among participants. Also, accelerometer measurements in Paper II were collected for one week, which may not reflect the individual's general physical activity behaviors. While Paper I reflects physical activity behaviors among 6,856 individuals with diabetes in Denmark, Paper II only reflects behaviors among 181 individuals with diabetes from a specific area of Denmark. It is therefore questionable which paper reflects the actual prevalence of physical activity adheres and non-adherers among Danish individuals with diabetes.

### **6.2.2. Determinants of physical activity**

In Paper I, we found that individuals with higher perceived stress, lower HRQoL, and comorbidities, including mental health conditions were less likely to engage in MVPA. These findings support previous studies showing an association between mental health conditions, distress, and physical activity among individuals with diabetes (128, 129). Individuals suffering from mental health conditions or distress may experience challenges concerning self-care in managing the diabetes condition compared to individuals with only somatic conditions. Additionally, Paper I showed a strong association between higher BMI and lower MVPA, which is consistent with results from previous studies (6, 28). Individuals with elevated BMI may experience feelings of discomfort, shame, and exercise-related anxiety, acting as barriers to participate in

physical activity (130-132). Interestingly, the findings of Paper II revealed that participants with prediabetes were less physically active compared to age- and sex-matched counterparts with no diabetes, however, when adjusting for BMI, these differences were no longer significant. Whereas in participants with diabetes, the differences in physical activity compared with participants with no diabetes were still significant after adjusting for BMI. This suggests that the observed differences among participants with prediabetes and no diabetes were explained by BMI.

While Paper I revealed that comorbidities, BMI, stress, and HRQoL were determinants of physical activity, Paper II showed that when adjusting for these determinants, physical activity remained significantly lower among individuals with diabetes when compared to those without diabetes. These results indicate that the diabetes condition itself is associated with reduced physical activity levels. However, due to the nature of the study design, we cannot conclude whether inactivity leads to the development of diabetes or if diabetes itself contributes to lower physical activity levels.

### **6.2.3. Psychological determinants of time spent sedentary**

The primary results of Paper III showed an association between higher well-being and lower total daily sedentary activity in individuals with diabetes and prediabetes. Suffering from low well-being may prevent the individual with diabetes in various ways from engaging in physical activity leading to increases in sedentary time. Individuals with low well-being may withdraw socially and lack motivation, which reduces opportunities for participating in physical activities that involve social interaction (38, 39). Yet, considering that a sedentary lifestyle can contribute to low well-being through diminished energy, motivation, and various health challenges linked to diabetes, the relationship between well-being and sedentary activity may be cyclical where low well-being reinforces a sedentary lifestyle, and vice versa.

The association between well-being and sedentary activity found in Paper III is inconsistent with our supplemental analyses in Paper I, which showed no association between HRQoL and self-reported time spent on sedentary behavior during the day. Partially, however, this may be explained by the fact that although HRQoL and well-being are related concepts, they still have distinct meanings and focus on different aspects of an individual's life. While HRQoL refers to an individual's perception of their health and how it impacts their overall quality of life, well-being is a broader concept that encompasses various aspects of an individual's life such as life satisfaction, relationship, and satisfaction with work, including but not limited to health (133).

Interestingly, we observed different results in the two association analyses in Paper III with stress and well-being as exposures and sedentary activity as outcome. This may be explained by the differences between stress and well-being. Perceived stress reflects a state of emotional burden when demands exceed an individual's perceived resources (40), whereas well-being involves emotional, physical, and social parameters (36). It is important to note that the relationship between stress and well-being is bidirectional, because suffering from high levels of stress over a longer period may have a negative impact on the individual's well-being (134). On the other hand, individuals with high well-being may be more able to manage stressors, adapt to challenges, and have higher self-efficacy which may reduce the impact of stress (135).

Similar to the findings from Paper I, Paper III did not find an association between stress and sedentary activity in individuals with diabetes. However, a systematic review by Teychenne et al. (136) revealed conflicting findings regarding the relationship between sedentary behavior and stress among healthy adults depending on whether sedentary behavior was objectively measured or self-reported. In Paper I, sedentary behavior was self-reported, while Paper III focused on sedentary activity objectively measured. Self-reported methods may underestimate sedentary time compared to device-measured assessments, and studies indicate that device-measured sedentary behavior is more strongly associated with health outcomes, particularly mortality, than self-reported sitting behaviors (137). Additionally, self-reported sedentary behavior might capture context-specific behaviors, such as watching TV or time spent sitting at work, where certain types of sedentary behavior may be stronger related with stress than others (136, 138). Given that individuals with diabetes tend to be more inactive, sedentary, and experience higher levels of stress compared to healthy counterparts, as shown in paper I-III, the relationship between stress and sedentary activity may be more pronounced within the diabetes population. Also, there may be large differences on the association between stress and sedentary activity depending on the duration of stress.

In Paper III, we observed that most participants with low well-being were challenged by several factors, including more comorbidities, obesity, suffering from pain, minimal engagement in MVPA, and high levels of total sedentary activity. Further, Paper I showed that the prevalence of comorbidities, obesity, higher levels of stress, and lower HRQoL was significantly associated with lower MVPA. It is likely to believe that all these factors may lead to lower well-being, suggesting that suffering from low well-being comes with additional challenges that may prevent the individual from being physically active and decrease time spent sedentary. Therefore, it seems highly relevant

to target improvements in well-being in diabetes management. One potential approach to achieve this could involve integrating social support into existing diabetes treatment strategies, as social support is essential in helping individuals initiate and maintain physical activity habits (61, 65). Being a part of an exercise community can be essential for some people with chronic conditions to feel supported in managing efforts of daily physical activity engagement (61). However, these communities often require facilitation by peers or healthcare professionals (61, 65), e.g., group-based exercise organized by patients or sports associations. In relation to this, as the developed intervention from Paper IV showed to be feasible, this could be an example of how to create a physical exercise community for individuals with diverse preferences and schedules. Being a part of a physical exercise community may provide opportunities to share experiences, challenges, and coping strategies that may reduce stress and improve well-being.

#### **6.2.4. Balance between engagement in physical activity and sedentary activity**

Paper II revealed that participants with diabetes had a less active daily profile when compared to participants with prediabetes or those without diabetes, particularly during the period from 12:00 pm to 3:00 pm compared to participants with no diabetes after adjustments for age, sex, and diabetes-related determinants of activity. Moreover, the sedentary profiles from Paper III showed a steep increase in sedentary activity from 6:00 pm until night in participants with diabetes and prediabetes, but a slightly higher amount among those with diabetes. These results indicate that many individuals with diabetes may have a more inactive daily pattern compared to individuals with prediabetes and those without diabetes.

Considering the observed small amounts of daily MVPA and high amounts of sedentary time among individuals with diabetes in paper II and III, it seems important to focus on both behaviors as they are interrelated and associated with the risk of all-cause mortality (30). Dunstan et al. (51) have illustrated these interacting influences, showing that individuals who sit the longest and do the least amount of physical activity have the highest risk of death. Therefore, increasing physical activity and reducing time spent sedentary seem equally important as opportunities for risk reduction (51). In healthy adults, the most efficient and effective way to improve and/or maintain good cardiometabolic health is suggested to be prioritizing a balance of more time on MVPA and less time sedentary (139). However, as our results in Paper II and III showed, even engaging in daily MVPA may seem challenging for individuals with diabetes. Therefore, other approaches focusing

on the balance between engagement in physical activity intensities and limit time spent sedentary could be considered to reach feasible and sustainable health behaviors in this population.

One approach is to focus on increasing LPA rather than exercise based MVPA among inactive individuals with diabetes. This could offer a seemingly equally effective approach, particularly if they suffer from other determinants such as obesity and comorbidities that prevent them from engaging in exercise-type activities with higher intensities (52, 140). This approach aligns with the WHO recommendations, emphasizing that any level of physical activity is preferable to none, as even engaging in some physical activity can positively impact an individual's health (21).

A second approach is to place brief intermittent non-exercise physical activity bouts of MVPA during the day, which is associated with substantially lower mortality among adults (141). This approach may be a more accessible and feasible alternative to achieve the benefits of physical activity for those who are unwilling or unable to exercise in their leisure time due to barriers of participating in structured exercise (141).

A third approach is to focus on reducing sedentary activity. Based on the steep increase in sedentary activity from 6:00 pm until night in the sedentary profiles from Paper III, there is a great potential to reduce sedentary activity in the evening. Replacing sedentary activity with physical activity of any intensity is strongly recommended for adults and older adults with chronic conditions (21). Further, reductions in sedentary activity could be placed in the evening to avoid several prolonged sedentary bouts according to recommendations from ADA (22).

As paper I-III showed, individuals with diabetes have different physical activity and sedentary behaviors and different factors determines their ability to engage in physical activity and reduce sedentary activity. To accommodate these differences as well as individual preferences, opportunities, and resources, healthcare professionals should consider all different approaches to ensure the most sustainable treatment for the individual.

#### **6.2.5. Personalized medicine**

Among participants with diabetes in Paper I, 16% were completely inactive, corresponding to zero hours of weekly MVPA based on self-reported physical activity. Further, inactive individuals with diabetes had lower levels of education, which indicates that social inequality in engagement in physical activity is present among individuals with diabetes. Based on objectively measured physical activity, Paper II showed that 33% of participants with diabetes were highly inactive daily,

corresponding to less than 5 minutes of MVPA during a day when standardized on age and sex. Social inequality is highly associated with the prevalence and complications of T2D (142, 143). This includes a 10% higher risk of developing severe diabetes-related complications and a 26% higher risk of premature mortality among individuals with lower levels of education (144). With a large sociodemographic and geographically represented population, the results of Paper I highlight the nationwide challenges of social inequality among individuals with diabetes and their ability to be regularly active. Moreover, the findings of Paper II support these challenges since this study is based on data from a socio-economically disadvantaged area (140, 145).

Achieving and maintaining a physically active lifestyle can be a challenge for individuals with diabetes, and some may not even view daily activity as a crucial aspect of managing their diabetes (61). Although patients receive support and counselling on physical activity, their ability to act upon this depends on their level of health literacy. Health literacy is associated with older age, lower education, and chronic conditions (146). Both Paper I and Paper II found that individuals with diabetes were older and lower educated when compared with individuals no diabetes. Further, both papers revealed that most individuals with diabetes suffer from at least one chronic condition indicating that most individuals with diabetes are multimorbid. This supports the importance of implementing a personalized medicine approach in physical activity interventions, which has been highlighted to improve patient health and experience by offering different interventions based on individual characteristics, needs, and preferences (147).

Individuals with diabetes who are sufficiently physically active may not need support from healthcare professionals, peers, or family to initiate physical activity. However, directing resources towards sustaining their physical activity levels through easily accessible, long-term interventions emphasizing social support or employing activity trackers and apps could be beneficial (61, 67, 148), as Paper IV demonstrated. Acknowledging that inactive individuals may require not only additional, but also more intensive and long-term support, is relevant to reach increasement in physical activity. This may involve continuous guidance from healthcare professionals to increase their physical activity levels, sustain these changes over time, and ultimately achieve health-related benefits. Paper I and II also revealed that around 35-60% were sufficiently physically active according to the WHO recommendations. Consequently, physical activity interventions for individuals with diabetes should be concentrated on those who stand to benefit the most, conserving

resources for those who may not. The utilization of physical activity screening tools, such as wearable accelerometer-based devices, could help identify individuals with diabetes requiring additional support to modify their physical activity behaviors, facilitating a personalized medicine approach (58). Moreover, it is also important to include the individual's preferences and motivation in strategies for increasing and maintaining physical activity in their daily life (149, 150). Such approaches empower healthcare professionals to tailor interventions for patients with diabetes based on their individual needs to have a physically active lifestyle.

#### **6.2.6. Feasibility of an online physical exercise intervention**

Paper IV showed that the combination of a co-created online physical exercise intervention with group meetings supported by an activity watch in individuals with T2D was feasible in terms of completion of intervention, adherence, and improvement of physical activity. However, the results suggest that amendments regarding participant recruitment, burden of objectively measured physical activity, and adverse events are needed before investigating effectiveness in a future RCT.

As Paper IV showed, the developed intervention was feasible and acceptable for individuals with T2D with higher educational levels when compared to the general population with T2D. The study in Paper IV was developed in close collaboration with the DDA, therefore, recruitment of participants was done solely through the DDA. Members of this patient association are a selected group of Danish individuals with T2D, because the majority has an upper secondary or vocational education and live with their spouse (151). Low socioeconomic status, older age, poor health status, and low digital health literacy are key determinants that seem to be the reason for disparities in access to and utilization of digital health solutions (152). Based on the findings from another study by Thorsen et al. (153) from 2020, implementation of digital health solutions in the care of T2D should be based on a comprehensive consideration of mental well-being, emotional distress, and readiness for health technology to identify those who are in need for social support, self-management education, and extensive digital support. Moreover, Thorsen et al. conclude that a one-size-fits-all approach to digital implementation in healthcare will potentially increase the risk of treatment failure among the most vulnerable with T2D (153). In Paper IV, we found that participants had high mental well-being, primarily moderate perceived stress and high educational level which is expected to be related to high readiness for health technology (152). This suggests that the study population seemed to be a subgroup that was particularly relevant for digital health

implementation. Nevertheless, online physical exercise combined with group sessions may still have great potential to be a specific delivery model for selected subgroups with diabetes.

The decision to integrate online physical exercise, online group meetings, and incorporate activity watches was driven by the purpose of aligning with individuals' preferences in terms of content, timing, and location, as highlighted in the study by Thorsen et al. (61). This approach aimed to seamlessly integrate into participants' daily lives. Our objective was to design an intervention that not only catered to individual needs but also fostered self-motivation and capability to enhance daily physical activity. While we did not expect a significant increase in daily physical activity solely from the 30-minute of online physical exercise, the combination of this component with the other two elements (group meetings and activity watches) was intended to boost participants' confidence and ability to increase their daily physical activity levels. As Paper I revealed, 60% of inactive individuals with diabetes were motivated to be more physically active. Consequently, employing behavior change techniques such as peer-support through group meetings and feedback from activity watches becomes pertinent to empower individuals in initiating and sustaining efforts to change their physical activity habits more effectively (154).

Considering that Paper II showed that 33% of participants with diabetes were highly inactive (<5 min/MVPA daily), providing a rather simple intervention as 30 minutes of online physical exercise weekly may be a feasible way to reach some improvements in physical activity. Moreover, the online group meeting intended to provide a 'safe space' for the participants to share their experiences with peers and receive social support to adopt their physical activity behaviors. Although limited by the small sample size and lack of a control group, we found that participants increased their daily MVPA and steps from baseline to postintervention. Participants exhibited strong adherence to both online physical exercise sessions and group meetings, suggesting that changes in secondary outcomes were related to the completion of the intervention (155). Results of the secondary outcomes imply that the intervention achieved its intended objectives, enabling participants to adopt and maintain new physical activity behaviors in their daily lives with support from their online group and the activity watch. Nevertheless, it is relevant to validate these findings through a properly powered RCT.

Physical exercise interventions delivered online have raised concerns about safety and adverse events due to the limited capacity of the healthcare system for responding promptly (155). A



systematic review and meta-analysis examining exercise interventions delivered via videoconferencing for individuals with chronic conditions found no increase in exercise-related adverse events or serious adverse events among the intervention groups in the included studies (155). In Paper IV, one serious adverse event was reported due to hospitalization with Benign Paroxysmal Positional Vertigo. Since participating in physical exercise is not a risk factor for developing Benign Paroxysmal Positional Vertigo (156), we are not convinced that the reported serious adverse event is linked to the study intervention. Nevertheless, for any potential future RCT, it is recommended to gather information regarding adverse events weekly throughout the intervention phase. This can be achieved through the utilization of questionnaires, text messages, and hospital records to ensure that all adverse events are identified.

In Paper IV, participants were required to wear accelerometers for a minimum of seven days before, during, and after the intervention. Results showed that four participants found the number of measurement days with accelerometers too burdensome. The three measurement periods had only a few weeks in-between, which might account for the perceived burden by some participants. Despite this, overall compliance remained high. To ensure representative data of individual physical activity levels, a minimum of four days of valid accelerometer data is recommended for adults and older adults (157). The opting for a seven-day measurement period was a deliberate choice, aiming to capture sufficient valid data while accounting for potential measurement errors. Given that the study intervention focused primarily on individuals' ability to improve and maintain daily physical activity, we anticipated weekly variations. Consequently, we chose three measurement periods to observe changes before, during, and after the intervention. In a potential future RCT, the intervention period would most likely be longer than eight weeks to thoroughly investigate the intervention effectiveness. Hence, the measurement periods would be spread more out.

### **6.3. Methodological considerations**

*In an attempt to minimize the possibility of bias in all aspects of the included papers in this PhD thesis, different methodological strengths and limitations have been considered. As there are several methodological similarities between Paper I-III, the methodological considerations will be combined in the section below, while the methods of Paper IV will be discussed in a separate section.*

### 6.3.1. Paper I-III

#### *Definition of diabetes*

While the definition of diabetes was solely based on self-reported information in Paper I, Paper II and III included HbA1c measures from the blood samples and the use of diabetes medication to define and categorize diabetes status. In Paper I-III, we could not distinguish between type 1 and 2 diabetes among participants, which would have been preferable due to etiologically differences. However, since T2D accounts for 85-95% of diabetes cases in high-income countries (1), the findings of the papers will primarily be applicable to this patient group.

Information regarding diabetes complications and the duration of the diabetes disease were unavailable in Paper I-III. This would have been relevant information to include in the studies, as we would expect large differences in physical activity engagement based on the number of complications and duration of diabetes. To accommodate the potential age- and sex-related differences between individuals with diabetes, prediabetes, and no diabetes, all analyses in Paper I-III were standardized on age and sex.

#### *Measurement of physical activity and sedentary activity*

Physical activity and sedentary behavior were measured subjectively in Paper I using questions about minutes and hours spent on MVPA and VPA activities and sedentary behaviors such as reading, eating, transportation etc. The self-reported data can lead to different types of information bias, including social desirability bias regarding lifestyle questions, such as diet, alcohol, smoking, and physical activity, which could cause results to be underestimated (125). Another way information bias may have been introduced is through recall bias, e.g., the participant does not remember the exact amount of time being physically active or sedentary. Recall bias is expected to increase random measurement error, however, it is not expected to be different between physically active and inactive individuals leading to wider confidence intervals for the descriptive analyses and bias towards the null-hypothesis in associations analyses (158).

The questions about weekly MVPA are reported to provide an acceptable, but weak estimate of an individual's level of physical activity (84). Moreover, the assessment of MVPA in the DNHS from 2017 followed the former WHO recommendations concerning MVPA bouts of a minimum of 10 minutes (21). This questions the absolute distribution of adherence to WHO recommendations for physical activity in Paper I.

A major strength in Paper II and III is the use of accelerometers to assess 24-hour physical activity and sedentary activity under free-living conditions with a median of six valid measurement days among all participants. As Paper II focused on physical activity intensities, only data from the back-worn accelerometer were used. Whereas Paper III included data from both accelerometers to detect time spent in a sitting, reclined, or lying position, and thereby achieving a more precise estimate of time spent on total sedentary activities during a day. However, by using this method, we were not able to determine activities done seated, therefore, misclassification of time spent sedentary may have been introduced. Another limitation related to this, is that the accelerometry measurements used in this study were not able to accurately capture non-ambulatory activities such as resistance training.

Paper III had a focus on sedentary activity, therefore, we chose a restricted period from 7:00 am to 10:00 pm and that participants should have at least 10 hours of awake time during a measurement day to avoid including time spent sleeping. Although this restricted timeframe was suggested to be a strength to avoid time spent sleeping, it might have limited the ability to capture all sedentary activity. Paper II was restricted to 6:00 am to 11:59:59 pm to capture physical activity intensities during waking hours. This emphasizes that although accelerometer measurements are inherently objective, various factors can influence the collected data, and the results may depend strongly on the data cleaning and processing protocols (157, 159). Although, our study participants in Paper II and III provided a median of six days with valid accelerometer data, it is important to keep in mind that one week of measurement may not reflect an individual's habitual physical activity and sedentary activity.

### *Selection bias*

Paper I consists of a relatively large nationwide sample that strengthens the generalizability of the results. Among the participants, 5.6% reported having diabetes, a prevalence that is slightly higher when compared to a Danish study from 2020 using registry data, which reported an overall prevalence of 0.5% for type 1 diabetes and 4.4% for T2D (160). As individuals with certain negative health conditions and behaviors are more likely to refrain from responding to health surveys (161), selection bias may have arisen from non-response, particularly in Paper I. However, statistical weights provided by the DNHS enabled us to account for non-response to decrease selection bias and missing data to ensure a nationally representative analysis (87). Despite the use of

statistical weights, citizens living alone, with non-Western background, or at younger age were not highly represented in the study population affecting the generalizability of the findings.

Paper II and III used data from the LOFUS study where inhabitants from a socioeconomically disadvantaged area of Denmark were randomly invited to participate (91, 162). Given that low socio-economic status is associated with a higher incidence of T2D (163), we would expect a higher proportion of participants with diabetes in Paper II and III compared to the general population. This is expected to lower overall risk of selection bias in Paper II and III. However, the proportion of individuals with diabetes was almost similar to the one we found in Paper I. Further, the participation rate in LOFUS was highest among middle-aged, females, Danish citizens, and those with high socio-economic status (164). Therefore, the patterns and differences in activity observed may not be comparable to all socioeconomic backgrounds.

The LOFUS health examinations have shown reasonably good participation rates compared with rates from surveys in urban, economically privileged areas (165). However, participation in the accelerometer assessment was offered as an additional, voluntary health examination which may have introduced selection bias. In total, 7,208 participants in the LOFUS study were eligible for accelerometer assessment. Of those, 40% declined to wear accelerometers. It is unsure whether the accelerometer assessment introduced selection bias as we did not investigate differences between participants and non-participants.

Paper III showed that 65% of participants with diabetes had moderate to high stress, which is higher than Paper I in which 50% out of 6,856 participants with diabetes had moderate to high stress (PSS-score  $\geq 14$ ). The cut-off for moderate to high stress in Paper I was higher, which indicates that the prevalence of participants with diabetes and moderate to high stress might be similar to Paper III if the cut-offs were the same. As LOFUS data are collected from a socio-economically disadvantaged area of Denmark (88), we would expect the prevalence of participants with stress to be higher when compared with our nationwide study, however, it is likely that those with the highest levels of stress have declined to participate in the accelerometer measurement.

### *Cross-sectional study design*

As Paper I-III have a cross-sectional study design, it is important to point out the limitations of the causal interpretations because exposures and outcomes were assessed simultaneously. Therefore, we cannot draw any conclusions on the direction or causal nature of the associations. Further, the

study design introduces other potential challenges, such as confounding. To control for confounding in Paper I-III, adjustments were made in the multiple regression analyses to isolate the association of interest in each paper. Our use of DAGs to identify biased paths prior to commencing the statistical analyses enabled us to theoretically avoid confounding estimates. In addition, residual and unknown confounding cannot be ruled out.

In Paper I-III, we treat sedentary activity isolated from physical activity, and vice versa. This may be a limitation to the papers, as both physical activity and sedentary activity constitute integral parts of the 24-hour movement behavior continuum (23). Moreover, sleeping behaviors would be relevant to include as they undergo as a part of the 24-hour movement behavior continuum (23). Particularly in Paper III, the observed variations in sedentary patterns across stress and well-being levels in our study population could arise from a complex interplay of physical activity compositions, such as differences in MVPA, or other unidentified factors. The observed differences across stress and well-being groups underscore the challenge of unravelling the inherent relationship between these behaviors in our study population. However, our observations of distinct sedentary patterns linked to well-being, and the absence of a difference in sedentary time associated with stress levels, are not artifacts but evident findings. Nonetheless, it remains unclear whether stress or well-being directly influences these observed differences in sedentary behavior, or if they result from more complex factors, including the overall composition of physical activity.

### **6.3.2. Paper IV**

The feasibility study in Paper IV was guided by pre-defined research progression criteria serving as benchmarks to systematically evaluate the success of the intervention and study design.

A major strength of Paper IV is the use of a co-creation process and “the Future Workshop” to develop the intervention in collaboration with the DDA and individuals with T2D (109). A co-creation process offers enhanced stakeholder engagement, improved acceptability and adherence, and early identification of barriers and facilitators (72). Additionally, participants provided postintervention feedback to provide us with firsthand perspectives on the intervention.

Although Paper IV has several strengths, the feasibility study is constrained by several limitations. The absence of a control group poses challenges in drawing firm conclusions on the effectiveness of the intervention and which components of the intervention that drives our results. Additionally, the methods used for collecting information on adverse events may not have captured all events during

the intervention. Therefore, we cannot with certainty claim that the intervention is completely safe for individuals with T2D. Furthermore, the introduction course about the project was held shortly before baseline measurements began, which raises concerns about a potential effect that could have influenced baseline results and led to an underestimation of the intervention's effect over time. Although co-creation was used to enhance generalizability, recruiting participants was challenging in this feasibility study, as mentioned earlier. Consequently, it remains uncertain whether our intervention would be feasible in a more diverse population of individuals with T2D, particularly those with lower educational levels and digital readiness, low mental well-being, and emotional distress. Therefore, before advancing to an RCT, an improved recruitment strategy is needed. When comparing characteristics with Paper I, those participating in Paper IV reported higher stress, were more obese, and had more comorbidities. However, the major difference between these two study populations is educational level, where 50% of participants in Paper IV were higher educated. Acknowledging these limitations is crucial for a nuanced interpretation of the outcomes of Paper IV and highlights areas for refinement in future research endeavors.

## **7. Conclusions**

This PhD thesis encompassed four distinct papers, each shedding light on different facets of physical activity and sedentary activity in individuals with diabetes. Our findings showed that on a nationwide level, 40% of individuals with diabetes do not meet the WHO recommendations of physical activity. Remarkably, among those, 60% expressed motivation to become more physically active. The findings of objectively measured physical activity showed that 63% of individuals with diabetes were non-adherers to the WHO recommendations, while numbers on sedentary activity surpassed 10-11 hours daily. Further, when compared to individuals with prediabetes and no diabetes, individuals with diabetes had a less physically active daily pattern, particularly in the afternoon and with a steep increase in sedentary activity in the evening. These findings underscore the importance of addressing physical inactivity and sedentary lifestyles in this population.

The findings of the associations analyses revealed that the prevalence of comorbidities, higher BMI, higher perceived stress, and lower HRQoL were significantly associated with lower engagement in weekly MVPA in individuals with diabetes. Further, higher well-being was found to contribute to lower daily sedentary activity in individuals with diabetes. However, the lower engagement in

physical activity when compared to individuals with prediabetes and those without diabetes, were not fully explained by other major determinants of physical activity. This underscores the necessity for tailored interventions that recognize these factors to enhance physical activity engagement. Thus, an intervention combining online physical exercise, groups sessions, and activity watches may be a feasible approach to accommodate some of these factors and other barriers for participating in physical activity.

Altogether, the findings of this thesis emphasize the importance of acknowledging differences in physical activity and sedentary activity behaviors among individuals with diabetes and how these differences could be accounted for and integrated in future tailored interventions to enhance physical activity engagement in this population.

## **8. Future perspectives**

### **8.1. Clinical implications**

From a clinical perspective, the insights gained from this PhD thesis on physical activity behaviors in individuals with diabetes offer valuable implications for healthcare professionals. Further, the evidence presented in this thesis underlines the critical role of physical activity in diabetes management, extending beyond conventional recommendations.

The findings advocate for a holistic approach that not only emphasizes the importance of regular physical activity, but also recognizes the individualized challenges and activity patterns within the diabetes population. Given the diverse levels of physical activity engagement in individuals with diabetes, healthcare professionals should consider when to target specific physical activity intensities or reductions in time spent sedentary based on the individual's characteristics, abilities, and needs. Further, this PhD thesis provides a nuanced understanding of psychosocial factors influencing physical activity, opening avenues for holistic interventions that consider mental well-being alongside physical health.

The importance of employing diverse physical activity delivery models in individuals with diabetes lies in recognizing the differences of this population. Healthcare professionals should consider addressing factors such as increased BMI, the prevalence of comorbidities in addition to diabetes,

reduced HRQoL and mental well-being or high levels of stress and how these factors influence activity behaviors. Further, tailoring interventions to individual preferences, addressing accessibility challenges, providing psychosocial support, and incorporating varied behavior change strategies are essential considerations to include. The utilization of digital health interventions should be considered as they have the potential to enhance and support physical activity behaviors in subgroups of individuals with diabetes and can be delivered in unconventional and cost-effective ways. By embracing the diversities within this population, healthcare professionals can enhance the effectiveness and inclusivity of interventions aiming to promote and maintain physical activity behaviors.

## **8.2. Future studies**

Future research should build upon the insights gained from this PhD thesis to address crucial gaps and enhance the effectiveness and sustainability of interventions targeting physical activity behaviors in individuals with diabetes.

As this PhD thesis elaborates, physical activity engagement among individuals with diabetes is alarmingly challenged. Although individuals with diabetes are offered supervised exercise-based rehabilitation to support physical activity changes by the municipalities in Denmark, Paper I-III have now revealed that most individuals seem to struggle to maintain their adapted behaviors. During the transition from being a patient with diabetes in the healthcare system to an individual with diabetes can be experienced as a vulnerable period (166). In this period, the responsibility of maintaining physical activity behaviors often lies with the individual with no or very little support from healthcare professionals (167) which commonly results in a decline in physical activity over time (168) due to lack of support and motivation (61, 169). Thus, there is a need for an increased focus on this period to ensure that individuals with diabetes proceed with their adapted behaviors and are able to maintain the behaviors following supervised exercise-based rehabilitation. The transition is, however, only the first step. To enhance long-term physical activity behaviors, interventions should evolve around individual preferences and local societal opportunities. Such research projects call for close collaboration with the municipalities, sports and patient associations, and importantly, the patients. As this PhD thesis provides detailed knowledge about physical activity behaviors among individuals with diabetes and subgroups of this population, these



new insights can provide new perspectives on development and implementation of interventions of such research projects aiming to increase and maintain physical activity behaviors. The experiences obtained from Paper IV are relevant in this context as we developed an intervention in collaboration with individuals with T2D and the DDA. Although the next step seems to be upscaling the study from Paper IV to an RCT, it may be relevant to consider incorporating the experiences and the intervention into a broader research project in which online physical exercise combined with group sessions could undergo as one of many delivery models to individuals with diverse preferences. Thus, ensuring the implementation and sustainability of the developed research project.

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# Appendix I

## Paper I

Determinants of physical activity among 6856 individuals with diabetes: a nationwide cross-sectional study

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# Determinants of physical activity among 6856 individuals with diabetes: a nationwide cross-sectional study

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## ABSTRACT

**Introduction** The aims of this cross-sectional study were to (1) describe habitual physical activity and adherence to WHO recommendations, and (2) investigate the association of comorbidity, obesity, stress, and health-related quality of life (HRQoL) with moderate to vigorous physical activity (MVPA) among individuals with diabetes.

**Research design and methods** This study included 6856 participants with diabetes from the Danish National Health Survey from 2017. The primary outcome measure was weekly MVPA. Exposures included self-reported number of conditions, body mass index (BMI), perceived stress, and HRQoL. Mean difference in MVPA across exposures was estimated by multiple linear regression analyses.

**Results** Forty per cent of individuals with diabetes were not adherent to WHO recommendations for physical activity. Individuals with diabetes had higher BMI, more comorbidities, higher perceived stress, and lower HRQoL. Individuals with three or more comorbidities were significantly associated with lower weekly MVPA (−0.48 hours/week, 95% CI −0.88 to −0.07) compared with individuals with no comorbidity. Furthermore, overweight or obese (class I–III) individuals engaged in significantly less weekly MVPA (obese class III vs normal weight: −1.98 hours/week, 95% CI −2.49 to −1.47). Higher perceived stress was significantly associated with lower weekly MVPA (−1.76 hours/week, 95% CI −2.18 to −1.34) versus low perceived stress. Finally, having low physical and mental HRQoL was associated with lower weekly MVPA (−0.93 hours/week, 95% CI −1.19 to −0.66 and −0.39 hours/week, 95% CI −0.71 to −0.08 respectively vs moderate or high HRQoL).

**Conclusions** We found that 40% of individuals with diabetes do not engage regularly in adequate physical activity. Comorbidities, higher BMI, higher perceived stress, and lower HRQoL were associated with less engagement in physical activity. This study suggests that subgroups of individuals with diabetes are at higher risk of physical inactivity.

## INTRODUCTION

Physical inactivity alone is estimated to cause 7% of the burden of type 2 diabetes.<sup>1</sup> On the other hand, engaging in regular physical activity is a cornerstone of diabetes management to prevent long-term diabetes complications, declines in quality of life and premature

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ No previous large-scale study has provided a detailed description of habitual physical activity among individuals with diabetes and associated factors.

## WHAT THIS STUDY ADDS

⇒ Forty per cent of individuals with diabetes do not engage regularly in adequate physical activity.  
⇒ Having comorbidities, higher body mass index, higher perceived stress, and lower health-related quality of life is significantly associated with lower moderate to vigorous physical activity among individuals with diabetes.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Subgroups of individuals with diabetes are at higher risk of physical inactivity and might need additional support or tailored interventions to increase their physical activity level.

mortality.<sup>2,3</sup> According to the WHO and the American Diabetes Association,<sup>4,5</sup> adults living with diabetes are recommended to do at least 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity (or an equivalent combination) aerobic physical activity weekly.<sup>4,5</sup> Living with diabetes can be very stressful and significantly affect the individual's quality of life.<sup>6,7</sup> Individuals with diabetes may worry about existing and future complications and comorbidities, as well as feeling guilty and ashamed of not adhering to lifestyle recommendations, for example, in terms of body mass index (BMI) and physical activity.<sup>8</sup> Meeting the WHO recommendations of regular physical activity is a major challenge among individuals with diabetes,<sup>9</sup> but some studies report that about 40%–45% of individuals with diabetes do adhere to the recommendations<sup>10,11</sup> and their treatment should thus not necessarily revolve around increasing physical activity. Morbidity, obesity, stress, and lower health-related quality of life

(HRQoL) are associated with decreased habitual physical activity in the general population.<sup>12–15</sup> Given that individuals with diabetes are at high risk of suffering from all these factors,<sup>6 16 17</sup> it is likely that physical activity among individuals with diabetes is also associated with these factors. Availability of such information would be an important resource when designing and promoting a physical activity intervention taking individual characteristics, needs and preferences into account, and thereby spending the resources on those in most need. However, no previous large-scale studies have provided a detailed description of habitual physical activity among individuals with diabetes and associated factors.

Therefore, the aims of this study were to (1) describe habitual physical activity and adherence to WHO recommendations, and (2) investigate the association of comorbidity, obesity, stress, and HRQoL with moderate to vigorous physical activity (MVPA) among individuals with diabetes based on data from a large nationwide Danish survey.

## RESEARCH DESIGN AND METHODS

Reporting of this cross-sectional study followed the ‘Strengthening the Reporting of Observational Studies in Epidemiology’ checklist.<sup>18</sup>

### Setting and data sources

We used data from the cross-sectional nationwide Danish National Health Survey (DNHS) from 2017. The overall aim of the DNHS is to monitor the status and trends in physical and mental health in the adult Danish population ( $\geq 16$  years). A detailed description of the DNHS design is available on the DNHS web page (<https://www.danskernessundhed.dk/>).<sup>19 20</sup> In 2017, a total of 312 349 individuals were randomly drawn from the population using the Danish Civil Health Registration System and invited via a secure electronic mail service (Digital Post) or regular postal service to participate in the survey. The questionnaire was fully or partially completed (sex, age, and at least one other question answered) by 183 372 respondents (58.7%).<sup>20</sup>

### Participants

The present study included participants with ‘Diabetes’ and ‘No known diabetes’. Following the categorization of diabetes from DNHS, respondents were defined as ‘Having diabetes’ if they had answered ‘I have diabetes now’ or ‘I have had diabetes’ and ‘I suffer from sequela due to the diabetes’. The question on diabetes did not distinguish between types of diabetes; therefore, the respondents covered the whole spectrum of diabetes. Out of 183 372 respondents, 10 216 individuals reported to have diabetes. Respondents with complete data on outcome, exposure, and confounder variables were considered eligible for the present study.

### Outcome variables

The outcomes of interest were self-reported MVPA (hours/week), adherence to WHO recommendations of

physical activity and sedentary behavior, and total sedentary behavior (hours/day). MVPA was assessed with the question: ‘During a regular week, how much time do you spend on moderate and vigorous physical activities, where you can feel your pulse and your breathing increase (eg, walking, cycling as transport or recreational activity, hard gardening, running or exercise sports)? Indicate only activities lasting at least 10 min’. Respondents replied in hours and minutes.

Adherence to WHO recommendations was assessed with the question regarding MVPA and the question: ‘How much time of the above-mentioned physical activities do you spend in a regular week on vigorous physical activities? These are activities where your pulse is substantially increased, you sweat, and which cause you to be out of breath and to find it hard to talk (eg, swimming, running, cycling at high speed, strength training or ball games)’. Adherence to WHO recommendations was dichotomized to ‘Following WHO recommendations’ or ‘Not following WHO recommendations’. Respondents were categorized as ‘Following WHO recommendations’ if they reported at least 150 min/week of moderate intensity, at least 75 min/week of vigorous intensity, or an equivalent combination.<sup>4</sup>

In addition, self-reported MVPA was categorized into four levels of habitual physical activity in accordance with the WHO recommendations: (1) inactive: 0 hour/week; (2) inadequate: participants do not meet recommendations (150–300 min/week of moderate intensity or 75–150 min/week of vigorous intensity); (3) adequate: participants meet recommendations, but not more than 300 min/week of moderate intensity or 150 min/week of vigorous intensity; and (4) optimal: participants with more than 300 min/week of moderate intensity or 150 min/week of vigorous intensity.

Total sedentary behavior was assessed with the question: ‘On a typical weekday/workday, how much time do you spend on sitting down in each of the following situations? Please consider your total sitting time and distribute it in each of the following categories’. Respondents reported minutes and hours spent on (1) transport (eg, in car, bus or train; not cycling); (2) work/school/education (eg, sitting by the desk or at meeting); (3) leisure time: by screen (eg, television, computer, tablet, smartphone); (4) leisure time: other (eg, meals, reading, social gatherings). All questions regarding MVPA and sedentary behavior have been validated.<sup>21</sup> Motivation for being more physically active was assessed with the question: ‘Do you want to be more physically active?’.

### Exposures

#### Comorbidity

Self-reported information on selected long-term conditions (excluding diabetes) and sequela were used to assess comorbidity. Respondents reported whether they had or have had selected long-term conditions, and whether they were suffering from sequelae due to the specific long-term condition. The definition of comorbidity was based on diagnoses organized in 10 groups of different body systems according to Willadsen *et al.*<sup>22</sup> In

this study, there were only seven groups due to lack of information on conditions in all body systems, and since diabetes was the only endocrine condition in the survey, it was excluded from the comorbidity variable. The seven groups were: (1) lung, (2) musculoskeletal, (3) mental, (4) cancer, (5) neurological, (6) cardiovascular, and (7) sensory organs.

The variable was categorized as a count variable, counting the numbers of comorbidities from zero to three or more from different body systems including diabetes. Suffering from several long-term conditions within the same body system, for example, hypertension and myocardial infarction, would still only count as one comorbidity.

Individuals with mental comorbidities engage less regularly in physical activity compared with individuals with only somatic comorbidities.<sup>23 24</sup> Therefore, a variable differentiating between comorbidities with and without a mental health condition was created.

### Obesity

Self-reported data on height and weight were used to calculate BMI ( $\text{kg}/\text{m}^2$ ). BMI was categorized into five groups: underweight/normal weight (BMI <25.0), overweight (BMI  $\geq$ 25.0 to <30.0), obese class I (BMI  $\geq$ 30.0 to <35.0), obese class II (BMI  $\geq$ 35.0 to <40.0), and obese class III (BMI  $\geq$ 40), as defined by the WHO.<sup>25</sup>

### Stress

Self-reported psychological stress was assessed using the Danish version of Cohen's 10-item Perceived Stress Scale (PSS).<sup>26 27</sup> PSS was categorized into three as follows: (1) low perceived stress (scores ranging from 0 to 13), (2) moderate perceived stress (scores ranging from 14 to 26), and (3) high perceived stress (scores ranging from 27 to 40).<sup>27</sup>

### Health-related quality of life

Self-reported HRQoL (physical and mental health) was assessed using the 12-item Short-Form Health Survey and was categorized into a physical and mental scale.<sup>28 29</sup> A physical score of 50 or less was categorized as 'Low physical HRQoL', and a mental score of 42 or less was categorized as 'Low mental HRQoL'.<sup>30</sup>

### Covariates

The following covariates are suggested to be potential independent risk factors of the four exposures (comorbidity, obesity, stress, and HRQoL) and the outcome (physical activity): age, sex, ethnicity, marital status, educational level, alcohol consumption, smoking, and diet. Directed acyclic graphs<sup>31</sup> of the assumed causal relations between exposures and outcome of the primary analysis are available in online supplemental file 1. Marital status was dichotomized into 'Married or living with partner' or 'Living alone'. Educational level was assessed using the respondents' highest level of education and categorized into three: (1) primary and lower secondary education, (2) upper secondary or vocational,

and (3) higher education. Ethnicity was categorized into three groups: Danish, other Western, and non-Western background. Smoking was categorized into (1) smoker, (2) ex-smoker, (3) never smoked. Alcohol consumption was measured by the number of drinks of beer, wine and spirits consumed in a typical week and categorized in accordance with the national recommendations from the Danish Health Authority: (1) no alcohol (0 drink), (2) below low risk (men >0 and <14 drinks, women >0 and <7 drinks), (3) above low risk (men  $\geq$ 14 and  $\leq$ 21 drinks, women  $\geq$ 7 and  $\leq$ 14 drinks), (4) high risk (men >21 drinks, women >14 drinks). Eating habits were measured using the diet score dividing the respondents into three health levels based on their diet: (1) healthy diet, (2) medium healthy diet, and (3) unhealthy diet.<sup>32</sup>

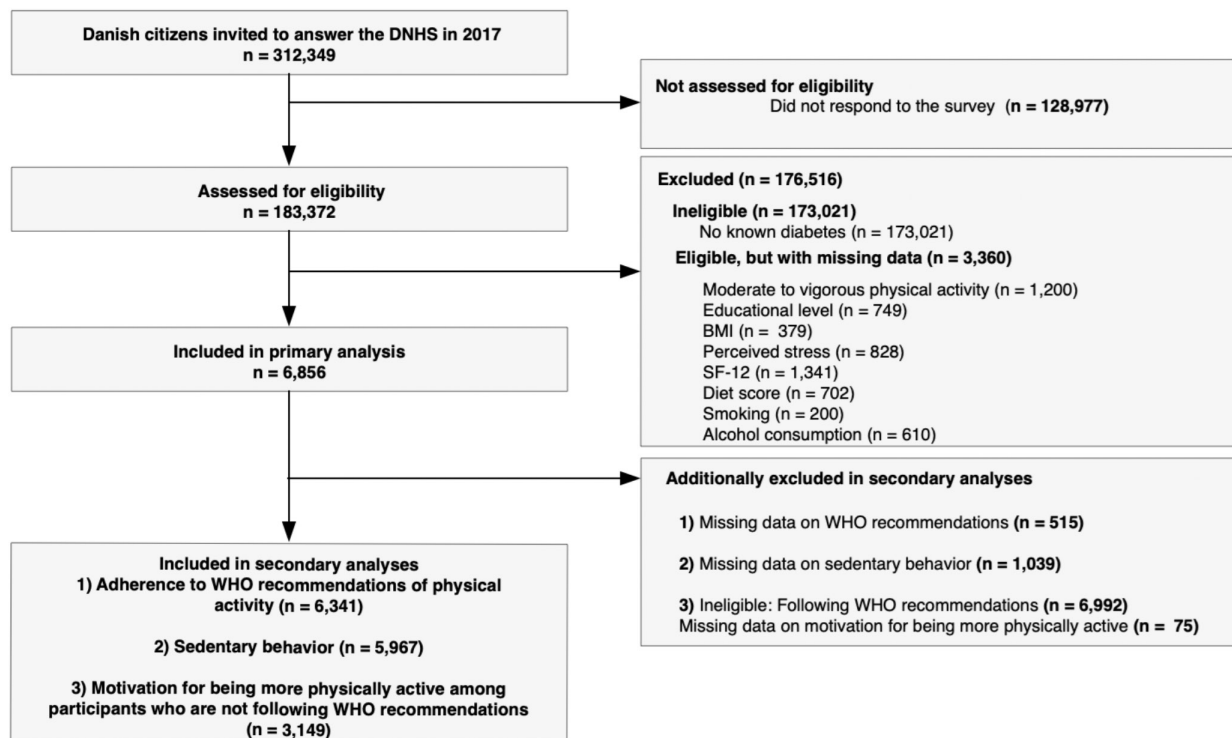
### Statistical analyses

A statistical analysis plan was developed (online supplemental file 2) and openly available (<https://osf.io/25u4g/>) prior to commencing the analyses. Cross-tabulations were conducted to describe habitual physical activity among individuals with diabetes and individuals with no known diabetes and to display potential subgroup differences.

Descriptive statistics are presented as numbers and percentages or means and SDs or medians and IQR. Four multiple linear regression analyses were conducted to investigate the associations between the exposures (comorbidity, obesity, stress, and HRQoL) and the outcome MVPA. Results of the multiple linear regression analyses are presented as mean differences with 95% CIs across levels of exposures with no comorbidity, underweight or normal weight, low perceived stress, and moderate to high HRQoL as reference categories.

To explore the associations between the same four exposures and adherence to WHO recommendations of physical activity, four multiple logistic regression analyses were performed. Results of the logistic regression analyses are presented as prevalence ORs with 95% CI. Furthermore, four multiple linear regression analyses were performed with total sedentary behavior as outcome.

All models are reported crude and adjusted for age, sex, ethnicity, marital status, educational level, alcohol consumption, smoking, and diet. Furthermore, the four exposures were potential independent risk factors in the individual model; therefore, the variables were included as confounders in the individual model (online supplemental file 1). Post hoc analyses of comorbidities and MVPA excluding adjustment of BMI were performed to investigate the size of difference in MVPA between numbers of comorbidities allowing for adiposity levels to be different across comorbidities, because obesity is a strong determinant of a wide range of morbidities. In addition, cross-tabulations were conducted describing proportions and characteristics of participants with diabetes who were not following WHO recommendations of physical activity and their motivation for being more physically



**Figure 1** Flow chart of all included participants in the primary analysis and the three secondary analyses from the Danish National Health Survey (DNHS) 2017. BMI, body mass index; SF-12, 12-item Short-Form Health Survey.

active. Statistically, weights provided by the DNHS were included in all models to account for non-response by certain population groups. The weights were computed by Statistics Denmark and account for differences such as age, sex, educational level, income, socioeconomic group, municipality of residence, marital status, ethnic background, healthcare utilization and research protection.<sup>33</sup> All statistical analyses were conducted in STATA/BE V.17.0 using an  $\alpha$  level of 0.05, two sided.

## RESULTS

Out of 183372 responses, 10216 participants reported they had diabetes. Of these, 6856 participants had complete data on outcome, exposures, and covariates in the primary analysis (figure 1).

### Participant characteristics

Characteristics of participants with diabetes with and without complete data and participants with no known diabetes are presented in table 1. Due to differences in age and sex between diabetes status, direct standardization was performed on participants with no known diabetes based on the age and sex distribution among participants with diabetes. Only 60% of those with diabetes met the WHO recommendations compared with 70% of those without diabetes. Participants with diabetes had higher BMI, more comorbidities, higher perceived stress, and lower HRQoL.

### Participant characteristics by level of habitual physical activity

Characteristics of participants with diabetes stratified by level of habitual physical activity according to WHO Guidelines of Physical Activity and Sedentary Behavior are presented in table 2. Out of 6341 participants, 2530 (38.8%) had optimal amount of habitual physical activity and 955 (16.4%) were inactive. Inactive participants had lower levels of education and more unhealthy eating habits, higher prevalence of obesity class II and III, higher prevalence of three or more comorbidities, higher perceived stress, and lower HRQoL.

### Associations of MVPA and comorbidities

Table 3 represents the results from the primary analysis regarding associations between exposures and MVPA (hours/week) in participants with diabetes. Having diabetes with three or more comorbidities including mental health conditions had significantly lower weekly MVPA after adjustments ( $-0.48$  hours/week, 95% CI  $-0.88$  to  $-0.07$ ) compared with individuals with no comorbidity, whereas three or more comorbidities excluding mental health conditions were non-significant after adjustments ( $-0.54$  hours/week, 95% CI  $-0.76$  to  $0.04$ ) compared with no comorbidity. Post hoc analyses showed significant lower weekly MVPA among individuals with two comorbidities and three or more comorbidities including mental health conditions without adjustment of BMI ( $-0.58$  hours/week, 95% CI  $-0.98$  to  $-0.18$  and

**Table 1** Characteristics of participants with diabetes with and without complete responses and no known diabetes

	Diabetes (complete data)	Diabetes (incomplete data)	No known diabetes
n (%) b21	6856 (8.4)*	10216 (8.8)*	173021 (91.2)
<b>Marital status</b>			
Married/living with partner	4928 (63.7)	6977 (61.1)	119029 (66.8)
Living alone	1928 (36.3)	3239 (38.9)	53992 (33.2)
<b>Educational level</b>			
Primary	1113 (19.8)	1848 (22.6)	18478 (16.0)
Upper secondary	4071 (58.9)	5563 (58.3)	86947 (55.3)
Higher	1672 (21.3)	2056 (19.1)	53911 (28.7)
<b>Ethnic background</b>			
Danish	6320 (88.1)	9387 (87.0)	159429 (91.6)
Western	187 (3.9)	273 (4.0)	5847 (4.3)
Non-Western	349 (7.9)	556 (9.0)	7745 (4.1)
<b>Alcohol consumption (drinks consumed weekly)</b>			
No alcohol	2161 (35.5)	3372 (39.4)	35 883 (22.0)
Below low risk	3440 (47.3)	4551 (44.4)	88587 (54.0)
Above low risk	753 (10.4)	1027 (9.8)	24361 (16.1)
High risk	502 (6.8)	656 (6.4)	10967 (7.8)
<b>Smoking</b>			
Smoker	1309 (19.8)	1935 (20.8)	33017 (19.3)
Ex-smoker	3023 (42.9)	4388 (41.9)	52 149 (39.2)
Never smoked	2524 (37.3)	3693 (37.3)	79529 (41.5)
<b>Diet score</b>			
Unhealthy	997 (14.9)	1522 (16.6)	23609 (16.5)
Medium healthy	4669 (68.2)	6325 (66.3)	105169 (65.5)
Healthy	1190 (16.9)	1667 (17.1)	29405 (17.9)
<b>Obesity</b>			
Underweight/normal	1492 (23.1)	2170 (23.2)	78 160 (43.9)
Overweight	2584 (37.2)	3740 (36.9)	57078 (39.5)
Obese class I	1725 (24.6)	2436 (24.3)	18805 (12.6)
Obese class II	691 (9.5)	980 (9.8)	4980 (2.9)
Obese class III	364 (5.6)	511 (5.8)	2146 (1.1)
<b>Comorbidities including mental health conditions</b>			
No comorbidity	839 (11.6)	1205 (11.9)	59297 (27.3)
One comorbidity	1813 (25.1)	2653 (25.0)	53 182 (30.2)
Two comorbidities	1989 (28.6)	2980 (28.4)	35944 (23.9)
Three or more comorbidities	2215 (34.5)	3378 (34.7)	24598 (18.6)
<b>Perceived stress</b>			
Low perceived stress	3739 (50.1)	4771 (46.5)	96095 (61.2)
Moderate perceived stress	2826 (44.9)	4207 (48.2)	57962 (36.1)
High perceived stress	291 (5.0)	410 (5.3)	5217 (2.7)
<b>HRQoL</b>			
Low physical HRQoL	4715 (71.8)	6335 (73.7)	60 680 (50.6)
Low mental HRQoL	1845 (30.6)	2567 (32.8)	36 103 (20.8)
<b>Adherence to WHO recommendations of physical activity</b>			
Following recommendations	2457 (59.1)	4902 (58.4)	102 881 (68.9)
Not following recommendations	3884 (40.9)	3224 (41.6)	40 578 (31.1)

Data are presented as n (%).

n is different due to variations in complete responses in each variable.

\*Proportion of individuals with diabetes compared with proportion of individuals without diabetes.

HRQoL, health-related quality of life.

**Table 2** Characteristics of participants with diabetes stratified by level of habitual physical activity

	Level of habitual physical activity*			
	Inactive	Inadequate	Adequate	Optimal
n (%)	955 (16.4)	1502 (23.5)	1354 (21.3)	2530 (38.8)
Sex				
Male	547 (57.8)	912 (60.1)	785 (57.8)	1558 (62.2)
Female	408 (42.2)	590 (39.9)	569 (42.2)	942 (37.8)
Age (years)	64 (53; 74)	64 (54; 72)	62 (53; 71)	63 (52; 71)
Marital status				
Married/living with partner	640 (59.8)	1097 (66.6)	981 (65.6)	1841 (66.1)
Living alone	315 (40.2)	405 (33.4)	373 (34.4)	689 (33.9)
Educational level				
Primary	211 (24.8)	229 (17.2)	191 (16.2)	365 (16.3)
Upper secondary	577 (59.6)	887 (60.0)	794 (60.4)	1488 (58.9)
High	167 (15.6)	386 (22.7)	369 (23.4)	677 (24.8)
Ethnic background				
Danish	877 (86.4)	1394 (88.7)	1256 (87.8)	2347 (88.9)
Western	33 (5.7)	45 (3.9)	27 (2.9)	67 (3.7)
Non-Western	45 (7.8)	63 (7.4)	71 (9.3)	116 (7.3)
Smoking				
Smoker	231 (24.5)	315 (22.8)	253 (19.9)	420 (18.8)
Ex-smoker	431 (43.4)	666 (42.6)	579 (40.0)	1117 (42.1)
Never smoked	293 (32.1)	521 (34.6)	522 (40.1)	993 (37.1)
Diet score				
Unhealthy	255 (26.3)	274 (20.1)	139 (10.5)	255 (10.0)
Medium healthy	594 (62.5)	1044 (68.8)	971 (70.9)	1702 (68.1)
Healthy	106 (11.2)	184 (11.1)	244 (18.7)	573 (21.9)
Alcohol consumption (drinks consumed weekly)				
No alcohol	415 (45.6)	453 (33.8)	369 (31.3)	716 (31.9)
Below low risk	380 (38.0)	736 (46.8)	758 (53.8)	1336 (50.1)
Above low risk	78 (7.7)	168 (10.7)	144 (9.3)	317 (11.9)
High risk	82 (8.7)	145 (8.8)	83 (5.6)	161 (6.1)
MVPA in leisure time (hours/week)	0 (0; 0)	1 (0.5; 1.5)	2.5 (2; 3.25)	6 (4.5; 9)
Total sedentary behavior (hours/day)	9 (6.5; 12)	8.5 (6; 12)	8.25 (6; 11.6)	8.2 (6; 11.7)
Obesity				
Underweight/normal	150 (16.5)	270 (18.4)	271 (21.3)	686 (28.9)
Overweight	331 (33.9)	536 (35.0)	514 (37.4)	1017 (38.6)
Obese class I	238 (24.2)	430 (28.2)	365 (26.1)	548 (21.4)
Obese class II	142 (14.4)	168 (11.0)	133 (9.5)	199 (7.6)
Obese class III	94 (11.0)	98 (7.4)	71 (5.7)	80 (3.5)
Comorbidities including mental health conditions				
No comorbidity	76 (8.3)	140 (8.8)	171 (13.5)	391 (16.3)
One comorbidity	191 (19.3)	373 (24.3)	381 (25.9)	738 (28.2)
Two comorbidities	272 (27.9)	461 (30.2)	420 (29.5)	689 (26.7)
Three or more comorbidities	416 (44.5)	528 (36.7)	382 (31.1)	712 (28.8)
Perceived stress				
Low perceived stress	411 (40.2)	778 (46.3)	759 (50.6)	1566 (58.9)

Continued



**Table 2** Continued

	Level of habitual physical activity*			
	Inactive	Inadequate	Adequate	Optimal
Moderate perceived stress	455 (50.0)	657 (47.8)	546 (44.9)	897 (37.7)
High perceived stress	89 (9.8)	67 (5.9)	49 (4.5)	67 (3.3)
HRQoL				
Low physical HRQoL	820 (86.3)	1137 (76.8)	930 (70.0)	1450 (58.8)
Low mental HRQoL	955 (43.6)	1502 (34.1)	1354 (28.1)	2530 (23.4)

n=6341.  
 Data are presented as number and proportion (%) except from age, MVPA and sedentary behavior, which are presented as median and IQR.  
 \*Level of habitual physical activity was categorized in accordance with the 'WHO Guidelines of Physical Activity and Sedentary Behavior': (1) inactive=0 hour/week, (2) inadequate=participants do not meet recommendations (150–300 min/week of moderate intensity or 75–150 min/week of vigorous intensity), (3) adequate=participants meet recommendations, but not more than 300 min/week of moderate intensity or 150 min/week of vigorous intensity, and (4) optimal=participants with more than 300 min/week of moderate intensity or 150 min/week of vigorous intensity of physical activity.  
 HRQoL, health-related quality of life; MVPA, moderate to vigorous physical activity.

–0.85 hours/week, 95% CI –1.25 to –0.45) compared with individuals with no comorbidity. The analyses excluding mental health conditions showed also significant results without adjustment of BMI (–0.51 hours/week, 95% CI –0.89 to –0.12 and –0.72 hours/week, 95% CI –1.12 to –0.32).

### Associations of MVPA and obesity

Overweight or obese (class I–III) individuals engaged in significantly less MVPA after adjustments (overweight: –0.61 hours/week, 95% CI –0.94 to –0.29; obese class I: –1.08 hours/week, 95% CI –1.43 to –0.74; obese class II: –1.43 hours/week, 95% CI –1.85 to –1.01; obese class III: –1.98 hours/week, 95% CI –2.49 to –1.47) compared with underweight and normal weight individuals.

### Associations of MVPA and perceived stress

Moderate and high perceived stress were significantly associated with lower weekly MVPA after adjustments (–0.59 hours/week, 95% CI –0.83 to –0.34 and –1.76 hours/week, 95% CI –2.18 to –1.34) compared with low perceived stress.

### Associations of MVPA and HRQoL

At last, low physical and mental HRQoL were associated with lower weekly MVPA after adjustments (–0.93 hours/week, 95% CI –1.19 to –0.66 and –0.39 hours/week, 95% CI –0.71 to –0.08) compared with moderate or high HRQoL. The pattern of association of comorbidity, obesity, and stress with MVPA appeared consistent with an inverse graded relationship.

### Adherence to WHO recommendations

The estimated associations of the logistic regression models between exposures and adherence to WHO recommendations appeared similar to the linear models (online supplemental file 3).

### Associations of sedentary behavior and determinants

Results of sedentary behavior showed significant associations between obese class II and III and higher weekly sedentary behavior compared with normal weight individuals with diabetes (for more details see online supplemental file 4).

### Motivation for being more physically active

Table 4 shows the distribution and characteristics of participants with diabetes who are not following WHO recommendations of physical activity and their motivation for being more physically active. Younger participants were more motivated for being more physically active. In addition, the proportion of motivated participants was highest among obese class II and III compared with obese class I, overweight, and underweight/normal. Distribution and characteristics of participants with diabetes who are following the WHO recommendations of physical activity and their motivation for being more physically active are available in online supplemental file 5.

### DISCUSSION

We found that 40% of individuals with diabetes from this nationwide population were not adherent to WHO recommendations for physical activity as measured by self-report. Inactive individuals with diabetes were less educated, had more unhealthy eating and smoking habits, higher BMI, more comorbidities, higher perceived stress, and lower HRQoL. The primary analysis showed that higher BMI, higher perceived stress, lower HRQoL, and having two comorbidities and three or more comorbidities were associated with lower weekly MVPA. However, when comorbidities only included somatic conditions, the association was only significant when participants had three or more comorbidities. Obesity, high perceived stress, and low physical HRQoL were the most remarkable determinants of low physical activity with mean differences of at least

**Table 3** Linear regressions on the associations of determinants with MVPA in participants with diabetes**Therefore, the aims of this**

	MVPA (hours/week)					
	Crude		Multivariable adjusted		Multivariable adjusted (excluding BMI)†	
	β (95% CI)*	P value	β (95% CI)	P value	β (95% CI)	P value
Comorbidities including mental health conditions‡						
No comorbidity	(Reference)		(Reference)		(Reference)	
One comorbidity	-0.38 (-0.79 to 0.02)	0.064	-0.08 (-0.48 to 0.34)	0.688	-0.29 (-0.69 to 0.11)	0.161
Two comorbidities	-0.73 (-1.13 to -0.34)	0.001§	-0.31 (-0.70 to 0.09)	0.135	-0.58 (-0.98 to -0.18)	0.004§
Three or more comorbidities	-1.04 (-1.44 to -0.65)	0.001§	-0.48 (-0.88 to -0.07)	0.021§	-0.85 (-1.25 to -0.45)	0.001§
Comorbidities excluding mental health conditions‡						
No comorbidity	(Reference)		(Reference)		(Reference)	
One comorbidity	-0.27 (-0.66 to 0.12)	0.0175	-0.04 (-0.34 to 0.43)	0.823	-0.16 (-0.55 to 0.23)	0.417
Two comorbidities	-0.65 (-1.03 to -0.27)	0.001§	-0.23 (-0.61 to 0.16)	0.243	-0.51 (-0.89 to -0.12)	0.010§
Three or more comorbidities	-0.91 (-1.29 to -0.53)	0.001§	-0.54 (-0.76 to 0.04)	0.081	-0.72 (-1.12 to -0.32)	0.001§
Obesity¶						
Underweight/normal	(Reference)		(Reference)			
Overweight	-0.61 (-0.93 to -0.29)	0.001§	-0.61 (-0.94 to -0.29)	0.001§		
Obese class I	-1.12 (-1.47 to -0.77)	0.001§	-1.08 (-1.43 to -0.74)	0.001§		
Obese class II	-1.49 (-1.92 to -1.07)	0.001§	-1.43 (-1.85 to -1.01)	0.001§		
Obese class III	-2.05 (-2.58 to -1.52)	0.001§	-1.98 (-2.49 to -1.47)	0.001§		
Stress**						
Low perceived stress	(Reference)		(Reference)			
Moderate perceived stress	-0.68 (-0.92 to -0.44)	0.001§	-0.59 (-0.83 to -0.34)	0.001§		
High perceived stress	-1.90 (-2.29 to -1.51)	0.001§	-1.76 (-2.18 to -1.34)	0.001§		
HRQoL††						
<i>Physical score</i>						
Moderate to high physical HRQoL	(Reference)		(Reference)			
Low physical HRQoL	-1.35 (-1.59 to -1.09)	0.001§	-0.93 (-1.19 to -0.66)	0.001§		
<i>Mental score</i>						
Moderate to high mental HRQoL	(Reference)		(Reference)			
Low mental HRQoL	-0.90 (-1.15 to -0.65)	0.001§	-0.39 (-0.71 to -0.08)	0.015§		

n=6856.  
 Crude and adjusted models were weighted for non-response.  
 \*β coefficients and 95% CIs represent mean difference in MVPA (hours/week) compared with the reference.  
 †Post hoc analyses of comorbidities and MVPA excluding adjustment of BMI.  
 ‡Each multivariable model was adjusted as follows: age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, BMI.  
 §Significant results (p<0.05).  
 ¶Each multivariable model was adjusted as follows: age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, comorbidity.  
 \*\*Each multivariable model was adjusted as follows: age, sex, educational level, marital status, smoking, BMI, comorbidity.  
 ††Each multivariable model was adjusted as follows: age, sex, educational level, marital status, smoking, BMI, comorbidity, stress.  
 BMI, body mass index; HRQoL, health-related quality of life; MVPA, moderate to vigorous physical activity.

1 hour of lower weekly MVPA compared with references. Post hoc analyses showed significant lower weekly MVPA among individuals with two comorbidities and three or more comorbidities.

Among individuals with diabetes who did not meet the WHO recommendations, 60% were motivated for being more physically active, with higher motivation among young, middle-aged and obese individuals.

The prevalence of adherence to the WHO recommendations found in this study is inconsistent with two previous cross-sectional studies outside Denmark. A study by Martinez-Harvell *et al*<sup>11</sup> from 2020 found that 53.5% of

25 980 participants with diabetes from the USA did not meet the recommendations of physical activity (150 min/week of MVPA, or 75 min/week of vigorous intensity at least three times/week). A Scottish study by Salman *et al*<sup>34</sup> from 2019 found that 65.9% of 1259 participants did not meet the recommended levels of physical activity (150 min/week moderate or 75 min/week vigorous physical activity or equivalent combination). The inconsistency might be explained by differences in how physical activity was quantified and the populations included. Our study included a large population with diabetes from all regions of Denmark, which increases the generalizability to the

**Table 4** Distribution of insufficiently physically active participants and their motivation for being more physically active

	Motivated	Not motivated	Don't know
n (%)	1914 (59.8)	604 (19.2)	631 (21.0)
Sex			
Male	1089 (59.6)	389 (20.3)	360 (20.1)
Female	825 (60.1)	215 (17.7)	271 (22.2)
Age (categories)			
16–34 years	59 (72.5)	6 (9.2)	13 (18.3)
35–54 years	414 (77.1)	47 (9.4)	72 (13.6)
55–64 years	545 (65.6)	131 (14.9)	147 (19.4)
65–74 years	592 (56.1)	211 (21.6)	206 (22.3)
≥75 years	304 (41.4)	209 (30.8)	193 (27.8)
Obesity			
Underweight/normal	285 (52.3)	138 (26.7)	106 (21.0)
Overweight	642 (57.6)	244 (22.6)	214 (19.8)
Obese class I	489 (58.4)	141 (16.6)	192 (25.0)
Obese class II	289 (71.2)	44 (11.2)	65 (17.6)
Obese class III	177 (72.6)	27 (9.6)	41 (18.9)
Comorbidities including mental health conditions			
No comorbidity	162 (61.5)	64 (23.0)	43 (15.5)
One comorbidity	412 (59.7)	141 (18.9)	151 (21.3)
Two comorbidities	556 (57.5)	184 (20.2)	193 (22.3)
Three or more comorbidities	784 (61.0)	215 (18.0)	244 (21.0)
Stress			
Low perceived stress	820 (59.5)	296 (21.5)	258 (19.0)
Moderate perceived stress	871 (60.6)	248 (18.1)	281 (21.0)
High perceived stress	121 (62.0)	22 (11.9)	47 (26.1)
HRQoL			
<i>Physical score</i>			
Moderate to high physical HRQoL	359 (66.9)	107 (18.9)	83 (14.2)
Low physical HRQoL	1395 (59.8)	415 (18.2)	473 (22.0)
<i>Mental score</i>			
Moderate to high mental HRQoL	1103 (59.3)	373 (20.5)	353 (20.2)
Low mental HRQoL	651 (63.8)	149 (15.1)	203 (21.1)

n=3149 (n differs due to variations in complete responses in each variable).  
 Data are presented as n (%).  
 HRQoL, health-related quality of life.

whole country thereby extending previous findings. Even though our results are inconsistent with previous studies, our results still indicate that physical activity interventions targeting individuals with diabetes are needed.

We found that individuals with higher perceived stress, lower HRQoL and comorbidities including mental health conditions are less likely to engage in regular physical activity. These findings support previous studies showing an association between mental health conditions, distress, and physical activity among individuals with diabetes.<sup>35 36</sup> Individuals suffering from mental health conditions or distress may experience challenges

concerning self-care in managing the diabetes condition compared with individuals with only somatic conditions. We also found that higher BMI and lower HRQoL were associated with lower MVPA, which support the results from other studies.<sup>11 34 37</sup> Individuals with poor HRQoL and elevated BMI may suffer from discomfort, fatigue, shame and fear of exercise as barriers to engage in regular physical activity.<sup>38–40</sup>

No other studies have described and investigated the characteristics and correlates of physical activity among individuals with diabetes who are completely inactive corresponding to 0 hour of weekly MVPA. Results showed

that inactive individuals with diabetes had lower levels of education, which indicates that social inequality in engagement in physical activity is present among individuals with diabetes. Social inequality is highly associated with prevalence and complications of type 2 diabetes.<sup>41 42</sup> This includes a 10% higher risk of developing severe diabetes-related complications, and 26% higher risk of premature mortality among individuals with lower levels of education.<sup>43</sup> With a large sociodemographic and geographic represented population, the results of the present study highlight the nationwide challenges of social inequality among individuals with diabetes and their ability to engage in regular physical activity.

### Clinical implications

Based on our results, healthcare providers may need more targeted approaches to reach those in most need of physical activity interventions to increase the reach and motivation as well as the success of the interventions. Tailored interventions that are adapted to individuals with lower levels of education, higher BMI, more comorbidities, higher perceived stress, and lower HRQoL might be needed to help improve diabetes self-management and physical activity level among all individuals with diabetes and thereby help prevent the development of other chronic conditions, diabetes-related complications and premature mortality. It seems important to develop or adapt current diabetes management and physical interventions to increase reach and motivation on an individual level among insufficiently active individuals to increase the health of the population and prevent the development of other chronic conditions. In our study, most individuals with diabetes who were not sufficiently active were motivated to increase their physical activity level (60%), which suggests that other factors prevent them from increasing their physical activity level. Previous studies have found that mental health, lack of time and energy, working schedule, economic circumstances, and social support are reasons for not being more physically active.<sup>38 44–46</sup> These reasons are also important to consider when designing and promoting a physical activity intervention.

### Strengths and limitations

The present study is based on a relatively large nationwide sample, which strengthens the generalizability of the results. The sample of participants with self-reported diabetes was 5.6%, which is slightly higher than the prevalence of diabetes in a recently published study in Denmark that found an overall prevalence of 0.5% of type 1 diabetes and 4.4% of type 2 diabetes in 2016.<sup>47</sup> Another strength of this study is the data on perceived stress, HRQoL and weekly MVPA, which were provided with validated questionnaires.<sup>21 26 28</sup> Furthermore, this study applied statistically weights provided by the DNHS to account for non-response and ensure a nationally representative analysis.<sup>33</sup>

The results of this study should be interpreted with the following limitations in mind. It was not possible to distinguish between type 1 and type 2 diabetes among participants,

which would have been preferable due to etiological differences. Since type 2 diabetes accounts for 85%–95% of diabetes cases in high-income countries,<sup>48</sup> the findings of this study will primarily be applicable to this patient group. In addition, information regarding diabetes complications and duration of the diabetes disease was not available, and the sample answering could potentially be skewed. Data were collected through self-reported questionnaires, which introduces information bias, including social desirability bias regarding lifestyle questions, such as diet, alcohol, smoking, and physical activity. Individuals with certain negative health conditions and behaviors are more likely to refrain from responding to health surveys.<sup>49</sup> Thus, the absolute prevalence of diabetes might be underestimated, and the presented characteristics might not be representative for all subgroups of individuals with diabetes, while the estimated levels of MVPA might be overestimated due to desirability bias. Despite the use of statistical weights to reduce the possible impact of non-response bias on the estimates, citizens living alone, or with non-Western background or at younger age were not highly represented in the study population affecting the generalizability of the findings.

The comorbidity variable created in this study does not include all the conditions, and not all conditions affect the individual's ability to be physically active. Questions regarding weekly MVPA are reported to provide an acceptable but weak estimate of participants' level of physical activity, which questions the absolute distribution of adherence to WHO recommendations of physical activity.<sup>21</sup> In addition, results might be different if assessment of MVPA was following the WHO recommendations from 2020, where physical activity of less than 10 min bouts has been removed.<sup>4</sup> Finally, the cross-sectional study design is a limitation, as reverse causation, uncontrolled confounding, and information bias cannot be ruled out. A prospective study design and/or objective measurement tools are suggested for further research to support the findings of this study.

### CONCLUSION

In this nationwide survey, we found that having comorbidities, higher BMI, higher perceived stress, and lower HRQoL were significantly associated with lower MVPA. Suffering from obesity, high perceived stress, and low physical HRQoL were the most remarkable determinants of low MVPA. Furthermore, we found that 40% of individuals with diabetes do not engage regularly in adequate physical activity, and 60% of those who do not meet the WHO recommendations for physical activity are motivated for being more physically active.

Our study suggests that subgroups of individuals with diabetes are at risk of physical inactivity and might need additional support or tailored interventions to increase their physical activity level.

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SRM wrote the first draft of the manuscript. STS reviewed and commented on all drafts of the manuscript. All authors contributed to the critical revision and final manuscript. All authors read and approved the final manuscript. SRM is the guarantor and takes responsibility for the conduct and the overall content of the article.

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**Data availability statement** Data are available upon reasonable request. All data used in the current study were derived from the DNHS. Data are available through application to the National Institute of Public Health, University of Southern Denmark.

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# Supplementary material

## Supplement S1

**Supplementary table 1.** Logistic regressions on the association of determinants with adherence to recommendations<sup>a</sup> in participants with diabetes

	Crude		Multivariable adjusted	
	POR [95 % CI]	<i>p</i> value	POR [95 % CI]	<i>p</i> value
<b>Comorbidities including mental conditions<sup>1</sup></b>				
No comorbidities	1.00 (Reference)		1.00 (Reference)	
One comorbidity	0.69 [0.55; 0.86]	0.001*	0.84 [0.67; 1.06]	0.133
Two comorbidities	0.53 [0.43; 0.66]	0.001*	0.70 [0.56; 0.88]	0.002*
Three or more comorbidities	0.42 [0.34; 0.51]	0.001*	0.59 [0.47; 0.74]	0.001*
<b>Comorbidities excluding mental conditions<sup>1</sup></b>				
No comorbidities	1.00 (Reference)		1.00 (Reference)	
One comorbidity	0.76 [0.62; 0.94]	0.011*	0.94 [0.75; 1.17]	0.573
Two comorbidities	0.57 [0.47; 0.70]	0.001*	0.76 [0.61; 0.94]	0.011*
Three or more comorbidities	0.46 [0.37; 0.56]	0.001*	0.65 [0.52; 0.81]	0.001*
<b>Obesity<sup>2</sup></b>				
Underweight /Normal	1.00 (Reference)		1.00 (Reference)	
Overweight	0.74 [0.63; 0.88]	0.001*	0.75 [0.63; 0.89]	0.001*
Obese class I	0.58 [0.49; 0.69]	0.001*	0.62 [0.52; 0.75]	0.001*
Obese class II	0.45 [0.36; 0.56]	0.001*	0.48 [0.38; 0.61]	0.001*
Obese class III	0.33 [0.25; 0.43]	0.001*	0.36 [0.27; 0.48]	0.001*
<b>Stress<sup>3</sup></b>				
Low perceived stress	1.00 (Reference)		1.00 (Reference)	
Moderate perceived stress	0.65 [0.57; 0.73]	0.001*	0.71 [0.62; 0.80]	0.001*
High perceived stress	0.39 [0.29; 0.52]	0.001*	0.44 [0.32; 0.59]	0.001*
<b>HRQoL<sup>4</sup></b>				
<i>Physical score</i>				
Moderate to high physical HRQoL	1.00 (Reference)		1.00 (Reference)	
Low physical HRQoL	0.40 [0.35; 0.46]	0.001*	0.56 [0.48; 0.65]	0.001*
<i>Mental score</i>				
Moderate to high mental HRQoL	1.00 (Reference)		1.00 (Reference)	
Low mental HRQoL	0.54 [0.48; 0.62]	0.001*	0.69 [0.59; 0.82]	0.001*

n = 6,341

<sup>a</sup>Following WHO recommendations = at least 150 mins/week of moderate physical activity or at least 75 mins/week of vigorous physical activity or an appropriate combination hereby

POR = prevalence odds ratio; CI = confidence interval

Crude and multivariable adjusted prevalence odds ratios of following WHO recommendations of physical activity in relation to comorbidities, obesity, stress, and health-related quality of life. Significant results ( $p < 0.05$ ) are marked with \*

Crude and adjusted models were weighted for non-response. Each multivariable model was adjusted as follows: <sup>1</sup>Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, BMI. <sup>2</sup>Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, comorbidity.

<sup>3</sup>Age, sex, educational level, marital status, smoking, BMI, comorbidity. <sup>4</sup>Age, sex, educational level, marital status, smoking, BMI, comorbidity, stress.

## Supplement S2

**Supplementary table 2.** Linear regression on the associations of determinants with total sedentary behavior in participants with diabetes

	Total sedentary behavior h/day			
	Crude $\beta^a$ [95 % CI]	<i>p</i> value	Multivariable adjusted $\beta$ [95 % CI]	<i>p</i> value
<b>Comorbidities including mental conditions<sup>1</sup></b>				
No comorbidities	(Reference)		(Reference)	
One comorbidity	-0.30 [-0.75; 0.15]	0.187	-0.01 [-0.45; 0.43]	0.973
Two comorbidities	-0.46 [-0.89; -0.02]	0.038*	-0.0004 [-0.43; 0.43]	0.998
Three or more comorbidities	-0.09 [-0.53; 0.35]	0.691	0.33 [-0.11; 0.77]	0.139
<b>Comorbidities excluding mental conditions<sup>1</sup></b>				
No comorbidities	(Reference)		(Reference)	
One comorbidity	-0.47 [-0.90; -0.03]	0.037*	-0.12 [-0.55; 0.31]	0.577
Two comorbidities	-0.50 [-0.92; -0.08]	0.020*	-0.004 [-0.42; 0.41]	0.984
Three or more comorbidities	-0.29 [-0.72; 0.15]	0.197	0.23 [-0.23; 0.65]	0.316
<b>Obesity<sup>2</sup></b>				
Underweight /Normal	(Reference)		(Reference)	
Overweight	-0.16 [-0.51; 0.18]	0.352	0.02 [-0.32; 0.35]	0.920
Obese class I	-0.02 [-0.39; 0.35]	0.898	0.15 [-0.22; 0.51]	0.427
Obese class II	0.66 [0.16; 1.15]	0.009*	0.63 [0.14; 1.12]	0.011*
Obese class III	1.15 [0.49; 1.80]	0.001*	1.05 [0.39; 1.71]	0.002*
<b>Stress<sup>3</sup></b>				
Low perceived stress	(Reference)		(Reference)	
Moderate perceived stress	0.15 [-0.11; 0.41]	0.270	-0.01 [-0.28; 0.25]	0.923
High perceived stress	0.92 [0.22; 1.62]	0.010*	0.55 [-0.14; 1.24]	0.116
<b>HRQoL<sup>4</sup></b>				
<i>Physical score</i>				
Normal physical HRQoL	(Reference)		(Reference)	
Low physical HRQoL	-0.09 [-0.36; 0.18]	0.529	0.12 [-0.18; 0.41]	0.438
<i>Mental score</i>				
Normal mental HRQoL	(Reference)		(Reference)	
Low mental HRQoL	0.42 [0.12; 0.71]	0.006*	0.14 [-0.21; 0.49]	0.426

n = 5,967

CI = confidence interval

<sup>a</sup>  $\beta$  coefficients and 95 % confidence intervals (95 % CI) represent mean difference in sedentary behavior h/day compared with the reference.

Significant results ( $p < 0.05$ ) are marked with \*

Crude and adjusted models were weighted for non-response. Each multivariable model was adjusted as follows: <sup>1</sup>Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, BMI. <sup>2</sup>Age, sex, ethnicity, educational level, marital status, diet, smoking, alcohol consumption, comorbidity. <sup>3</sup>Age, sex, educational level, marital status, smoking, BMI, comorbidity. <sup>4</sup>Age, sex, educational level, marital status, smoking, BMI, comorbidity, stress.



## Supplement S3

**Supplementary table 3.** Distribution of sufficiently physically active participants and their motivation for being more physically active

	Motivated	Not motivated	Don't know
<b>n (%)</b>	2,681 (55.6)	1,341 (27.3)	798 (17.3)
<b>Sex</b>			
Male	1,544 (53.0)	902 (30.1)	478 (16.9)
Female	1,137 (59.5)	439 (22.9)	320 (17.6)
<b>Age (categories)</b>			
16-34 years	127 (64.2)	40 (22.6)	22 (13.2)
35-54 years	607 (69.5)	153 (17.5)	92 (13.0)
55-64 years	785 (61.5)	278 (22.0)	191 (16.5)
65-74 years	851 (47.2)	576 (33.1)	343 (19.7)
≥75 years	311 (41.4)	294 (38.6)	150 (20.1)
<b>Obesity</b>			
Underweight /Normal	531 (47.3)	437 (36.2)	185 (16.5)
Overweight	1,034 (53.3)	573 (29.0)	320 (17.7)
Obese class I	678 (60.6)	239 (21.6)	192 (17.8)
Obese class II	276 (69.1)	58 (14.5)	66 (16.4)
Obese class III	144 (80.2)	17 (10.5)	16 (9.3)
<b>Comorbidities including mental conditions</b>			
No comorbidities	364 (54.0)	208 (29.2)	114 (16.8)
One comorbidity	752 (53.6)	434 (31.0)	208 (15.4)
Two comorbidities	771 (55.4)	381 (27.7)	226 (16.9)
Three or more comorbidities	794 (58.4)	318 (22.4)	250 (19.2)
<b>Stress</b>			
Low perceived stress	1,382 (50.7)	853 (32.7)	415 (16.6)
Moderate perceived stress	1,058 (60.5)	382 (21.3)	319 (18.3)
High perceived stress	105 (72.5)	23 (15.2)	17 (12.3)
<b>HRQoL</b>			
<i>Physical score</i>			
Normal physical HRQoL	1,822 (52.3)	1,043 (30.5)	564 (17.2)
Low physical HRQoL	636 (66.3)	182 (17.9)	150 (15.8)
<i>Mental score</i>			
Normal mental HRQoL	850 (52.3)	564 (34.1)	233 (23.6)
Low mental HRQoL	1,608 (57.9)	661 (23.6)	481 (18.6)

n = 4,820 (n differs due to variations in complete responses in each variable)

Data are presented as number (%)

Abbreviations: HRQoL = Health-related quality of life.




# Appendix II

## Paper II

Detailed descriptions of physical activity patterns among individuals with diabetes and prediabetes: the Lolland-Falster Health Study

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# Detailed descriptions of physical activity patterns among individuals with diabetes and prediabetes: the Lolland-Falster Health Study

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## ABSTRACT

**Introduction** This study aimed to describe objectively measured physical activity patterns, including daily activity according to day type (weekdays and weekend days) and the four seasons, frequency, distribution, and timing of engagement in activity during the day in individuals with diabetes and prediabetes and compared with individuals with no diabetes.

**Research design and methods** This cross-sectional study included data from the Danish household-based, mixed rural-provincial population study, The Lolland-Falster Health Study from 2016 to 2020. Participants were categorized into diabetes, prediabetes, and no diabetes based on their glycated hemoglobin level and self-reported use of diabetes medication. Outcome was physical activity in terms of intensity (time spent in sedentary, light, moderate, vigorous, and moderate to vigorous physical activity (MVPA) intensities), adherence to recommendations, frequency and distribution of highly inactive days (<5 min MVPA/day), and timing of engagement in activity assessed with a lower-back worn accelerometer.

**Results** Among 3157 participants, 181 (5.7 %) had diabetes and 568 (18.0 %) had prediabetes. Of participants with diabetes, 63.2% did not adhere to the WHO recommendations of weekly MVPA, while numbers of participants with prediabetes and participants with no diabetes were 59.5% and 49.6%, respectively. Around a third of participants with diabetes were highly inactive daily (<5 min MVPA/day) and had >2 consecutive days of inactivity during a 7-days period. Mean time spent physically active at any intensity (light, moderate, and vigorous) during a day was lower among participants with diabetes compared with participants with no diabetes and particularly from 12:00 to 15:00 (mean difference of -6.3 min MVPA (95% CI -10.2 to -2.4)). Following adjustments, significant differences in physical activity persisted between diabetes versus no diabetes, but between participants with prediabetes versus no diabetes, results were non-significant after adjusting for body mass index. **Conclusions** Inactivity was highly prevalent among individuals with diabetes and prediabetes, and distinct daily activity patterns surfaced when comparing these groups with those having no diabetes. This highlights

## WHAT IS ALREADY KNOWN ON THIS TOPIC?

⇒ Engagement in regular physical activity is a cornerstone of type 2 diabetes management and prevention, but no studies have investigated differences in objectively measured physical activity between individuals with diabetes, prediabetes, and no diabetes (normal blood glucose levels based on glycated hemoglobin).

## WHAT THIS STUDY ADDS?

⇒ This study found that most individuals with diabetes and prediabetes were insufficiently physically active and a third with diabetes was highly inactive (<5 min MVPA/day).  
⇒ Differences in daily and weekly patterns of physical activity were observed across diabetes status, but after adjusting for body mass index, the differences between individuals with prediabetes and no diabetes were equalized.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ This study highlights the need to optimize current diabetes treatment and prevention at the individual level and group level to better use resources and accommodate the large differences in engagement in physical activity among individuals with diabetes.

a need to optimize current diabetes treatment and prevention to accommodate the large differences in activity engagement.

## INTRODUCTION

Regular physical activity is a cornerstone of type 2 diabetes management and prevention.<sup>1</sup> Inactive adults have a substantially higher risk of developing type 2 diabetes and a range of other chronic conditions compared with those adhering to the physical activity recommendations.<sup>2, 3</sup> While the general

recommendation is to be physically active throughout the week, a specific recommendation for adults with type 2 diabetes is to spread the activity over at least 3 days per week and have no more than two consecutive days of inactivity.<sup>4</sup> This recommendation refers to a whole-day approach, which is considered a way to achieve regular physical activity for individuals with diabetes, who are unable to engage in more structured exercise. Indeed, previous short-term experiments found that increasing volume of activities of daily living favorably affect postprandial glucose metabolism in prediabetes and type 2 diabetes.<sup>5,6</sup> Although regular physical activity among individuals with diabetes is important, the whole-day physical activity pattern is largely unknown. Most population-based studies used self-reported instruments to assess physical activity and reported that a large proportion of individuals with diabetes did not adhere to physical activity recommendations.<sup>7,8</sup> However, numbers in these reports may be inaccurate, for example, due to social desirability and recall bias. Studies using accelerometer-based device measurements are needed to scrutinize the daily physical activity pattern across diabetes status to inform future physical activity interventions that can help to use resources in diabetes treatment and prevention.<sup>9</sup>

This study aimed to describe objectively measured physical activity patterns, including daily activity according to day type (weekdays and weekend days) and the four seasons, frequency, distribution, and timing of engagement in activity during the day among individuals with diabetes and individuals with prediabetes and compare these patterns with individuals with no diabetes. We also aimed to investigate whether there were any distinct differences in physical activity patterns across diabetes status, while considering other important diabetes-related determinants of activity such as obesity, comorbidities, and mental well-being.

## METHODS

This study is reported in accordance with the ‘Strengthening the Reporting of Observational Studies in Epidemiology’ checklist.<sup>10</sup>

### Setting and data sources

Data were derived from the Danish household-based population study: The Lolland-Falster Health Study (LOFUS) that collected data in a mixed rural-provincial area between February 2016 and February 2020. Inhabitants  $\geq 18$  years were randomly selected from the Danish Civil Registration System and invited to participate with their household members of all ages. The data collection in LOFUS encompassed questionnaires, a site visit including physical examinations, and biological samples. Detailed information about the LOFUS study protocol is described by Jepsen *et al.*<sup>11</sup> In continuation of the physical examinations, a subsample was asked to wear accelerometers.<sup>12</sup> Between February 2017 and November 2018, families were included if at least one adult and one child

agreed to accelerometer assessment. From December 2018 to February 2020, all participants were eligible for inclusion.<sup>13</sup>

Written informed consent from participants was obtained at the site visit.<sup>11</sup>

### Study population

In total, 7208 adults (above 18 years) participating in LOFUS were eligible to wear accelerometers. The present study included LOFUS participants with valid accelerometer data and information about diabetes status.

### Exposure

#### Diabetes status

Data on glycated hemoglobin (HbA1c) from blood samples were used to classify participants’ diabetes status. Participants were categorized as ‘Having diabetes’ if one of the following criteria were met: (1) HbA1c  $\geq 48$  mmol/mol, or (2) HbA1c  $< 48$  mmol/mol and self-reported use of antidiabetic medication (insulin and other diabetes medication). ‘Having prediabetes’ was defined as: HbA1c between  $< 48$  mmol/mol and  $\geq 39$  mmol/mol according to the American Diabetes Association (ADA) and no self-reported use of antidiabetic medication.<sup>4</sup> Participants were categorized as having ‘No diabetes’ if HbA1c were  $< 39$  mmol/mol and there was no self-reported use of antidiabetic medication.

### Outcome

#### Physical activity

Physical activity was measured using Axivity AX3 (Axivity, Newcastle, UK) accelerometers that were attached to the skin using adhesive plaster and placed on the lower back.<sup>12</sup> Axivity AX3 accelerometers have previously shown to be valid when measuring physical activity in individuals with and without functional impairments.<sup>14,15</sup>

Participants were instructed to wear the accelerometers consecutively for 7 days, including during sleep and water activities. By evaluating acceleration and temperature data from the accelerometer, raw valid wear periods were identified. The intensity cut-points for adults were as follows: light: 100 counts, moderate: 3522, and vigorous: 6016.<sup>13</sup> A minimum of 22 hours of wear time was the criterion for valid data for a day. We included participants with minimum three valid weekdays and one valid weekend day of measurement. Time spent in different physical activity intensities was determined by generating ActiGraph counts using 10 s epochs from the raw acceleration<sup>16</sup>, and time spent sedentary (sitting and lying) was determined using the method by Skotte *et al.*<sup>17</sup> Data were processed as described in Petersen *et al.*<sup>13</sup>

The following physical activity outcomes were included:

- ▶ Sedentary behavior (SB): Hours spent daily on sedentary activity weighted by 5/7 for weekdays and 2/7 for weekend days.
- ▶ Light physical activity (LPA): Minutes spent daily on light intensity activity.

- ▶ Moderate physical activity (MPA): Minutes spent daily on moderate intensity activity.
- ▶ Moderate to vigorous physical activity (MVPA): Minutes spent daily on moderate to vigorous intensity activity.
- ▶ Vigorous physical activity (VPA): Minutes spent daily on vigorous intensity activity.

### Adherence to recommendations

Adherence to the WHO recommendations of weekly physical activity and SB was assessed with MPA and VPA. The WHO recommends that adults engage in at least 150 min of MPA or 75 min of VPA weekly.<sup>18</sup> Importantly, these guidelines imply that time spent in VPA is effectively 'double-counted' compared with MPA, reflecting the greater intensity of VPA. Therefore, when calculating adherence on a daily level (necessary due to the varying number of valid measurement days among participants), we derived the total daily MVPA as follows:  $MVPA = MPA + (VPA * 2)$ .  $MVPA < (150 \text{ min}/7 \text{ days})$  was categorized as 'Not following recommendations' and  $MVPA \geq (150 \text{ min}/7 \text{ days})$  as 'Following recommendations'.

Adherence to the ADA recommendations of daily physical activity (engagement in  $\geq 30$  min MVPA/day) was calculated by summarizing daily MVPA and categorized into: (1) Sufficient physical activity:  $\geq 30$  min MVPA/day, (2) Some physical activity:  $\geq 5$  min MVPA/day and  $< 30$  min MVPA/day, and (3) Highly inactivity:  $< 5$  min MVPA/day.<sup>4 19</sup> The cut-off between high inactivity and some physical activity was applied because it has been suggested to provide the minimum clinical important difference among inactive adults.<sup>20</sup>

### Covariates and variables to describe participant characteristics

Information about age and sex of the participants came from the Civil Registration System, whereas other background information stemmed from the LOFUS Questionnaire.<sup>21</sup>

### Self-reported measures

Marital status was dichotomized into: 'Married or living with partner' or 'Living alone'. Highest level of education was categorized as follows: (1) Primary or lower secondary education, (2) Upper secondary or vocational education, and (3) Higher education. Occupational status was categorized into (1) Employed, (2) Unemployed, (3) Sick leave, (4) Retired, (5) Student and (6) Other.

Self-reported information on a variety of long-term conditions was used to assess comorbidity in addition to diabetes. The definition of comorbidity was based on the 10 body system groups according to Willadsen *et al.*<sup>22</sup> In addition, participants were asked to add if they had any other condition(s). All 'other' conditions were coded into the 10 groups by first author SRM and coauthor LBJ independently following the classification by Tang *et al.*<sup>23</sup>

Psychological stress was obtained with Cohen's 10-item Perceived Stress Scale.<sup>24</sup> Stress was classified as: (1) Low

perceived stress (scores from 0 to 13), (2) Moderate perceived stress (scores from 14 to 26), and (3) High perceived stress (scores from 27 to 40).

Mental well-being was obtained with the WHO-5 Well-Being Index. The scoring of the WHO-5 was done by multiplying the raw score by 4 to obtain a percentage score ranging from 0 to 100.<sup>25</sup> A higher score indicated a better mental well-being. Scores  $< 50$  were categorized as low mental well-being. Long-lasting chronic pain was reported as Yes or No, and use of selected medication was obtained from the questionnaire. We used information on use of insulin, other diabetes medication, cholesterol-lowering medication, and diuretics.

### Objectively measures

Participants' height and weight were obtained at the health examination to calculate body mass index (BMI) ( $\text{kg}/\text{m}^2$ ). BMI was categorized into: Underweight/normal weight ( $\text{BMI} < 25$ ), overweight ( $\text{BMI} \geq 25 - < 30$ ), obese class I ( $\text{BMI} \geq 30 - < 35$ ), obese class II ( $\text{BMI} \geq 35 - < 40$ ), and obese class III ( $\text{BMI} \geq 40$ ), as defined by the WHO.<sup>26</sup> HbA1c were used to classify controlled glycemic level for adults: Controlled glycemic level ( $\text{HbA1c} < 53 \text{ mmol}/\text{mol}$ ); Uncontrolled glycemic level ( $\text{HbA1c} \geq 53 \text{ mmol}/\text{mol}$ ).<sup>4</sup>

### Statistical analyses

Prior to commencing the analyses, a statistical analysis plan was developed and stored as openly available (<https://osf.io/34t2c/>). Some deviations from the plan were made in some of the analyses to fit the models due to low participant numbers in the diabetes group.

The `dstat` function in STATA<sup>27</sup> was used to describe statistical distributions by diabetes status with standardization of age and sex. Descriptive characteristics of participants with diabetes, prediabetes, and no diabetes were summarized as numbers and proportions or means and standard errors. The distribution and comparison of daily SB, LPA, MPA, VPA, and MVPA in total, during weekdays, and weekend days by diabetes status were estimated with median and quantiles (25th and 75th centiles). Difference in MVPA percentiles between diabetes status by weekdays, weekend days, and season of the year were estimated with coefficients and 95% CI. Adherence to recommendations of physical activity was distributed and displayed with numbers and proportions. Differences across diabetes status were investigated using Wald test within regression models, which varied based on outcome distribution, to adjust for age and sex by testing the null hypothesis that all coefficients are jointly zero.

The distribution of 0, 1, 2, 3, 4, 5, 6, and  $\geq 7$  inactive days and the prevalence of  $> 2$  consecutive inactive days were estimated by diabetes status with adjustment for age, sex, and number of days with valid accelerometer data.<sup>27</sup> Zero-inflated Poisson regression models were used to predict number of days with inactivity during a 7-day period of measurement by diabetes status adjusted

for age and sex and with number of valid days with accelerometer data as exposure time.

Mixed linear regression models with adjustment for age and sex were used to estimate and display the daily activity profile (mean time spent physically active at any intensity over the waking hours (per 15 min)) of weekdays and weekend days by diabetes status. Savitzky-Golay smoothing filter with an order of 3 and length of 15 was used to generate a smoothed trend based on the point estimates for every 15 min obtained from the mixed model. The order of 3 was chosen to reflect the expected pattern in physical activity data, with the length of 15 determined iteratively to best describe the general trend in the data. Based on visual inspection of the plot, we conducted post hoc analyses of daily activity profiles with additional adjustments of occupational status, BMI, and stress to investigate if differences in daily activity profile could be explained by other major determinants of inactivity. Finally, multiple quantile regression models on daily physical activity intensities and diabetes status were performed with additional adjustments to investigate if any differences by diabetes status were explained by other factors. Therefore, Model 1 was adjusted for age and sex; Model 2 was adjusted for age, sex, and BMI; and Model 3 was adjusted for age, sex, BMI, comorbidities, stress, mental well-being, and chronic pain.

All statistical analyses were performed using the software STATA BE V.17.0 and R statistical software (R Core Team, Vienna, Austria) V.4.2.2 (November 10, 2022), RStudio (RStudio, Boston, Massachusetts, USA) V.2022.07.2.

## RESULTS

Of the 3157 participants with valid accelerometer data and information on diabetes status, 181 (5.7 %) participants had diabetes, 568 (18.0 %) participants had prediabetes, and 2408 (76.3 %) participants had no diabetes (flow chart in online supplemental file 1).

Median (25th and 75th centiles) age was 67.8 (60.7–73.8) years among participants with diabetes, 65.1 (54.5–72.2) years among participants with prediabetes, and 51.1 (40.1–65.4) years among participants with no diabetes. The proportion of men was higher among participants with diabetes (59.1 %) compared with participants with prediabetes (46.1 %) or no diabetes (44.7 %). Characteristics of participants with diabetes, prediabetes, and no diabetes, standardized on age and sex, are displayed in [table 1](#). A larger proportion of participants with diabetes were on sick leave or retired, had higher BMI, and more comorbidities compared with participants with prediabetes or no diabetes. Further, participants with prediabetes had higher BMI and more comorbidities compared with participants with no diabetes.

Among participants with diabetes, 63.2% did not adhere to the WHO recommendations of weekly MVPA, while 59.5% of participants with prediabetes and 49.6% of participants with no diabetes did not follow the

recommendations. The proportion of participants with diabetes who was highly inactive daily (<5 min MVPA/day) was 33.0% ([table 2](#) and online supplemental file 2). The percentage point difference in highly inactive participants with diabetes (reference) compared with prediabetes and no diabetes was –14.7% (95% CI –18.2 to –11.4) and –20.1% (95% CI –25.9 to –15.1), respectively (online supplement 2).

The 25th, 50th, and 75th centiles of MVPA were significantly higher among participants with no diabetes compared with participants with diabetes (difference p25: 6.1 min/day, 95% CI 4.9 to 7.3, difference p50: 11.9 min/day, 95% CI 9.9 to 14.0, and difference p75: 10.0 min/day, 95% CI 4.2 to 15.9) (online supplemental files 3 and 4). No variations in seasonal distribution of daily MVPA by diabetes status were present (online supplemental file 5).

After adjustment for sex, there was no age-related differences in MVPA (min/day) between participants with diabetes and no diabetes except for a difference in the lowest centile (p25) of MVPA (4.2 min/day difference among participants  $\geq 65$  years and 7.9 min/day difference among participants <65 years,  $p=0.02$  for interaction (for more information see online supplemental file 6)).

Mean time spent physically active at any intensity during a weekday and a weekend day was lower among participants with diabetes compared with participants with prediabetes and no diabetes ([figure 1](#)). Participants with diabetes were significantly less physically active in the early afternoon (from 12:00 to 15:00) compared with participants with no diabetes (–6.3 min, 95% CI –10.2 to –2.4,  $p=0.001$ ). Additional adjustments for BMI, stress, and occupational status showed similar daily activity profiles across diabetes status (online supplemental files 7–9).

Among participants with diabetes, 33.2% had more than two consecutive days with high inactivity (<5 min/day of MVPA) during a 7-day period ([table 3](#)) which is at a rate that is 2.30 (95% CI 1.80 to 2.94) and 1.36 (95% CI 1.12 to 1.66) times higher compared with participants with prediabetes and participants with no diabetes, respectively, after adjustment for age and sex. Predicted number of days with high inactivity during a 7-day period were higher among participants with diabetes (2.2 days, 95% CI 1.98 to 2.37) compared with participants with prediabetes (1.75 days, 95% CI 1.63 to 1.87) and no diabetes (1.47 days, 95% CI 1.40 to 1.54) (online supplemental file 10).

Participants with diabetes had significantly lower median LPA, MPA, MVPA, and higher median SB after adjustments for BMI and other major determinants compared with participants with no diabetes. Additionally, participants with prediabetes had significantly lower median MPA, MVPA, and higher SB compared with participants with no diabetes when adjusting for age and sex. After adjusting for BMI, these differences were no longer significant ([table 4](#)). Further, participants with prediabetes had significantly higher median LPA and

**Table 1** Characteristics of participants with diabetes, prediabetes, and no diabetes

N (%)	Diabetes	Prediabetes	No diabetes	P value
	181 (5.7)	568 (18.0)	2408 (76.3)	
Marital status				0.294
Married/living with partner	136 (79.1)	421 (78.2)	1853 (81.4)	
Living alone	36 (20.9)	118 (21.8)	423 (18.6)	
Educational level				0.060
Primary or lower secondary	31 (17.8)	42 (7.9)	182 (8.0)	
Upper secondary or vocational	105 (60.7)	331 (61.6)	1286 (56.3)	
Higher	33 (19.2)	144 (26.7)	701 (30.7)	
Other	4 (2.3)	20 (3.8)	114 (5.0)	
Occupational status				<0.001*
Employed	74 (43.9)	326 (62.1)	1313 (58.4)	
Unemployed	2 (1.1)	9 (1.7)	29 (1.3)	
Absent (sick leave)	25 (14.6)	34 (6.4)	90 (4.0)	
Retired	56 (33.2)	145 (27.5)	724 (32.2)	
Student	12 (7.3)	1 (0.1)	74 (3.3)	
Other	0 (0)	11 (2.1)	17 (0.7)	
BMI categories				<0.001*
Underweight /Normal	35 (20.2)	143 (26.0)	961 (40.6)	
Overweight	49 (28.2)	189 (34.3)	919 (38.8)	
Obese class I (BMI ≥30–<35)	59 (34.4)	148 (26.8)	351 (14.8)	
Obese class II (BMI ≥35–<40)	23 (13.4)	50 (9.1)	103 (4.4)	
Obese class III (BMI ≥40)	7 (3.8)	21 (3.8)	34 (1.4)	
Comorbidities				<0.001*
No comorbidities	55 (30.2)	181 (31.9)	818 (34.0)	
One comorbidity	51 (28.2)	160 (28.1)	789 (32.8)	
Two comorbidities	38 (21.0)	131 (23.1)	509 (21.1)	
Three or more comorbidities	37 (20.6)	96 (16.8)	292 (12.1)	
Perceived stress				0.696
Low perceived stress	15 (9.1)	42 (8.2)	163 (7.4)	
Moderate perceived stress	147 (89.5)	463 (90.2)	1994 (90.6)	
High perceived stress	2 (1.4)	8 (1.6)	44 (2.0)	
Mental well-being				0.001*
Moderate to high mental well-being	135 (81.8)	415 (80.2)	1927 (86.0)	
Low mental well-being	30 (18.2)	102 (19.8)	313 (14.0)	
Suffers from chronic pain	65 (37.5)	185 (34.5)	648 (28.4)	<0.001*
Use of medication				
Insulin	58 (33.8)	–	–	–
Other diabetes medication	81 (47.4)	–	–	–
Cholesterol-lowering medication	74 (43.1)	99 (18.9)	225 (10.0)	<0.001*
Diuretics	40 (23.6)	40 (7.8)	150 (6.7)	<0.001*
HbA1c level	54.1 (1.45)	40.7 (0.08)	34.3 (0.05)	<0.001*
Controlled glycemic level (HbA1c level <53mmol/mol)	102 (56.6)	–	–	–
Median number of valid days with accelerometer measurement	6 (6–7)	6 (6–7)	6 (6–7)	0.074

Categorical data are presented as n and proportion (%) with standardization on age and sex. Continuous data are presented with mean and SE due to standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference). Wald test was used to joint test coefficients for categories of diabetes. The null hypothesis for the Wald test in this context is that all coefficients associated with diabetes status are simultaneously zero, implying no effect of diabetes status on the outcome of interest after adjusting for age and sex. Significant results ( $p < 0.05$ ) are marked with\*. n varies due to variations in complete responses for each variable. BMI, body mass index; HbA1c, glycated hemoglobin.

**Table 2** Distribution of daily SB, LPA, MPA, VPA, and MVPA and adherence to recommendations among participants with diabetes, prediabetes, and no diabetes

	Diabetes n=181	Prediabetes n=568	No diabetes n=2408	P value
Total				
SB	11.6 (10.0–12.6)	11.0 (9.9–12.1)	10.8 (9.7–11.9)	<0.001*
LPA	156.4 (123.4–214.8)	197.8 (158.2–230.4)	194.2 (156.7–234.0)	<0.001*
MPA	8.5 (2.8–18.4)	12.5 (5.9–23.8)	15.8 (8.1–26.1)	<0.001*
VPA	0.6 (0.1–2.3)	1.2 (0.4–3.2)	1.6 (0.5–4.4)	<0.001*
MVPA	9.3 (3.5–22.9)	14.3 (6.6–27.8)	18.9 (9.6–32.1)	<0.001*
Weekdays				
SB	11.6 (10.2–12.8)	11.1 (9.9–12.2)	11.0 (9.9–12.1)	<0.001*
LPA	151.6 (122.7–214.8)	195.4 (155.8–235.2)	192.0 (154.5–237.9)	<0.001*
MPA	7.5 (2.8–19.0)	13.2 (5.7–23.8)	15.8 (7.8–27.0)	<0.001*
VPA	0.5 (0.2–2.5)	1.2 (0.3–3.0)	1.5 (0.5–4.2)	<0.001*
MVPA	8.8 (3.2–22.1)	14.6 (6.5–26.9)	18.4 (9.2–31.8)	<0.001*
Weekend days				
SB	10.7 (9.7–12.3)	10.9 (9.6–12.1)	10.4 (9.2–11.7)	<0.001*
LPA	175.5 (118.0–225.8)	187.2 (137.9–238.8)	190.7 (146.2–237.4)	<0.001*
MPA	7.8 (2.3–17.2)	8.3 (3.7–19.7)	12.9 (5.3–26.7)	<0.001*
VPA	0.5 (0.1–2.0)	0.9 (0.3–2.5)	1.3 (0.3–3.8)	<0.001*
MVPA	9.3 (2.5–24.9)	9.7 (4.2–23.3)	15.7 (6.2–31.7)	<0.001*
Adherence to WHO recommendations on weekly physical activity *				<0.001*
Following recommendations	67 (36.8)	230 (40.5)	1214 (50.4)	
Not following recommendations	114 (63.2)	338 (59.5)	1194 (49.6)	
Adherence to ADA recommendations on daily physical activity †				<0.001*
High inactivity	60 (33.0)	104 (18.3)	308 (12.8)	
Some physical activity	90 (49.8)	350 (61.6)	1430 (59.4)	
Sufficient physical activity	31 (17.2)	114 (20.1)	670 (27.8)	

Data are standardized on age and sex and presented as medians and quantiles (25th and 75th centile) or n and proportion (%). Wald test was used to join test coefficients for categories of diabetes. The null hypothesis for the Wald test in this context is that all coefficients associated with diabetes status are simultaneously zero, implying no effect of diabetes status on the outcome of interest after adjusting for age and sex. Significant results ( $p < 0.05$ ) are marked with \*.

\*Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity:  $\geq 150$  min MVPA or  $\geq 75$  min VPA weekly or an equivalent combination.

†Distribution of adherence to recommendations on daily physical activity according to ADA. High inactivity:  $< 5$  min MVPA/day, Some activity:  $\geq 5$  min MVPA/day and  $< 30$  min MVPA/day, Sufficient activity:  $\geq 30$  min MVPA/day.

ADA, American Diabetes Association; LPA, light physical activity; MPA, moderate physical activity; MVPA, moderate to vigorous physical activity; SB, sedentary behavior; VPA, vigorous physical activity.

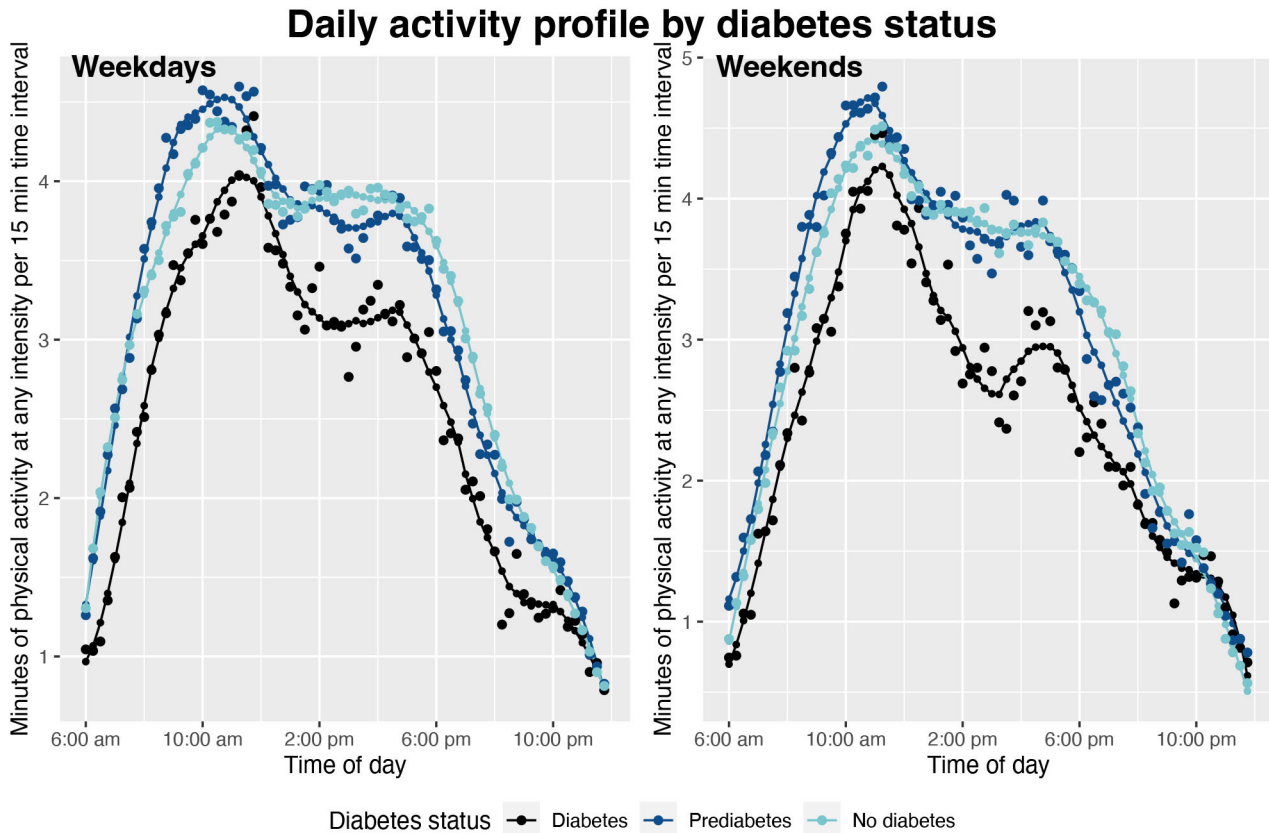
lower SB after adjustments compared with participants with diabetes (online supplemental file 11).

## DISCUSSION

We found that a large proportion of participants with diabetes and prediabetes were insufficiently physically active. Also, results revealed that over a third of

participants with diabetes and prediabetes met the WHO recommendations for weekly physical activity. Participants with diabetes engaged significantly less in physical activity during weekdays and weekend days and had a higher frequency of highly inactive days compared with participants with prediabetes or no diabetes. These differences were evident even after adjustment for other major





**Figure 1** Daily activity profiles by diabetes status are presented as mean time (minutes per 15 min interval) spent physically active at any intensity (light physical activity (LPA) was the threshold for detection of physical activity at any intensity) during a weekday and a weekend day adjusted for age and sex. The points represent the raw age-adjusted and sex-adjusted estimates, and the fitted line represents a smoothing trend based on the point estimates. The smoothed trend was generated using a *sgolay* filtering with an order of 3 and length 15.

**Table 3** The prevalence for accumulating 0, 1, 2, 3, 4, 5, 6, and 7 days of high inactivity (<5 min MVPA/day) among participants with diabetes, prediabetes, and no diabetes

	Diabetes n=181	Prediabetes n=568	No diabetes n=2408
Inactive days during a week	%	%	%
0 day	33.6	44.0	52.9
1 day	13.6	17.4	17.0
2 days	10.3	10.3	8.4
3 days	9.2	7.3	7.1
4 days	4.4	5.9	4.4
5 days	11.3	4.9	4.2
6 days	11.6	7.7	4.3
≥7 days	6.0	2.4	1.7
Consecutive days with high inactivity			
>2 days	33.2	19.9	15.1

Data are presented as proportion (%) with standardization on age, sex, and number of valid days with accelerometer measurement. MVPA, moderate to vigorous physical activity.

determinants of physical activity such as BMI and prevalent comorbidities. Participants with prediabetes were also less physically active compared with age-matched and sex-matched participants with no diabetes. However, after adjusting for BMI, these differences were no longer significant.

### Comparison with other studies

Most prior studies used self-reported instruments and only estimated adherence to the recommendations of physical activity in individuals with diabetes.<sup>7 8 28 29</sup> We identified few studies that used device-based measurements among individuals with diabetes or prediabetes to report physical activity intensities and adherence to WHO recommendations. A Danish study by Domazet *et al*<sup>30</sup> found that 62% of individuals with a median age of 61.8 years and newly diagnosed type 2 diabetes met the recommendations. A Swedish population-based study by Hult *et al*<sup>31</sup> found that 43% of 70-year-old adults with diabetes adhered to the WHO recommendations. In our study, participants with diabetes had a median age of 67.8 years and only 36.8% adhered to the WHO recommendations. Furthermore, our study participants were resident in a socioeconomically disadvantaged area of Denmark,<sup>32</sup> which could explain the differences in results between the studies as physical activity is typically lower in

**Table 4** Quantile regression models on daily LPA, MPA, VPA, MVPA, and SB by diabetes status with additional adjustment for other major determinants of physical activity

	Model 1* n=2746 β (95% CI)	P value	Model 2† n=2746 β (95% CI)	P value	Model 3‡ n=2746 β (95% CI)	P value
<b>Total LPA (min/day)</b>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	1.6 (−5.2 to 8.4)	0.649	3.4 (−4.0 to −10.7)	0.371	4.0 (−3.1 to 11.2)	0.269
Diabetes	−42.9 (−54.1 to −31.7)	<0.001*	−30.0 (−42.2 to −17.7)	<0.001*	−35.3 (−47.2 to −23.3)	<0.001*
<b>Total MPA (min/day)</b>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	−3.7 (−5.5 to −1.9)	<0.001*	−1.5 (−3.3 to 0.3)	0.107	−1.5 (−3.3 to 0.3)	0.103
Diabetes	−10.0 (−12.9 to −7.0)	<0.001*	−5.1 (−8.2 to −2.1)	0.001*	−4.8 (−7.8 to −1.7)	0.002*
<b>Total VPA (min/day)</b>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	−0.3 (−0.7 to 0.004)	0.053	−0.1 (−0.4 to 0.2)	0.444	−0.2 (−0.5 to 0.3)	0.242
Diabetes	−0.7 (−1.2 to −0.2)	0.011*	−0.3 (−0.8 to 0.2)	0.294	−0.2 (−0.8 to 0.3)	0.368
<b>Total MVPA (min/day)</b>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	−4.7 (−6.8 to −2.6)	<0.001*	−1.1 (−3.3 to 1.0)	0.307	−2.1 (−4.1 to 0.03)	0.054
Diabetes	−11.6 (−15.1 to −8.1)	<0.001*	−5.5 (−9.1 to −1.9)	0.003*	−5.5 (−9.0 to −2.0)	0.002*
<b>Total SB (hours/day)</b>						
No diabetes	(reference)		(reference)		(reference)	
Prediabetes	0.1 (−0.1 to 0.3)	0.219	0.04 (−0.1 to 0.2)	0.663	0.05 (−0.1 to 0.2)	0.608
Diabetes	0.7 (0.4 to 1.0)	<0.001*	0.4 (0.1 to 0.7)	0.007*	0.5 (0.2 to 0.8)	0.001*

β coefficients and 95% CI represent median difference in LPA, MPA, VPA, MVPA (min/day) and SB (hours/day) compared with participants with no diabetes as the reference. Significant results (p<0.05) are marked with\*.

\*Model 1: Multivariable regression model adjusted for age and sex.

†Model 2: Multivariable regression model adjusted for age, sex, and BMI.

‡Model 3: Multivariable regression model adjusted for age, sex, BMI, comorbidities, stress, mental well-being, and chronic pain.

BMI, body mass index; LPA, light physical activity; MPA, moderate physical activity; MVPA, moderate to vigorous physical activity; SB, sedentary behavior; VPA, vigorous physical activity.

individuals with low socioeconomic status.<sup>33 34</sup> Swindell *et al*<sup>35</sup> found that mean MVPA among overweight and prediabetic women and men was 26.2 min/day and 31.6 min/day, respectively. Participants were 15 years younger and volunteers in a lifestyle intervention which could explain why we found a lower median daily MVPA (14.3 min/day) among participants with prediabetes in our study.<sup>35</sup>

Steeves *et al*,<sup>36</sup> using the National Health and Nutrition Examination Survey (NHANES) data from 2003 to 2006, also reported lower physical activity levels among those with diabetes and a noticeable drop in the afternoon, similar to our findings. They found comparable activity levels between individuals with prediabetes and normoglycemic individuals, as well. However, unlike their study, which focused solely on adults over the age of 60 years, our study included a broader range of participants.<sup>36</sup> Importantly, comparisons of results between studies using accelerometer-measured physical activity is challenged by a lack of consensus about the method used in the data reduction process.<sup>37 38</sup>

### Highly inactive days

Our study provides new insights into physical activity patterns distributed over a week, which have not been addressed in prior studies.<sup>4</sup> We found that 33.0% of participants with diabetes were highly inactive (<5 min MVPA/day), and 33.2% had more than two consecutive highly inactive days during a 7-day period, while numbers were 12.8% and 15.1% among participants with no diabetes. Achieving and maintaining a physically active lifestyle can be a challenge for individuals with diabetes, and some may not even view daily activity as a crucial aspect of managing their diabetes.<sup>39</sup> Many physical activity intervention programs for adults with type 2 diabetes have been developed, but a limited number of these interventions focus on implementation and maintenance.<sup>40</sup> Given the high proportion of participants not adhering to physical activity recommendations in our study, especially among those with diabetes, efforts on an individual level and societal level are needed to promote physical activity and improve health.<sup>41 42</sup> Among

others, this may be accomplished by offering exercise communities and support and increasing accessibility and flexibility for participation such as digital solutions or group-based interventions.<sup>39 43</sup> Our study also revealed that around 20%–40% of participants with diabetes and prediabetes were sufficiently active daily and weekly according to the ADA and WHO recommendations. The observed differences in engagement in physical activity within individuals with diabetes and prediabetes suggest a need of rethinking how diabetes treatment and prevention is delivered to the individual. Personalized medicine has been highlighted as a clinical approach aiming to improve patient health and experience and reducing costs.<sup>44</sup> Individuals with diabetes and prediabetes who are sufficiently physically active may not need support from, for example, health professionals, peers, or family to become physically active, however, resources could be spent on supporting these individuals to maintain their physical activity level through easily accessible long-term physical activity interventions with a focus on social support or physical activity monitoring with activity trackers or apps.<sup>39 43 45</sup> Furthermore, it is important to note that inactive individuals, especially those with diabetes, may require not only additional, but also more intensive, and long-term support. This could include continuous guidance from healthcare professionals to increase their physical activity levels, sustain these changes over time, and ultimately achieve health-related benefits. Therefore, physical activity interventions for individuals with diabetes should be concentrated on those who will benefit from it, and spare resources for those who will not. Physical activity screening tools might be needed to be able to reach out to those individuals with diabetes who may need extra support to change their physical activity behavior. Wearable accelerometer-based devices could be used as a screening tool to introduce a personalized medicine approach to identify and stratify individuals with diabetes and prediabetes into subgroups based on their habitual physical activity levels and patterns.<sup>46</sup> Furthermore, it is also important to include the individual's preferences and motivation in terms of increasing and maintaining physical activity in their daily life.<sup>47 48</sup> These approaches would enable clinicians to treat patients with diabetes and prediabetes individually based on their needs to have a physically active lifestyle.

### Daily physical activity patterns

Differences in the daily activity profile across diabetes status were also revealed in our study. Participants with diabetes were particularly less physically active during the period from 12:00 to 15:00 compared with participants with no diabetes after adjustments for diabetes-related determinants of activity. Although speculative, a possible explanation of the lower levels of activity among participants with diabetes in the early afternoon could be higher with more prolonged postprandial glucose excursions compared with individuals with prediabetes and individuals with no diabetes.<sup>49</sup> Postprandial hyperglycemia and

hyperinsulinemia may cause increased fatigue following a meal, which might dampen motivation for activity in the postprandial period.<sup>50 51</sup> The results indicate that many individuals with diabetes may have a more inactive daily pattern compared with individuals with prediabetes and individuals with no diabetes. In addition, since total volume of physical activity has been reported being equally strongly associated with cardiometabolic health as MVPA,<sup>35 52</sup> a whole-day approach should be considered when increasing physical activity in individuals with diabetes. Focusing on increasing LPA in a whole-day perspective rather than exercise-based MVPA in a short timeframe among inactive individuals with diabetes could offer a seemingly equally effective approach, particularly if they suffer from other determinants such as obesity and comorbidities that prevent them from engaging in exercise-type activities with higher intensities.<sup>6 7</sup> Considering the low levels of physical activity among participants with diabetes in the present study, replacing a significant part of the day spent being sedentary with LPA may be more feasible for some to overcome possible barriers of engagement in higher intensity activities. This approach is also in accordance with the WHO recommendations highlighting that doing some physical activity is better than none, because engagement in some physical activity will still be beneficial for the individual's health.<sup>18</sup>

### Strengths and limitations of the study

The present study has several strengths. To the best of our knowledge, this is the first population-based study to detail both the time spent in varying physical activity intensity domains and the weekly distribution of inactive days, specifically contrasting these characteristics across individuals with different diabetes statuses.<sup>11</sup> Further, HbA1c measures from the blood samples were used to categorize diabetes status, which also enabled us to include individuals with prediabetes, however, we were not able to distinguish between type 1 and 2 diabetes in this study. Another strength is the use of accelerometry to assess 24-hour physical activity behavior under free-living conditions with a median of six valid days among all participants. Also, we controlled for age-related and sex-related differences in activity patterns across diabetes status in all analyses and performed additional adjustments in our regression models to investigate if factors such as comorbidities, stress, chronic pain, and obesity, that are more prevalent in diabetes, could explain differences in activity across diabetes status.<sup>53–55</sup>

This study also has several potential limitations. Lolland-Falster is a socioeconomically disadvantaged area of Denmark,<sup>32</sup> and given that low socioeconomic status is associated with higher incidence of type 2 diabetes,<sup>56</sup> we would expect the proportion of participants with diabetes to be larger compared with the general population. However, out of 3157 participants 5.7% had diabetes which corresponds with latest available data on diabetes prevalence in Denmark.<sup>7</sup> Participation in the LOFUS Study and the accelerometer assessment was voluntary

which may have introduced selection bias. The participation rate in LOFUS was highest among the middle-aged population, women, Danish citizens and those from a high socioeconomic status.<sup>57</sup> Therefore, the patterns and differences in activity observed may not be representative of other populations. Also, the sample size of participants with diabetes in this study was modest, which might also affect the generalizability of the study. There may be other diabetes-related determinants of physical activity that were not captured by those included that could explain differences in activity patterns across diabetes status. Furthermore, accelerometry measurements used in the study are not able to accurately capture non-ambulatory activities such as resistance training. Lastly, because of the cross-sectional study design, we cannot draw any conclusions on direction or causal nature of the associations.

### Conclusion

We found that a large proportion of individuals with diabetes and individuals with prediabetes were insufficiently physically active. Most individuals with diabetes engaged less in physical activity during the day in terms of overall daily levels of activity, frequency, and distribution of highly inactive days and timing of engagement in activity compared with individuals with no diabetes. Among individuals with prediabetes, we found that they were less physically active compared with their age-matched and sex-matched counterparts with no diabetes. This difference, however, diminished when adjusting for BMI. Also, we found that more than a third of individuals with either diabetes or prediabetes were engaging in sufficient levels of physical activity. This emphasizes the necessity to tailor diabetes treatment and prevention strategies to the wide-ranging physical activity habits seen within these populations, ensuring resources are used in the most effective manner.

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**Data availability statement** Data are available upon reasonable request. All data used for this study were derived from the Lolland-Falster Health Study (LOFUS). Research groups can apply to the LOFUS steering group for access to use LOFUS data. Each project must adhere to the rules and regulations on research ethics and data protection.

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## Supplementary material

### Supplement S1

**Supplementary table 1.** Daily MVPA percentile difference between groups of diabetes status.

	p25		p50		p75	
	$\beta$ [95 % CI]	<i>p</i> -value	$\beta$ [95 % CI]	<i>p</i> -value	$\beta$ [95 % CI]	<i>p</i> -value
<i>Total MVPA (min/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	3.2 [1.9; 4.6]	<0.001*	6.6 [4.2; 9.0]	<0.001*	5.1 [-1.1; 11.3]	0.108
No diabetes	6.1 [4.9; 7.3]	<0.001*	11.9 [9.9; 14.0]	<0.001*	10.0 [4.2; 15.9]	0.001*

$\beta$  coefficients and 95 % confidence intervals (95 % CI) represent estimated difference in daily MVPA (min/day) (25<sup>th</sup> percentile, 50<sup>th</sup> percentile and 75<sup>th</sup> percentile) within each percentile of MVPA by diabetes status with diabetes as the reference. Data are standardized on age and sex. Significant results ( $p < 0.05$ ) are marked with \*.

### Supplement S2

**Supplementary table 2.** Daily MVPA median (p50) difference between weekdays and weekends by diabetes status.

	Diabetes		Prediabetes		No diabetes	
	$\beta$ [95 % CI]	<i>p</i> -value	$\beta$ [95 % CI]	<i>p</i> -value	$\beta$ [95 % CI]	<i>p</i> -value
<i>Total MVPA (min/day)</i>						
Weekdays	(reference)		(reference)		(reference)	
Weekends	-1.2 [-2.1; -0.3]	0.012*	-2.2 [-3.3; -1.1]	<0.001*	-2.3 [-3.1; -1.6]	<0.001*

$\beta$  coefficients and 95 % confidence intervals (95 % CI) represent estimated difference in daily MVPA (min/day) (50<sup>th</sup> percentile) between weekdays and weekends by diabetes status with diabetes as the reference. Data are standardized on age and sex. Significant results ( $p < 0.05$ ) are marked with \*.

### Supplement S3

**Supplementary table 3.** Estimated distribution of daily MVPA (p25, p50, and p75) by diabetes status and season.

	<i>MVPA (min/day)</i>		
	p25 $\beta$ [95 % CI]	p50 $\beta$ [95 % CI]	p75 $\beta$ [95 % CI]
<i>Diabetes</i>			
Winter	1.3 [-0.2; 2.7]	5.2 [2.9; 7.6]	16.5 [9.9; 23.0]
Spring	2.4 [0.5; 4.4]	5.7 [3.1; 8.5]	17.1 [7.7; 26.4]
Summer	1.8 [0.7; 3.6]	4.3 [1.9; 6.8]	12.9 [4.2; 21.7]
Autumn	2.2 [-0.1; 4.5]	5.9 [2.9; 8.8]	12.5 [7.5; 17.6]
<i>Prediabetes</i>			
Winter	5.7 [3.9; 7.6]	14.1 [11.1; 17.1]	27.8 [23.7; 31.9]
Spring	6.2 [4.4; 8.1]	13.3 [9.8; 16.7]	27.1 [21.4; 32.8]
Summer	3.8 [2.2; 5.4]	10.1 [7.4; 12.8]	24.2 [18.5; 29.9]
Autumn	4.6 [2.6; 6.7]	11.9 [8.8; 15.1]	26.5 [19.5; 33.5]
<i>No diabetes</i>			
Winter	9.8 [8.5; 11.1]	19.7 [17.9; 21.4]	33.4 [30.8; 36.0]
Spring	9.6 [8.1; 11.1]	19.8 [17.8; 21.9]	33.7 [30.7; 36.8]
Summer	9.4 [7.9; 10.9]	17.4 [15.2; 19.5]	30.6 [27.4; 33.8]
Autumn	9.3 [7.9; 10.7]	17.8 [15.9; 19.6]	31.2 [28.0; 34.4]

$\beta$  coefficients and 95 % confidence intervals (95 % CI) represent estimated daily MVPA (min/day) (25<sup>th</sup> percentile, 50<sup>th</sup> percentile and 75<sup>th</sup> percentile) by diabetes status and season. Data are standardized on age and sex.

## Supplement S4

**Supplementary table 4.** Predicted MVPA (min/day) between diabetes status and age groups.

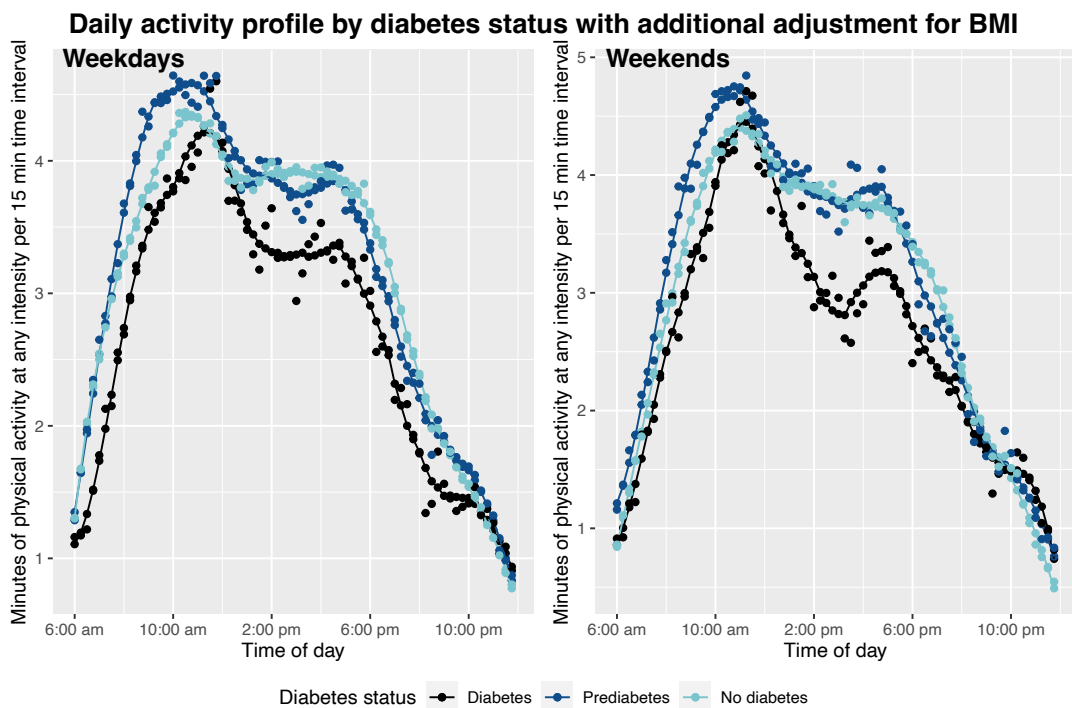
	p25		p50		p75	
	Margin [95 % CI]	<i>p</i> -value	Margin [95 % CI]	<i>p</i> -value	Margin [95 % CI]	<i>p</i> -value
<i>&lt;65 years</i>						
Diabetes	4.2 [0.8; 7.6]	(reference)	8.3 [3.2; 13.3]	(reference)	20.7 [13.6; 27.8]	(reference)
Prediabetes	7.3 [5.6; 9.0]	0.107	14.8 [12.3; 17.4]	0.023*	27.3 [23.7; 30.8]	0.103
No diabetes	12.1 [11.4; 12.7]	<0.001*	21.7 [20.7; 22.7]	<0.001*	34.8 [33.4; 36.2]	<0.001*
<i>≥65 years</i>						
Diabetes	1.0 [-1.9; 3.8]	(reference)	3.4 [-0.8; 7.7]	(reference)	9.9 [3.9; 15.9]	(reference)
Prediabetes	4.0 [2.2; 5.7]	0.076	10.5 [7.9; 13.1]	0.007*	25.1 [21.4; 28.7]	<0.001*
No diabetes	5.2 [4.0; 6.4]	0.007*	13.5 [11.8; 15.3]	<0.001*	26.1 [23.7; 28.5]	<0.001*

n = 2,746

Margins and CI 95 % represent predicted average values of MVPA (min/day) in p25, p50, and p75 between diabetes status and age groups (<65 years and ≥65 years) based on fitted quantile regression models adjusted for sex.

*p*-values represent differences in MVPA (min/day) in each age group between diabetes and prediabetes, and diabetes and no diabetes. Significant results (*p*<0.05) are marked with \*.

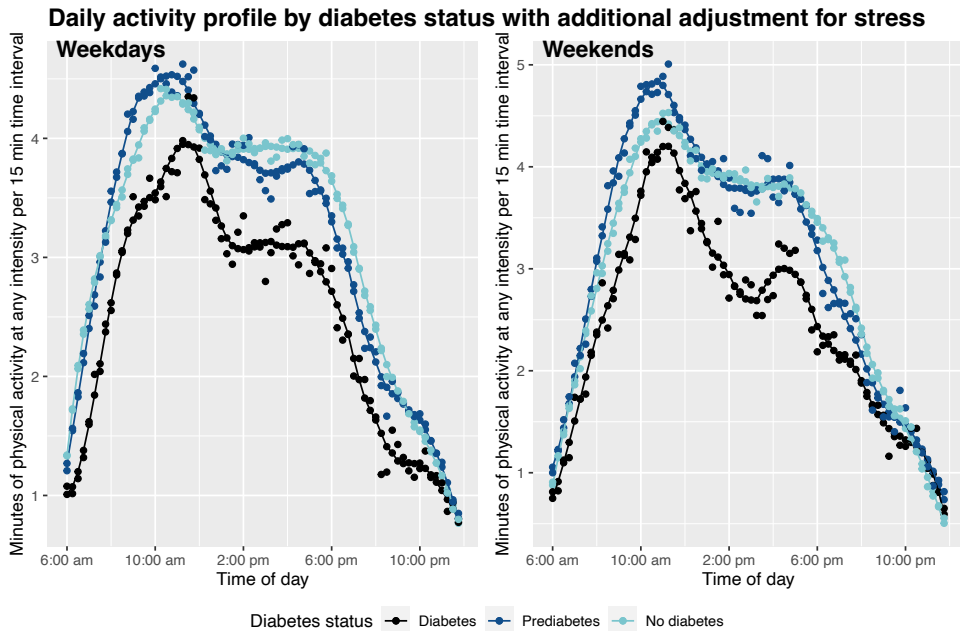
## Supplement S5



**Supplementary figure 1.** Daily activity profiles by diabetes status are presented as mean time (minutes per 15 minutes interval) spent being physically active at any intensity (LPA was the threshold for detection of physical activity at any intensity) during a weekday and weekend day adjusted for age, sex, and BMI. The points represent the raw estimates, and the fitted line represents a smoothing trend based on the point estimates. The smoothed trend was generated using a *sgolay* filtering with an order of 3 and length 15.

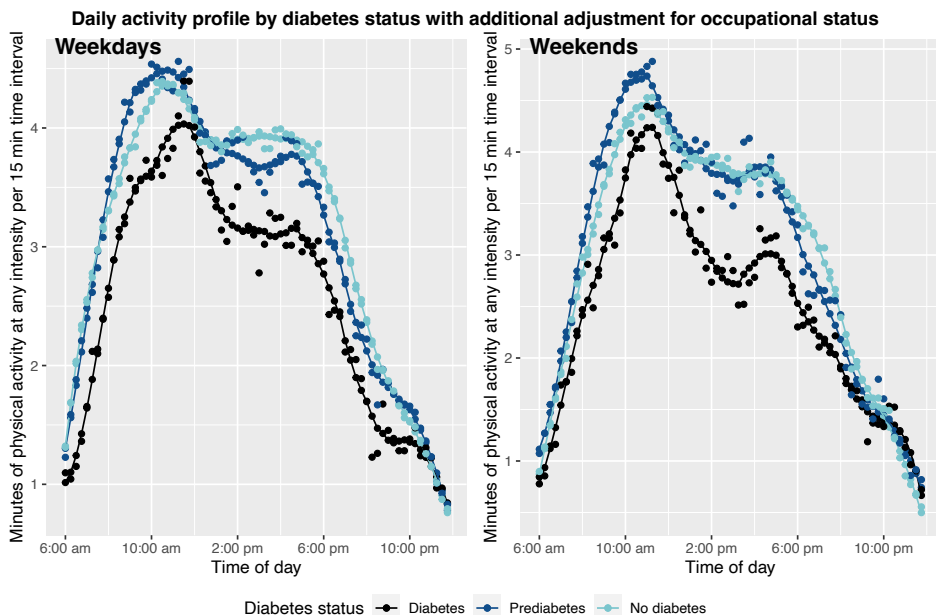


## Supplement S6



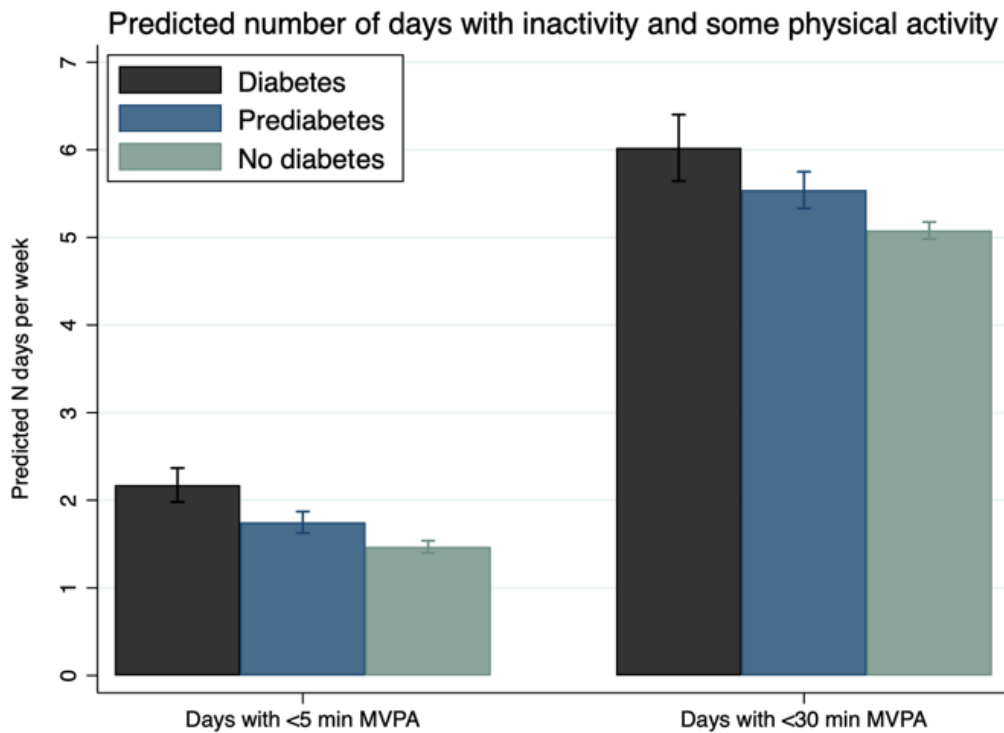
**Supplementary figure 2.** Daily activity profiles by diabetes status are presented as mean time (minutes per 15 minutes interval) spent being physically active at any intensity (LPA was the threshold for detection of physical activity at any intensity) during a weekday and weekend day adjusted for age, sex, and stress. The points represent the raw estimates, and the fitted line represents a smoothing trend based on the point estimates. The smoothed trend was generated using a sgolay filtering with an order of 3 and length 15.

## Supplement S7



**Supplementary figure 3.** Daily activity profiles by diabetes status are presented as mean time (minutes per 15 minutes interval) spent being physically active at any intensity (LPA was the threshold for detection of physical activity at any intensity) during a weekday and weekend day adjusted for age, sex, and occupational status. The points represent the raw estimates, and the fitted line represents a smoothing trend based on the point estimates. The smoothed trend was generated using a sgolay filtering with an order of 3 and length 15.

## Supplement S8



**Supplementary figure 4.** Predicted number of days (95 % CI) with highly inactivity (<5 min MVPA/day) and some physical activity (<30 min MVPA/day) during the median of 7-days period with adjustments for age and sex.

## Supplement S9

**Supplementary table 5.** Quantile regression models on daily LPA, MPA, VPA, MVPA and SB between participants with diabetes and participants with prediabetes with additional adjustment for other major determinants of physical activity

	Model 1 <sup>a</sup> n = 630		Model 2 <sup>b</sup> n = 630		Model 3 <sup>c</sup> n = 630	
	$\beta$ [95 % CI]	p-value	$\beta$ [95 % CI]	p-value	$\beta$ [95 % CI]	p-value
<i>Total LPA (min/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	44.1 [31.9; 56.4]	<0.001*	32.9 [19.7; 46.2]	<0.001*	31.2 [19.1; 43.3]	<0.001*
<i>Total MPA (min/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	6.1 [3.4; 8.8]	<0.001*	3.7 [0.7; 6.6]	0.015*	2.8 [-0.4; 6.0]	0.091
<i>Total VPA (min/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	0.4 [0.1; 0.7]	0.012*	0.2 [-0.1; 0.5]	0.242	0.2 [-0.1; 0.5]	0.245
<i>Total MVPA (min/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	6.5 [3.3; 9.7]	<0.001*	4.2 [0.7; 7.6]	0.018*	3.3 [-0.1; 6.7]	0.057
<i>Total sedentary behavior (hour/day)</i>						
Diabetes	(reference)		(reference)		(reference)	
Prediabetes	-0.6 [-1.0; -0.3]	0.001*	-0.3 [-0.7; 0.01]	0.056	-0.4 [-0.8; -0.1]	0.021*

$\beta$  coefficients and 95 % confidence intervals (95 % CI) represent median difference in LPA, MPA, VPA, MVPA (min/day) and sedentary behavior (hour/day) compared with participants with diabetes as the reference. Significant results (p<0.05) are marked with \*.

<sup>a</sup> Model 1: Multivariable regression model adjusted for age and sex

<sup>b</sup> Model 2: Multivariable regression model adjusted for age, sex, and BMI

<sup>c</sup> Model 3: Multivariable regression model adjusted for age, sex, BMI, comorbidities, stress, mental well-being, and chronic pain

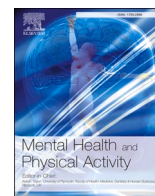
# Appendix III

## Paper III

Sedentary activity, sedentary bouts, and patterns of total daily sedentary activity, and their relationship with stress and well-being in individuals with diabetes and prediabetes: The Lolland-Falster Health Study

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## Sedentary activity, sedentary bouts, and patterns of total daily sedentary activity, and their relationship with stress and well-being in individuals with diabetes and prediabetes: The Lolland-Falster Health Study

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### ABSTRACT

**Aims:** This study aimed to investigate the cross-sectional associations of stress and well-being with the total amount of sedentary activity and sedentary bouts in adults with diabetes and prediabetes. A secondary aim was to explore the sedentary activity pattern during a day in adults with diabetes and prediabetes.

**Methods:** This cross-sectional study from the Danish Lolland-Falster Health Study categorized participants into diabetes (including both type 1 and type 2 diabetes) and prediabetes based on their HbA1c level and self-reported use of diabetes medication. Exposures were Perceived Stress Scale (scores  $\geq 18$  = moderate to high stress) and WHO-5 Well-Being Index (scores  $\leq 50$  = low well-being). Outcomes were total daily sedentary activity and sedentary bouts assessed with thigh-worn and back-worn accelerometers.

**Results:** Among the 562 included adult participants, 15 % had low well-being and 65 % had moderate to high stress. Higher well-being was associated with lower total sedentary activity in participants with diabetes ( $-1.1$  min/day, 95 % CI  $-2.0$ ;  $-0.2$ , for every 1-point increase in WHO-score) and participants with prediabetes ( $-0.6$  min/day, 95 % CI  $-1.1$ ;  $-0.05$ , for every 1-point increase in WHO-score). No association was found between stress and sedentary activity. During a day, participants with diabetes were more sedentary with a mean difference of  $-0.7$  h/day (95 % CI  $-1.1$ ;  $-0.4$ ) when compared with participants with prediabetes.

**Conclusions:** This study found that higher well-being is associated with lower total daily sedentary activity in individuals with diabetes and prediabetes, while no association between stress and sedentary activity was found. These findings imply that individuals with diabetes and prediabetes and low well-being may need additional support to reduce time spent on daily sedentary activity.

### 1. Background

Diabetes has become one of the most prevalent chronic conditions worldwide (*International Diabetes Federation. IDF Diabetes Atlas, 10th edn., 2021*), and regular physical activity plays an important role in

diabetes management and prevention (*Colberg et al., 2016; Kanaley et al., 2022*). However, reduction in sedentary activity, defined as total amount of time spent in a sitting, reclined or lying position during waking hours, has become an important focus in diabetes management due to the detrimental health effects (*Kerr & Booth, 2022*). Therefore,

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adults with diabetes are recommended to reduce sedentary time and place small “doses” of light physical activity every 30 min throughout the day to break up sitting time in addition to the general recommendations of physical activity (American Diabetes Association, 2022; Kanaley et al., 2022). As both physical inactivity and high sedentary activity influences the risk of all-cause mortality, targeting sedentary activity is still important to reduce risk even though an individual is sufficiently physically active (Dunstan, Dogra, Carter, & Owen, 2021).

Living with diabetes can be very stressful due to additional demands of self-management in terms of physical activity, diet, and medication (Dennick, Sturt, & Speight, 2017). Depression, anxiety, high perceived stress, and low well-being are more prevalent in individuals living with diabetes compared to the general population (Huang, Brown, Ewigman, Foley, & Meltzer, 2007; Jing et al., 2018; Mortensen et al., 2022; Perrin, Davies, Robertson, Snoek, & Khunti, 2017). While perceived stress reflects a state of emotional burden when demands exceed an individual's perceived resources (Sheldon Cohen, 1988), well-being involves emotional, physical, and social parameters (World Health Organization, 2022). Studies within the field of diabetes indicate that low well-being may have a substantial negative impact upon diabetic control and self-care in relation to the diabetes (Gonzalez et al., 2007; Gonzalez, Shreck, Psaros, & Safren, 2015; Papanas et al., 2010). Furthermore, a recent Danish nationwide cross-sectional study found that individuals with diabetes who suffered from high perceived stress and low health-related quality of life (HRQoL) were less likely to engage in regular physical activity (Mortensen et al., 2022). These results suggest that stress and well-being in individuals with diabetes may challenge their ability to adhere to lifestyle recommendations.

While reaching the recommended levels of physical activity may be challenging, targeting reductions in time spent sedentary may seem like a more feasible strategy for this population. Despite the high prevalence of stress and low well-being in individuals with diabetes, it has yet to be investigated to what extent these factors are associated with a sedentary lifestyle among individuals with diabetes and prediabetes. Such knowledge could provide important insights about whether individuals with high levels of stress or low well-being may need additional support to enhance time spent non-sedentary to prevent the development of diabetes in individuals with prediabetes and future diabetes-related comorbidities and complications in those with diabetes.

The aim of this study was to investigate the associations of stress and well-being with the total amount of sedentary activity, characterized by sitting, reclining, and lying during waking hours, and durations of continuous sedentary bouts in adults with diabetes or prediabetes. A secondary aim was to explore the daily sedentary activity pattern during a day in adults with diabetes and prediabetes. We hypothesized that higher stress and lower well-being were associated with higher sedentary outcomes.

## 2. Methods

### 2.1. Setting and data sources

This cross-sectional study used data from a subsample of the participants in the Danish household-based, mixed rural-provincial population study; The Lolland-Falster Health Study (LOFUS) that aimed to establish baseline information on the health status of inhabitants of Lolland-Falster. Data were collected between February 2016 and February 2020. Inhabitants  $\geq 18$  years were randomly selected from the Danish Civil Registration System and invited to participate with their household members of all ages. Those who agreed to participate received a web-based questionnaire prior to a site visit with physical examinations and collection of biological samples. Detailed information about the LOFUS study protocol is available in Jepsen et al. (Jepsen et al., 2020). At the end of the physical examination, a subsample of the participants was asked to wear accelerometers (Petersen, Brønd, Benfeldt, & Jepsen, 2022). During the period spanning from February 2017

to November 2018, families were considered eligible for inclusion if minimum one adult and one child consented to participate in accelerometer assessment. Subsequently, from December 2018 to February 2020, eligibility for inclusion was extended to all LOFUS participants (Petersen et al., 2020).

LOFUS was approved by Region Zealand's Ethical Committee on Health Research (SJ-421) and the Danish Protection Agency (REG-024-2015) and registered in Clinical Trials (NCT02482896). Data storage and management for the present study were approved by the Danish Data Protection Agency through the University of Southern Denmark (Journal nr.: 11.396). Written informed consent was obtained at the site visit (Jepsen et al., 2020).

This study is reported in accordance with the “Strengthening the Reporting of Observational Studies in Epidemiology” (STROBE) checklist (Vandenbroucke et al., 2014).

### 2.2. Study population

In total, 7208 LOFUS participants (18 years or above) were eligible to wear accelerometers. LOFUS participants were included in the present study if they provided valid accelerometer data and information regarding diabetes status, perceived stress, and well-being.

The diabetes status of the participants was defined using information about their glycated hemoglobin level (HbA1c) obtained from a venous blood sample during the physical examination and analyzed using TOSOH-G8 (Tosoh Bioscience, Belgium) (Jepsen et al., 2020) and their self-reported use of antidiabetic medication. Participants were defined as “Have diabetes” if one of the following criteria were met: 1) HbA1c  $\geq 48$  mmol/mol, or 2) HbA1c  $< 48$  mmol/mol and self-reported use of antidiabetic medication.

Using the LOFUS data, it was not possible to distinguish between type 1 and type 2 diabetes. Participants with HbA1c levels between  $< 48$  mmol/mol and  $\geq 39$  mmol/mol and no self-reported use of antidiabetic medication were categorized as “Have prediabetes” according to the American Diabetes Association (ADA) (American Diabetes Association, 2022).

### 2.3. Exposures

**Stress (PSS).** Self-reported psychological stress over the past month was obtained with Cohen's 10-item Perceived Stress Scale (PSS) included in the LOFUS questionnaire. All items were summed into a total score ranging from 0 to 40, and a higher score indicates higher perceived stress (Cohen, Kamarck, & Mermelstein, 1983).

**Well-being (WHO-5).** Self-reported mental well-being over the last two weeks was assessed using the WHO-5 Well-Being Index (World Health Organization, 1998). Each question was scored from 0 (none of the time) to 5 (all of the time), however, scoring of the WHO-5 followed the recommendations by multiplying the raw score by 4 to obtain a percentage score ranging from 0 to 100. The total score of WHO-5 covers the entire dimension from the complete absence of well-being (score of 0) to the highest imaginable level of well-being (score of 100) (Topp, Østergaard, Søndergaard, & Bech, 2015).

### 2.4. Outcome

**Sedentary activity.** Sedentary activity and physical activity were assessed using two Axivity AX3 (Axivity, Newcastle UK) accelerometers placed on the lower back and the front of the right thigh, respectively. Participants were instructed to wear the accelerometers continuously for seven consecutive days (24 h/day), including during sleep and water activities and to reapply the accelerometers if they fell off (Petersen et al., 2022).

A minimum wear time of 22 h out of 24 h was the criterion for valid data for a day. Data for a measurement period were considered valid if the participant obtained at least three valid weekdays and one valid

weekend day. Valid data on sedentary activity required data from both accelerometers and a minimum of 10 h awake time. For calculation of total daily sedentary activity and physical activity, data were weighted by 5/7 for weekdays and 2/7 for weekend days. Time spent sedentary (sitting, reclined, or lying) was determined using the validated method described by Skotte et al. (Crowley et al., 2019; Skotte, Korshøj, Kristiansen, Hanisch, & Holtermann, 2014). Physical activity intensities were determined by generating ActiGraph counts using 10-s epochs from the raw acceleration (Brønd, Andersen, & Arvidsson, 2017). Data processing is described in detail in Petersen et al. (Petersen et al., 2020).

In the present study, the following sedentary activity and physical activity variables were included:

- Total sedentary activity (hours/day and minutes/day): Total time spent in a sitting, reclined, or lying position between 7:00 a.m. and 10:00 p.m. during a day, which was presumed to correspond to the waking hours for an adult.
- Sedentary bouts (number/day): A sedentary bout was classified if the individual had been in a sitting or lying position for at least 10 s duration.
- Categories of sedentary bouts in terms of duration on a given day: <1 min,  $\geq 1$  to <3 min,  $\geq 3$  to <10 min,  $\geq 10$  min to <30 min, and  $\geq 30$  min.
- Prolonged sedentary bouts (number/day): Sedentary bouts of >30 min during a given day.
- Breaks in sedentary activity in terms of duration on a given day: A break in sedentary activity during waking hours was defined as a transition from a sitting, reclined, or lying position of at least 10 s duration to any of the following positions/activities of at least 10 s duration during waking hours: Stand, move, walk, and run. The following categories of breaks in sedentary activity were made based on the distribution: <1 min,  $\geq 1$  min to <3 min,  $\geq 3$  min to <10 min, and  $\geq 10$  min.
- Moderate to vigorous physical activity (MVPA): Minutes per day spent in moderate to vigorous intensity activity measured from the lower back-worn accelerometer. The intensity cut-points for moderate and vigorous in adults were 3522 and 6016 counts (Petersen et al., 2020).

### 2.5. Participant characteristics and covariates

Information about age and sex of the participants came from the Civil Registration System, and other background information stemmed from the LOFUS questionnaire (Egholm et al., 2020).

**Self-reported measurements.** Marital status was dichotomized into: “Married or living with partner” or “Living alone”. Highest level of education was categorized into 1) Primary, lower secondary, or other education, 2) Upper secondary (shorter length education (2–3 years)) or vocational education, and 3) Higher education (medium (3–4 years) and longer (>4 years) length higher education). Self-reported occupational status was categorized into 1) Employed, student, or other, 2) Unemployed or absent due to sick leave, and 3) Retired. Information on a variety of long-term conditions was used to assess the prevalence of comorbidity in addition to diabetes. The definition of comorbidity was based on the ten body system groups (lung, musculoskeletal, endocrine (excluding diabetes), mental conditions, cancer, neurological, gastrointestinal, cardiovascular, kidney, sensory organs) according to Willadsen et al. (Willadsen et al., 2018). The comorbidity variable was categorized as follows: 1) No comorbidities, 2) One comorbidity from one body system, 3) Two or more comorbidities from two different body systems. Long-lasting chronic pain was reported as Yes or No.

**Body mass index (BMI).** Participants’ height and weight were obtained at the health examination to calculate BMI ( $\text{kg}/\text{m}^2$ ) and categorized into three following the definitions from the World Health Organization (World Health Organization, 2000): Underweight/normal weight ( $\text{BMI} < 25$ ), overweight ( $\text{BMI} \geq 25$ –<30), and obese ( $\text{BMI} \geq 30$ ).

### 2.6. Statistical analyses

A statistical analysis plan (SAP) with detailed information about variables and the chosen analyses was developed prior to commencing the analyses (Mortensen, Grøntved, et al., 2023). However, the stress categories were changed due to low numbers in the original developed categories from the SAP. A variable that distinguished between the prevalence of low stress (scores below <18) and moderate to high stress (scores  $\geq 18$ ) was developed, because this cut-off corresponds to the upper quintile of PSS levels in Denmark and is associated with higher mortality (Prior et al., 2016). Likewise, a variable for well-being distinguishing between the prevalence of low well-being (scores  $\leq 50$ ) and moderate to high well-being was developed based on previous research (Topp et al., 2015).

We used the `dstat` function in STATA (Jann, 2022) to describe and test statistical distributions by diabetes status (diabetes and prediabetes) and groups of stress and well-being with standardization for age and sex. Participant characteristics and estimation of sedentary outcomes and MVPA of participants with diabetes and prediabetes with low and moderate to high levels of stress or well-being were summarized and presented in tables.

Multiple linear regression models were performed to investigate the association between the exposures stress and well-being and total sedentary activity in participants with diabetes and prediabetes. In these models, stress and well-being were treated as continuous variables, and total sedentary activity was converted from h/day to min/day to represent the differences in a better readability. Additionally, multiple quantile regression models were performed to investigate the association between stress and well-being (exposures) and sedentary bouts and prolonged sedentary bouts in participants with diabetes and prediabetes. Models with stress were adjusted for age and sex in the first model, and additionally adjusted for educational level, occupational status, marital status, BMI, and comorbidities in the second model. Models with well-being were adjusted for the same covariates, but the second model also included chronic pain. The included variables were suggested a priori based on previous literature and hypotheses of the potential biasing paths between exposures and outcomes using Directed Acyclic Graphs (DAGs) (Shrier & Platt, 2008) (for more information see SAP).

Mixed linear regression models were used to estimate and subsequently display the daily sedentary profile (mean time spent on sedentary activity over the waking hours (per 15 min)) between participants with diabetes and participants with prediabetes. We used a Savitzky-Golay smoothing filter with an order of 3 and length of 15 to generate a smoothed trend based on the point estimates for every 15-min obtained from the mixed model. Three models were performed to investigate the extent to which differences in the sedentary pattern between individuals with diabetes and prediabetes were explained by stress or well-being. The first one was adjusted for age and sex, the second one for age, sex, and stress, and the third model for age, sex, and well-being.

All statistical analyses were performed in STATA/BE 17.0 and R statistical (R Core Team, Vienna, Austria) software version 2023.06.0 + 421. RStudio (RStudio Inc., Boston, MA, USA) version 2022.07.2 using an  $\alpha$ -level of 0.05 two-sided, and assumption checks were performed for all statistical tests.

### 3. Results

We included 562 participants, of whom 144 (26 %) had diabetes, and 418 had prediabetes (74 %) (Fig. 1 – Flowchart). Among all participants, 65 % had moderate to high stress and 15 % had low well-being. Additionally, among those with diabetes, 65 % had moderate to high stress and 19 % had low well-being, while the corresponding numbers among those with prediabetes were 66 % and 14 %. Characteristics of participants with diabetes and prediabetes across categories of stress and well-being are presented in Tables 1 and 2.

Among participants with diabetes and prediabetes, time spent on

## Flowchart of included participants

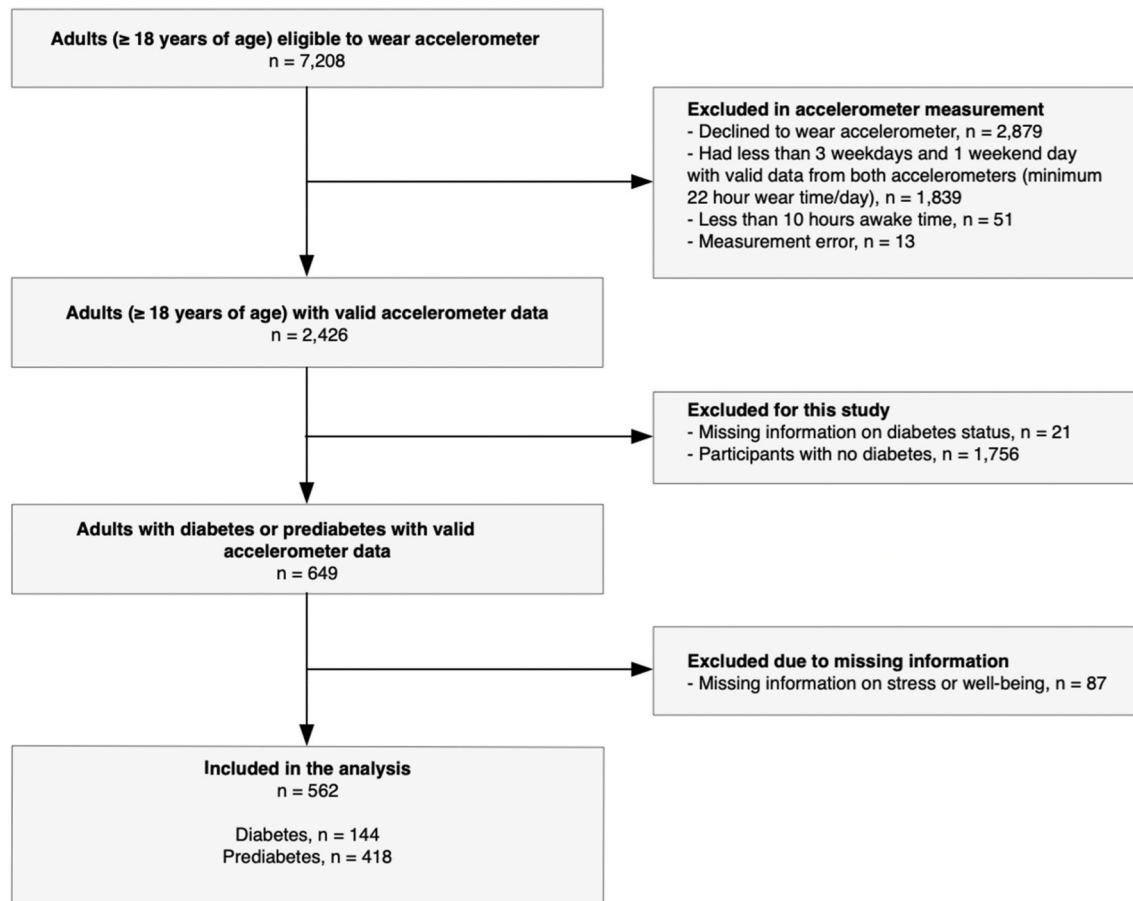


Fig. 1. Flowchart of included participants in the present study.

Table 1

Age- and sex standardized characteristics of participants with diabetes and prediabetes with low and moderate to high levels of stress.

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low stress	Moderate/high stress	Low stress	Moderate/high stress	Low stress	Moderate/high stress
n (%)	50 (35 %)	94 (65 %)	144 (34 %)	274 (66 %)	194 (34 %)	368 (65 %)
Married/Living with partner	38 (76.2)	78 (83.0)	108 (75.3)	223 (81.9)	146 (75.6)	300 (81.8)
Educational level						
Primary, lower secondary or other education	15 (30.5)	9 (10.0)	16 (11.4)	40 (14.8)	31 (16.0)	47 (12.8)
Upper secondary or vocational education	29 (58.1)	60 (63.4)	99 (69.6)	159 (58.3)	128 (66.8)	219 (59.9)
Higher education	6 (11.5)	25 (26.6)	27 (19.0)	73 (26.9)	33 (17.2)	100 (27.3)
Occupational status						
Employed, student, other	19 (39.0)	24 (25.9)	65 (46.0)	101 (38.7)	85 (44.2)	127 (35.9)
Unemployed, absent due to sick leave	4 (7.4)	13 (14.6)	2 (1.2)	19 (7.1)	6 (2.9)	31 (8.7)
Retired	27 (53.6)	54 (59.5)	75 (52.8)	142 (54.2)	102 (52.9)	196 (55.4)
BMI categories <sup>a</sup>						
Underweight/normal weight	8 (16.4)	9 (10.4)	32 (22.7)	71 (26.6)	40 (18.1)	81 (23.0)
Overweight	10 (20.6)	30 (33.8)	55 (39.6)	111 (41.7)	65 (32.3)	140 (39.4)
Obese	30 (63.0)	50 (55.8)	52 (37.6)	84 (31.7)	82 (49.7)	134 (37.8)
Suffers from chronic pain	21 (42.3)	48 (51.6)	40 (28.4)	102 (37.4)	60 (31.6)	150(41.0)
Comorbidities						
No comorbidities	9 (18.6)	11 (11.4)	33 (22.8)	47 (17.2)	42 (21.9)	57 (15.5)
1 comorbidity	18 (36.6)	21 (22.8)	51 (35.7)	78 (28.6)	70 (36.1)	102 (27.7)
≥2 comorbidities	22 (44.8)	62 (65.8)	60 (41.5)	148 (54.1)	82 (42.1)	209 (56.8)

n varies due to variations in complete responses within each variable.

Categorical data are presented as n and proportion (%) with standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference).

<sup>a</sup>BMI categories: Underweight/normal weight (<25.0), Overweight (BMI ≥25-<30), and obese (BMI ≥30).

**Table 2**

Age- and sex standardized characteristics of participants with diabetes and prediabetes with low and moderate to high levels of well-being.

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being
n (%)	28 (19 %)	116 (81 %)	57 (14 %)	361 (86 %)	85 (15 %)	477 (85 %)
Married/Living with partner	19 (67.1)	97 (83.2)	40 (71.3)	292 (81.2)	59 (70.2)	388 (81.6)
Educational level						
Primary and lower secondary or other education	3 (11.4)	22 (18.6)	10 (18.1)	47 (13.1)	13 (14.7)	67 (14.1)
Upper secondary or vocational education	19 (68.8)	68 (58.7)	33 (57.1)	225 (63.1)	52 (61.4)	295 (62.3)
Higher education	6 (19.8)	26 (22.7)	14 (24.8)	85 (23.8)	20 (23.9)	112 (23.6)
Occupational status						
Employed, student, other	9 (30.9)	35 (30.9)	19 (34.8)	152 (43.3)	27 (33.0)	187 (40.5)
Unemployed, absent due to sick leave	7 (26.0)	9 (8.4)	7 (13.2)	13 (3.7)	15 (17.8)	22 (4.8)
Retired	12 (43.1)	69 (60.7)	28 (52.0)	185 (53.0)	40 (49.3)	253 (54.7)
BMI categories <sup>a</sup>						
Underweight/normal weight	2 (8.8)	16 (15.0)	12 (21.4)	89 (25.5)	14 (16.7)	107 (23.2)
Overweight	5 (18.7)	32 (28.8)	23 (40.3)	144 (41.3)	27 (32.3)	176 (38.4)
Obese	20 (72.5)	62 (56.1)	21 (38.3)	116 (33.2)	43 (51.0)	176 (38.4)
Suffers from chronic pain	21 (75.1)	47 (40.9)	39 (68.9)	105 (29.5)	60 (71.0)	153 (32.3)
Comorbidities						
No comorbidities	0 (0)	19 (16.4)	4 (7.7)	74 (20.4)	5 (5.8)	92 (19.3)
1 comorbidity	5 (19.5)	34 (29.4)	11 (19.2)	123 (34.0)	16 (18.9)	160 (33.5)
≥2 comorbidities	23 (80.5)	63 (54.2)	42 (73.1)	164 (45.5)	64 (75.3)	225 (47.2)

n varies due to variations in complete responses within each variable.

Categorical data are presented as n and proportion (%) with standardization on age and sex (entropy balancing with the distribution of age and sex in the total sample as the reference).

<sup>a</sup>BMI categories: Underweight/normal weight (<25.0), Overweight (BMI ≥25-<30), and obese (BMI ≥30).

total sedentary activity, number of sedentary bouts, durations of sedentary bouts, and breaks in sedentary activity were almost similar between those with moderate to high stress and those with low stress. Daily median MVPA among participants with diabetes and moderate to high stress were 4.8 min/day (IQR: 1.5–12.4), while those with low stress had a median of 8.0 min MVPA/day (IQR: 1.9–17.7) (Table 3). Participants with low well-being and diabetes spent on average 11.0 h/day ±1.8 on total sedentary activity, while those with prediabetes were sedentary 10.2 h/day ±1.9. Further, median MVPA among those with diabetes and low well-being was 4.8 min/day (IQR: 0.8–9.0), whereas those with moderate to high well-being had a median MVPA of 5.4 min/day (IQR: 1.8–18.1) (Table 4).

Table 5 represents the results of the primary analyses. Among participants with diabetes or prediabetes, no association between stress (PSS) and total sedentary activity was found. Higher well-being (WHO-

5) was significantly associated with lower total sedentary activity after adjustments in participants with diabetes (−1.1 min/day, 95 % CI -2.0; −0.2, for every 1-point increase in WHO-5) and participants with prediabetes (−0.6 min/day, 95 % CI -1.1; −0.05, for every 1-point increase in WHO-5). No association was observed between sedentary bouts, prolonged bouts and stress. In participants with prediabetes, higher well-being was associated with a lower number of sedentary bouts after adjustments (−0.2 bouts/day, 95 % CI -0.3; −0.06, for every 1-point increase in WHO-5). Moreover, higher well-being was significantly associated with a lower number of prolonged sedentary bouts in participants with diabetes after adjusting for age and sex, but results became insignificant in the fully adjusted model.

Participants with diabetes spent on average more time on sedentary activity during the whole day when compared with participants with prediabetes after adjusting for age and sex. In both groups, a decline in

**Table 3**

Distribution of age- and sex standardized total sedentary activity, sedentary bouts, duration of breaks in sedentary activity, and MVPA among participants with diabetes, prediabetes, and total sample with low and moderate to high levels of stress.

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low stress	Moderate/high stress	Low stress	Moderate/high stress	Low stress	Moderate/high stress
n (%)	50 (35 %)	94 (65 %)	144 (34 %)	274 (66 %)	194 (35 %)	368 (65 %)
Total sedentary activity (h/day)	10.1 ± 1.8	10.3 ± 1.8	9.4 ± 1.7	9.5 ± 1.6	9.6 ± 1.8	9.7 ± 1.7
Sedentary bouts (n/day)	49 (42–59)	49 (40–59)	50 (43–62)	53 (43–67)	50 (43–62)	51 (43–65)
Prolonged sedentary bouts (>30 min) (n/day)	5 (5–7)	6 (5–7)	5 (4–6)	5 (4–6)	5 (4–6)	5 (4–6)
Sedentary bout duration (n/day)						
<1 min.	13 (10–19)	13 (9–18)	15 (11–20)	16 (11–24)	15 (10–20)	15 (11–22)
≥1 to <3 min.	8 (7–12)	9 (6–11)	9 (7–12)	9 (7–13)	9 (7–12)	9 (7–12)
≥3 to <10 min.	11 (8–15)	11 (9–14)	12 (9–16)	12 (9–16)	12 (9–16)	12 (9–16)
≥10 min to <30 min	10 (9–12)	10 (8–12)	10 (8–12)	10 (9–12)	8 (10–12)	10 (8–12)
Breaks in sedentary activity duration (n/day)						
<1 min.	18 (13–27)	16 (12–24)	19 (13–25)	20 (14–29)	19 (13–25)	19 (14–27)
≥1 to <3 min	12 (9–16)	12 (9–16)	12 (10–16)	12 (9–16)	12 (10–16)	12 (9–16)
≥3 to <10 min.	10 (8–12)	11 (9–13)	12 (9–14)	12 (9–14)	11 (9–14)	12 (9–14)
≥10 min.	7 (6–9)	7 (5–9)	9 (7–10)	9 (7–10)	8 (6–10)	8 (6–10)
MVPA (min/day)	8.0 (1.9–17.7)	4.8 (1.5–12.4)	10.6 (4.6–23.7)	12.1 (5.1–26.6)	9.3 (3.9–22.0)	9.9 (3.6–24.7)

Data are standardized on age and sex. Continuous data are presented as means with standard deviations or medians and interquartile range (25th and 75th quartile).



**Table 4**

Distribution of age- and sex standardized total sedentary activity, sedentary bouts, duration of breaks in sedentary activity, and MVPA among participants with diabetes, prediabetes, and total sample with low and moderate to high levels of well-being.

	Diabetes n = 144		Prediabetes n = 418		Total sample n = 562	
	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being	Low well-being	Moderate/high well-being
n (%)	28 (19 %)	116 (81 %)	57 (14 %)	361 (86 %)	85 (15 %)	477 (85 %)
Total sedentary activity (h/day)	11.0 ± 1.8	10.1 ± 1.7	10.2 ± 1.9	9.4 ± 1.6	10.5 ± 1.9	9.6 ± 1.6
Sedentary bouts (n/day)	51 (38–68)	48 (40–58)	57 (47–75)	51 (43–66)	57 (43–72)	51 (43–64)
Prolonged sedentary bouts (>30 min) (n/day)	6 (5–8)	6 (5–7)	5 (4–7)	5 (4–6)	6 (4–7)	5 (4–6)
Sedentary bout duration (n/day)						
<1 min.	13 (10–17)	13 (9–19)	18 (10–24)	15 (11–22)	17 (10–23)	15 (10–22)
≥1 to <3 min.	8 (6–12)	8 (6–11)	9 (7–13)	9 (7–13)	9 (7–13)	9 (6–12)
≥3 to <10 min.	11 (8–15)	11 (8–14)	12 (10–17)	12 (9–16)	12 (9–16)	12 (9–16)
≥10 min to <30 min	10 (9–12)	10 (8–12)	10 (8–12)	10 (8–12)	10 (8–12)	10 (8–12)
Breaks in sedentary activity (n/day)						
<1 min.	16 (13–24)	17 (12–25)	23 (18–31)	19 (14–26)	22 (15–31)	19 (13–26)
≥1 to <3 min	12 (10–15)	12 (9–16)	13 (11–17)	12 (9–16)	13 (10–17)	12 (9–16)
≥3 to <10 min.	10 (8–14)	11 (9–13)	11 (9–13)	12 (9–14)	11 (8–13)	12 (9–14)
≥10 min.	6 (4–7)	8 (6–10)	7 (5–10)	9 (7–10)	6 (4–9)	9 (7–10)
MVPA (min/day)	4.8 (0.8–9.0)	5.4 (1.8–18.1)	9.4 (1.9–17.5)	12.2 (5.0–26.3)	6.3 (1.8–13.3)	10.7 (4.0–25.3)

Data are standardized on age and sex. Continuous data are presented as means with standard deviations or medians and interquartile range (25th and 75th quartile).

**Table 5**

Cross-sectional association between stress and well-being and total sedentary activity, sedentary bouts, and prolonged sedentary bouts among participants with diabetes and prediabetes.

	Diabetes			
	Model 1 <sup>a</sup> n = 141		Model 2 <sup>b</sup> n = 141	
	β [95 % CI]	p-value	β [95 % CI]	p-value
<b>Stress (PSS)</b>				
Total sedentary activity (min/day) <sup>c</sup>	0.7 [-2.7; 4.0]	0.683	-0.9 [-4.5; 2.7]	0.632
Sedentary bouts (n/day) <sup>d</sup>	-0.5 [-1.1; 0.2]	0.153	-0.4 [-1.1; 0.4]	0.327
Prolonged sedentary bouts (n/day) <sup>d</sup>	0.04 [-0.03; 0.1]	0.216	-0.02 [-0.1; 0.05]	0.551
<b>Well-being (WHO-5)</b>				
Total sedentary activity (min/day) <sup>c</sup>	-1.2 [-2.0; -0.4]	0.003*	-1.1 [-2.0; -0.2]	0.023*
Sedentary bouts (n/day) <sup>d</sup>	0.02 [-0.1; 0.2]	0.767	-0.05 [-0.2; 0.1]	0.605
Prolonged sedentary bouts (n/day) <sup>d</sup>	-0.02 [-0.03; -0.01]	0.002*	-0.01 [-0.03; 0.002]	0.100
	Prediabetes			
	Model 1 n = 403		Model 2 n = 403	
	β [95 % CI]	p-value	β [95 % CI]	p-value
<b>Stress (PSS)</b>				
Total sedentary activity (min/day) <sup>c</sup>	0.7 [-1.6; 3.0]	0.528	0.3 [-1.8; 2.4]	0.795
Sedentary bouts (n/day) <sup>d</sup>	0.33 [-0.2; 0.8]	0.195	0.22 [-0.2; 0.7]	0.333
Prolonged sedentary bouts (n/day) <sup>d</sup>	0.003 [-0.03; 0.04]	0.834	-0.02 [-0.06; 0.02]	0.383
<b>Well-being (WHO-5)</b>				
Total sedentary activity (min/day) <sup>c</sup>	-1.0 [-1.5; -0.5]	<0.001*	-0.6 [-1.1; -0.05]	0.034*
Sedentary bouts (n/day) <sup>d</sup>	-0.1 [-0.2; 0.04]	0.191	-0.2 [-0.3; -0.06]	0.004*
Prolonged sedentary bouts (n/day) <sup>d</sup>	-0.01 [-0.02; 0.001]	0.076	0.001 [-0.01; 0.01]	0.886

Significant results ( $p < 0.05$ ) are marked with \*.

Well-being: Model 1: Multivariable regression model adjusted for age and sex.

Well-being: Model 2: Multivariable regression model adjusted for age, sex, educational level, occupational status, marital status, BMI, comorbidities, and chronic pain.

<sup>a</sup> Stress: Model 1: Multivariable regression model adjusted for age and sex.

<sup>b</sup> Stress: Model 2: Multivariable regression model adjusted for age, sex, educational level, occupational status, marital status, BMI, and comorbidities.

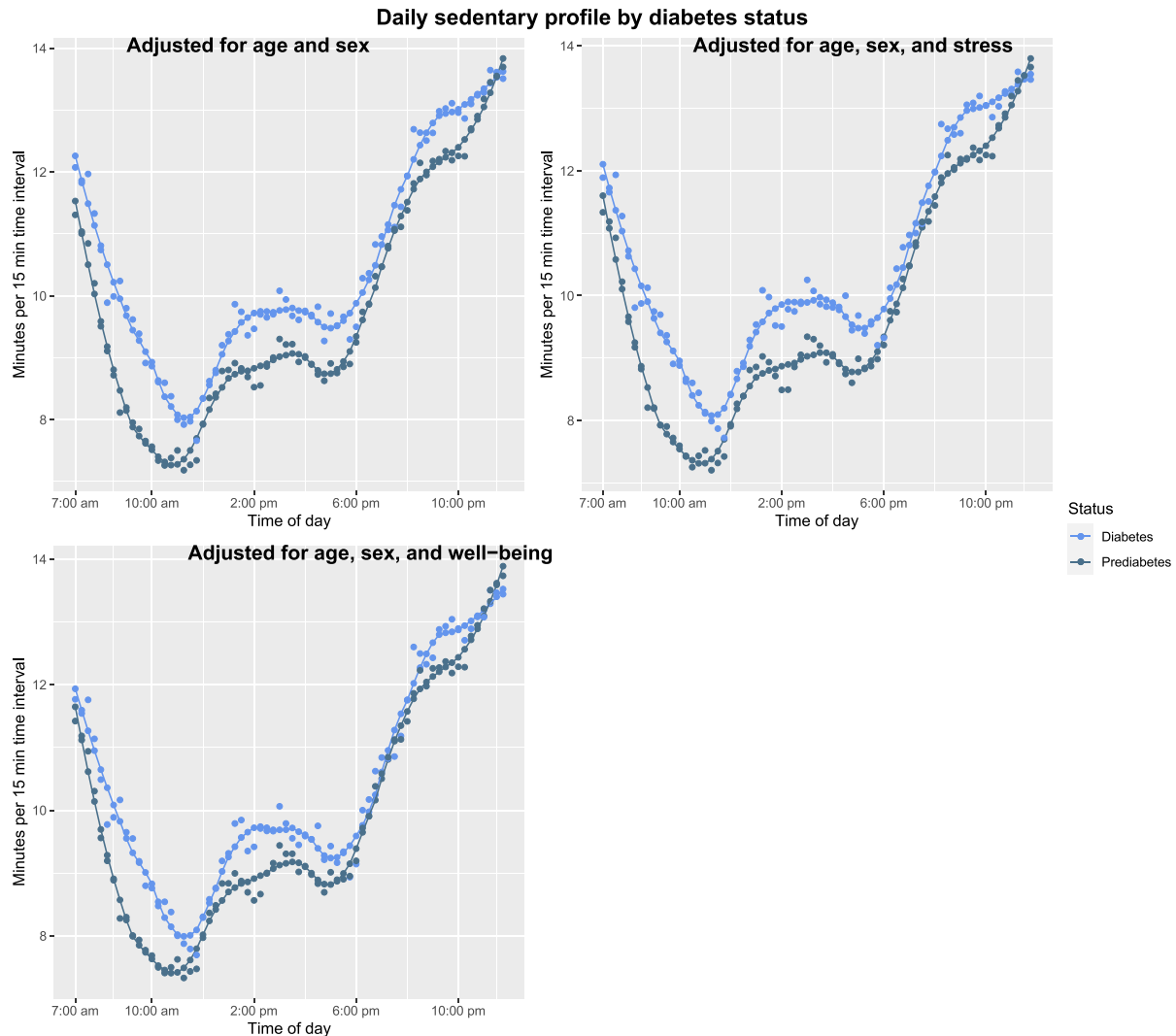
<sup>c</sup> Linear regression. β coefficients and 95 % confidence intervals (95 % CI) represent mean difference in total sedentary activity (min/day) per 1 point increase in PSS or WHO-5.

<sup>d</sup> Quantile regression. β coefficients and 95 % confidence intervals (95 % CI) represent difference in the median of sedentary bouts (n/day) and prolonged sedentary bouts (n/day) per 1 point increase in PSS or WHO-5.

sedentary activity was observed from 7:00 a.m. to 10:00 a.m., followed by an increase in sedentary activity which was stabilized until 6:00 p.m., and then a steep increase occurred until night. Mean difference in total daily sedentary activity between participants with diabetes and participants with prediabetes was  $-0.7$  h/day (95 % CI  $-1.1$ ;  $-0.4$ ) when adjusting for age and sex, and when stress was included in the analysis, the difference was similar  $-0.7$  h/day (95 % CI  $-1.1$ ;  $-0.4$ ). However, when adjusting for well-being in addition to age and sex, the difference between groups in total sedentary activity during a day was attenuated with a mean difference of  $-0.6$  h/day (95 % CI  $-1.0$ ;  $-0.4$ ) (Fig. 2).

#### 4. Discussion

We found that higher well-being was significantly associated with lower total sedentary activity in participants with diabetes and participants with prediabetes. No association between stress and total sedentary activity was found. Participants with diabetes and prediabetes and low well-being were more sedentary and had lower daily MVPA compared with participants with moderate to high well-being. Further, participants with diabetes and prediabetes and moderate to high stress were as sedentary as those with low stress. During a day, participants with diabetes spent slightly more time on sedentary activity compared



**Fig. 2.** Daily sedentary profiles by diabetes status are presented as mean time (minutes per 15 min interval) spent on sedentary activity during a day adjusted for age and sex, stress, and well-being, respectively. The points represent the raw age- and sex adjusted estimates, and the fitted line represents a smoothing trend based on the point estimates.

with participants with prediabetes, and these differences between groups became even smaller when adjusting for well-being.

#### 4.1. Comparison with existing research

In a prior study on a national cohort of individuals with diabetes (Mortensen et al., 2022), we found no association between HRQoL and time spent on sedentary behavior during a day among individuals with diabetes. This is inconsistent with the association between higher well-being and lower total daily sedentary activity demonstrated in the current study. Partially, however, it may be explained by the fact that although well-being and HRQoL relates, they are not the same. While HRQoL specifically evaluates the impact of health on the individual's quality of life, well-being encompasses a broader spectrum of life satisfaction, including relationships, satisfaction with work etc. (Sfeatcu et al., 2014; Spiro & Bossé, 2000).

Similar to the current results, our prior study (Mortensen et al., 2022) did not find an association between stress and sedentary behavior in individuals with diabetes. Sedentary behavior was self-reported in our prior study, which is suggested to generally under-report time spent sedentary when compared to device-measures (Prince et al., 2020). However, a systematic review by Teychenne et al. (Teychenne et al., 2019) found divergent results in the relationship between sedentary behavior and stress among healthy adults depending on objectively measured and self-reported sedentary behavior. Further, self-reported sedentary behavior may capture context-specific behaviors, such as watching TV or time sitting at work, in which some types of sedentary behavior may be stronger related with stress than others (Pedersen et al., 2022; Teychenne et al., 2019). As individuals with diabetes are more inactive, sedentary, and have higher levels of stress compared to healthy individuals (Martinez-Harvell, Goluboff, Rodriguez, Castro, & Barenco, 2020; Mortensen et al., 2022; Mortensen, Skou, et al., 2023), stress and sedentary activity may be stronger related within the diabetes population.

#### 4.2. Well-being and sedentary activity

In this study, we found that lower well-being was associated with higher daily sedentary activity.

Low well-being may prevent individuals with diabetes in various ways from engaging in physical activity and thereby leading to increases in sedentary time. Individuals with low well-being may experience social withdrawal and lack motivation, reducing opportunities for engaging in physical activities that involve social interaction (Gonzalez et al., 2007, 2015). However, as a sedentary lifestyle can contribute to low well-being by reductions in energy, motivation, and other health challenges associated with diabetes, the relationship between well-being and sedentary activity may be cyclical where low well-being reinforces sedentary lifestyle, and vice versa.

The observed association between well-being and total daily sedentary activity after adjustments was  $-1.1$  min/day among participants with diabetes and  $-0.6$  min/day among participants with prediabetes for every 1-point increase in WHO-5. A 10-point change on the WHO-5 is considered to be clinically relevant (Bech, Lunde, Bech-Andersen, Lindberg, & Martiny, 2007), which in this study would correspond to a reduction in sedentary time of 11 min/day among individuals with diabetes and 6 min/day in individuals with prediabetes. Whether this reduction in total sedentary time is of relevance is questionable. However, according to the risk matrix on the interacting influences of sedentary behavior and physical activity on all-cause mortality in men and women (regardless of health status) by Dunstan et al. from 2021 (Dunstan et al., 2021), daily sitting time should be reduced to below 8 h/day to decrease the risk of all-cause mortality. Therefore, a reduction of 11 min/day in sedentary activity would most likely not influence the risk of all-cause mortality in our study, as the mean sedentary time was 11.0 h/day among participants with diabetes and low well-being and

10.2 h/day among those with prediabetes and low well-being. As the risk matrix shows, opportunities for risk reduction include both increases in physical activity (including walking and MVPA), reductions in time spent sitting, or a combination of both. Hence, if a 11 min/day reduction in sedentary activity is replaced with physical activity, the risk of all-cause mortality will be reduced from high to medium (Dunstan et al., 2021). However, it is important to note that the risk matrix may be different among individuals suffering solely from diabetes, because individuals with diabetes are at higher risk of complications that may increase the risk of premature mortality (Ahmad, Lim, Lamptey, Webb, & Davies, 2022). In addition, comparisons of results between studies measuring sedentary behavior are challenged by lack of consensus about the method used in the data reduction process (J. H. Migueles et al., 2017; Jairo H. Migueles et al., 2022).

#### 4.3. Sedentary patterns

The amounts of daily sedentary activity among participants with diabetes and prediabetes in our study were remarkably high. Consequently, it is important to provide recommendations on reductions in sedentary activity to individuals with diabetes and prediabetes irrespective of their level of stress and well-being. Also, a study by Cooper et al. (Cooper et al., 2014) emphasized the potential benefits of reducing sedentary time, particularly among the least active individuals with type 2 diabetes. Considering the small amounts of daily MVPA and the sedentary profiles among participants with diabetes and prediabetes observed in this study, there is a great potential to increase physical activity in the evening, because the profiles showed a steep increase in sedentary activity from 6:00 p.m. until night. Replacing sedentary activity with physical activity of any intensity is strongly recommended for adults and older adults with chronic conditions (World Health Organization, 2020). From a whole-day perspective (Davies et al., 2022) and based on the sedentary profiles found in this study, reductions in sedentary activity should be placed in the evening to avoid several prolonged sedentary bouts. Furthermore, the observed sedentary pattern in the evening could occur due to barriers in engagement in physical activity, such as lack of motivation, support from family or peers, or maybe the available physical activity interventions do not accommodate with the individual's needs (Korkiakangas, Alahuhta, & Laitinen, 2009; Lidgaard, Schwennesen, Willaing, & Faerch, 2016; Thorsen et al., 2022).

#### 4.4. Targeted interventions

In this study, we observed that most participants with low well-being were challenged by several factors, including more comorbidities, suffering from pain, minimal engagement in MVPA, and high levels of total sedentary activity. Although these factors were also prevalent among participants with diabetes and moderate to high stress, the proportions were remarkably high among those with low well-being. This suggests that having low well-being comes with additional challenges that may prevent the individual from engaging in physical activity as well as decreasing time spent sedentary. Given that these factors are closely linked to physical activity engagement and the fact that more than half of participants reported moderate to high stress, targeting improvements of well-being and reductions in stress could be highly relevant in diabetes management (Cradock et al., 2021; Mortensen et al., 2022). One potential approach to achieve this could involve integrating social support into existing diabetes treatment strategies, as this is essential in helping individuals initiate and maintain physical activity habits (Thorsen et al., 2022; Walker, Valentiner, & Langberg, 2018). Importantly, individuals consider social support as a resource that they are not able or responsible to mobilize (Thorsen et al., 2022). Therefore, social support should be organized as a part of the diabetes treatment structured by health professionals to ensure an establishment of a community that individuals with diabetes will keep attending.

#### 4.5. Strengths and limitations

A major strength of this study is the use of two accelerometers (one on the lower back and the other on the right thigh) to assess sedentary activity under free-living conditions. By using data from two accelerometers, we were able to detect time spent in a sitting, reclined, or lying position, and thereby obtaining a more precise estimate of time spent on total sedentary activities during a day. Further, we chose a limited period of waking hours (from 7:00 a.m. to 10:00 p.m.) to avoid including time spent sleeping, and participants had at least a total of four measurement days with a minimum of 10 h awake time. Another strength is the standardization of age and sex that was used in all analyses to increase comparison between participants with diabetes and prediabetes, and the adjustment of confounders that are suggested to be related to the outcomes and exposures.

The study has some limitations that are important to mention. First, the sample size of participants with diabetes was relatively small, especially among those with low well-being and low stress. Therefore, the observed differences between the groups of stress and well-being should be interpreted carefully. Further, it was voluntary to participate in the LOFUS study and the accelerometer measurement which may have introduced selection bias. In this study, we were unable to distinguish between type 1 and type 2 diabetes, which may have driven the association towards zero, as individuals with type 2 diabetes have distinct activity patterns due to older age, obesity, and other contextual factors compared to those with type 1 diabetes (Ahmad, Sargeant, Yates, Webb, & Davies, 2022). Our data showed that 65 % of participants with diabetes had moderate to high stress, which is higher than other studies from Denmark. Bo et al. (Bo, Pouwer, Juul, Nicolaisen, & Maindal, 2020) found that 46 % out of 216 individuals with early-onset type 2 diabetes had high stress level (PSS-score  $\geq 18$ ), while our previous cross-sectional study found that 50 % of 6856 individuals with diabetes had moderate to high stress (PSS-score  $\geq 14$ ) (Mortensen et al., 2022). LOFUS data are collected from a socio-economically disadvantaged area of Denmark (Poulsen, Eriksson, Christiansen, & Wingstrand, 2022), whereas the studies by Bo et al. and Mortensen et al. are based on national survey data (Bo et al., 2020; Mortensen et al., 2022). Therefore, we would expect the prevalence of stress to be higher when compared with other studies, however, those with highest levels of stress might still have declined to participate in the accelerometer measurement.

Although accelerometer measurement has its strengths in this study, our restricted timeframe may limit the study's ability to capture all sedentary activity. As we were not able to determine activities done seated, misclassification of time spent sedentary may have been introduced. Further, we did not account for seasonal differences in this study, however, in a previous study using the same data, we found no seasonal differences (Mortensen, Skou, et al., 2023). Additionally, it is important to keep in mind that one week of measurement with a median of six valid days may not reflect the individual's general sedentary activity.

The observed differences in sedentary patterns across levels of stress and well-being in our study population should not be interpreted as direct evidence of causation. These variations may stem from a complex interplay of physical activity compositions, including differences in MVPA, or other unidentified factors. The differences in MVPA observed across groups of stress and well-being further highlight the challenge of disentangling the inherent relationship between these behaviors within our study population. Yet, our observations of distinct sedentary patterns related to well-being, and the lack of a difference in sedentary time associated with stress levels, are not artifacts but evident findings. However, it remains unclear whether stress or well-being directly causes these observed differences in sedentary activity, or if they are due to more complex factors, including the overall composition of physical activity. Such complexities underscore the need for further research to elucidate the causal pathways connecting psychological factors, physical activity, and sedentary lifestyle.

## 5. Conclusion

We found that higher well-being scores were associated with lower total daily sedentary activity in individuals with diabetes and prediabetes, while no association was found between stress and sedentary outcomes. Results showed that individuals with diabetes and prediabetes and low well-being were more sedentary and had lower daily MVPA compared with individuals with moderate to high well-being. Further, individuals with moderate to high stress were as sedentary as individuals with low stress. During a day, individuals with diabetes spent more time on sedentary activity when compared with individuals with prediabetes. Our findings imply that individuals with diabetes and prediabetes and low well-being may need additional support to reduce time spent on daily sedentary activity, highlighting the importance of holistic approaches to diabetes management that address both physical and mental health aspects. Future studies should address mental health outcomes in relation to types and domains of sedentary behavior, as differences may exist.

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### CRedit authorship contribution statement

**Sofie Rath Mortensen:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Anders Grøntved:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Jan Christian Brønd:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Mathias Ried-Larsen:** Writing – review & editing, Visualization, Supervision, Conceptualization. **Therese Lockenwitz Petersen:** Writing – review & editing, Supervision, Data curation. **Lars Bo Jørgensen:** Writing – review & editing, Investigation. **Randi Jepsen:** Writing – review & editing, Data curation. **Lars Hermann Tang:** Writing – review & editing, Supervision. **Søren T. Skou:** Writing – review & editing, Visualization, Supervision, Conceptualization, Validation, Methodology, Investigation.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data is available from the LOFUS steering committee upon reasonable request

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# Appendix IV

## Paper IV

### Online Physical Exercise and Group Sessions to Increase and Maintain Physical Activity in Individuals with Type 2 Diabetes: A Single-Arm Feasibility Study

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Article

# Online Physical Exercise and Group Sessions to Increase and Maintain Physical Activity in Individuals with Type 2 Diabetes: A Single-Arm Feasibility Study

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**Abstract:** Current physical activity interventions for individuals with Type 2 diabetes do not accommodate the needs of the individual in terms of content, time, and location. The aim of this study was to evaluate the feasibility and acceptability of an 8-week high intensity online physical exercise intervention combined with online group meetings and supported by an activity watch in individuals with Type 2 diabetes. This study was designed as a one-armed feasibility study and the intervention was developed using a co-creation approach. A total of 19 individuals with Type 2 diabetes participated in eight weeks of 30 min online physical exercise intervention followed by 30 min online group meetings in smaller groups once a week. Outcomes included pre-defined research progression criteria, secondary measurements of health parameters, and participant feedback. Most research progression criteria reached a level of acceptance, with the exception of participant recruitment, burden of objectively measured physical activity, and adverse events, where changes are needed before continuing to an RCT. Combining online physical exercise with online group meetings supported by an activity watch is feasible and acceptable in individuals with Type 2 diabetes with a higher educational level compared to the general population with Type 2 diabetes.

**Keywords:** Type 2 diabetes; physical activity; online physical exercise; accelerometer; feasibility studies; eHealth; wearables



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## 1. Introduction

Engaging in physical activity behaviors is a key component in Type 2 diabetes management to improve health, quality of life, and prevent complications and premature mortality [1]. Increased physical activity is also considered a cornerstone in the treatment of hyperglycemia [1]. Hence, adults with Type 2 diabetes are recommended to engage in at least 150 min moderate- to vigorous-intensity weekly physical activity, to reduce the time spent sedentary, and break up sitting time with frequent activity breaks [1–3]. However, many individuals experience difficulties maintaining their motivation for physical activity [4,5]. Current physical activity interventions do not accommodate the needs of content, time, and location to preserve the individual's daily life while increasing physical activity [6]. During recent years and throughout the COVID-19 pandemic, the use of digital information and communication technologies in healthcare has increased significantly [7]. The use of activity wearables and internet-based interventions for physical activity promotion are recommended in adults with Type 2 diabetes to adopt and maintain a physically active lifestyle [8]. Physical activity interventions delivered online (online



physical exercise) could potentially meet the need of more physical activity interventions that enable the individual to attend the intervention despite a lack of resources and time, or geographical distances [6,9]. However, attending online physical exercise classes could result in a social distance causing reduced relational and mental effects and lower adherence to physical exercise sessions [9,10]. Social support is essential for individuals for managing efforts of engagement in physical activity and increase long-term adherence to physical activity interventions [6]. Combining online physical exercise with online group meetings could potentially offer health-related benefits and increase maintenance of daily engagement in physical activity through emotional and social support from individuals with similar challenges. The co-creation method involves patients in the development of health interventions, and it is an effective tool to improve adherence, satisfaction, and effectiveness [11,12]. The feasibility and effectiveness of a co-created online physical exercise intervention combined with online group meetings are yet undiscovered, although it might have a great potential to pave the way for permanent and free disease management among individuals with Type 2 diabetes. Therefore, the aim of this study was to evaluate the feasibility, fidelity, and acceptability of an 8-week high intensity online physical exercise program combined with online group meetings and supported with an activity watch in individuals with Type 2 diabetes. Outcomes included pre-defined research progression criteria, secondary subjective and objective measurements of a range of health parameters, and participant feedback.

## 2. Materials and Methods

### 2.1. Study Design

This study was designed as a one-armed feasibility study because most progression criteria were related to the received intervention. No blinding was applied in the present study. The study was carried out from 16 March to 18 May 2022 at the Centre for Physical Activity Research, Rigshospitalet, Copenhagen, Denmark. Reporting of the study followed the CONSORT extension to randomized pilot and feasibility trials [13] (Supplementary Material Table S1). This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Capital Region of Denmark (Protocol code: H-2106295 and date of approval: 13 January 2022) and retrospectively registered in clinicaltrials.gov (NCT05668442).

### 2.2. Participants

Participants were eligible if they were above 18 years of age, diagnosed with Type 2 diabetes by a general practitioner and with access to a computer, smartphone, or tablet. The exclusion criteria were participation in another intervention study simultaneously or within the last 3 months, and if the participant's general practitioner had advised against participation in exercise [14].

Participants were recruited from January to March 2022 from the Capital Region of Denmark and Region Zealand using several recruitment strategies such as posters on the website of the Danish Diabetes Association, via contacts from local organizations within the Danish Diabetes Association, posters in the local Diabetes Centre in Copenhagen, and lastly, participants with Type 2 diabetes from a previous trial at Centre for Physical Activity Research (CFAS) who were informed about the project through a social media forum. Potential participants underwent telephone screening with the project coordinator (MEP) to determine eligibility of participation.

### 2.3. Study Intervention

In this section, the framework of the development and design of the intervention and how it was conducted are described. First, the background for the theoretical choice of co-creation as a method with the involvement of the findings from Thorsen et al. [6], will be presented. Second, an introduction of the application of the co-creation process and a prototyping phase in practice and how it formed the actual intervention will occur.

### 2.3.1. Development of the Intervention

The rationale of developing the intervention was inspired by the findings of Thorsen et al. [6]. The study found three central themes as barriers to physical activity: (1) Physical activity conflicts with everyday life, (2) lack of physical activity opportunities and possibilities in technology, and (3) lack of community and social support. Together with the co-creation approach, these three themes created the framework for the intervention in this study. Firstly, the framework for the proposed intervention involved a physical exercise intervention that the participants could assess from their own digital device in different timeslots of a weekly day. Furthermore, the Garmin Vivofit 4 activity watch was suggested for the intervention due to its utility: small size, one year of battery life, price, and widgets. Secondly, following the online physical exercise session, it was proposed that the participants were divided into small online groups to establish relationships and social support. Lastly, the participants decided the content and agenda of the group room together. The intervention intended to initiate engagement in physical activity and support participants' ability and motivation to increase and maintain daily physical activity by themselves.

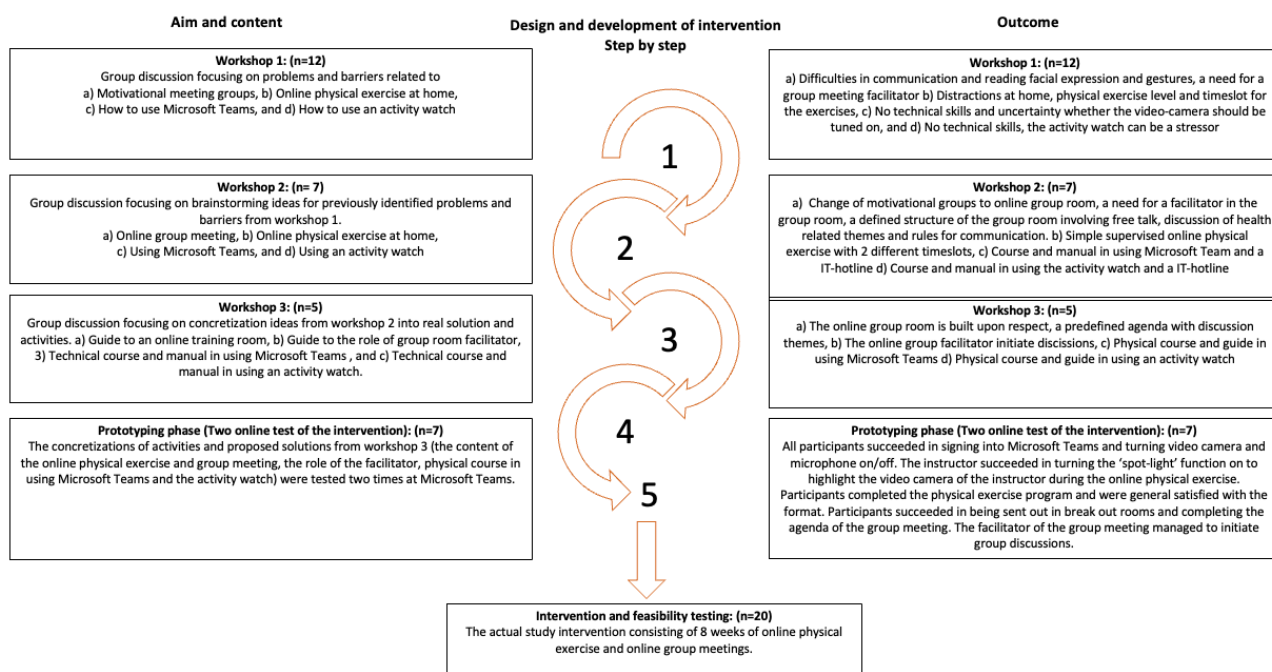
Co-creation is built upon collaborations between end-users (the target population), stakeholders (people who have interest or are involved in the intervention), and academic researchers (university researchers or health-related practitioners), all working together towards a common understanding [12]. We conducted three co-workshops, a prototyping phase, and an introduction course from September 2021 to March 2022. Prior to initiating the co-creation process, stakeholders were identified via a stakeholder analysis focusing on mapping local stakeholders [15]. Stakeholders included individuals that were diagnosed with Type 2 diabetes ( $n = 12$ ), health science researchers ( $n = 4$ ), physiotherapists and professionals from sports science ( $n = 3$ ), and consultants from the Danish Diabetes Association ( $n = 2$ ). When partnership between all the stakeholders was established, information about the framework of the intervention was explained with the purpose of engaging the stakeholders in agreeing on a common goal. Afterwards, all the stakeholders were invited to a series of three face-to-face co-workshops. The first co-workshop focused on problem exploration, including identifying key challenges and barriers linked to the online physical exercise and community format. The following two co-workshops were inspired by "the Future Workshop" model focusing on idea generation and proposing solutions to the previously identified barriers and concretizing those ideas into real solutions and actions [16]. Afterwards, intervention content was tested in the prototyping phase with the purpose of early identification of potential issues [12]. The delivery and content of the intervention were tested using a small sample of end-users ( $n = 7$ ) through two intervention sessions. During the test sessions, observations and feedback were obtained and refinements to the intervention were made. Following this, delivery and content were tested again. The result of the prototyping phase was the final prototype (i.e., the actual intervention) (Figure 1) [12].

### 2.3.2. Intervention

The intervention was standardized and described in accordance with the template for intervention description and replication checklist that was developed for telehealth-interventions (TIDieR-Telehealth) [17] (Supplementary Material Table S2). As a part of the intervention, participants physically attended an introduction course before baseline testing that aimed to educate the participants in the use of Microsoft Teams, Garmin activity watches, and accelerometers.

The participants were invited to participate in 8-weeks of online physical exercise of 30 min followed by 30 min of group meeting in smaller groups once a week from March to May 2022. The participants attended the online intervention through the platform Microsoft Teams from their own devices (e.g., computer, smartphone, tablet). The intervention was scheduled on Wednesdays; one session from 10:00 to 11:00, and the other from 17:00 to

18:00. Prior to the intervention start, the participants were placed in one of the scheduled sessions as desired to accommodate other activities in their daily life.



**Figure 1.** Design and development of the intervention using a co-creation approach. The development consisted of five steps: (1–3) three co-workshops, (4) a prototyping phase, and (5) the actual intervention.

The 30 min physical exercise program was delivered by the project coordinators (SRM (MSc Physiotherapy) and MEP (MSc Sports science and clinical biomechanics)) and consisted of a short warm-up, followed by an interval-type circuit physical exercise program consisting of bodyweight aerobic and strength exercises targeting individuals with Type 2 diabetes aimed to benefit glycemic control [8,18,19]. The interval circuit physical exercise program was intended to reach an intensity level corresponding to 16 on the Borg scale [20]. The participants were instructed in using the Borg scale, and right after the physical exercises, the participants reflected and evaluated on their reached intensity level (more detailed information about the physical exercise program is available in Supplementary Material Table S3). Following the online physical exercise, the participants were sent out in smaller predefined groups of three to five participants using the break-out room function in Microsoft Teams to conduct an online group meeting. The online group meeting served as a platform for discussion and evaluation of the online physical exercise, diabetes-related issues, and other aspects that the participants found important. Each group discussion was facilitated by a participant who had volunteered to be a facilitator prior to the intervention. The facilitators received information about how to facilitate a discussion and inspiration to the discussion topics. In addition, the facilitators were contacted by the project coordinator (MEP) by telephone after the first three online sessions to evaluate the group discussions, and afterwards the facilitators could call MEP if needed. In all other aspects, the facilitators participated in the study on equal terms in the same way as all other participants. The participants were encouraged to set personal weekly activity goals following the SMART goals structure [21] to increase self-management of habitual physical activity and evaluate their activity goals in the group discussions.

As a part of the intervention, the participants received a Garmin Vivofit 4 activity watch which they were encouraged to wear throughout all 8-weeks. Garmin activity watches were included in the study as an element to facilitate weekly activity goals and ongoing evaluation of their daily physical activity to discuss in the groups. The Garmin activity

watches were chosen because they have a long battery life and a simple design to increase adherence. There were four participants that wore Garmin Forerunner 245 to compare heart rate with self-reported intensity (Borg scale) during the online physical exercise.

#### 2.4. Outcomes

The outcomes included pre-defined research progression criteria, objective measurement of habitual physical activity, self-reported outcomes of a range of health parameters, and participant feedback from questionnaires. In addition, general demographic information, including age, sex, marital status, educational level, and ethnicity, and information regarding the participants' diabetes condition, including time of diagnose, complications, medication, and HbA1c level measured by their general practitioner, were obtained from the baseline questionnaire.

##### 2.4.1. Primary outcomes

Pre-defined research progression criteria in preparation for a definitive randomized controlled trial (RCT) based on a traffic light system of green (continue without changes), amber (changes needed to improve study design and feasibility), and red (major changes are needed) [22] were the primary outcomes in this study (Table 1).

Recruitment of participants was evaluated by calculating the number of participants that were recruited within three months. Retention was evaluated by calculating the percentage of participants who provided baseline and postintervention data out of the total number of participants at baseline. To evaluate adherence to online physical exercise and group meetings, the participants received a short web-based questionnaire every week right after the online physical exercise and group meetings to respond whether they attended the sessions. Adherence was calculated by counting the number of completed online physical exercises and group meetings separately, divided by the eight planned sessions. Along with the weekly questions regarding adherence to online physical exercise and group meetings, the participants wrote down their activity goal for the forthcoming week and if they completed the activity goal from the previous week.

To evaluate improvement of habitual physical activity, all the participants were instructed to wear two Axivity AX3 (Axivity, Newcastle, UK) accelerometers for seven consecutive days before, during, and after the intervention [23]. The participants received the accelerometers by post before the measurement periods and were instructed in how to wear the accelerometers. The accelerometers were attached with a patch; one was placed on the right thigh and the other on the right side of the lower back. Accelerometer data were considered valid if the participant had minimum 22 h wear time out of 24 h that were possible. A measurement period was considered valid if the participant had at least three valid weekdays and one valid weekend day. According to the World Health Organization Guidelines on Physical Activity and Sedentary Behavior, doing some physical activity is better than none, and some physical activity will still benefit the individual's health [2]. Therefore, any improvement in habitual physical activity (daily counts per minute) from baseline to post-intervention among participants was considered as an improvement in terms of the research progression criteria. The experienced burden of objectively measured physical activity was evaluated with a questionnaire at post-intervention regarding the participants' satisfaction with applying and wearing the accelerometers during the intervention. The participants scored their experienced severity of adverse events in the post-intervention questionnaire following the structure of the patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE<sup>®</sup>) [24]. In addition, the participants were told to contact the project coordinators (SRM and MEP) if they experienced any adverse events during the intervention. Minor adverse events covered dizziness, acute and prolonged musculoskeletal pain, and minor falls. Serious adverse events covered life-threatening events, disability, permanent damage, or hospitalization [25].

**Table 1.** Research progression criteria for continuing to definitive RCT.

Outcome	Green	Amber	Red
Participant recruitment	24 participants recruited within 3 months	Fewer than 24 participants recruited within 3 months	Fewer than 12 participants recruited within 3 months
Completion of intervention	Minimum 75% of the participants complete postintervention	Minimum 50% of the participants complete postintervention	Fewer than 50% of the participants complete postintervention
Adherence to online physical exercise sessions <sup>1</sup>	Minimum 75% of the participants complete more than half of the online physical exercise sessions	Minimum 50% of the participants complete more than half of the physical exercise sessions	Fewer than 50% of the participants complete more than half of the physical exercise sessions
Adherence to online group meetings <sup>2</sup>	Minimum 75% of the participants complete more than half of the group meeting sessions	Minimum 50% of the participants complete more than half of the group meeting sessions	Fewer than 50% of the participants complete more than half of the group meeting sessions
Adherence to activity goals <sup>3</sup>	Minimum 75% of the participants set goals	Minimum 50% of the participants set goals	Fewer than 50% of the participants set goals
Burden of objectively measured physical activity	Minimum 80% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Minimum 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Fewer than 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again
Improvement of physical activity <sup>4</sup>	Minimum 50% of the participants have achieved improvements in physical activity at postintervention	Minimum 25% of the participants have achieved improvements in physical activity at postintervention	Fewer than 25% of the participants have achieved improvements in physical activity at postintervention
Adverse events	No or minor adverse events related to the intervention at postintervention	Fewer than five serious adverse events related to the intervention at postintervention	Five or more serious adverse events related to the intervention at postintervention

Research progression criteria based on traffic light system: Green (continue), amber (changes to protocol must be discussed before continuing), and red (do not proceed unless the issue can be solved) [22]. <sup>1</sup> At the beginning and end of the online physical exercise sessions all the participants note if they were participating. <sup>2</sup> At the beginning and end of each of the group meetings all the participants note if they were participating. <sup>3</sup> Activity goals that were assessed during the group meetings. <sup>4</sup> Any improvement in objectively measured physical activity (count per minute for the day).

## 2.4.2. Secondary Outcomes

### Objective Outcomes

In addition to any improvement in physical activity, other aspects of habitual physical activity among the participants were explored as secondary outcomes. Activity intensity types were determined by generating ActiGraph counts using 10 s epochs from the raw acceleration data measured at the back [26]. The following activity intensity types were included: light physical activity (LPA), moderate physical activity (MPA), vigorous physical activity (VPA), moderate–vigorous physical activity (MVPA), and sedentary behavior (time spent sitting and lying) (SB). Activity intensities were additionally used to assess whether the participants adhered to the WHO recommendations of physical activity and sedentary behavior ( $\geq 150$  min. MVPA or  $\geq 75$  min. VPA weekly) and the recommendations on daily physical activity according to the American Diabetes Association (ADA) and the Danish Health Authority ( $\geq 30$  min. daily MVPA, which were categorized as (1) inactive day:  $< 5$  min. MVPA, (2) day with some activity:  $\geq 5$  min. and  $< 30$  min. MVPA, and (3) day with sufficient activity:  $\geq 30$  min. MVPA) [2,3]. The total daily step counts were included and determined by an algorithm by Godfrey et al. [27].

### Self-Reported Outcomes

Baseline and post-intervention questionnaires were used to obtain secondary self-reported outcomes. The participants reported their height and weight, which was calculated into a body mass index (BMI) ( $\text{kg}/\text{m}^2$ ). Cohen's 10-item Perceived Stress Scale (PSS) was used to assess the participants' perceived stress, and a higher score indicated a higher perceived stress [28]. Mental well-being was assessed using the WHO5-Well-Being Index. Questions were scored from 0 (none of the time) to 5 (all of the time), and the raw scores were then multiplied by 4 to obtain a percentage score ranging from 0 to 100, where scores of  $\geq 50$  indicated a moderate to high mental well-being [29]. The Bayliss Burden of Illness Measure was used to obtain information about the number of chronic conditions and to what extent the condition interfered with daily life activities on a 5-point Likert scale of 1 (not at all) to 5 (a lot). The total scores represent the total morbidities and the total score of burden [30]. The participants' self-perceived beliefs about their own abilities related to performing an activity were measured with the questionnaire "Self-Efficacy for Managing Chronic Disease 6-Item Scale" (SEMCD6). A higher score reflects a greater self-efficacy [31]. In addition, self-rated feelings of loneliness were assessed with the UCLA 3-Item Loneliness Scale. Each item was scored with points ranging from "hardly ever or never" (1 point) to "often" (3 points), and a higher score indicates a higher level of perceived loneliness [32].

### Participant Feedback

The participants (both facilitators and regular participants) received a questionnaire at post-intervention about their satisfaction with the following topics: the communication between the project coordinators and participants, introduction course, online physical exercise sessions, online group meetings, setting weekly activity goals and prioritization of them, use of Microsoft Teams and Garmin watches, burden of tasks in the project, and the experience of being and having a facilitator in the online group meetings. The participants responded to what extent they agreed/disagreed with a list of statements within the abovementioned topics.

A voluntary evaluation day was held at the end of the project where the participants were encouraged to suggest potential improvements of the study design and procedures.

### 2.5. Sample Size

No sample size calculation was performed, but according to the rationale for a feasibility study, regulatory, and statistical considerations, at least 12 participants should be included to obtain a precise and representable mean and variance [33].

### 2.6. Statistical Analysis

Before the analyses were commenced, a statistical analysis plan was developed and openly available <https://osf.io/3nphj/> (accessed on 14 June 2022).

Cross-tabulations were conducted to describe the participant's characteristics. Research progression criteria were presented with descriptive statistics in accordance with the traffic light system on the per protocol population. Continuous data were presented as the mean and standard deviation or as the median and interquartile range. Categorical data were presented as the number and proportion. Changes in secondary outcomes from baseline to postintervention were reported with median and interquartile ranges (IQR) or as a number and proportions. No hypothesis-testing was carried out in this feasibility study in accordance with the CONSORT extension to randomized pilot and feasibility trials [13]. All statistical analyses were performed using Stata, Version 17, (StataCorp, College Station, TX, USA) and R statistical (R Core Team, Vienna, Austria) software version 4.2.2 (10 November 2022), RStudio (RStudio Inc., Boston, MA, USA) version 2022.07.2.

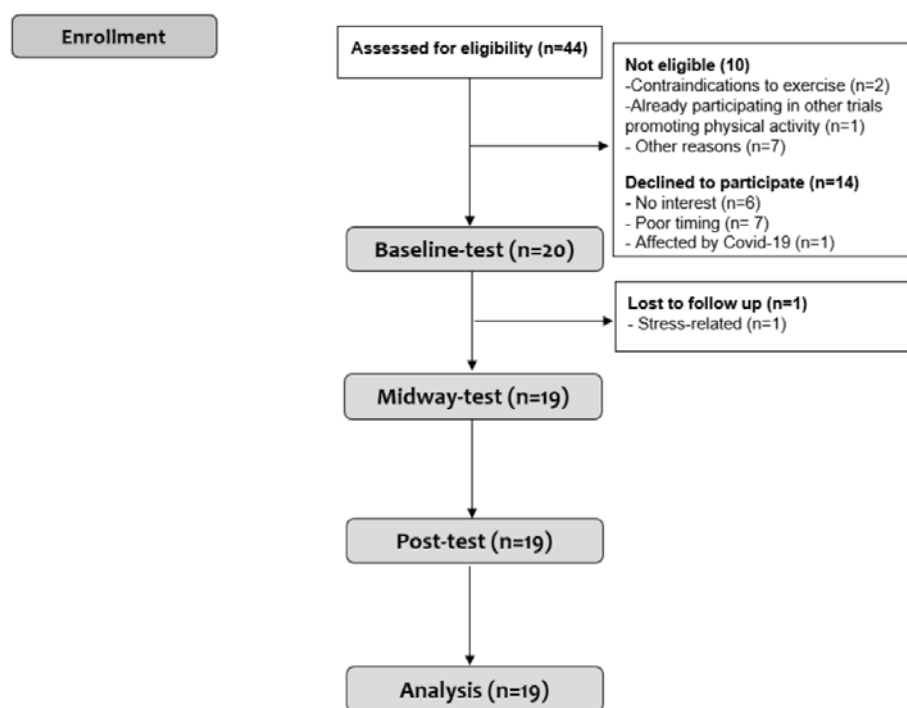
### 2.7. Deviations from the Protocol

We originally planned to collect information on adverse events at the end of every week during the intervention. However, as the participants already received several

weekly questionnaires, we decided to collect detailed information about adverse events at post-intervention instead and informed participants, that they should contact the project coordinators (SRM and MEP) if they experienced any adverse events during the intervention. Furthermore, we decided not to perform a sensitivity analysis on differences in measuring daily steps between Garmin watches and accelerometers because of the small sample size.

### 3. Results

A total of 44 individuals were assessed for eligibility from 14 February to 10 March 2022, 20 participants were allocated to the intervention, and 19 participants were included in the analyses (Figure 2).



**Figure 2.** Flowchart of participant enrolment, follow-up, and analysis. Other reasons for declining to participate were stress and other mental disorders ( $n = 3$ ), personal reasons ( $n = 1$ ), residing abroad ( $n = 1$ ), and loss of spouse ( $n = 1$ ).

There were 8 females and 12 males aged  $60.4 \pm 8.7$  and diagnosed with Type 2 diabetes that were included. Most participants had completed higher education, were overweight or obese, reported moderate perceived stress, and did not follow the WHO recommendations of physical activity (Table 2).

**Table 2.** Baseline characteristics of participants.

Characteristics	
Age, years	$60.4 \pm 8.7$
Women, $n$ (%)	8 (40.0)
Ethnicity, $n$ (%)	18 (90.0)
Living alone, $n$ (%)	6 (30.0)
Educational level, $n$ (%)	
Primary education	3 (15.0)
Upper secondary or vocational	7 (35.0)
Higher education	10 (50.0)
BMI, $n$ (%)	

Table 2. Cont.

Characteristics	
Underweight/Normal	0
Overweight	8 (40.0)
Obese Class I	8 (40.0)
Obese Class II	3 (15.0)
Obese Class III	1 (5.0)
Diet score (healthy/medium healthy/unhealthy) <sup>a</sup>	7/10/3
Alcohol consumption (no alcohol/below risk group/above risk group) <sup>b</sup>	7/12/1
Smoking status (smoker/ex-smoker/never smoked)	1/10/9
Adherence to WHO recommendations on weekly physical activity <sup>c</sup> , <i>n</i> (%)	
Following recommendations	5 (25.0)
Not following recommendations	15 (75.0)
Adherence to recommendations on daily physical activity <sup>d</sup> , <i>n</i> (%)	
Inactivity	3 (15.0)
Some physical activity	13 (65.0)
Sufficient physical activity	4 (20.0)
WHO-5-Well-Being Index total score, (0–100)	78 [72–80]
Bayliss burden of illness measure	
Median number of comorbidities reported	4 [2.5–6]
Median disease burden reported	5.5 [1.5–9]
SEMCD6, (0–10)	8 [5.7–8.7]
PSS total score, <i>n</i> (%)	
Low perceived stress	1 (5.0)
Moderate perceived stress	16 (80.0)
High perceived stress	3 (15.0)
Loneliness scale, (3–9)	3 [3–5]
Self-reported HbA1c (mmol/mol) <sup>*</sup>	47 [38–48]

*n* = 20. Data are presented as number (proportion), means ( $\pm$  standard deviation), or median [interquartile range]. Abbreviations: BMI: body mass index, WHO: World Health Organization, SEMCD6; Self-Efficacy for Managing Chronic Disease 6-Item Scale, PSS: Perceived Stress Scale. <sup>a</sup> Self-reported dietary habit were categorized into three items based on a diet score. <sup>b</sup> Self-reported alcohol consumption was categorized in accordance with the recommendations from the Danish Health Authority. <sup>c</sup> Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity:  $\geq 150$  min MVPA or  $\geq 75$  min VPA weekly or an equivalent combination. <sup>d</sup> Distribution of adherence to recommendations of daily physical activity according to ADA and the Danish Health Authority. Complete inactivity:  $< 5$  min/day of MVPA, some activity:  $\geq 5$  min/day and  $< 30$  min/day MVPA, and sufficient activity:  $\geq 30$  min/day MVPA. \* *n* = 14 due to missing data.

### 3.1. Primary Outcomes

Most research progression criteria reached a level of acceptance (i.e., green, continue to a RCT without changes), except for the criteria regarding participant recruitment, burden of objectively measured physical activity, and adverse events, which were amber (i.e., changes needed to improve study design and feasibility) (Table 3). Our target was to recruit 24 participants within three months, however, due to delayed acceptance from the Ethics Committee, we only had two months to recruit participants. Out of 19 participants, 15 (79.0%) reported that the number of days wearing the accelerometer was appropriate, which was only one percent from meeting the criterion for green. During the intervention, one participant cancelled an online physical exercise due to hospitalization with benign paroxysmal positional vertigo. The participant attended the online physical exercise the following week. Half or more of the online physical exercise sessions and group meetings were completed by 17 (89.5%) and 16 (84.2%) participants, respectively. The median [IQR] self-reported intensity (Borg scale) during the online physical exercises was 15.4 [14.4–16.8] and the median [IQR] measured heart rate with Garmin Forerunner 245 watches was 115 [111–121]. More than half of the participants with valid accelerometer data had im-



proved their habitual physical activity from baseline to post-intervention. A total of nine participants reported minor adverse events, such as muscle pain and dizziness.

**Table 3.** Research progression criteria results to evaluate whether to progress with a definitive RCT.

Research Progression Criteria		Evaluation
Participant recruitment, actual <i>n</i> /desired <i>n</i>	20/24	Amber
Participants who completed the intervention, <i>n</i> (%) *	19/20 (95.0)	Green
Adherence to online physical exercise sessions		
Participants who completed half of the online physical exercise sessions, <i>n</i> (%)	17/19 (89.5)	Green
Adherence to online group meetings		
Participants who completed half of the online group meetings, <i>n</i> (%)	16/19 (84.2)	Green
Adherence to goalsetting		
Participants who set activity goals, <i>n</i> (%)	19/19 (100.0)	Green
Burden of objectively measured physical activity		
Participants who did not find the attachment and shipping too time-consuming, <i>n</i> (%)	17/19 (89.5)	Green
Participants who found the numbers of days wearing the accelerometer appropriate, <i>n</i> (%)	15/19 (79.9)	Amber
Improvement of physical activity		
Participants who improved physical activity from baseline to postintervention, <i>n</i> (%) **	10/19 (62.5)	Green
Adverse events		
Participants who experienced minor adverse events, <i>n</i> (%)	9/19	Green
Participants who experienced serious adverse events, <i>n</i> (%)	1/19	Amber

*n* = 19. The research progression criteria were based on the traffic light system [22]. \* 19/20 participants followed the intervention and had complete data on baseline and postintervention measurements. \*\* 16 participants had valid accelerometer data from baseline and postintervention.

### 3.2. Participant Feedback

Most of the participants (89.5%) were satisfied with the intervention and the project met their expectations. Furthermore, most (84.2%) found it motivating to do physical exercises with others even though it was conducted online. In addition, 68.4% felt a sense of solidarity in their smaller exercise groups. Some participants (26.3%) felt that they had to prioritize participating in the study activities over other activities in their everyday life to reach their weekly activity goal (Supplementary Material Table S4).

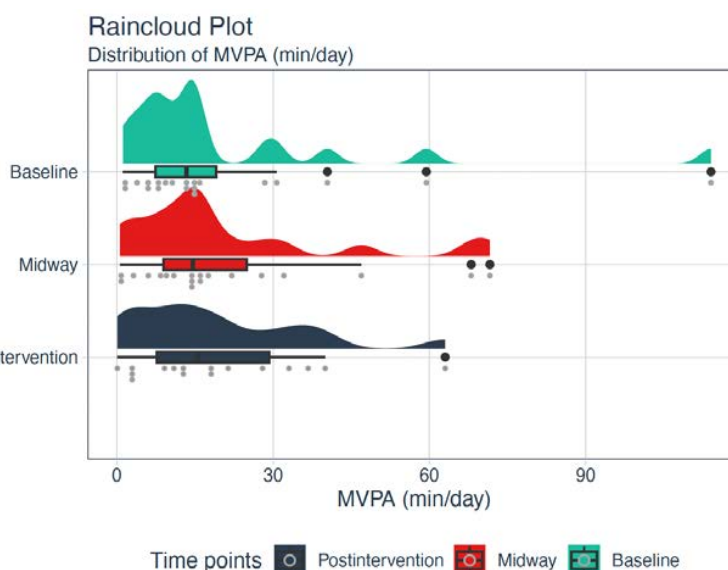
**Table 4.** Secondary outcomes on objectively measured habitual physical activity.

	Baseline (before Week 1)	Midway (after Week 4)	Postintervention (after Week 8)
Total			
SB	10.7 [9.4–11.6]	10.2 [8.9–10.5]	10.3 [9.0–10.8]
LPA	136.8 [111.7–155.4]	133.9 [109.5–162.6]	129.2 [113.7–149.7]
MPA	9.2 [5.7–18.9]	11.7 [4.7–16.5]	12.6 [4.6–29.5]
VPA	0.3 [0.1–1.2]	0.3 [0.1–0.9]	0.3 [0.1–0.6]
MVPA	11.8 [5.8–22.2]	14.3 [7.2–19.8]	15.5 [6.2–30.5]
Daily steps	6292 [4044–9336]	8519 [5197–12068]	7479 [4569–12780]
Weekdays			
SB	11.4 [9.4–12.9]	10.6 [7.8–12.0]	10.9 [7.3–12.6]
LPA	136.8 [108.6–165.5]	131.0 [109.0–168.7]	112.3 [76.4–165.5]
MPA	7.9 [3.1–21.4]	4.8 [1.7–20.5]	7.0 [1.4–21.5]
VPA	0.2 [0–0.6]	0.2 [0–0.5]	0.2 [0–0.4]
MVPA	8.3 [3.5–23.4]	5.7 [1.8–21.7]	7.6 [1.8–22.7]
Daily steps	6620.5 [3775–9844]	7298 [3508–12273]	5910 [2709–13243]

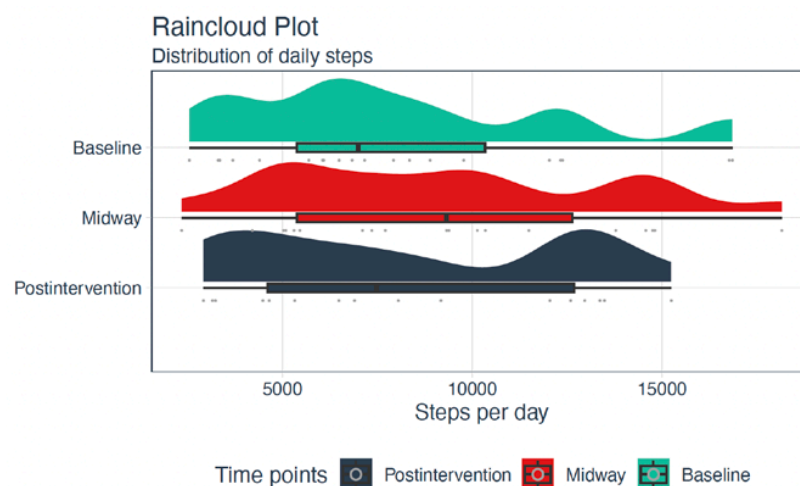
**Table 4.** Cont.

	Baseline (before Week 1)	Midway (after Week 4)	Postintervention (after Week 8)
<b>Weekends</b>			
SB	9.7 [6.1–11.2]	10.7 [9.3–11.6]	10.8 [9.2–11.8]
LPA	113.2 [70.7–172.3]	155.6 [118.5–195.2]	152.8 [93.7–189.3]
MPA	5.7 [0.8–11.7]	10.2 [1.8–19.8]	7.0 [3.3–33.2]
VPA	0.2 [0–0.3]	0.2 [0–0.5]	0.2 [0–0.7]
MVPA	6.0 [1.2–12.3]	11.8 [2.0–23.3]	9.3 [3.3–37.2]
Daily steps	4468 [1820–9216]	9405 [5237–14784]	9786 [4326–14252]
<b>Adherence to WHO recommendations on weekly physical activity<sup>a</sup></b>			
Following recommendations	4 (25.0)	4 (25.0)	6 (37.5)
Not following recommendations	12 (75.0)	12 (75.0)	10 (62.5)
<b>Adherence to recommendations on daily physical activity during a week<sup>b</sup></b>			
Days with inactivity	2.5 [1–6.5]	3 [1–5.5]	2.5 [1–5.5]
Days with some physical activity	5.5 [2.5–7.5]	3 [1–5]	2.5 [1–4]
Days with sufficient physical activity	0.5 [0–3]	0.5 [0–1.5]	1.5 [0–3]

*n* = 16 (participants with valid accelerometer data from baseline to postintervention). Data are presented as medians and interquartile range (IQR) (25th and 75th quartile) or *n* and proportion (%). Abbreviations: SB: sedentary behavior (hour/day), LPA: light physical activity (min/day), MPA: moderate physical activity (min/day), VPA: vigorous physical activity (min/day), MVPA: moderate to vigorous physical activity (min/day). <sup>a</sup> Adherence to recommendations on weekly physical activity according to WHO. Following recommendations of weekly physical activity: ≥150 min MVPA or ≥75 min VPA weekly or an equivalent combination. <sup>b</sup> Median [IQR] number of days during a week with inactivity (<5 min/day of MVPA), some activity (some activity: ≥5 min/day and <30 min/day MVPA), and sufficient activity (sufficient activity: ≥30 min/day MVPA) in accordance with recommendations on daily physical activity according to ADA and the Danish Health Authority.



**Figure 3.** Raincloud plot representing an illustration of data in a half-density distribution (the ‘cloud’) with individual raw data (the ‘rain’) and a boxplot below the ‘cloud’ of the total daily moderate to vigorous physical activity (MVPA) in minutes at baseline, midway, and post-intervention.



**Figure 4.** Raincloud plot representing an illustration of data in a half-density distribution (the ‘cloud’) with individual raw data (the ‘rain’) and a boxplot below the ‘cloud’ of the total daily steps at baseline, midway, and post-intervention.

**Table 5.** Secondary self-reported outcomes.

	Baseline (before Week 1)	Postintervention (after Week 8)
BMI	31.2 [28.7–33.7]	31.2 [28.2–32.7]
PSS total score, (0–40)	20 [18–23]	19 [17–22]
Loneliness scale, (3–9)	3 [3–5]	3 [3–5]
SEMCD6, (0–10)	8 [4.8–8.8]	8.3 [6.7–9.0]
WHO-5 Wellbeing Index total score, (0–100)	80 [72–80]	80 [72–84]
Bayliss burden of illness measure		
Median number of comorbidities	4 [3–7]	3 [2–6]
Median disease burden reported	6 [1–9]	7 [2–14]

$n = 19$  (participants with complete data on self-reported secondary outcomes from baseline to post-intervention). Data are presented as medians and quantiles (25th and 75th percentile). Abbreviations: BMI: body mass index, WHO: World Health Organization, SEMCD6: Self-Efficacy for Managing Chronic Disease 6-Item Scale, PSS: Perceived Stress Scale.

### 3.3. Secondary Outcomes

The median total daily MPA, MVPA, and steps among participants increased from baseline to post-intervention (Figures 3 and 4 and Table 4). Large individual differences in total daily MVPA were present among participants at baseline, which were equalized post-intervention to some degree (Figure 3). In addition, the median total daily SB decreased from baseline (10.7 h, IQR: 9.4–11.6) to post-intervention (10.3 h, IQR: 9.0–10.8). Number of days with sufficient physical activity during a week according to the recommendations from ADA and the Danish Health Authority increased from baseline (0.5 day, IQR: 0–3) to post-intervention (1.5 days, IQR: 0–3).

The median total PSS score among the participants was one point lower at post-intervention. The number of comorbidities that were reported decreased at post-intervention, however, the median disease burden that was reported increased (Table 5).

## 4. Discussion

We found that the combination of a co-created online physical exercise intervention with group meetings supported by an activity watch in individuals with Type 2 diabetes was feasible in terms of completion of intervention, adherence to online physical exercises,

group meetings, activity goals, and an improvement of physical activity. However, the data suggest that adjustments regarding participant recruitment, burden of objectively measured physical activity, and adverse events are needed before investigating effectiveness in a future RCT.

The criteria of participant recruitment did not reach an acceptable level (green) partly due to the slow processing of the project application from the Ethics Committee, which led to a shortening of the recruitment period. Initially, the participants were recruited solely through the Danish Diabetes Association. However, due to slow rates of inclusion, participants from a previous project with a physical exercise intervention were also invited to participate [34]. Members of the Danish Diabetes Association are a selected group of Danish individuals with Type 2 diabetes, because the majority has an upper secondary or vocational education and live with their spouse [35]. The participants in this study were higher educated and had healthier lifestyle behaviors compared to the members of the Danish Diabetes Association and the general population with diabetes [35,36]. Therefore, we expect the study population to be a selected group of individuals with diabetes with higher health literacy, digital health literacy, and greater motivation for attending physical activity intervention studies [37,38]. The facilitators of the group meetings were all participants who had been engaged in either the co-creation process or the previous project with physical exercise intervention [34]. We expected the facilitators to be particularly committed and motivated to the project, which may also have influenced the other participants' engagement in the project. As such, it is unclear if our intervention would also be feasible in a broader population of individuals with Type 2 diabetes with lower educational level, health literacy, and digital competences. An improved recruitment strategy is needed before proceeding to an RCT, and a new feasibility study might be required to develop a final recruitment strategy to target a wider population with Type 2 diabetes. In Denmark, general practitioners are the most frequent and first contact to the healthcare system for individuals with diabetes [39]. Recruiting participants through general practitioners could be a potential strategy to avoid a selected study population of individuals with Type 2 diabetes. Also, e-health and m-health strategies for weight loss have proven relevant and feasible in this context [40], supporting the relevance to recruit from general practitioners.

Physical exercise interventions that are delivered online are associated with more concerns about safety and adverse events due to the diminished ability for the healthcare system to take immediate action [41]. A systematic review and meta-analysis of exercise interventions delivered via videoconferencing for individuals with chronic conditions found no increased number of exercise-related adverse events and serious adverse events in the intervention groups of the included studies [41]. In our study, one serious adverse event was reported because of hospitalization with benign paroxysmal positional vertigo. However, since engagement in physical exercise is not a risk factor of developing benign paroxysmal positional vertigo [42], we do not believe that the reported serious adverse event is related to the intervention of the study. In a potential future RCT, information about adverse events should be collected weekly during the intervention period with questionnaires or text messages and via hospital records to ensure that all adverse events are identified.

The participants wore accelerometers for three periods of at least seven days before, during, and after the intervention. A total of four participants found the number of measurement days with accelerometers too burdensome. The three measurement periods were very close to each other with only few weeks in between, which could explain why some participants found the accelerometer measurements burdensome. In spite of this, the compliance was still high. A minimum of four days valid accelerometer data among adults and older adults is recommended to ensure representative data of the individual's physical activity level [43]. A total of seven days of measurement were chosen to obtain enough valid data despite the potential occurrence of measurement errors. The study intervention was primarily focused on the individual's own ability to increase and maintain daily physical activity, and we expected variations in physical activity from week to week. Therefore, we

decided to measure physical activity three times to follow the changes before, during, and after the intervention. In a potential future RCT, the intervention period would most likely be longer than eight weeks to investigate the effectiveness of the intervention. Furthermore, the measurement during the intervention might not be needed. Hence, the measurement periods would be spread more out.

The rationale for combining online physical exercise with online group meetings and including Garmin activity watches was to accommodate the individual's needs in terms of content, time, and location to preserve their daily life based on the findings from Thorsen et al. [6]. In addition, we intended to develop an intervention that supported the individual's ability and motivation to increase daily physical activity by themselves. We did not expect the 30 min online physical exercise in eight weeks to increase daily physical activity significantly, but in combination with the other two components (group meetings and Garmin watches) we aimed to increase the participants' confidence and ability to increase daily physical activity. Although limited by the small sample size and lack of control group, we found that participants increased their daily MVPA and steps from baseline to follow-up. Adherence to the online physical exercise sessions and group meetings were high among the participants, suggesting that changes in secondary outcomes were related to completion of the intervention [41]. The results of the secondary outcomes suggest that the intervention worked as intended, and participants managed to increase and maintain new physical activity behaviors in their daily life with support from their online group and activity watch. However, these findings need confirmation in an appropriately powered RCT.

This feasibility study has several limitations. Firstly, the study is limited by its design with a lack of control group and inability to ensure blinding, which precludes any firm conclusions on the effectiveness of the intervention and which components of the intervention drive our results. Secondly, the method that was used to collect information of adverse events might not have captured all adverse events during the intervention. Therefore, we cannot claim with certainty that the intervention is completely safe for individuals with Type 2 diabetes. Thirdly, the introduction course about the project was held few days before baseline measurements began, which could potentially have affected the results of baseline measurements and lead to an underestimation of the effect over time.

## 5. Conclusions

An intervention including online physical exercise, group sessions, and activity watches is feasible and acceptable for individuals with Type 2 diabetes with a higher educational level as compared to the general population with Type 2 diabetes. To claim feasibility, acceptability, and safety among the general population with Type 2 diabetes and before we can continue to a full-scale RCT, a recruitment strategy that successfully targets this population must be developed. In addition, minor changes regarding how adverse events are collected and the timing of periods with accelerometer measurements must be considered. A future RCT will demonstrate whether the intervention is also effective in increasing and maintaining physical activity in this population.

**Supplementary Materials:** The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/ijerph20042893/s1>, Table S1: CONSORT 2010 checklist; Table S2: The TIDieR Checklist; Table S3: Description of content in the interval circuit physical exercise program; Table S4: Participant feedback.

**Author Contributions:** Conceptualization, all authors; Methodology, all authors; Formal analysis, S.R.M.; Investigation, S.R.M. and M.E.P.; Data curation, S.R.M.; Writing—original draft preparation, S.R.M. and M.E.P.; Writing—review and editing, all authors; Visualization, S.R.M. and M.E.P.; Supervision, M.R.-L. and S.T.S.; Project administration, S.R.M., M.E.P. and M.R.-L.; Funding Acquisition, M.R.-L. All authors have read and agreed to the published version of the manuscript.

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**Informed Consent Statement:** Informed consent was obtained from all the subjects involved in the study.

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## Supplementary material

### Supplement S1

**Supplementary table 1.** Description of content in the interval circuit physical exercise program

X<sub>1</sub>, intended intensity (Borg scale)

X<sub>2</sub>, number of repetitions

X<sub>3</sub>, number of sets

X<sub>4</sub>, number of exercises (minus warm up and cool down)


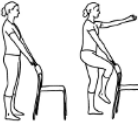

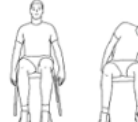
X<sub>5</sub>, duration of each exercise (seconds)

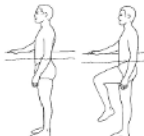


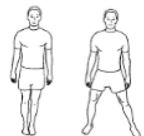

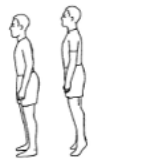
X<sub>6</sub>, rest in-between exercises (seconds)

X<sub>7</sub>, rest in-between sets (minutes)

X<sub>8</sub>, sessions per week

X <sub>1</sub>	X <sub>2</sub>	X <sub>3</sub>	X <sub>4</sub>	X <sub>5</sub>	X <sub>6</sub>	X <sub>7</sub>	X <sub>8</sub>
16	As many repetitions as possible	2	8	40	20	2	1

Exercise type	Specific exercises	Progression	Regression	Illustration
<b>Warm up</b>	Different movements and slightly increasing pace			
<b>Strength exercises (Set 1)</b>	Repeated sit-to-stand from a chair	- No support from armrests - No use of chair (squats)	- Use support from armrests	
	Diagonally raises with support from a chair	- No support from chair - Move opposite elbow to knee in one movement following the diagonally raises	- Raise knees supporting both hands to chair	
	Press ups at a wall	- Increase distance from feet to wall	- Decrease distance from feet to wall	
	Side flexion (sitting position)	- Raise arms - Standing with wide distance between feet with knees slightly flexed – do side flexions with raised arms	- Decrease side flexion	

<b>Aerobic exercises (Set 2)</b>	Knee raises (standing position)	- Increase pace	- Support from a chair or wall	
	Air-boxing	- Increase pace - Do small footsteps while boxing	- Decrease pace	
	“Twist”	- Increase pace	- Decrease pace	
	Step sideways	- Increase pace - Include arms	- Decrease pace - Support from a chair or wall	
<b>Balance /cool down exercises</b>	One-leg standing	- Look in different directions - Do smaller movements with arms - Close eyes in small periods	- Support from a chair or wall - Stand on both legs; look in different directions, do smaller movements etc.	
	Toe-stand	- Stand on one leg	- Support from a chair or wall	
<b>Stretch out</b>	Stretch out major muscle groups			

## Supplement S2

**Supplementary table 2. Participant feedback**

Statements	<i>n</i> , % that responded “Highly agree” or “Agree”
<i>General satisfaction with the project</i>	
The project met my expectations	17 (89.5)
I will recommend the project to others	19 (100.0)
I participated in the project because I wanted to	19 (100.0)
Information about the content of the project was appropriate	18 (94.7)
<i>Participation and communication</i>	
The communication from the project coordinator was understandable	19 (100.0)
The project coordinator was reachable during the project	18 (94.7)
The number of emails, calls and text messages was adequate	18 (94.7)
<i>Online physical exercise</i>	
The online physical exercise met my expectations	18 (94.7)
I felt safe turning the video camera on during the online physical exercises	18 (94.7)
The introduction to Borg-scale was appropriate	17 (89.5)
The level of the physical exercises was adjusted to my level	15 (79.0)
It was motivating to do physical exercises with others even though it was behind a screen	16 (84.2)
I will recommend the online physical exercise to others	19 (100.0)
<i>Online group meetings</i>	
I felt comfortable turning the video camera on during online group meetings	19 (100.0)
The group supported me to be active in every life	13 (68.4)
Being a part of a smaller online group motivated me to participate in the online physical exercises	13 (68.4)
I felt we had a sense of solidarity in the smaller online group	13 (68.4)
<i>Activity goals</i>	
I was able to set a realistic weekly activity goal	18 (94.7)
The smaller group supported me to reach my weekly activity goal	13 (68.4)
I had to down prioritize other things to reach my weekly activity goal	5 (26.3)
<i>Microsoft Teams</i>	
The introduction to Microsoft Teams was sufficient	16 (84.2)
I felt comfortable using Microsoft Teams	18 (94.7)
I experienced technical issues with Microsoft Teams	7 (36.8)
I got the necessary support and help to use Microsoft Teams	15 (79.0)
<i>Garmin watches</i>	
The introduction to Garmin watches was sufficient	15 (79.0)
I got the necessary support and help to use the Garmin watch	15 (79.0)
The Garmin watch’s measurement of steps motivated me to be physically active	14 (73.7)
The Garmin watch was useful to set weekly activity goals	14 (73.7)
The Garmin watch was useful to reach my weekly activity goal	13 (68.4)
<i>The role of the facilitator in the group meetings (questions only for facilitators)</i>	
The introduction to the facilitator role was sufficient	4 (66.7)
I used the proposed agenda in the group meetings	6 (100.0)
It was time and energy consuming to be a facilitator	1 (16.7)
<i>The role of the facilitator in the group meetings (questions only for participants)</i>	
The facilitator had a structured agenda in the group meetings	10 (76.9)
The facilitator managed to start and direct the group discussions	10 (76.9)
<i>The burden of tasks in the project</i>	
The number of questionnaires was too much in the beginning of the project	2 (10.5)
The number of questionnaires was too much during the project	3 (15.8)
The number of questionnaires was too much in the end of the project	4 (21.1)
The number of smaller tasks e.g., make note of steps and intensity minutes, was appropriate	17 (89.5)
The introduction to attaching the accelerometers was sufficient	17 (89.5)
Attaching and returning the accelerometers were too time consuming	2 (10.5)
The number of days wearing the accelerometers was appropriate	13 (68.4)

*n* = 19

Satisfaction questionnaire from postintervention. Participants responded to what degree they agreed or not with the statements.

# **Appendix V**

## **Statistical analysis plan for Paper I**

The statistical analysis plan was uploaded at Open Science Framework (<https://osf.io/25u4g/>)

## **Statistical analysis plan**

### **Running title**

Determinants of physical activity among individuals with diabetes: a cross-sectional study

### **Authors**

Sofie Rath Mortensen, Peter Lund Kristensen, Cathrine Juel Lau, Mathias Ried-Larsen, Anders Grøntved, Søren Thorgaard Skou

### **Contributors and roles in the SAP**

*Responsible for writing the SAP:* PhD-student Sofie Rath Mortensen (PT, MSc)

### **Brief background**

Engagement in regular physical activity is a cornerstone of type 2 diabetes management to prevent long-term diabetes complications and premature mortality. Morbidity, obesity, stress, and health-related quality of life are all factors that may determine decreased habitual physical activity in general population. Given that individuals with diabetes are at high risk of suffering from these factors, it is likely that individuals with diabetes have different physical activity patterns. No previous large-scale studies have provided a detailed description of habitual physical activity among individuals with diabetes. Availability of such information would be an important resource for planning future treatment courses taking individual characteristics, needs and preferences into account when designing and promoting a physical activity intervention.

### **Primary aim**

To provide descriptive data on habitual physical activity and investigate the association of morbidity, obesity, stress, and health-related quality of life with physical activity among individuals with diabetes based on data from The Danish National Health Survey from 2017.

### **Secondary aim**

To investigate the association of morbidity, obesity, stress, and health-related quality of life with sedentary behavior among individuals with diabetes based on data from The Danish National Health Survey from 2017.

### **Methods**

#### **Study design**

The study design is cross-sectional. Reporting of the study will be followed by the STROBE checklist (1).

#### **Data sources**

Responders of The Danish National Health Survey (DNHS) in 2017 will be included. The DNHS was based on six mutually exclusive random subsamples; one in each of the five Danish administrative regions, and one national sample. 312,349 individuals were invited via a secure electronical mail service (Digital Post) or regular postal service to participate in the survey. Mandatory questions of the survey for all subsamples will be used in this project (appendix 5).

#### **Variables**

##### Exposures

*Comorbidity (excluding diabetes)* (categorical)

- Self-reported information on selected long-term conditions (excluding diabetes) and sequela from question 10-11 were used to assess comorbidity. Respondents reported whether they have or have had selected long-term conditions. If respondents reported they have had a long-term condition, they reported whether they were suffering from sequelae due to the specific long-term condition.
- The definition of multimorbidity will be based on diagnoses organized in 10 groups of different body systems according to Willadsen et al. (2). In this study there will only be 7 groups due to lack of information on gastrointestinal and genitourinary diseases from the survey, and the endocrine body system will be excluded since diabetes is not a part of the comorbidity-variable in the present study. The 7 groups will be: 1) Lung (asthma and bronchitis), 2) Musculoskeletal (osteoarthritis, rheumatoid arthritis, osteoporosis, and back diagnoses), 3) Mental (temporary mental disease and long-term mental disease), 4) Cancer, 5) Neurological (stroke and migraine), 6) Cardiovascular (hypertension, angina pectoris, and myocardial infarction), and 7) Sensory organs (tinnitus and cataract).
- The variable will be categorized as follows: 1) Have diabetes and no comorbidities, 2) Have diabetes and one comorbidity from one body system, 3) Have diabetes and two comorbidities from two different body systems, 4) Have diabetes and three or more comorbidities from at least three different body systems. Suffering from several long-term conditions within the same body system, e.g., hypertension and myocardial infarction, will still only count as one comorbidity.
- Studies have found that a decreased mental health status among individuals with comorbidities is associated with lower physical activity (3, 4). Therefore, a variable differentiating between having diabetes and comorbidities with and without a mental disease will be created.

#### *Obesity (categorical)*

- Self-reported data on body weight and height were obtained from question 38-39.
- Body mass index (BMI) ( $\text{kg}/\text{m}^2$ ) will be calculated and categorized into the following groups: underweight/normal weight ( $\text{BMI} < 25.0$ ), overweight ( $\text{BMI} \geq 25.0 - < 30.0$ ), obese class I ( $\text{BMI} \geq 30.0 - < 35.0$ ), obese class II ( $\text{BMI} \geq 35.0 - < 40.0$ ), and obese class III ( $\text{BMI} \geq 40$ ), as defined by the World Health Organization (5).

#### *Stress (categorical)*

- Self-reported psychological stress was obtained with Cohen's 10-item Perceived Stress Scale (PSS) (6) from question 8.
- The PSS will be categorized into three as follows:
  - o Scores ranging from 0-13 will be considered low perceived stress
  - o Scores ranging from 14-26 will be considered moderate perceived stress
  - o Scores ranging from 27-40 will be considered high perceived stress

#### *Health-related quality of life (categorical)*

- Self-reported health-related quality of life was obtained with the 12-item Short-Form Health Survey (SF-12) from question 1-7 (7).
- The SF-12 score is divided into a physical and mental score and each variable was dichotomized following the recommendations (8):
  - o Physical: A score of 50 or less determines a physical condition
  - o Mental: A score of 42 or less may be indicative of clinical depression

### Primary outcome

#### *Moderate to vigorous physical activity (MVPA) h/week (continuous)*

- Respondents reported hours and minutes spent weekly on moderate and vigorous physical activities in question D-E.
- MVPA in hours and minutes weekly will be calculated into hours.

### Secondary outcomes

#### *Adherence to the WHO recommendations of physical activity and sedentary behavior (binary)*

- Adherence to the WHO recommendations of physical activity and sedentary behavior was assessed with information regarding hours and minutes spent on weekly MVPA from question D-E.
- Following the WHO recommendations:  $\geq 150$  mins/week of moderate intensity or  $\geq 75$  mins/week of vigorous intensity or an appropriate combination hereby.
- Not following the WHO recommendations:  $< 150$ - $300$  mins/week of moderate intensity or  $< 75$  mins/week of vigorous intensity (9).

#### *Total sedentary behavior h/day (continuous)*

- In question F, respondents reported hours and minutes spent daily sedentary on the following: work, transport, screen time and other sedentary activities, such as eating, social gatherings etc.
- Total sedentary behavior h/day will be calculated by adding hours and minutes from the abovementioned categories and then calculated into hours.

### Covariates

The listed covariates below are suggested to adjust for in the analyses due to possible confounding: Age, sex, ethnicity, marital status, educational level, alcohol consumption, smoking, and diet may be independent risk factors of the four exposures (comorbidity, obesity, stress, and health-related quality of life) and the outcome (physical activity).

Furthermore, the four exposures may be independent risk factors in the individual model, therefore, the variables comorbidity, obesity, stress, and health-related quality of life will be included as potential confounders in each model. Directed Acyclic Graphs (DAGs) of the assumed causal relations between exposures and outcome of the primary analysis have been created (appendix 1-4).

#### *Age (continuous)*

- Calculated age at Jan 11<sup>th</sup>, 2017, from CPR-register

#### *Sex (binary)*

- From CPR-register
- Categorizations: Male, Female

#### *Ethnicity (categorical)*

- From CPR-register
- Categorizations: Born in Denmark, Western, Non-Western

#### *Marital status (binary)*

- Based on question G and CPR-register
- Marital status was categorized into: Married or Living with partner, Living alone

#### *Educational level (categorical)*

- Educational level was defined as the highest completed education, and the variable was obtained from question 50-51
- Educational level was categorized into the following: Primary (<10 years), Upper secondary or vocational (10-12 years), Higher education ( $\geq 13$  years)

#### *Alcohol consumption (categorical)*

- Respondents were asked about their weekly alcohol consumption in question 24
- Alcohol consumption was categorized in accordance with the national recommendations from the Danish Health Authority and the risk of alcohol-related diseases for men and women:
  - o No alcohol (0 drinks – both men and women)
  - o Below low risk (men  $>0$  &  $<14$  drinks, women  $>0$  &  $<7$  drinks)
  - o Above low risk (men  $\geq 14$  &  $\leq 21$  drinks, women  $\geq 7$  &  $\leq 14$  drinks)
  - o High risk (men  $>21$  drinks, women  $>14$  drinks)

#### *Smoking (categorical)*

- Information regarding respondents smoking habits was obtained from question 13
- Smoking was categorized into the following: Smoker, Ex-smoker, Never smoked

#### *Diet (categorical)*

- Frequency and self-rated dietary habits were obtained from question 27-32
- Diet was calculated and categorized in accordance with the Dietary Quality Score: Unhealthy, Medium healthy, Healthy (10)

### **Statistical methods**

#### Statistical software

STATA/BE 17.0

#### Sample size

The survey was fully or partially completed by 183,372 respondents (58.7 %). Respondents with diabetes and complete data on outcome, exposures and covariates will be considered as eligible for the analytical sample of the primary aim. Following the categorization of diabetes from DNHS, respondents were defined as “Having diabetes” if they had answered “I have diabetes now” or “I have had diabetes” and “I suffer from sequelae due to the diabetes”. According to this categorization, 10,216 respondents have diabetes. Respondents with complete data on primary outcome, exposures and covariates will be 6,856. The secondary analysis will have a smaller sample size due to fewer complete responses.

#### Missing data

The percentage of missing data for the primary outcome (MVPA) among individuals with diabetes is 11.8 %. For the secondary outcome (WHO recommendations) the percentage of missing data is 20.5 %, and for the outcome total sedentary behavior the percentage of missing data is 20.0 %. To reduce the possible impact of non-response bias on the estimates, calibration weighting from NATSUP will be applied.

A supplementary table comparing characteristics of responders with non-responders among individuals with diabetes will be conducted.



### Primary analyses

Cross-tabulations will be conducted to describe habitual physical activity among individuals with diabetes and to display potential subgroup differences.

Table 1 (participant characteristics) will be standardized on age and sex due to expected large differences between “Individuals with diabetes” and “Individuals with no known diabetes”.

Both crude and multivariable adjusted associations will be estimated.

Four multivariable linear regression analyses will be conducted to investigate the association between selected determinants and MVPA. Adjustments will differentiate from each analysis according to DAGs (supplements 1-4). Model assumptions of linear regressions will be assessed:

- 1) Exposure: Comorbidity with and without mental diseases  
Adjustments: Age, alcohol consumption, diet, educational level, ethnicity, sex, marital status, obesity, and smoking
- 2) Exposure: Obesity  
Adjustments: **Age, alcohol consumption, diet, educational level, ethnicity, sex, marital status, comorbidity, and smoking**
- 3) Exposure: Stress  
Adjustments: Age, educational level, sex, marital status, obesity, comorbidity, and smoking
- 4) Exposure: Health-related quality of life  
Adjustments: Age, educational level, sex, marital status, obesity, comorbidity, smoking, and stress

### Secondary analyses

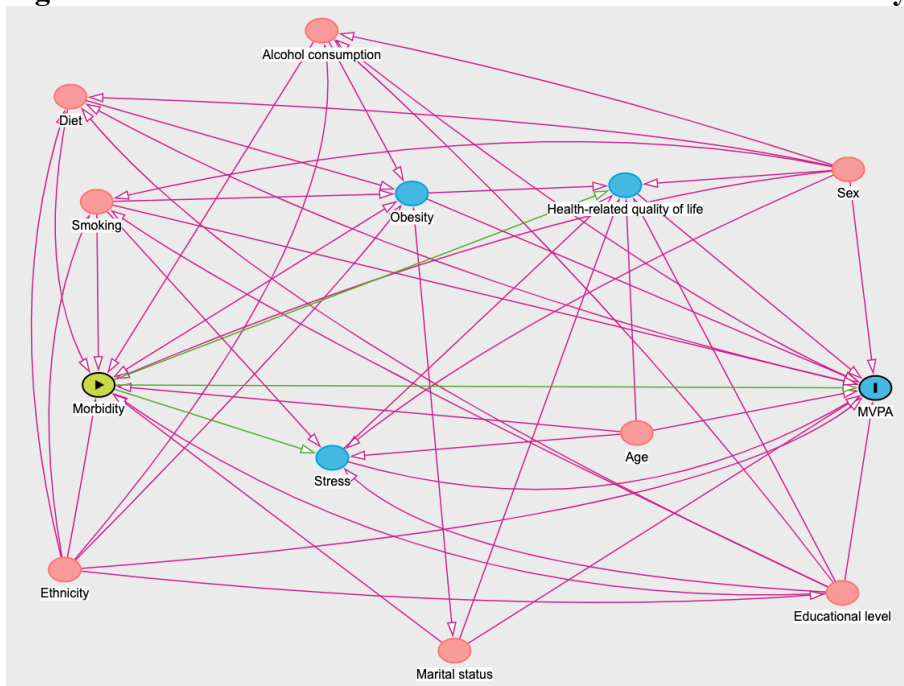
Four multivariable logistic regression analyses will be conducted with the same exposures and adjustments as the abovementioned. Using multivariable logistic regression analyses with the WHO guidelines of physical activity as outcome (binary). Model assumptions of logistic regressions will be examined by linearity between independent variables and log odds of outcome.

Furthermore, four multivariable linear regression analyses will be conducted to investigate the secondary aim with sedentary behavior in leisure time as outcome and comorbidity, obesity, stress, and health-related quality of life as exposures. Adjustments in the secondary analyses will be the same as the primary analyses. Model assumptions will be assessed.

At last, cross-tabulations will be conducted to describe proportions of whether inactive participants with diabetes who are motivated for being more physically active. The cross-tabulations will be conducted in subgroups of age and sex due to expected differences in motivation of behavioral changes.

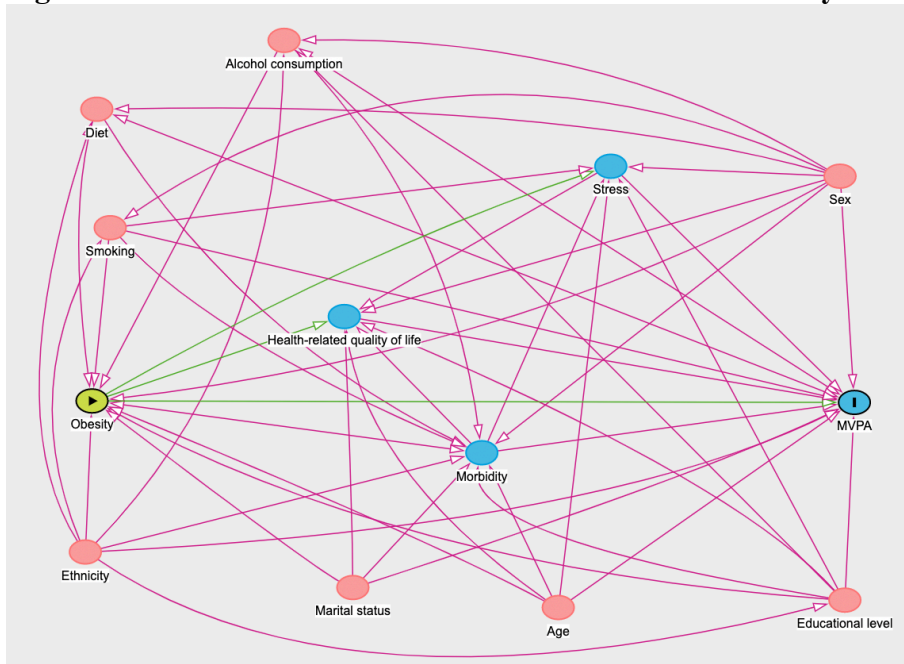
## Supplements

**Fig. s1. DAG of the assumed causal relations between comorbidity and MVPA.**



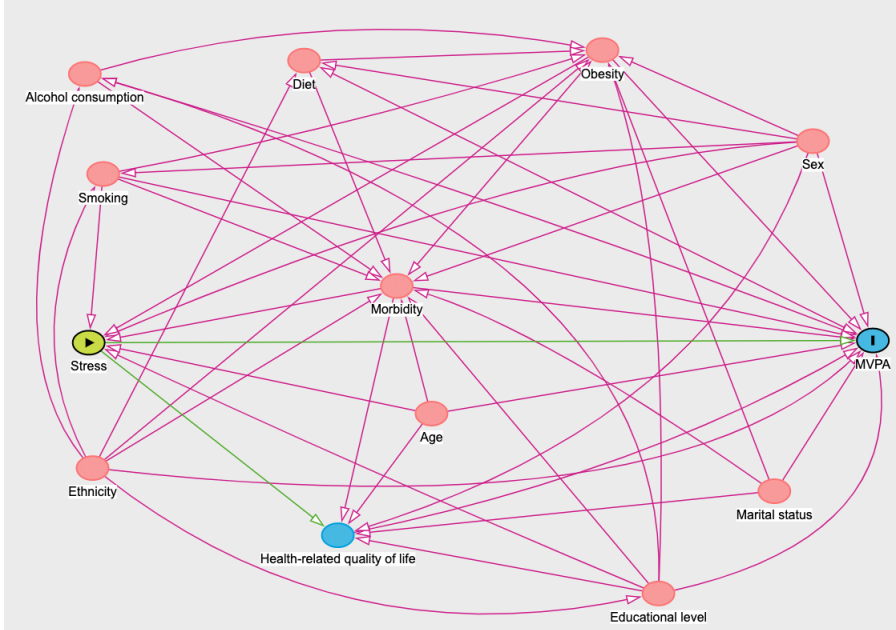
Directed Acyclic Graph (DAG) of the assumed causal relations between exposure (comorbidity), outcome (MVPA) and covariates in the primary analyses. Green line reflects the assumed causal paths. Red line and variables reflect possible confounding paths.

**Fig. s2. DAG of the assumed causal relations between obesity and MVPA.**



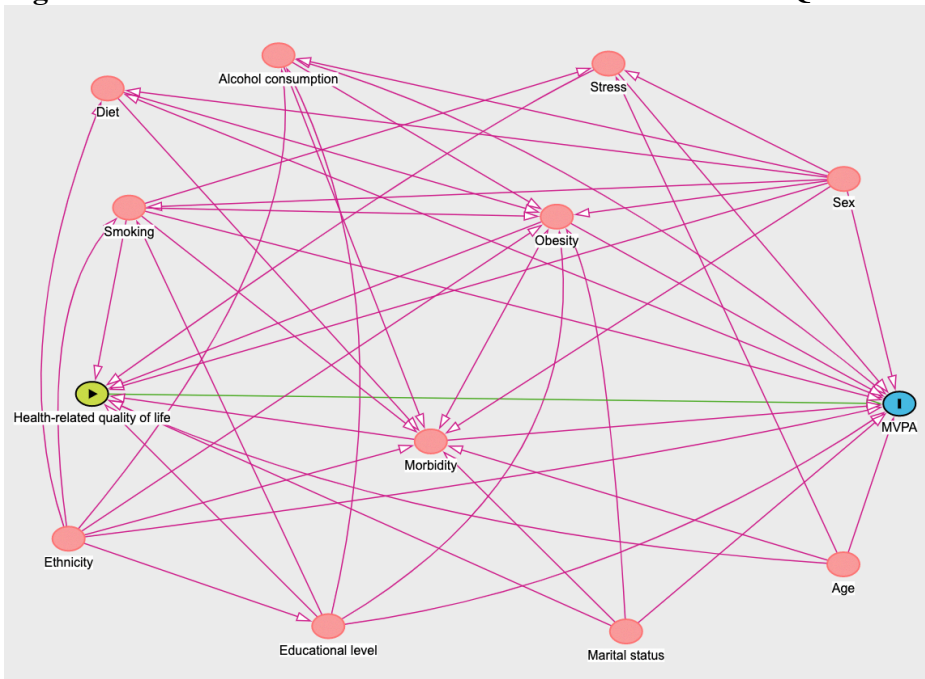
Directed Acyclic Graph (DAG) of the assumed causal relations between exposure (obesity), outcome (MVPA), and covariates in the primary analyses. Green line reflects the assumed causal paths. Red line and variables reflect possible confounding paths.

**Fig. s3. DAG of the assumed causal relations between stress and MVPA.**



Directed Acyclic Graph (DAG) of the assumed causal relations between exposure (stress), outcome (MVPA), and covariates in the primary analyses. Green line reflects the assumed causal paths. Red line and variables reflect possible confounding paths.

**Fig. s4. DAG of the assumed causal relations between HRQoL and MVPA.**



Directed Acyclic Graph (DAG) of the assumed causal relations between exposure (HRQoL), outcome (MVPA), and covariates in the primary analyses. Green line reflects the assumed causal paths. Red line and variables reflect possible confounding paths.

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# **Appendix VI**

## **Statistical analysis plan for Paper II**

The statistical analysis plan was uploaded at Open Science Framework (<https://osf.io/34t2c/>)

**Running title**

Detailed descriptions of physical activity patterns among individuals with prediabetes and diabetes: The Lolland-Falster Health Study

**Authors**

Sofie Rath Mortensen, Søren Thorgaard Skou, Jan Christian Brønd, Mathias Ried-Larsen, Randi Jepsen, Lars Bo Jørgensen, Lars Hermann Tang, Therese Lockenwitz Petersen, Neda Bruun Rasmussen, Anders Grøntved

**Contributors and roles in the SAP**

*Researcher responsible for writing the SAP:* PhD student Sofie Rath Mortensen (PT, MSc)

**Brief background**

Diabetes is a major public health challenge, and the prevalence of diabetes is predicted to increase rapidly because of the high prevalence of prediabetes and the conversion to type 2 diabetes (1, 2). Engagement in regular physical activity is a cornerstone of type 2 diabetes management. Adults with diabetes are recommended to exercise daily to enhance insulin action, or at least have no more than 2 consecutive days of inactivity. In addition, weekly engagement in physical activity should include at least 150 min. of moderate to vigorous intensity spread over at least 3 days (3). Despite the importance of physical activity for type 2 diabetes, it is largely unknown to what extent physical activity patterns vary among individuals with prediabetes and diabetes. Recent developments of technological wearable devices provide new possibilities to describe detailed patterns of physical activity, physical postures, sleep characteristics, and other physiological factors over long time periods. The second-by-second continuous assessment offer many opportunities to advance research also among individuals with diabetes and other chronic conditions (4). No previous large-scale studies have provided a detailed description of objectively assessed habitual physical activity patterns among individuals with prediabetes and diabetes. Availability of such information would be an important resource for planning future treatment courses taking individual characteristics, needs, and preferences into account when designing a physical activity intervention.

**Overall aim**

To describe physical activity behaviors and patterns among individuals with prediabetes and diabetes and compare these patterns with individuals with no known diabetes.

**Specific aims**

- I. To describe engagement in total daily light, moderate, and vigorous physical activity according to age, sex, day-type (weekend vs. weekday), and season among individuals with diabetes and prediabetes
- II. To describe the distribution of the number of inactive days/week and consecutive inactive days among individuals with diabetes and prediabetes
- III. To describe the physical activity profile (sedentary, light, moderate- and vigorous activity) during waking hours on week- and weekend days among individuals with diabetes and prediabetes
- IV. To statistically compare distributions of physical activity in I, II, and III according to diabetes status (no known diabetes/prediabetes/diabetes) while controlling for age and sex, and further investigate if any differences by diabetes status are explained by other major determinants of physical activity such as body composition, other prevalent chronic disease, stress, mental well-being, and chronic pain.

## Methods

### Study design

The study design is cross-sectional. Reporting of the study will be followed by the STROBE checklist (5).

### Data sources

Data will be derived from the Danish Lolland-Falster Health Study (LOFUS), which is a Danish household-based prospective cohort study that aims to establish determinants of health in a disadvantaged, mixed rural-provincial area. LOFUS was conducted between 8<sup>th</sup> of February 2016 and 13<sup>th</sup> of February 2020. The data collection in LOFUS encompassed questionnaires, a site visit including physical examinations, and biological samples (6).

### Measurements

#### *Diabetes definition*

##### *Diabetes*

Participants will be defined as “Have diabetes” if one of the following criteria are met:

- 1) HbA1c  $\geq 48$  mmol/mol, or
- 2) HbA1c  $< 48$  mmol/mol and use of self-reported antidiabetic medication.

It is not possible to distinguish between type 1 and type 2 diabetes due to lack of information.

##### *Prediabetes*

Participants with HbA1c levels between  $\geq 39$  mmol/mol and  $\leq 47$  mmol/mol were categorized as prediabetic according to the American Diabetes Association (ADA) (7).

##### *Participants with no known diabetes*

Participants will be defined as “No known diabetes” if HbA1c levels are below 39 mmol/mol and no self-reported use of antidiabetic medication.

#### *Outcomes*

##### *Physical activity patterns*

Objectively measured physical activity was assessed using two Axivity AX3 (Axivity, Newcastle UK) accelerometers placed on lower back and the front of the right thigh. Participants were instructed to wear the accelerometers for seven consecutive days during all time (24 hours/day), including during sleep and water activities.

A minimum of 22 hours of wear time out of 24 hours was the criteria for valid data for a day. Data for a measurement period will be considered as valid, if the participant has at least 3 valid weekdays and 1 valid weekend. For calculation of total daily physical activity, data will be weighted by 5/7 for weekdays and 2/7 for weekends.

The following physical activity intensities will be included in the present study:

- Sedentary activity: Time spent on sedentary activity
- Light physical activity (LPA): Time spent on light intensity activity
- Moderate physical activity (MPA): Time spent on moderate intensity activity
- Vigorous physical activity (VPA): Time spent on vigorous intensity activity

- Moderate to vigorous physical activity (MVPA): Time spent on moderate to vigorous intensity activity

The included activity types were determined by generating ActiGraph counts using 10 seconds-epochs from the raw acceleration measured at the back (8).

#### *Adherence to the recommendations of physical activity and sedentary behavior*

Adherence to the World Health Organization (WHO) recommendations of weekly physical activity and sedentary behavior will be assessed with objectively measured MVPA and VPA.

- $\geq 150$  minutes MPA or  $\geq 75$  minutes VPA weekly or an equivalent combination will be considered as following the recommendations.

Adherence to the recommendations of daily physical activity according to the American Diabetes Association and the Danish Health Authority will be assessed with objectively measured daily MVPA. The distribution of MVPA during a week will be categorized into number of days with:

- 1) Sufficient physical activity:  $\geq 30$  minutes/day MVPA
- 2) Some physical activity:  $\geq 5$  minutes/day and  $< 30$  minutes/day MVPA
- 3) Inactivity:  $< 5$  minutes/day of MVPA

#### *Variables to describe participant characteristics*

##### *Age (continuous)*

- Age of the participants when attending health examinations.

##### *Marital status (categorical)*

- Participants were asked “*What is your legal marital status?*” and “*Do you live permanently in a paperless cohabitation?*”. The two questions will be combined into one variable differentiating between status of cohabitant: Married/living with partner; Living alone.

##### *Educational level (categorical)*

- Self-reported information on participants’ educational level was obtained from the questionnaire.
- Educational level will be categorized into: Primary ( $< 10$  years), Upper secondary or vocational (10-12 years), Higher education ( $\geq 13$  years).

##### *Obesity (categorical)*

Participants’ height and weight was obtained at the health examinations to calculate the body mass index (BMI) ( $\text{kg}/\text{m}^2$ ). Height was measured with SECA 216 Wall-mounted height measure, and weight was measured with Tanita Body Composition Analyzer (BC-420MA III or Electronic scale Tanita WB 150 SMA) (6).

BMI will be categorized into the following: underweight/normal weight (BMI  $< 25.0$ ), overweight (BMI  $\geq 25.0$ - $< 30.0$ ), obese class I (BMI  $\geq 30.0$ - $< 35.0$ ), obese class II (BMI  $\geq 35.0$ - $< 40.0$ ), and obese class III (BMI  $\geq 40$ ), as defined by the World Health Organization (9).

##### *Comorbidities (excluding diabetes) (categorical)*

Self-reported information on selected long-term conditions (excluding diabetes) were obtained from the questionnaire and will be used to assess comorbidity.

The definition of comorbidity will be based on diagnoses organized in ten groups of different body systems according to Willadsen et al. (10).



Participants were asked to add if they had any other condition(s). All “other” conditions will be coded into the ten groups of body systems following the classification by Tang et al. (11). The classification in this study will differ from Tang et al. by including hypertension, but excluded other risk factors (e.g., increased cholesterol).

The variable will be categorized as follows: 1) Have diabetes and no comorbidities, 2) Have diabetes and one comorbidity from one body system, 3) Have diabetes and two comorbidities from two different body systems, 4) Have diabetes and three or more comorbidities from at least three different body systems. Suffering from several long-term conditions within the same body system, e.g., hypertension and angina pectoris, will still only count as one comorbidity.

#### *Stress (categorical)*

Self-reported psychological stress was obtained with Cohen’s 10-item Perceived Stress Scale (PSS) (12) from the questionnaire.

The PSS will be categorized into three as follows:

- Scores ranging from 0-13 will be considered low perceived stress
- Scores ranging from 14-26 will be considered moderate perceived stress
- Scores ranging from 27-40 will be considered high perceived stress

#### *Mental well-being (categorical)*

Self-reported mental well-being was obtained with the WHO-5 Well-Being Index (13). Each question is scored from 0 (none of the time) to 5 (all of the time), however, scoring of the WHO-5 in this study will follow the recommendations to multiply the raw score by 4 to obtain a percentage score ranging from 0-100 (14). A higher score indicates a better perceived health-related quality of life. Scores <50 will be categorized as low mental well-being, and scores  $\geq 50$  will be categorized as moderate to high mental well-being.

#### *Chronic pain (binary)*

- Participants were asked “Do you have long-lasting/chronic pain, that has lasted for 6 months or more?” with Yes/No as answer categories, which will be the categories of this variable.

#### *Medication (continuous)*

- Self-reported use of selected medical preparation was obtained from the questionnaire. Number of participants taking the following medical preparation will be reported:
  - o Insulin
  - o Other diabetes medication
  - o Cholesterol-lowering medication
  - o Diuretics

#### *HbA1c-level and glycemic control (continuous and binary)*

- Level of HbA1c was obtained from the biological samples and will be reported as continuous data.
- Glycemic control will be dichotomized following the definition of a reasonable controlled glycemic level for adults from the ADA (15): Controlled glycemic level (HbA1c-level <53 mmol/mol); Uncontrolled glycemic level (HbA1c-level  $\geq 53$  mmol/mol).

## Statistical methods

### Statistical software

STATA/BE 17.0 and RStudio Version 1.4.1106

### Sample size

A total of 3,158 participants have provided valid data on accelerometer and information regarding diabetes status, and out of those, 181 participants have diabetes, 568 participants have prediabetes, and 2,409 participants have no known diabetes, based on the abovementioned definitions.

### Missing data

Accelerometer data were received as complete data, therefore, there are no missing data on primary outcomes.

Out of 3,187 above 18 years of age with valid accelerometer data, 0.9 % are missing information regarding diabetes status.

### Primary analyses

Characteristics of participants with diabetes, prediabetes and participants with no known diabetes will be described and displayed in table 1. Table 1 will be standardized on age and sex due to expected differences between participants with prediabetes, diabetes, and no known diabetes.

The distribution of total daily LPA, MPA, VPA, MVPA and SB by age among individuals with prediabetes and diabetes and no known diabetes will be estimated and graphically displayed. Due to the expected zero-inflated physical activity data (in particular MVPA and VPA) we will use quantile regression with age as the independent variable using fractional polynomials to account for an expected curved relationship of age with physical activity. Based on the model, fitted quantiles of activity (i.e., median, 25<sup>th</sup> and 75<sup>th</sup> percentile) by age will be estimated and displayed graphically and in a table. These analyses will also be done by sex and day-type (weekend vs. weekday). Also, to explore differences across the distributions in total daily LPA, MPA, VPA, and MVPA in detail by diabetes status, estimated density and quantile functions will be carried out with entropy balancing of age and sex (16).

The distribution (i.e., 25<sup>th</sup> and 75<sup>th</sup> percentile) of total daily MVPA by season will be estimated by diabetes status (winter, spring, summer, and autumn) using quantile regression.

To investigate if any differences by diabetes status are explained by BMI, stress, other chronic diseases, mental well-being, and chronic pain, regression models on daily MVPA and diabetes status will be performed with additional adjustment for these factors. Because BMI distributions may be large across diabetes status and body composition is a strong determinant of activity, we will in a separate analysis consider adjustment for BMI only (in addition to age and sex).

### Explorative analyses

The prevalence of two and three or more consecutive inactive days and rate of inactive days per week will be estimated by season using probability distribution function and flexible parametric modelling respectively.

The percentage of individuals with 0, 1, 2, 3, 4, 5, 6, and 7 inactive days (count data) will be estimated by diabetes status with adjustment for age and sex using probability distribution function and flexible parametric modelling will be used to compare the rate of consecutive inactive days by diabetes status with adjustment for age and sex. To accommodate that participant will have 4 to 7 consecutive days of monitoring, right censoring will be employed in the flexible parametric

modelling analysis. Also, the prevalence of two and three or more consecutive days with inactivity in accordance with the ADA will be compared by diabetes status with adjustment for age- and sex.

Finally, the physical activity profile over the waking hours of weekdays and weekend days will be estimated by diabetes status. Mixed quantile regression with adjustment for age and sex will be used to obtain fitted quantiles of activity (i.e., median, 25<sup>th</sup> and 75<sup>th</sup> percentile) by time of day (per 15 min) will be estimated and displayed graphically. We will pursue functional data analysis (FDA) to statistically compare daily activity profiles by diabetes status, but we may turn to a simpler stratified approach (analysis stratified in time-segments) if we are unsuccessful with using FDA.

Due to expected age-related differences in physical activity, we may stratify some analyses by below and above 65 years of age.

The results will be presented in one or two papers.

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# **Appendix VII**

## **Statistical analysis plan for Paper III**

The statistical analysis plan was uploaded at Open Science Framework (<https://osf.io/7bnyp/>)

**Running title**

Sedentary activity and sedentary bouts, and their relationship with stress and well-being in individuals with diabetes and prediabetes: The Lolland-Falster Health Study

**Authors**

Sofie Rath Mortensen, Anders Grøntved, Jan Christian Brønd, Mathias Ried-Larsen, Therese Lockenwitz Petersen, Lars Bo Jørgensen, Randi Jepsen, Lars Hermann Tang, Søren Thorgaard Skou

**Contributors and roles in the SAP**

*Researcher responsible for writing the SAP:* PhD-student Sofie Rath Mortensen (PT, MSc)

**Brief background**

Diabetes has become one of the most prevalent chronic conditions worldwide (1), and regular physical activity plays an important role in type 2 diabetes management and prevention (2, 3). However, reduction in sedentary activity, such as sitting and lying down during waking hours, has become an increased focus in diabetes management (4). Therefore, adults with type 2 diabetes are recommended to reduce sedentary time and place small “doses” of light physical activity every 30 minutes throughout the day to break up sitting time in addition to the recommendations of physical activity (3, 5). Living with diabetes can be very stressful due to demands of self-management in terms of adherence to lifestyle recommendations such as physical activity, diet, and medication, which is also known as diabetes distress. Depression, anxiety, high perceived stress, and low well-being, are more prevalent in individuals living with diabetes compared to the general population (6-9). Studies within the field of diabetes indicate that low well-being may have a substantial negative impact upon diabetic control and self-care in relation to the diabetes (10). Furthermore, a recent Danish nationwide cross-sectional study found that individuals with diabetes who suffered from high perceived stress and low health-related quality of life were less likely to engage in regular physical activity (6). These results suggest that stress and well-being in individuals with diabetes may challenge their ability to adhere to lifestyle recommendations. Despite the high prevalence of stress and low well-being in individuals with diabetes, it is yet undiscovered to what extent these factors are associated with a sedentary lifestyle among individuals with diabetes and prediabetes. Such knowledge could provide more insights into recommendations in diabetes treatment and prevention to enhance time spent non-sedentary when individuals with diabetes or prediabetes suffer from high levels of stress and low well-being.

**Aims**

The aim of this study is to investigate the associations of stress and well-being with the total amount of sedentary activity, characterized by sitting, reclined, and lying during waking hours, and durations of continuous sedentary bouts in individuals with diabetes and prediabetes. A secondary aim is to explore the daily sedentary activity pattern during a day in individuals with diabetes and prediabetes.

**Methods****Study design**

The study design is cross-sectional and reporting of the study will be followed by the STROBE checklist (11).

**Data sources**

Data will be derived from the Danish Lolland-Falster Health Study (LOFUS), which is a Danish household-based prospective cohort study that aims to establish determinants of health in a disadvantaged, mixed rural-provincial area. LOFUS was conducted between 8<sup>th</sup> of February 2016 and 13<sup>th</sup> of February 2020. The data collection in LOFUS encompassed questionnaires, a site visit including physical examinations, and biological samples (12).

## Measurements

### Definition of diabetes

Participants will be defined as “Have diabetes” if one of the following criteria are met:

1. HbA1c  $\geq 48$  mmol/mol, or
2. HbA1c  $< 48$  mmol/mol and self-reported use of antidiabetic medication.

It is not possible to distinguish between type 1 and type 2 diabetes due to lack of information.

Participants with HbA1c levels between  $\geq 39$  mmol/mol and  $< 48$  mmol/mol and no self-reported use of antidiabetic medication will be categorized as “Have prediabetes” according to the American Diabetes Association (ADA) (13).

### Outcomes

#### *Sedentary and physical activity variables*

Objectively measured sedentary and physical activity were assessed using two Axivity AX3 (Axivity, Newcastle UK) accelerometers placed on the lower back and the front of the right thigh. Participants were instructed to wear the accelerometers for seven consecutive days during all time (24 hours/day), including during sleep and water activities (14).

A minimum of 22 hours of wear time out of 24 hours was the criteria for valid data for a day. Data for a measurement period will be considered as valid, if the participant has at least three valid weekdays and one valid weekend day. For calculation of total daily sedentary activity, data will be weighted by 5/7 for weekdays and 2/7 for weekends.

Time spent sedentary was determined using the method described by Skotte et al. (15), and physical activity intensities were determined by generating ActiGraph counts using 10-seconds epochs from the raw acceleration (16). Data processing is described in detail in Petersen et al. (17).

The following sedentary and physical activity variables will be included in the present study:

- Total sedentary activity (hours/day): Total time spent in a sitting, reclined or lying position from 7:00 AM to 10:00 PM during a day which is presumed to correspond to the waking hours for an adult. Differences between waking time and sleeping during weekdays and weekend days were checked, however, the distributions were almost similar. Therefore, we chose the same waking hours (7:00 AM to 10:00 PM) for both weekdays and weekend days.
- Total number of daily sedentary bouts: A sedentary bout will be measured if the individual has been in a sitting or lying position for at least 10 seconds duration.
- Categories of sedentary bouts in terms of duration:  $< 1$  min.,  $\geq 1$  to  $< 3$  min.,  $\geq 3$  to  $< 10$  min.,  $\geq 10$  min. to  $< 30$  min., and  $\geq 30$  min.
- Number of prolonged sedentary bouts: Sedentary bouts of  $> 30$  min. daily.
- Categories of breaks in sedentary time in terms of duration: A break in sedentary time during waking hours will be defined as a transition from a sitting, reclined or lying position of at least 10 seconds duration to any of the following positions/activities of at least 10 seconds duration during waking hours: Stand, move, walk, and run. The following categories were made based on the distribution:  $< 1$  min.,  $\geq 1$  min. to  $< 3$  min.,  $\geq 3$  min. to  $< 10$  min., and  $\geq 10$  min.
- Moderate to vigorous physical activity (MVPA): Minutes spent on moderate to vigorous intensity activity.

### Exposures

#### *Stress (binary)*

Self-reported psychological stress was obtained with Cohen's 10-item Perceived Stress Scale (PSS) (18) from the questionnaire. The PSS is categorized into three: Scores from 0-13 = low perceived stress, Scores from 14-26 = moderate perceived stress, and Scores from 27-40 = high perceived stress. For the primary aim, we will collapse the categories into a binary variable distinguishing between low perceived stress (scores from 0-13) and moderate to high perceived stress (scores from 14-40) because of low numbers in the highest category.

A variable that distinguishes between the prevalence of diabetes, prediabetes, and low or moderate to high perceived stress based on the abovementioned definitions will be developed and categorized as: 1) Diabetes and low perceived stress, 2) Diabetes and moderate to high perceived stress, 3) Prediabetes and low perceived stress, and 4) Prediabetes and moderate to high perceived stress. For the second aim, the stress variable will be handled as a continuous variable.

#### *Well-being (binary)*

Self-reported mental well-being was obtained with the WHO-5 Well-Being Index (19). Each question is scored from 0 (none of the time) to 5 (all of the time), however, scoring of the WHO-5 in this study will follow the recommendations to multiply the raw score by 4 to obtain a percentage score ranging from 0-100 (10). A higher score indicates a better perceived mental well-being. Scores <50 will be categorized as low well-being, and scores  $\geq 50$  will be categorized as moderate to high well-being in the first aim.

A variable that distinguishes between the prevalence of diabetes, prediabetes, and low or moderate to high well-being based on the abovementioned definitions will be developed and categorized as: 1) Diabetes and low well-being, 2) Diabetes and moderate to high well-being, 3) Prediabetes and low well-being, and 4) Prediabetes and moderate to well-being. For the second aim, the well-being variable will be handled as a continuous variable.

### Variables to describe participant characteristics and covariates

#### *Age (continuous)*

- Age of the participants when attending health examinations.

#### *Marital status (categorical)*

- Participants were asked "What is your legal marital status?" and "Do you live permanently in a paperless cohabitation?". The two questions will be combined into one variable differentiating between status of cohabitant: Married/living with partner; Living alone.

#### *Educational level (categorical)*

- Self-reported information on participants' educational level was obtained from the questionnaire.
- Educational level will be categorized into: Primary and lower secondary or other (<10 years), Upper secondary or vocational (10-12 years), and Higher education ( $\geq 13$  years).

#### *Occupational status (categorical)*

- Self-reported information on participant's employment status was obtained from the questionnaire.



- Employment status will be categorized into the following based on the answer categories from the questionnaire:
  - o Employed (Employed, Both employed and self-employed, Self-employed)
  - o Unemployed (Unemployed)
  - o Not working due to sick leave or early retirement (In rehabilitation, Chronic illness (3 or more month), In early retirement due to invalidity)
  - o Retired (Retired – private pension, Old age pensioner)
  - o Student (Student, Primary or secondary school student, Apprentice)
  - o Other (Military conscript, Family worker, Stay at home parent, Other)

#### *Body Mass Index (categorical)*

- Participants' height and weight were obtained at the health examinations to calculate the body mass index (BMI) ( $\text{kg}/\text{m}^2$ ). Height was measured with SECA 216 Wall-mounted height measure, and weight was measured with Tanita Body Composition Analyzer (BC-420MA III or Electronic scale Tanita WB 150 SMA) (12).
- BMI will be categorized into the following: underweight/normal weight ( $\text{BMI} < 25.0$ ), overweight ( $\text{BMI} \geq 25.0 - < 30.0$ ), obese ( $\text{BMI} \geq 30.0$ ) as defined by the World Health Organization (20).

#### *Comorbidities (excluding diabetes) (categorical)*

- Self-reported information on selected long-term conditions (excluding diabetes) was obtained from the questionnaire and will be used to assess comorbidity.
- The definition of comorbidity will be based on diagnoses organized in ten groups of different body systems (Lung, Musculoskeletal, Endocrine, Mental, Cancer, Neurological, Gastrointestinal, Cardiovascular, Kidney, and Sensory organs) according to Willadsen et al. (21).
- Participants were asked to add if they had any other condition(s). All “other” conditions were coded into the ten groups of body systems following the classification by Tang et al. (22). The classification in this study differs from Tang et al. by including hypertension, but excluding other risk factors (e.g., increased cholesterol).
- In the predefined questions regarding chronic conditions, diabetes was the only one in the endocrine group. Therefore, the endocrine comorbidity group included all other conditions (obtained from the question regarding “other” conditions), except from diabetes.
- The variable will be categorized as follows: 1) No comorbidities, 2) One comorbidity from one body system, 3) Two or more comorbidities from two different body systems. Suffering from several long-term conditions within the same body system, e.g., hypertension and angina pectoris, will still only count as one comorbidity.

#### *Chronic pain (binary)*

- Participants were asked “Do you have long-lasting/chronic pain, that has lasted for 6 months or more?” with Yes/No as answer categories, which will be the categories of this variable.

## **Statistical methods**

### Sample size

2,146 participants have provided valid data on accelerometer from the lower back and the right thigh and information regarding diabetes status, perceived stress and well-being. Furthermore, we added additional criteria for inclusion in the present study will be: 1) above 18 years of age, 2) a

minimum of 10 hours awake time, and 3)  $\geq 4$  hours of daily total sedentary time (estimated to be a realistic minimum of total sedentary time, therefore, accelerometer data  $< 4$  hours of total sedentary time will be considered as a measurement error). Out of the 2,146 participants, 145 have diabetes and 418 have prediabetes based on the abovementioned criteria and will be included in the present study.

### Descriptive analyses

Characteristics of participants with diabetes, prediabetes, and the total sample divided into subgroups based on the categories of perceived stress and well-being will be described and displayed in a table 1.

The distribution of total sedentary activity (sitting, reclined, and lying), sedentary activity bouts, categories of sedentary activity bouts in terms of duration, breaks in sedentary activity, categories of breaks in sedentary activity in terms of duration among participants with diabetes, prediabetes, and the total sample (diabetes + prediabetes) across categories of stress and well-being will be described in a table 2.

Both table 1 and 2 will be standardized on age and sex due to expected differences between participants with diabetes and prediabetes in the LOFUS sample.

### Analyses of associations

The cross-sectional associations between the exposures stress and well-being and the outcome total sedentary activity in participants with diabetes and prediabetes will be examined using linear regression models as the first choice. However, if the assumptions regarding distribution of residuals and homoscedasticity are not met, quantile regression models will be performed.

For the association between the exposures stress and well-being and the outcomes sedentary activity bouts and prolonged sedentary activity bouts in participants with diabetes and prediabetes, linear regression models will be performed. If model assumptions of linear regression are not met, we will conduct quantile regression or negative binomial regression models.

For the association between stress and each outcome (total sedentary activity, sedentary activity bouts, and prolonged sedentary activity bouts), two models will be performed. Model 1 will be adjusted for age and sex, and Model 2 will include additional adjustments of educational level, occupational status, marital status, BMI, and comorbidities. Also, for the association between well-being and each outcome, two models will be performed. Model 1 will be adjusted for age and sex, and Model 2 will include additional adjustments of educational level, occupational status, marital status, BMI, comorbidities, and chronic pain.

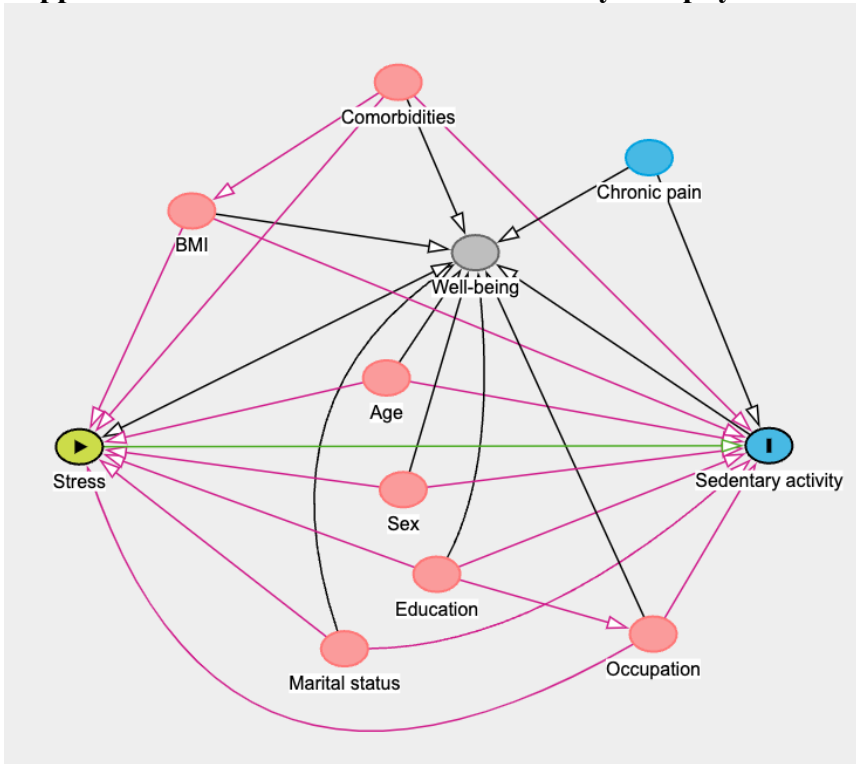
The included variables in the analyses were suggested a priori to be potential biasing paths between the exposures and outcomes according to the directed acyclic graphs (DAGs) (Supplement 1 and 2).

The daily sedentary activity pattern during weekdays and weekend days between participants with diabetes and participants with prediabetes will be investigated using mixed linear regression models with adjustment of age and sex. Further, we will add adjustment of stress to a second model, and a third model will be adjusted for well-being to investigate the influence of stress and well-being in the daily sedentary activity pattern. Savitzky-Golay smoothing filter will be used to generate a smoothed trend based on the point estimates for every 15-minutes obtained from the mixed model.

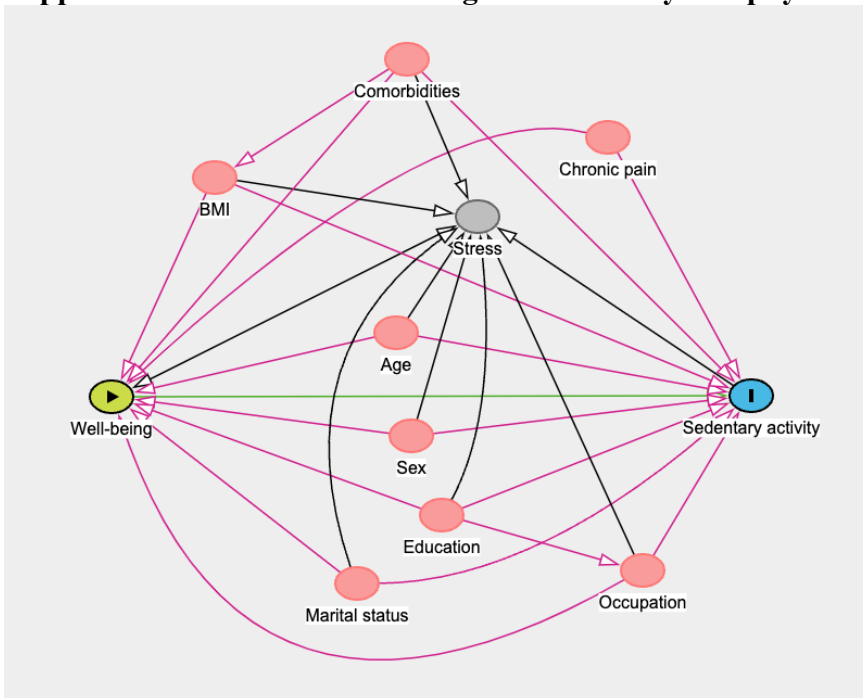
Some of the covariates may be recoded to continuous variables or collapsed into smaller categories depending on the fit of the model. All statistical analyses will be performed in STATA/BE 17.0 and

R statistical (R Core Team, Vienna, Austria) software version 2023.06.0+421. RStudio (RStudio Inc., Boston, MA, USA) version 2022.07.2 using an  $\alpha$ -level of 0.05 two-sided.

**Supplement 1 – DAG of stress and sedentary and physical activity outcomes.**



**Supplement 2 – DAG of well-being and sedentary and physical activity outcomes.**



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# **Appendix VIII**

## **Statistical analysis plan for Paper IV**

The statistical analysis plan was uploaded at Open Science Framework (<https://osf.io/3nphj/>)

*Statistical Analyses Plan (SAP)*

**Running title**

Feasibility of an online training community among individuals with type 2 diabetes: a one arm study

Version 1.0

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## **Brief background**

Physical activity is one of the cornerstones of type 2 diabetes (T2D) treatment and leads to an improved disease prognosis, increased functioning, and better quality of life, as well as reduced risk of developing micro- and macro-complications (1-3). It is well-established that supervised structured exercise consisting of aerobic exercise, strength training, or both combined can improve glucose control in patients with T2D (3, 4, 5). Adults living with T2D are recommended to do at least 150-300 minutes per week of moderate intensity or 75-150 minutes of vigorous intensity of physical activity (PA) or an equivalent combination on a weekly basis (6, 7). Throughout the Covid-19 pandemic, the use of digital information and communication technologies in healthcare, also known as e-based solutions or eHealth, has increased significantly (8). Currently it is well known that E-based solutions can be individualized and support individuals in managing their own illnesses and maintaining or increasing PA (9, 10). Evidence suggests that individuals with T2D who participate in and commit to exercise groups and use body-worn activity monitors such as pedometers and heart rate monitors are more successful in increasing and/or maintaining engagement in physical activity (11). In recent years, online training for individuals with chronic conditions have emerged as it enables participation in physical activity for individuals who have previously been challenged to participate due to limited resources or time, geographical distances, and sparse infrastructure (12). In 2022 a study investigated the effects of live-streamed tele-exercise during Covid-19-related lockdowns and demonstrated that live-streamed tele-exercise was an efficacious way to enhance physical activity; however, the adherence to the exercise program was a big challenge (13).

Combining an online training intervention with online group meetings could offer individuals with T2D social and mental support, while also conferring improved physical health-related benefits. No previous study has yet investigated the feasibility and/or potential benefits of combining online training with online group meetings.

### ***Study objective***

The aim of the trial is to evaluate the feasibility, fidelity, and acceptability of 8-week high intensity online training community supported by an activity watch in patients with type 2 diabetes.



## Study design

The present study is a one arm feasibility intervention study, and the primary outcome of the intervention is based on Research Progression Criteria for continuing to a full scale randomized controlled trial derived from a traffic light system (green - the intervention can continue to full scale, amber – the intervention can continue, but need changes in protocol and lastly red – the intervention can't continue, unless the specific problem(s) can be solved) (28). Reporting of the study will follow the CONSORT checklist (14). The study will be conducted between Marts 2022 to the end of May 2022. This study was approved by the Scientific Ethical Committee of the Capital Region of Denmark (Approval number: H-2106295) and registered at ISRCTN. Individuals with T2D were recruited within Capital Region of Denmark and Region of Zealand. Recruitment of participants was conducted via advertisements on the Facebook page of The Danish Diabetes Association, Diabetes magazines, local diabetes organizations, support from the Danish Diabetes Association, and from a contact list of participants with T2D from a previous experiment at CFAS.

## Study outcomes

### *Primary outcomes*

The primary outcome in this study is the predefined Research Progression criteria, which are presented in table 1.

**Table 1:** Research progression criteria for continuing or implement Online Training Community

Outcome	Can be implemented	Continue, but changes to the protocol must be discussed	Do not proceed implementation unless the issue can be solved
Participant recruitment	24 participants recruited within 3 months	Fewer than 24 participants recruited within 3 months	Fewer than 12 participants recruited within 3 months
Completion of intervention	Minimum 75% of the participants complete post intervention	Minimum 50% of the participants complete post intervention	Fewer than 50% of the participants complete post intervention
Adherence to the training sessions <sup>1</sup>	Minimum 75% of the participants complete more than half of the online training sessions	Minimum 50% of the participants complete more than half of the online training sessions	Fewer than 50% of the participants complete more than half of the online training sessions

Adherence to the group meetings <sup>2</sup>	Minimum 75% of the participants complete more than half of the group meeting sessions	Minimum 50% of the participants complete more than half of the group meeting sessions	Fewer than 50% of the participants complete more than half of the group meeting sessions
Adherence to goalsetting <sup>3</sup>	Minimum 75% of the participants set goals	Minimum 50% of the participants set goals	Fewer than 50% of the participants set goals
Difficulty in participating in the objectively measured physical activity	Minimum 80% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Minimum 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again	Fewer than 70% of the participants did NOT find the objective outcome measures of the study so difficult that they would not participate in the study again
Improvement of physical activity <sup>4</sup>	Minimum 50% of the participants have achieved improvements in physical activity at post intervention	Minimum 25% of the participants have achieved improvements in physical activity at post intervention	Fewer than 25% of the participants have achieved improvements in physical activity at post intervention
Adverse events	No or minor adverse events related to the intervention at post intervention	Fewer than five serious adverse events related to the intervention at post intervention	Five or more serious adverse events related to the intervention at post intervention
<sup>1</sup> At the start and end of each of the online training sessions all the participants note if they are participating. <sup>2</sup> At the start and end of each of the group meetings all the participants note if they are participating. <sup>3</sup> Goalsetting made in the group meetings. <sup>4</sup> Improvements in objectively measured physical activity types, which are listed further down in the SAP			

### ***Secondary outcomes***

A detailed description of all outcomes is listed below.

Time frame: 8 weeks

1. Change from baseline in perceived Stress
2. Change from baseline in mental well-being
3. Change from baseline in self-efficacy
4. Change from baseline in loneliness
5. Change from baseline in BMI
6. Change in diet habits
7. Satisfaction with the intervention after 8 weeks

## **Protocol deviations**

The target population was changed from only members of the Danish Diabetes Association to all individuals diagnosed with T2D.

Two of the Research progression criteria was changed after the study protocol was written. Firstly because of a definition error in Participant recruitment: amber was changed from “*24 participants recruited within 3 months*” to “*Fewer than 24 participants recruited within 3 months*” and red was changed from “*Fewer than 24 participants recruited within 3 months*” to “*Fewer than 12 participants recruited within 3 months*”.” Another change in the Research Progression Criteria was the definition of the **second feasibility outcome**, which was changed from “Completion of goalsetting” to “Completion of intervention”.

## **Study design**

The present study is a one arm feasibility intervention study, and the primary outcome of the intervention is based on Research Progression Criteria for continuing to a full scale randomized controlled trial derived from a traffic light system (green - the intervention can continue to full scale, amber – the intervention can continue, but need changes in protocol and lastly red – the intervention can’t continue, unless the specific problem(s) can be solved) (28). Reporting of the study will follow the CONSORT checklist (14). The study will be conducted between Marts 2022 to the end of May 2022. This study was approved by the Scientific Ethical Committee of the Capital Region of Denmark and registered at ISRCTN. Individuals with T2D were recruited within Capital Region of Denmark and Region of Zealand. Recruitment of participants was conducted via advertisements on the Facebook page of The Danish Diabetes Association, Diabetes magazines, local diabetes organizations, support from the Danish Diabetes Association, and from a contact list of participants with T2D from a previous experiment at CFAS.

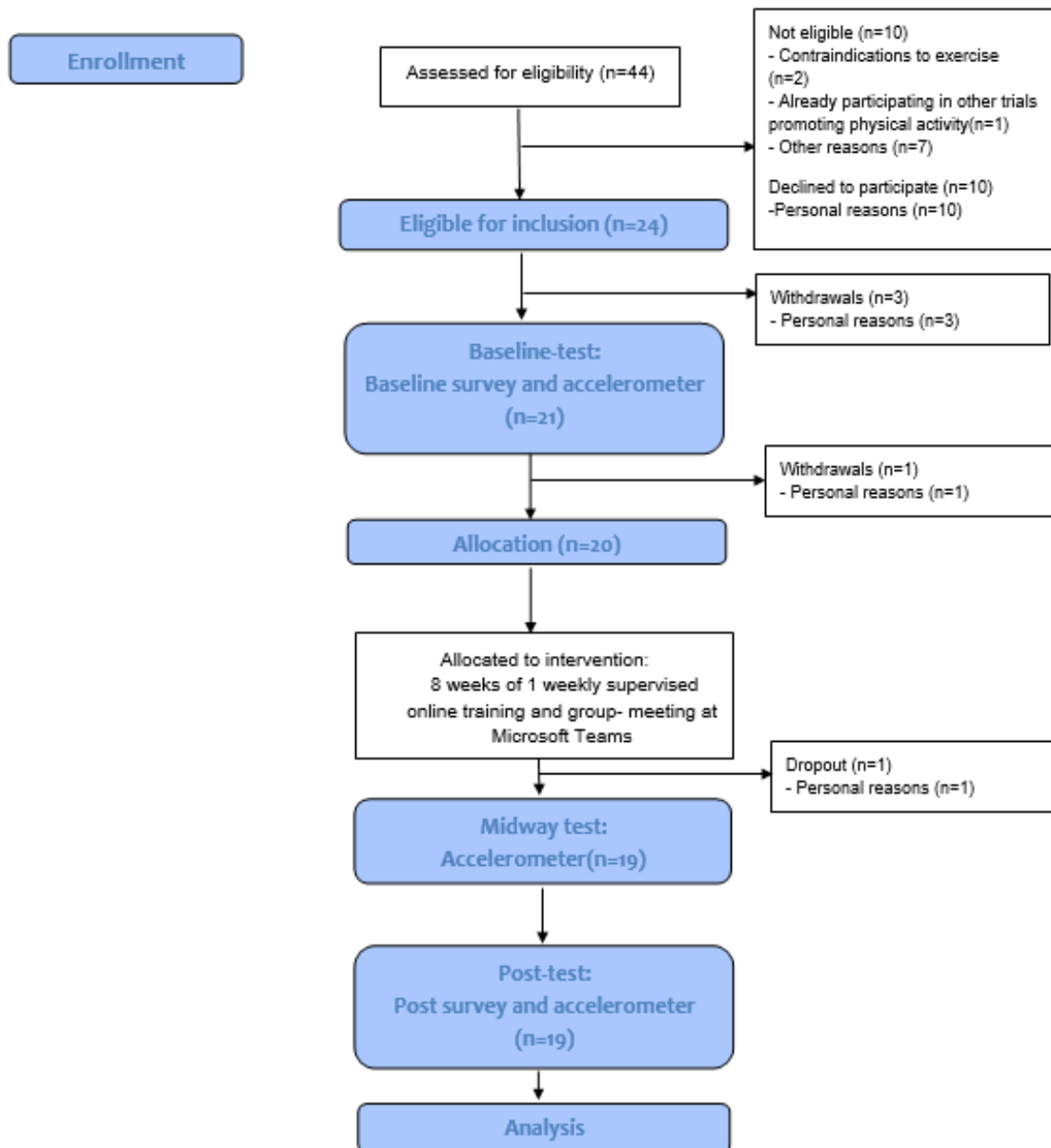
## **Sample size**

The sample size is based on the rationale of feasibility studies, regulatory and statistical considerations. According to this, at least 12 participants must be recruited (29). The intervention was fully or partly completed by 20 participants with diabetes.

The per protocol (PP) population will be defined as participants who followed the intervention with no major deviations and have complete data on baseline and postintervention measurements.

## Enrollment

The enrollment of the trial is illustrated in figure 1.



**Figure 1:** Flow diagram of participant enrolment.

## **Statistical analysis**

### *Statistical software*

All statistical analyses will be performed using STATA/BE 17.0 and RStudio Version 1.4.1106.

### *Participant characteristics*

Characteristics of participants will be presented with descriptive statistics (mean  $\pm$  standard deviation, median with interquartile range or frequency (%)). Cross tabulations will be conducted to describe participant characteristics. Furthermore, adherence to the online training sessions and online group meeting will be presented descriptively.

### *Primary analyses*

The primary outcomes of the study are as previously mentioned, Research Progression Criteria, and will be presented with descriptive statistics. The Research Progression Criteria will be evaluated based on the traffic light system of green (go), amber (amend) and red (stop) on the per protocol population.

### *Secondary analyses*

Within group changes from pre-to post-intervention on all secondary outcomes will be assessed. If continuous data fulfill assumptions for normality, within group changes will be presented with 95 % confidence intervals and standard deviations.

Outcomes related to training data recorded on Garmin activity watches (training intensity, training, mean and max intensity recorded with Garmin 245) will be presented descriptively.

Two different Garmin activity watches were handed out to the participants; Garmin 245 with a Heart Rate monitor, and Garmin Vivofit 4 without. A sensitivity analysis will be performed using a Bland-Altman plot to display differences in measuring daily steps between the two Garmin activity watches and accelerometers.

## Variables

### Primary outcome

- Progression criteria. Self-reported data/feedback from weekly questionnaires organized into categories related to:
  - Recruitment procedures
  - Completion of intervention
  - Adherence to goalsetting
  - Adherence to the online training intervention
  - Adherence to the online group meeting intervention
  - Difficulty participating in the objectively measured physical activity
  - Improvement of habitual physical activity
  - Adverse events.

#### *Adherence to online training (binary)*

- Information regarding adherence to online training will be obtained from a weekly questionnaire the participants will receive.
- Participants will answer the following questions with Yes/No as response categories:
  - Did you participate when the online training started?
  - Did you participate when the online training ended?

#### *Adherence to online group meeting (binary)*

- Information regarding adherence to online group meeting will be obtained from a weekly questionnaire the participants will receive.
- Participants will answer the following questions with Yes/No as response categories:
  - Did you participate when the online group meeting started? Yes/No
  - Did you participate when the online group meeting ended? Yes/No

#### *Adherence to individual goalsetting (binary)*

- Information regarding adherence to weekly goalsetting will be obtained from a weekly questionnaire.
- Participants will be asked if they completed their weekly goalsetting, and if not, they will be asked to describe why.

- I completed my goalsetting from the date x to the date x: Yes/No
- State a (possible) reason why you did not complete the goalsetting: \_\_\_\_\_
- Write down your new goal: \_\_\_\_\_

### *Completion of intervention*

- Information regarding completion of intervention will be obtained from the post intervention questionnaire and completion of the last measurement with the accelerometers.

### *Difficulty participating in objectively measured physical activity*

- Post intervention questionnaires will involve questions regarding how burdensome the participants found it to apply and wear the accelerometers during the intervention.

### *Adverse events (AE) and serious adverse events (SAE):*

- Self-reported data on adverse events and serious adverse events will be obtained via a post intervention survey.
- Questions addressing adverse events are made according to the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®) (15) structure and to describe the severity of prechosen symptoms such as dizziness, acute harm in the musculoskeletal system during the training and the hours afterwards, prolonged pain in the musculoskeletal system (at least 7 days without being able to train) and fall.
- The participants were asked to score the severity of pain from none to life threatening/a lot. (27)

### *Improvement of habitual physical activity*

- To evaluate improvement of physical activity behavior after the intervention, all participants were equipped with two Axivity AX3 (Axivity, Newcastle, UK) accelerometers for seven consecutive days before, during, and after the intervention. One was placed on the right thigh, and the other on the right side of the lower back attached with a patch (Fixomull stretch, BSN medical, Germany).

Accelerometer data will be considered valid, if the participant has minimum 22 hours wear

time out of 24 possible. A measurement period will be considered valid, if the participant has at least three valid weekdays and one valid weekend day.

- According to the World Health Organization Guidelines on Physical Activity and Sedentary Behavior, doing some physical activity is better than doing none, and some physical activity will still benefit the individual's health (30). Therefore, every improvement in physical activity from baseline to post intervention among participants will be considered as an improvement in terms of the Research progression criteria.

The following daily and weekly physical activity intensities and types will be included:

- Total minutes spent on light physical activity (LPA)
- Total minutes spent on moderate to vigorous physical activity (MVPA)
- Total minutes spent on vigorous physical activity (VPA)
- Total minutes spent on sedentary behavior (time spent sitting and lying)
- Total minutes spent on biking
- Total step counts

## **Secondary outcomes**

### *Stress (continuous)*

- Self-reported psychological stress was obtained with Cohen's 10-item Perceived Stress Scale (PSS) (16).
- The PSS will be presented as a continuous variable.
- Scoring of the PSS scale are interpreted as follows:
  - Scores ranging from 0-13 will be considered low perceived stress
  - Scores ranging from 14-26 will be considered moderate perceived stress
  - Scores ranging from 27-40 will be considered high perceived stress

### *Mental well-being (WHO) (continuous)*

- Self-reported mental well-being will be obtained with the WHO5-Well-Being Index (17).
- Questions are scored from 0 (none of the time) to 5 (all of the time).
- According to the recommendations, the raw score should be multiplied by 4 to obtain a percentage score ranging from 0-100 (reference).
- The score will be interpreted as follows:



- A score  $<50$  will be categorized as low mental well-being and describes as being at risk of developing stress and depression (25).
- A score  $\geq 50$  will be categorized as moderate to high mental well-being.

### *Comorbidity (categorical)*

- Many studies have found that there is a strong association between having a co-morbidity and reduced quality of life or mental health (18), and this emphasizes the argument for reporting co-morbidities in relation to mental health.
- The Bayliss Burden of Illness Measure is used to conduct information about the number of chronic diseases and self-reported burden of diseases among the participants (18).
- The questionnaire consists of a list of common diseases, where the participant answers whether he/she has the disease and to what extent the disease interferes with daily life activities on a 5-point Likert scale from 1 (not at all) to 5 (a lot).
- The total scores represent the total morbidities and the total score of burden (19).

### *Self-efficacy (continuous)*

- Participants' self-perceived beliefs about their own abilities related to performing a activity will be measured with the questionnaire “Self-Efficacy for Managing Chronic Disease 6-Item Scale” (SEMCD6) (20).
- SEMCD6 consist of questions what will be answered in a 10-point scale ranked from 1 (not confident at all) to 10 (totally confident).
- The total score of the scale is the mean and standard deviations of the six items.
- A higher score reflects a greater self-efficacy (20).

### *Loneliness (continuous)*

- Self-rated and subjective feeling of loneliness will be obtained with the UCLA 3-Item Loneliness Scale, which consists of three questions from the extended version consisting of 20 questions (21).

- Responses for each item ranges from “hardly ever or never” (1 point) to “often” (3 points). The total score will be calculated by summing all items, which ranges from 3 to 9.
- A higher score indicates a higher level of perceived loneliness.

#### *Diet (categorical)*

- Self-reported dietary habits were obtained with the Dietary Quality Score (22) and then categorized into following groups: Unhealthy, Medium healthy, Healthy.
- A minor error occurred in the questions regarding dietary habits, and therefore three of the questions had slightly different answer categories, but the development of the total score, will follow the Dietary Quality Score (22).

#### *BMI (continuous)*

- Self-reported data on weight and height will be obtained from the baseline survey.
- BMI will be presented as a continuous variable.

#### *Satisfaction with the intervention*

Post intervention participants will receive a questionnaire regarding their satisfaction with the project and this will be a way of evaluating the intervention (26). Participants will respond to what extent they agree/disagree with a list of statements. The statements will address the following topics:

- Overall experience of the project
  1. communication between the project manager and participants
  2. Online training (expectations, intensity, motivation)
  3. Online group meetings (communication, support, togetherness)
  4. Physical activity goalsetting in practice (succession with goals, and priorities)
  5. Microsoft Teams (introduction in using Microsoft Teams, technical problems, support to solve the problems)
  6. Garmin watches (introduction in using the Garmin watch, support to use the Garmin watch, motivation)

7. The facilitator-role during group meetings (introduction to the role, time spent on managing the role)
8. The participants' experience of the facilitator in group meetings
9. Burden of tasks in the project (number of questionnaires, log diaries, wearing accelerometers)

### Variables describing intervention intensity

#### *Training intensity (Self-perceived exertion)*

- Information regarding to intensity during the online training will be obtained with the Borg Scale to measure the degree of self-perceived exertion. The scale from 6 (corresponds to rest) to 20 (maximum effort). The scale is based assumption of a strong association between the degree of exertion, the workload and the heart rate. The degree of exertion measured with the Borg Scale (Rate of Perceived Exertion, RPE) (23) has shown moderate to high correlation with heart rate, oxygen uptake and respiration rate during a given work/training.
- In physical activity such as online training, the scale can be useful, and it is a practical toll for finding the desired intensity in training.
- Participants will answer the following questions with a number between 6 and 20 from the Borg Scale.

#### *Training intensity (Heart rate monitoring)*

- Information regarding to intensity during the online training will be obtained via a heart rate monitor in the 245 Garmin watch which 4 of the participants received before the intervention.
- Participants with Garmin 245 watches will answer the following questions regarding the mean and maximum intensity during the online training.

#### *Garmin watch data*

Intensity minutes (continuous):

- o At the end of every week during the intervention, the participants read from their Garmin activity watch and note the number of intensity minutes they have obtained.

- The participants write down their intensity minutes from the previous week in the questionnaire after the online training.
- Furthermore, participants are asked whether they believe the intensity minutes reflect their real weekly activities, and if not, they respond how many intensity minutes they believe they have obtained.

#### Daily steps (continuous)

- Throughout the intervention, the participants are wearing Garmin activity watches to measure their daily steps.
- At the end of every day, participants note their daily steps.
- In the weekly questionnaire, the participants report their daily steps for the previous week.

#### Variables describing general demographic information

##### Age (continuous)

- Self-reported and calculated age from CPR-number.

##### Sex (binary)

- Obtained from baseline questionnaire.
- Categorizations: Male, Female

##### Ethnicity (categorical)

- Self-reported

##### Educational level (categorical)

- Educational level was defined as the highest completed education.
- Educational level was categorized into the following: Primary (<10 years), Upper secondary or vocational (10-12 years), Higher education ( $\geq 13$  years).

##### Working situation (categorical)

- The participants were asked about their current work situation and the variable was obtained from questions.

- Work situation was categorized into the following: In ordinary work, In flexible work, Independent, Unemployed, e.g., social benefits or in activation, Rehabilitation, Pension, Early retirement, Education, Sick and Other.

#### *Living (categorical)*

- The participants were asked about their way of living (alone or cohabitant with children or without children) and the variable was obtained from questions.
- Living was categorized into the following: Living alone, living with partner or children.

#### *Alcohol consumption (categorical)*

- Respondents were asked about their weekly alcohol consumption (24).
- On behalf of the national recommendations of the Danish Health Authority and the risk factors of developing alcohol-related diseases for women and men, alcohol is categorized into following groups:
  - No alcohol (0 drinks – both men and women)
  - Below low risk (men >0 & <14 drinks, women >0 & < 7 drinks)
  - Above risk group (men  $\geq$ 14 & drinks, women  $\geq$ 7 drinks)

#### *Smoking (categorical)*

- Self-reported data regarding to the participants smoking habits was obtained and categorized into following groups: Smoker, Ex-smoker, Never smoked.

#### *Diabetes (categorical)*

- Self-reported information about the participants diabetes was obtained through 8 questions. Information of the following was obtained:
  - Their last measured hemoglobin A1c (HbA1c).
  - Diabetes complications: Retinopathy, neuropathy (nerve inflammation, e.g., sensory disturbances, pain in extremities, foot ulcers, sexual dysfunction, and diabetic foot.

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