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Design of the 10-year follow-up of the Healthy Ageing and Intellectual Disability study

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DECLARATIONS

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests statement

The authors declare that they have no competing interests.

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Author contributions

We would like to justify the authors' contribution by describing their involvement in the different phases of the writing process: 1) devising and shaping the research project (AO, TH, DM), 2) drafting the study protocol (MdL, AO, RE, MK), 3) writing the first draft of the manuscript (MdL), 4) critically revising the manuscript (AO, RE, MK, MvM, MvB, TH, PB, DM) and 5) drafting the manuscript, tables and figures to their final version (MdL, AO, RE). All authors have critically reviewed the content of this paper and have approved the final version of the manuscript.

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ABSTRACT

Introduction

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study in the Netherlands that started in 2008, including 1,050 older adults (≥50 years) with intellectual disabilities. The study is designed to gather more knowledge about the health and health risks of this ageing group. Compared to the amount of research in the general population, epidemiological research into the health of older adults with intellectual disabilities is still in its infancy. Longitudinal data on the health of this vulnerable and relatively unhealthy group is needed to be able to prioritize policy and care and to guide clinical decision making with regard to screening, prevention and treatment to improve healthy ageing.

Methods and analysis

This article presents a summary of the main findings of the HA-ID study up to now and describes the design of the 10-year follow-up in which a wide range of health data will be collected within five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders; 4) nutrition and nutritional state; and 5) frailty.

Ethics and dissemination

Ethical approval for the 10-year follow-up measurements of the HA-ID study is obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number: NL8564) and is conducted according to the principles of the Declaration of Helsinki.

KEY WORDS

Intellectual disability, healthy ageing, elderly, cohort study, epidemiology.

ARTICLE SUMMARY

Strengths and limitations of this study

- This protocol outlines the design of the 10-year follow-up of the HA-ID study, a prospective multicentre cohort study in which a heterogeneous group of 1,050 older adults with intellectual disabilities is followed over time.
- The longitudinal design of the study makes it possible to make statements about causality and to study health trajectories and health indicators, which is important to prioritize policy and care and to guide clinical decision making about screening, prevention and treatment to improve healthy ageing.
- The comprehensive set of measurements makes it possible to evaluate the health of older adults with intellectual disabilities from a broad perspective and to investigate the interrelationship between medical domains.
- The data collection consists of measurements that have been shown to be feasible, valid and reliable in older adults with intellectual disabilities, based on previously acquired knowledge and experience within the HA-ID study.
- Due to financial and feasibility reasons it has not been possible to perform follow-up measurements on a more regular basis.

INTRODUCTION

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study including older adults with intellectual disabilities (ID) in the Netherlands. The study was designed in response to the increasing longevity of people with ID and the lack of epidemiological data about their health and health risks at older age. The absence of this knowledge raised questions about how to organize care and support for this vulnerable and relatively unhealthy group [1]. Based on this need for knowledge, a consortium was established in 2006 consisting of three ID care organizations (Ipse de Bruggen, Amarant and Abrona) and the research group of Intellectual Disability Medicine of the Erasmus MC, University Medical Centre Rotterdam. The HA-ID consortium aims to: 1) increase knowledge on healthy ageing in people with ID by means of scientific research; 2) strengthen the scientific attitude of care professionals by means of participation in research and continuous education; and 3) innovate care by implementation of research outcomes. In 2008, the HA-ID study started with a focus on physical activity and fitness, nutrition and nutritional state, and mood and anxiety. A detailed description of the rationale and design of the baseline measurements can be found elsewhere [1]. After three and five years, follow-up measurements consisting of medical file research and questionnaires about the health of the participants were completed. During this follow-up period new topics were included; cardiovascular disease, frailty, mortality and causes of death [2].

Baseline results of the HA-ID study showed that older adults with ID experienced more health problems compared to peers in the general population, and that they experienced these problems at a younger age [3, 4]. Older adults with ID were earlier, and more severely frail than peers in the general population [5]. A high prevalence of polypharmacy [6], multimorbidity [6], sleep problems [7], major depressive disorders [8], dysphagia [9], obesity [10], sub-optimal nutritional intake [11], and low physical activity and fitness levels were found [12-15].

Based on data from the 3 and 5-year follow-up, frailty at baseline was predictive for the development of comorbidity [16], a decline in daily functioning and mobility [17], increased medication use [16], increased care intensity [18], and a higher mortality risk [19]. Also poor physical fitness was predictive for a decline in mobility [20], daily functioning [20, 21], and for a higher mortality risk [22]. The use of atypical antipsychotics, chronic kidney disease, abdominal obesity, a history of stroke, and a history of heart failure were predictive for developing cardiovascular disease (CVD) over a 3-year time period [23]. These first results from the longitudinal data of the HA-ID study provided important insights for policy and care on how to contribute to a better health of older adults with ID. The results of the HA-ID study have been used in the development of diagnostic instruments and guidelines [3, 24, 25], and to illustrate the vulnerability and poor health situation of people with ID, resulting in changes to the Dutch legislation with regard to long-term financing of support, care and treatment for people with ID.

Following the start of the HA-ID study, other research groups initiated longitudinal studies focusing on different aspects of health in adults with ID, such as the IDS-TILDA study in Ireland [26], the SAge-ID study in Australia

[27], and a longitudinal cohort study about dementia and mortality in persons with Down syndrome in the Netherlands [28]. Despite these initiatives, epidemiological research into the health of adults with ID is still extremely limited. Too little is known about the health of this aging group, and knowledge about changes in health status over time and early indicators for health problems. However, this knowledge is of importance to provide the evidence base for improving care and support of older adults with ID and to guide care providers in preparing themselves for this growing group of elderly with ID. Longitudinal research makes it possible to make statements about causality and in this way contributes, for example, to the identification of group-specific risk factors, groups at risk for specific diseases and other negative outcomes such as a decline in independence. This knowledge can be used in reducing the occurrence of specific risk factors and by timely identifying, monitoring and treating high risk groups. For this reason, more longitudinal studies focusing on the health of this specific group are urgently needed .

This article describes the design for the 10-year follow-up measurements of the HA-ID cohort. To gain more knowledge about changes in health status and indicators for health problems over time, a wide range of health data will be collected. Based on previous measurements and results, the focus will be on five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders (including sleep problems); 4) nutrition and nutritional state (including dysphagia); and 5) frailty. This article presents the design of the HA-ID cohort study, a summary of the main findings up to now, and provides an update of the planned measurements of the 10-year follow-up research themes.

METHODS AND ANALYSIS

STUDY COHORT

The HA-ID cohort consists of older adults with borderline to profound ID. All participants receive care or support from one of the care organizations of the HA-ID consortium. These organizations are geographically located in different regions in the Netherlands and provide care to a wide spectrum of individuals with ID in different care settings [1]. All individuals with ID within the consortium aged 50 years or older by September 2008, were eligible to participate and received an invitation. Ultimately, 1,050 of the 2,322 (45.2%) invited individuals with ID participated in the baseline measurements. Table 1 presents the baseline characteristics of the participants. The participant characteristics were largely comparable to the total invited group of individuals with ID, and formed a near-representative study population for the total Dutch population of older adults with ID receiving formal support or care [1].

<<INSERT TABLE 1 ABOUT HERE>>

Figure 1 summarizes the number of participants in the cohort over time. At baseline, measurements consisted of reviewing medical files, administering questionnaires, physical examinations with portable measuring equipment, fitness tests, observations, interviews, laboratory assessments, and diaries [1]. At the 3-year follow-up, medical files were reviewed, and professional caregivers completed questionnaires about the participant's health. Five years after the baseline measurements, causes of death were examined in the files of the deceased participants. The participants themselves were not actively involved in the data collection during these follow-up measurements. At the 3-year and 5-year follow-up, the cohort consisted of respectively 873 and 787 participants.

All individuals with ID who participated in the baseline measurements and still receive care or support from one of the participating care organizations will be invited to participate in the 10-year follow-up measurements. There is one exclusion criterion: individuals with ID who are so seriously ill that participating in the study is not desirable, based on shared decision making with caregivers and professionals, are excluded from physical measurements.

<<INSERT FIGURE 1 ABOUT HERE>>

INFORMED CONSENT PROCEDURE

Because not all individuals with ID are mentally capable to give informed consent, two separate consent procedures will be followed. A behavioural scientist evaluates whether the individual is able to understand the specifically designed study information to make an informed decision about participation. If an individual is able to make an informed decision, an easy-to-read information letter with supporting pictures and consent form are sent to him or her. Otherwise, an information letter and consent form are sent to the legal representative. The professional caregiver of the individual with ID will be informed about the study and the informed consent procedure in order to support the individual or legal representative in making their decision for participation.

RESEARCH THEMES

An outline of the published results for each research theme is presented, followed by a description of the data collection of the 10-year follow-up, with a specific focus on newly added measurements. In the 10-year follow-up, we also omitted measurements that turned out to be not feasible, valid or reliable, based on the baseline measurements. For clarity, these measurements are not listed separately below. An overview of all measurements at baseline, 3, 5 and 10-year follow-up can be found in table 2.

1. Cardiovascular disease

The HA-ID study provided many insights into the prevalence of CVD risk factors and the incidence CVD in older adults with ID. Prevalence of hypertension (53.0%), diabetes (13.7%), metabolic syndrome (44.7%), and chronic kidney disease (15.3%) was similarly high as in the general population [29, 30]. However, the prevalence of peripheral arterial disease (20.7%) and obesity in women (25.6%), measured by the Body Mass Index (BMI), was significantly higher than in the general population [10, 31]. The incidence of newly diagnosed CVD during a 3-year follow-up period was also examined. Incidence rates for myocardial infarction (2.8 per 1,000 person-years), stroke (3.2 per 1,000 person-years), and heart failure (12.8 per 1,000 person-years) were similar as in the general population [23]. The use of atypical antipsychotics, chronic kidney disease, abdominal obesity, a history of stroke, and a history of heart failure turned out to be predictive for developing CVD during the 3-year follow-up period [23].

The baseline measurements revealed underdiagnosis of CVD risk factors in the HA-ID cohort. For example, 54% of the participants with diabetes had not been previously diagnosed with this condition. For hypercholesterolemia this was the case in 46% of the participants, for hypertension in 50%, and for metabolic syndrome in 94% of the participants [29]. Atypical presentation of symptoms, limitations in communication, limited cooperation and resilience make diagnostics in people with ID more challenging [32]. This makes underdiagnosis a common problem in people with ID [4, 33]. For this reason, the CVD incidence described above is also probably underestimated [23].

With increasing longevity and an increased prevalence of some CVD risk factors, people with ID may be at higher risk of developing CVD. The 10-year follow-up of the HA-ID cohort provides opportunities to gain knowledge about CVD risk factors and the development of CVD over time in older adults with ID. The planned measurements for the 10-year follow-up are summarized in table 2. The presence of CVD risk factors, CVD, and CVD treatments/interventions over the past ten years will be assessed by reviewing medical files of all participants who participated in the baseline measurements, including the medical files of deceased participants.

Blood will be collected through venepuncture. Blood will be stored for 15 years at -80 degrees Celsius, to be able to analyse relevant biochemical markers now and in the future (table 2).

The following measurements were added to the physical examination to gain more insight into the presence of CVD and its risk factors. Body composition will be studied with Bioelectrical Impedance Analysis (BIA) using the Tanita

Body Composition Analyzer (Tanita DC-430 MA, Tanita, the Netherlands). An electrocardiogram will be performed to examine heart conditions. In addition, heart rate variability will be measured as a marker for the autonomic nervous system by wearing a heart rate monitor (Polar Vantage V HR H10, Polar Electro Oy, Finland) at rest for 5 minutes. Finally, different hemodynamic measurements (mean arterial pressure (mmHg), pulse pressure (mmHg), resting heart rate (bpm), stroke volume (mL), cardiac output (l/min), cardiac index (l/m*1/m), augmentation index (%), peripheral vascular resistance (s*mmHg/mL), and pulse wave velocity (m/s)) will be obtained with a non-invasive electronic blood pressure oscillometric monitoring system (Mobil-O-Graph 24h PWA Monitor, I.E.M. GmbH, Germany) [34]. Adding the Mobil-O-Graph provides more insight into the presence of arterial stiffness and central systolic blood pressure, two important risk factors for CVD and morbidity [35].

2. Physical activity, fitness and musculoskeletal disorders

The HA-ID study yielded important results concerning physical activity and fitness. Older adults with ID had very low physical activity and fitness levels [12, 14]. In short, most participants were categorized as 'low active' (5,000-7,449 steps/day; 25.3%) or 'sedentary' (<5,000 steps/day; 38.5%). Only 36.2% of the participants walked ≥7,500 steps/day [12]. These results are likely an underestimation of the problem, because physical activity levels were only measured in participants who were physically able to walk at a sufficiently high speed for the pedometers to provide a reliable measurement. In addition to these low physical activity levels, people with ID aged 50 years and over had physical fitness levels comparable to, or worse than, people in the general population aged 70 years and over [13, 14]. Data from the 3 and 5-year follow-up showed that these low physical fitness levels at baseline were indicative for a decline in daily functioning and mobility over the 3-year follow-up period, and a higher mortality risk over the 5-year follow-up period [20-22, 36]. Additionally, it was found that being fit is more important with regard to survival than obesity. People who were unfit had a four times higher mortality risk than people who were fit, regardless of obesity [36]. Because of the importance of physical fitness, suitable fitness tests for this population are essential. Based on our previous research examining the reliability and feasibility of eight physical fitness tests in older adults with ID [37, 38] we developed the ID-fitscan to assess the physical fitness levels of adults with ID [24]. In the 10-year follow-up measurements, physical activity and fitness levels will be assessed again (see table 2). Based on previous results and experiences, some changes were made to the measurements. Physical activity will be measured using the ActiGraph (wGT3X-BT Accelerometer, ActiGraph, USA), an instrument that is able to measure at very low walking speeds and provides more detailed information about the physical activity levels of the participant. Complementary to this, we will use the International Physical Activity Questionnaire – Short Form (IPAQ-SF) to collect physical activity data [39]. The ID-fitscan [24], supplemented with the two-minute step test [40], will be used to assess physical fitness. Physical fitness tests that turned out to be less suitable at the baseline measurements are excluded [24].

The 10-year follow-up will also focus on musculoskeletal disorders, in particular osteoarthritis. Osteoarthritis is common in older people in the general population, leading to pain, joint instability, limitations in daily activities, and a decreased quality of life [41, 42]. Little is known about the prevalence of knee and hip osteoarthritis in people

with ID. A high prevalence is expected because many factors that have been associated with osteoarthritis, such as obesity, poor physical fitness levels, poor motor skills, gait abnormalities, musculoskeletal complications, and developmental problems are more present in adults with ID than in the general population [14, 43-47]. Osteoarthritis of the hip and the knee will be assessed by applying the American College of Rheumatology (ACR) criteria for the diagnosis of osteoarthritis. These criteria contain clinical symptoms, consisting of pain and functional limitations of the joint and include radiological characteristics on X-rays as well [48]. The 10-year follow-up includes several tests to identify the presence of the ACR criteria, including physical examinations with pain observations (Rotterdam Elderly Pain Observation Scale (REPOS) filled out by the health professional performing the physical examination, supplemented by a Numeric Rating Scale observation filled out by the professional caregiver during the physical examination, and a face-scale for self-report of pain [49]). The REPOS will also be used to assess pain during rest and daily activities that may provoke osteoarthritis complaints. Also, the Animated Activity Questionnaire (AAQ) will be used to identify whether the participants experience complaints due to osteoarthritis during daily living activities, filled out by the professional caregivers of the participants [50]. Additional, data about gait characteristics that may be related to osteoarthritis will be collected through a structured observation. To signal pain, stiffness and range of motion the standardized questionnaires (the Hip disability and Osteoarthritis Outcome Score (HOOS) [51, 52] and the Knee disability and Osteoarthritis Outcome Score (KOOS) [53]) will be used.

3. Psychological problems and psychiatric disorders

At baseline, data was collected on the prevalence of depression and anxiety disorders. The prevalence of major depressive disorder was 7.6% [8], which is higher than the prevalence found in the general population (1.8% to 4.0%) [54]. Only 4.4% of the participants met the criteria for one of the anxiety disorders [8]. This was lower than expected, and lower than the prevalence in the general population (10.2% to 11.6%) [55]. This may be explained by the fact that proxy reports had to be used in 78% of the participants. It is difficult for informants, such as professional caregivers, to recognize symptoms of anxiety (e.g., pounding heart, worrying). This may have led to an underestimation of the prevalence of anxiety disorders.

In the general population there is a strong association between sleep problems and anxiety- and mood disorders [56]. Therefore, also data on sleep and sleep-wake rhythm was collected at baseline based on wrist-worn accelerometry (Actiwatch AW7, Cambridge Technology Ltd, Cambridge, United Kingdom [49, 50]). It was found that 23.9% of the participants lay awake for more than one hour before falling asleep. In addition, 63.1% lay awake for more than 90 minutes after sleep onset and before final morning awakening, 20.9% slept less than 6 hours, and 9.3% was already awake for more than 60 minutes before getting out of bed [57]. In total 72.1% of the participants were classified as having at least one of these sleep problems [57].

During the 10-year follow-up data about anxiety disorders, depression and sleep will be collected again, with some changes and additions to the baseline data collection (see table 2). The 10-year follow-up has been extended with data retrieval from the psychological files about the presence of mood disorders, autism spectrum disorder, attention

deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders, personality disorders, psychotic disorders, post-traumatic stress disorder, and cognitive disorders (including dementia). In older people with ID, there is an association between the presence of a mental health diagnosis and problem behaviour [58]. For this reason, data on problem behaviour will also be collected within the 10-year follow-up using the Aberrant Behaviour Checklist (ABC) [59]. The ABC is a widely used behaviour rating scale and measures problem behaviour using five subscales: irritability, lethargy, stereotypy, hyperactivity, and excessive speech. In addition, a potential objective biomarker for long-term stress in people with ID will be evaluated, which may contribute to future diagnostic assessment. Long-term stress over the past months will be retrospectively examined with a hair cortisol measurement. Recently published studies in the general population indicate that there is a strong association between the level of hair cortisol, life events and symptoms of anxiety and depression [60-63].

Data on sleep and sleep-wake rhythm will still be collected with accelerometry; however, we will now use the GENEActiv (Original, Activinsights Ltd, UK). Data from the GENEActiv are comparable to data collected by the Actiwatch that was used at baseline [64]. Extra questions about sleep hygiene and sleep circumstances are added to gain more knowledge about the influence of these factors on sleep in older adults with ID.

4. Nutritional intake and nutritional state

The baseline measurements of the HA-ID study yielded insights into the nutritional intake and nutritional state of older adults with ID. Three-day dietary records completed by professional caregivers revealed an inadequate dietary intake, with none of the participants meeting all Dutch recommendations for a healthy dietary intake. The food intake was too low in calories in 68.6% of the participants, too low in protein in 30.2%, too low in fiber in 98.2%, and too high in saturated fat in 89.5% of the participants [11]. Forty-two percent of the participants had a Vitamin-D deficiency, of which 9% had a severe Vitamin-D deficiency [65]. Vitamin-D supplementation was routinely provided to 45% of the participants, and this group had significantly higher mean Vitamin-D serum levels than those without supplementation. This calls for more attention for the prescription of Vitamin-D in older adults with ID [65]. These results also indicate that there is much room for improvement with regard to healthy nutrition.

Meal time observations using the Dysphagia Disorder Survey (DDS) [66] showed moderate to severe dysphagia in 51.7% of the participants, which is comparable to the prevalence in nursing homes [9]. In 89.5% of the participants with dysphagia this had not been previously diagnosed. The high degree of underdiagnosis illustrates the importance of screening and diagnosing dysphagia to prevent complications in clinical practice. Higher age, Down syndrome, mobility impairment, needing help with feeding, and use of benzodiazepines were positively and independently associated with dysphagia [9].

The prevalence of sarcopenia was also studied. Fourteen percent of the participants was classified as having sarcopenia. Sarcopenia developed at a relatively young age compared to the general population. With a prevalence of 12.7%, sarcopenia was already remarkably present in participants aged 50 to 64 years old [67]. Additionally, 43.9% of the participants had low bone quality. Female sex, higher age, more severe level of ID, mobility impairment, and anticonvulsant drug use were positively associated with low bone quality [68]. Higher BMI was

negatively associated with low bone quality [68]. These results provide directions for periodic screening of risk groups for low bone quality and target groups for prevention in clinical practice [68].

In the 10-year follow-up the baseline measurements will be repeated (see table 2). To gain more insight into the degree of malnutrition of older adults with ID, the Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) will be added to the data collection. The SNAQRC is a screening instrument for the early detection of undernutrition in a nursing and residential home setting. The screening tool uses a traffic light system in which BMI and four questions related to involuntary weight loss, loss of appetite, and eating with help are combined [69]. The SNAQRC will be completed by professional caregivers.

At baseline, a short dental file examination provided some data on the dental condition of the participants. In order to get a more extensive insight in the dental condition and dental hygiene of older adults with ID, the dental file review will be extended. Data will be collected on dental condition, premedication and sedation during check-up and treatment, dental prosthesis, enamel wear, the number of dentist and dental hygienist visits, the number of elements in the upper and lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis and periodontitis, mobile elements, and loss of dental elements due to trauma.

5. Frailty

Frailty is a clinically recognizable state of increased vulnerability resulting from age-associated decline in reserve and function across multiple physiologic systems [70]. Frailty leads to the deterioration of daily functioning and mobility, increased disability, development of comorbidity and increased care intensity [17, 71, 72]. As a result, signalling frailty could play a valuable role in care planning, potentially improving quality of life and increasing the life expectancy of frail people with ID. In the general population frailty is usually measured with tools such as the frailty phenotype [73]. However, we theorized that the ID population required a more specific approach than the available tools allow. Based on the baseline data the ID-Frailty Index was created, consisting of 51 items [3]. The ID-frailty Index focuses on multiple aspects of daily functioning, opposed to a larger focus on physical frailty and mobility impairment [74]. As a result the ID-frailty Index could be applied to a larger part of the study population than the frailty phenotype and was deemed more suitable to measure frailty in older adults with ID [74]. Furthermore, the ID-frailty index showed a stronger relationship with mortality than the frailty phenotype [74]. The 3-year follow-up data showed that higher scores on the ID-Frailty Index resulted in a greater risk of death [19]. Finally, the ID-Frailty Index was predictive for a decline in mobility, and an increase in disability, polypharmacy, and care intensity [16-18].

In the 10-year follow-up all previous measurements that were used to create the ID-Frailty index will be repeated (see table 2). This allows us to investigate the characteristics of frailty over time. In an attempt to further increase the practical and clinical usability of the ID-Frailty Index a shortened version of the index was developed. During the 10-year follow-up, the utility of this ID-Frailty Index Short Form will be further investigated.

General health data

In addition to these five research themes, data on other health variables will also be collected (table 2) which will not be discussed in detail.

PROCEDURE

To limit the burden and impact on participants and their professional caregivers, all measurements will be performed in a setting close to where the participants live. All measurements are carried out by test administrators consisting of professionals working in the care organizations. All test administrators will be trained to ensure accurate administration and correct scoring of the measurements. All measurements for a specific participant will be scheduled within one week. This test week consists of a physical examination performed by medical staff, fitness tests supervised by movement therapists or physiotherapists, observations to assess pain during activities of daily life performed by trained healthcare professionals, a meal time observation to screen for dysphagia performed by speech and language therapists, and a maximum of two interviews by trained and qualified professionals aimed at screening and diagnosing anxiety and depression. The participant will wear portable measuring equipment on the wrist and hip for seven days to monitor physical activity and sleep-wake rhythm. If separate consent is provided, blood samples and a tuft of scalp hair will be collected. For logistical reasons, the X-rays of the hip and knees take place outside this test week. All measurements together require a maximum time investment of four hours for each participant. However, the time investment per participant will likely vary, because not every participant is able to undergo all measurements. The study will not interfere with routine medical practice. In addition to measurements for which active involvement of the participants is needed, data from the medical, psychological, and dental files will be collected. The professional caregiver will be asked to complete questionnaires about the participant's health. A complete overview of all measurements within the HA-ID study can be found in table 2. After the test week, the participant's physician and behavioural scientist receive a report with a summary of the results of the measurements.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not involved in the design of this study.

STATISTICAL ANALYSIS

In line with the previous measurements, the 10-year follow-up will provide cross-sectional and longitudinal data. Different statistical analyses will be applied. Descriptive statistics are used to answer questions regarding prevalence and incidence of health conditions and possible risk factors. Multivariable regression analyses are used to answer questions regarding differences between subgroups and associations between variables considering possible confounders and adjust for these covariates. Survival analysis with Cox proportional hazards models will be used to investigate relationships between different factors (including age, sex, level of ID, comorbidity) and several health conditions and mortality over time. For repeated measurements, the dependency of measurements for the same participant will be adjusted by using generalized linear mixed-effects models (GLME).

IMPLICATIONS FOR PRACTICE

The HA-ID study so far has yielded knowledge of various health problems that are prevalent in older adults with ID, and how these compare to the general population. This knowledge has provided directions to improve care for adults with ID. The 10-year follow-up will provide more insight into the course of health over time and risk factors for health problems in older adults with ID. Research into CVD risk factors in this population, for example, is still very limited. More knowledge about CVD risk factors and possible group-specific risk factors will contribute to a better estimate of the cardiovascular risk profile of older adults with ID. The 10-year follow-up will also give more insight into how frailty develops over time and whether there are certain groups of people with ID that are at the highest risk for adverse outcomes.

What characterizes the HA-ID study is that it is a prospective multicentre cohort study in which, compared to other ID studies, a relatively large (n=1,050) and heterogeneous group of older adults with ID is followed over time. The extensive measurements enable us to evaluate the health of older adults with ID from a broad perspective and to investigate the interrelationship between medical domains such as cardiovascular disease, physical fitness, psychological problems and psychiatric disorders, nutrition, and frailty. Looking across research themes is especially important because multimorbidity is common in people with ID [4].

From experience we know that conducting epidemiological research into this field can be difficult and involves challenges in selecting suitable measuring instruments. Some measuring instruments require a certain level of cognitive, physical or verbal ability which may not be compatible with those of the participants. In order to be able to make comparisons with the general population, as many instruments as possible which are also used (in studies) in the general (older) population were selected. However, feasibility, validity, and reliability in older adults with ID were the leading criteria in the selection of measuring instruments, using previously acquired knowledge and experience within the HA-ID study. It was also considered how invasive and time-consuming instruments are, the level of feasibility for a large part of our population, the extent in which it is possible to perform the measurement at the care organizations, and the extent in which the instruments can be carried out by a large group of professionals without making concessions in terms of inter-rater reliability. In addition, the costs of the measuring instruments were considered, considering use in clinical practice. Within the HA-ID study there is a continuous search for innovative and feasible measuring instruments that can be implemented in the data collection.

A limitation of our study is that due to financial and feasibility reasons it has not been possible to perform follow-up measurements on a more regular basis. Fortunately, the presence of routine registrations performed by the care organizations in medical, psychological and dental files allows us to retrospectively collect data on the health of the participants over the past 10 years.

Results from the 10-year follow-up measurements are important to prioritize policy and care and to inform clinical decision making about screening, prevention and treatment to improve healthy ageing of adults with ID. For this reason, longitudinal data collected within the 10-year follow-up of the HA-ID cohort is of great added value.

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ETHICS AND DISSEMINATION

Just as for the previous parts of the HA-ID study (MEC-2008-234 and MEC-2011-309), ethical approval for the 10-year follow-up is obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number: NL8564) and follows the guidelines of the Declaration of Helsinki [75]. Local ethical committees and boards of individuals with ID and their representatives of the three involved care organizations were informed. Inclusion of the participants started in July 2020 and is ongoing.

ABBREVIATIONS

AAQ	Animated Activity Questionnaire
ABC	Aberrant Behaviour Checklist
ACR	American College of Rheumatology
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CVD	Cardiovascular disease
DDS	Dysphagia Disorder Survey
GLME	Generalized linear mixed-effects models
HA-ID	Healthy Ageing and Intellectual Disability
HOOS	Hip disability and Osteoarthritis Outcome Score
ID	Intellectual disabilities
IPAQ-SF	Physical Activity Questionnaire – Short Form
KOOS	Knee disability and Osteoarthritis Outcome Score
MEC	Medical Ethics Review Committee
NTR	Dutch Trial Register
REPOS	Rotterdam Elderly Pain Observation Scale
SNAQRC	Short Nutritional Assessment Questionnaire for Residential Care

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TABLE 1 **Baseline characteristics of the HA-ID cohort (n=1,050) [1]**

Characteristic		***n* (%)**
Sex	Male	539 (51)
	Female	511 (49)
Age		60 (11, 50-93)*
Residential status	Central setting	557 (53.0)
	Community-based	432 (41.1)
	Independent with ambulatory support	43 (4.1)
	With relatives	7 (0.7)
	Unknown	11 (1.1)
Level of care (ZZP-scores)	Only day care indication	6 (0.6)
	Only indication ambulant care	37 (3.5)
	Residence with minimal support (1 VG)	12 (1.1)
	Residence with support (2 VG)	39 (3.7)
	Residence with support and care (3 VG)	138 (13.1)
	Residence with support and intensive care (4 VG)	207 (19.7)
	Residence with intensive support and intensive care (5 VG)	325 (31.0)
	Residence with intensive support, care and regulation of behaviour (6 VG)	93 (8.9)
	(Enclosed) residence with very intensive support, care and regulation of behaviour (7 VG)	142 (13.5)
	Mental Health Care ZZP scores	2 (0.2)
	Unknown	49 (4.7)

* Median (interquartile range, range)

ZZP = the Dutch classification of levels of support, care and/or treatment as a basis for long-term financing (Zorgzwaartepakket) [76]

VG = Dutch abbreviation for intellectual disability

TABLE 2 Measurements within the HA-ID study: baseline, 3, 5 and 10-year follow-up per research theme*

Type	Outcome	Details	Moment of data collection			
			Baseline (2009-2010)	3-year follow-up (2012-2013)	5-year follow- up (2015)	10-year follow-up (2020-2021)
Demographics						
Medical file	Age	-	X		X	X
	Sex	-	X			
	Residential status	Central setting (with or without 24-hour support), community based (with or without 24-hour support), independent with ambulatory support (by appointment), with relatives, with partner, independent.	X			X
	Level of care	Care Intensity Packages (Dutch ZZP-scores) [76].	X			X
Cardiovascular disease						
Physical assessment	Brachial blood pressure*	Omron M7 (OMRON Healthcare, the Netherlands).	X			
	Central blood pressure and arterial stiffness	Mobil-O-Graph 24h PWA Monitor (IEM GmbH, Germany) including pulse wave velocity.				X
	Ankle-Arm-Index*	Omron M7 (OMRON Healthcare, the Netherlands) (arm). Boso classico and 8-MHz Doppler probe (Huntleigh MD II, United Kingdom) (ankle). Ankle-arm-index calculated: systolic blood pressure ankle divided by systolic blood pressure arm.	X			X
	Heart rate variability	Polar Vantage V HR H10 (Polar Electro Oy, Finland).				X
	Electrical activity of the heart	Electrocardiogram (ECG).				X
Venipuncture	Biochemical markers*	Fasting plasma levels: glucose, cholesterol (total/HDL*/LDL), haemoglobin (HB)*, haemoglobin A1c (HbA1c), triglyceride, C-reactive protein (CRP), interleukin 6 (IL-6), Tumour Necrosis Factor alpha (TNF alpha), albumin, vitamin D, calcium, creatinine, cystatin C, troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP) etc. The participants' blood is stored for 15 years at -80 degrees Celsius, in order to perform additional analyses afterwards.	X			X

Medical file	Cardiovascular disease*	Presence of CVD (heart failure, myocardial infarction, stroke, transient ischemic attack (TIA), cardiac arrhythmias, angina pectoris, aortic aneurysm, peripheral arterial disease (PAD), hypertension etc.), CVD risk factors (diabetes mellitus, central obesity, metabolic syndrome, rheumatoid arthritis, incriminating family history etc.), and treatments/ interventions (revascularization of the coronary artery, pacemaker, and implantable cardioverter-defibrillator (ICD)).	X			X
	Endocrine disorders*	Presence of endocrine disorders (such as diabetes mellitus*, hypercholesterolemia and metabolic syndrome).	X			X
Physical activity, fitness and musculoskeletal disorders						
Fitness assessment	Manual dexterity*	Box and block test [77].	X			X
	Reaction time	Auditive and visual reaction time test [78, 79].	X			
	Balance*	Berg Balance Scale [80].	X			
		Comfortable and maximum walking speed (5m) [24]*.	X			X
		Static balance test (for stances) [24].				X
	Grip strength*	Jamar Hand Dynamometer (#5030J1, Sammons Preston Rolyan, USA) [24].	X			X
	Muscle endurance	30s chair stand [24].	X			X
		5 times chair stand [24].				X
	Cardiorespiratory endurance	10m Incremental shuttle walking test [81]. Results of this test recalculated to VO2max [82].	X			
		2 minute step test [40], with heart rate monitor (Polar RS400, Polar Electro Oy, Finland).				X
	Flexibility	Extended version of Modified back saver sit and reach test [83, 84].	X			
Measurement at home	Physical activity	Pedometer NL-1000 (New Lifestyles, USA).	X			
		ActiGraph wGT3X-BT Accelerometer (ActiGraph, USA).				X
Questionnaires professional caregiver		Self-assembled questionnaire about the participants' habitual physical activity.	X			
		International Physical Activity Questionnaire – short version (IPAQ-s) [39].				X
	Activities of daily life/mobility	Animated Activity Questionnaire (AAQ) [50].				X
	Mobility*	Self-assembled questionnaire based on the Hauser Ambulation Index [85] and the characteristics of the Gross Motor Function Classification Scale [86].	X			X
	Falling	Self-assembled questionnaire about the number of falls in the last three months.				X

	Symptoms/ limitations related to (hip/knee) OA	Hip disability and OA Outcome Score (HOOS) [51, 52].				X
		Knee injury and OA Outcome Score (KOOS) [53].				X
	Use of lower extremity aids	Self-assembled questions about the presence/use of aids for extra support of the lower extremity (such as orthopaedic footwear, splints and braces).	X			X
Physical assessment	Clinical/ symptomatic OA	Physical examination to examine the ACR criteria for clinical osteoarthritis of the hip and the knee [87, 48]. The following tests will be performed [88]: palpable warmth of the knee joint, joint crepitus of the knee, bony enlargement of the knee joint, quadriceps wasting, bone margin tenderness, patellofemoral joint tenderness, anserine tenderness, tibiofemoral joint tenderness, bulge sign of the knee, range of motion flexion and extension of the knee, range of motion flexion and extension of the hip, range of motion endorotation and exorotation of the hip. In addition, the laxity of the joints will be tested [89] and the gait and the postural alignment will be observed [90].				X
Interview	Self-report pain	The participants undergo a comprehension test to test whether their self-reported pain on a face-scale is a valid measurement [49]. When they succeed they will be asked to grade their pain during examination of the joint tenderness, flexion of the joints and hip internal rotation on a face-scale.				X
Observation	Observed pain	The health care professional will perform the Rotterdam Elderly Pain Observation Scale (REPOS) to observe pain behaviour during the physical examination for OA. A NRS-obs will be asked from the professional caregiver as part of the REPOS observation [91].				X
Medical imaging	Radiographic hip/knee OA	X-rays of the hip and knee: anterior posterior (AP) view of both knees (if possible weight-bearing), lateral view of right and left knee, skyline view of the patellofemoral joint of right and left knee, AP view of pelvis, faux profile view of right and left hip (only made by participants who are able to stand up (with support)).				X
Medical file	Musculoskeletal disorders*	Presence of musculoskeletal disorders in the medical file (such as OA, scoliosis*, spasticity and bone fractures).	X			X
Psychological problems and psychiatric disorders						
Measurement at home	Sleep-wake & circadian rhythm	Actiwatch AW7 (Cambridge Technology Ltd, United Kingdom).	X			
		GENEActiv Original (Activinsights Ltd, United Kingdom).				X

Interview	Self-report depression	Inventory of Depressive Symptomatology Self Report (IDS-SR) [92]. Phrasing of the questions adapted to people with ID.	X			X
	Self-report anxiety	Glasgow Anxiety Scale for people with an Intellectual Disability (GAS-ID) [93].	X			X
		Hospital Anxiety and Depression Scale (HADS) – anxiety subscale [94]. Phrasing of the questions adapted to people with ID.	X			
	Quality of life	Intellectual Disability Quality of Life (IDQOL-16) [95].	X			
	Diagnostic interview depression and/or anxiety	Participants with scores above the preset cut-off scores on one of the depression or anxiety questionnaires are further examined using the Psychiatric Assessment Schedule for Adults with Developmental Disability ICD-10 version (PAS-ADD-10). Interviews are conducted with the participant or his/her caregiver [96].	X			X
Questionnaires professional caregiver	Informant-report depression and anxiety*	Anxiety, Depression, and Mood Scale (ADAMS) [97]*.	X			X
		Signaallijst Depressie Zwakzinnigen (SDZ) [98]*.	X			X
	Somatic complaints	Somatic complaints subscale of the Symptom Checklist-90 (SCL-90) [99].	X			
	Life-events	Self-assembled checklist about life events based on other checklists, earlier life event-studies and experience from professionals working with people with ID.	X			X
	Social outcome	Self-assembled checklist about number of contacts with family, friends and peers and visiting leisure-clubs.	X			
	Cognitive functioning*	Dementia questionnaire for people with intellectual disabilities (DMR) [100].	X			X
	Aberrant behaviour	Aberrant Behaviour Checklist (ABC) [59].				X
	Sleep problems	Self-assembled questions about sleep problems, including problems with falling asleep, and waking up early.	X			X
	Sleep hygiene	Self-assembled questions about sleep hygiene (such as sleeping conditions, bedtimes, sleeping rituals, eating habits and use of TV, smartphone or tablet before going to bed, and provided professional support).				X
Psychological file	Psychological problems and psychiatric disorders	Baseline: level of intellectual disability, autism, depression, anxiety, dementia, psychoses, other psychiatric disorders and serious behavioural problems. 10-year follow-up: baseline variables + mood disorders, autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders,	X			X

		personality disorders, psychotic disorders, post-traumatic stress disorder, cognitive disorders (including dementia), traumatizing, and support or treatment received by the participant.				
Medical file	Sleep disorders/sleep problems	Presence of sleep disorders/problems in the medical file (such as problems with falling asleep and waking up early).	X			X
Physical assessment	Cortisol concentration last month	A small hair sample of at least 1cm (length) will be taken from the posterior vertex close to the scalp [101].				X
Nutritional intake and nutritional state						
Physical assessment	Height*	-	X			X
	Weight*	-	X			X
	Fat percentage	Formulas Durnin and Womersly [102] for calculating fat percentage from the sum of four skinfolds: triceps, biceps, subscapular and suprailiacal. Thickness of skinfolds measured with skinfold calliper (Harpenden, Baty International, United Kingdom).	X			X
		Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X
	Body composition	Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X
	Body circumferences	Measuring tape for hip, calf* and upper arm circumference.	X			X
	Bone Quality*	Ultrasonometer (Lunar Achilles Insight, GE Healthcare, United States) for measuring bone stiffness calcaneus.	X			X
Diary	Food intake	Self-assembled 3-day food intake diary.	X			X
Meal time observation	Dysphagia*	Dysphagia Disorder Survey [66].	X			X
Questionnaires professional caregiver	Malnutrition*	Mini Nutritional Assessment (MNA) [103]*.	X			X
		Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) [69].				X
	Eating disorders*	Screening Tool of fEeding Problems (STEP) [104].	X			X
	Gastro-oesophageal reflux disease	GORD Questionnaire: self-assembled questionnaire consisting of 50 items involving risk factors and symptoms of gastro-oesophageal reflux disease.	X			
Dental file	Dental condition	Baseline: dental condition, premedication/sedation during check-up or treatment, dental prosthesis and enamel wear.	X			X

		10-year follow-up: baseline variables + number of dentist/dental hygienist visits, number of elements in the upper/lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis/periodontitis, mobile elements and loss of dental elements due to trauma.				
Medical file	Gastrointestinal diseases*	Presence of gastrointestinal disease in the medical file (such as gastroesophageal reflux disease*, gastric ulcer, constipation* and dysphagia*).	X			X
General health data						
Medical file	Aetiology of intellectual disability	Presence of the aetiology of the intellectual disability in the medical file (such as a specific genetic syndrome).	X			X
	Malignancies*	Presence of malignancies in the medical file.	X			X
	Pulmonary diseases*	Presence of pulmonary disease in the medical file (such as asthma*, chronic obstructive pulmonary disease* and sleep apnoea syndrome).	X			X
	Neurological disorders	Presence of neurological disorders in the medical file (such as dementia, epilepsy and Parkinson's disease).	X			X
	Diseases of the genitourinary system	Presence of diseases of the genitourinary system in the medical file (such as urinary tract infections, incontinence and renal failure).	X			X
	Visual and hearing impairments*	Presence of visual and hearing impairments in the medical file.	X			X
	Medication use*	Medication use (medicament and dosage) as stated in the medical file.	X			X
	Hospitalization*	Number of hospitalizations in the past period.				X
	Mortality	Date of death, as stated in the medical file.			X	X
	Cause of death	Cause of death, as stated in the medical file.			X	X
Questionnaires professional caregiver	Activities of daily life*	Barthel Index [105]*.	X			X
	Instrumental activities of daily life*	Questionnaire based on the Instrumental Activities of Daily Living of Lawton and Brody [106] and the Groningen Activities Restriction Scale [107].	X			X
	Daytime activities*	Self-assembled questions about daytime activities and/or work of the participant.	X			X
	Smoking	Self-assembled questions about the smoking habits of the participant (how many cigars, cigarettes and/or pipe per day + past smoking habits).	X			X

	Alcohol use	Self-assembled questions about the participant's alcohol consumption (alcohol use per day + alcohol use in the past).	X			X
	Drug use	Self-assembled questions about the drug use of the participant (use of cannabis and hard drugs per day + drug use in the past).				X
	Use of caffeinated drinks	Self-assembled questions about the use of caffeinated drinks (coffee, tea, Coke, energy drink and chocolate milk) by the participant.				X

*All outcomes / measurements with an asterisk are part of the overarching research theme 'frailty'

FIGURE LEGENDS

Fig.1 Flow chart that shows the number of participants in the HA-ID cohort over time

Figure presents 1) the number of participants eligible for participation in the HA-ID cohort, 2) the number of participants who participated in measurements, 3) and the numbers of participants who dropped out the cohort

Note from the Editors: Instructions for reviewers of study protocols

Since launching in 2011, BMJ Open has published study protocols for planned or ongoing research studies. If data collection is complete, we will not consider the manuscript.

Publishing study protocols enables researchers and funding bodies to stay up to date in their fields by providing exposure to research activity that may not otherwise be widely publicised. This can help prevent unnecessary duplication of work and will hopefully enable collaboration. Publishing protocols in full also makes available more information than is currently required by trial registries and increases transparency, making it easier for others (editors, reviewers and readers) to see and understand any deviations from the protocol that occur during the conduct of the study.

The scientific integrity and the credibility of the study data depend substantially on the study design and methodology, which is why the study protocol requires a thorough peer-review.

BMJ Open will consider for publication protocols for any study design, including observational studies and systematic reviews.

Some things to keep in mind when reviewing the study protocol:

- Protocol papers should report planned or ongoing studies. The dates of the study should be included in the manuscript.
- Unfortunately we are unable to customize the reviewer report form for study protocols. As such, some of the items (i.e., those pertaining to results) on the form should be scores as Not Applicable (N/A).
- While some baseline data can be presented, there should be no results or conclusions present in the study protocol.
- For studies that are ongoing, it is generally the case that very few changes can be made to the methodology. As such, requests for revisions are generally clarifications for the rationale or details relating to the methods. If there is a major flaw in the study that would prevent a sound interpretation of the data, we would expect the study protocol to be rejected.

BMJ Open

Healthy Ageing and Intellectual Disability study: summary of findings and the protocol for the 10-year follow-up study

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Healthy Ageing and Intellectual Disability study: summary of findings and the protocol for the 10-year follow-up study

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DECLARATIONS

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests statement

The authors declare that they have no competing interests.

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Author contributions

We would like to justify the authors' contribution by describing their involvement in the different phases of the writing process: 1) devising and shaping the research project (AO, TH, DM), 2) drafting the study protocol (MdL, AO, RE, MK), 3) writing the first draft of the manuscript (MdL), 4) critically revising the manuscript (AO, RE, MK, MvM, MvB, TH, PB, DM) and 5) drafting the manuscript, tables and figures to their final version (MdL, AO, RE). All authors have critically reviewed the content of this paper and have approved the final version of the manuscript.

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ABSTRACT

Introduction

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study in the Netherlands that started in 2008, including 1,050 older adults (aged ≥50) with intellectual disabilities. The study is designed to learn more about the health and health risks of this group as they age. Compared to the amount of research in the general population, epidemiological research into the health of older adults with intellectual disabilities is still in its infancy. Longitudinal data about the health of this vulnerable and relatively unhealthy group are needed so that policy and care can be prioritised and for guiding clinical decision making about screening, prevention and treatment to improve healthy ageing.

Methods and analysis

This article presents a summary of the previous findings of the HA-ID study and describes the design of the 10-year follow-up in which a wide range of health data will be collected within five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders; 4) nutrition and nutritional state; and 5) frailty.

Ethics and dissemination

Ethical approval for the 10-year follow-up measurements of the HA-ID study has been obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number NL8564) and has been conducted according to the principles of the Declaration of Helsinki.

KEY WORDS

Intellectual disability, healthy ageing, elderly, cohort study, epidemiology.

ARTICLE SUMMARY

Strengths and limitations of this study

- This protocol outlines the design of the 10-year follow-up of the HA-ID study, a prospective multicentre cohort study in which a heterogeneous group of 1,050 older adults with intellectual disabilities is followed over time.
- The longitudinal design of the study makes it possible to make statements about causality and to study health progress and health indicators, which is important for prioritising policy and care and guiding clinical decision making about screening, prevention and treatment to improve healthy ageing.
- The comprehensive set of measurements makes it possible to evaluate the health of older adults with intellectual disabilities from a broad perspective and to investigate the interrelationships between medical domains.
- The data collection consists of measurements that have been shown to be feasible, valid and reliable in older adults with intellectual disabilities, based on previously acquired knowledge and experience within the HA-ID study.
- For financial and feasibility reasons, it has not been possible to perform follow-up measurements on a more regular basis.

INTRODUCTION

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study including older adults with intellectual disabilities (ID) in the Netherlands. The study was designed in response to the increasing longevity of people with ID and the lack of epidemiological data about their health and health risks at older ages. The absence of this knowledge raised questions about how to organise care and support for this vulnerable and relatively unhealthy group [1]. Based on this need for knowledge, a consortium was established in 2006 consisting of three ID care organisations (Ipse de Bruggen, Amarant and Abrona) and the research group of Intellectual Disability Medicine of the Erasmus MC, University Medical Centre Rotterdam. The HA-ID consortium aims to 1) increase knowledge on healthy ageing in people with ID through scientific research; 2) strengthen the scientific attitude of care professionals through participation in research and continuous education; and 3) innovate care by implementing research outcomes. In 2008, the HA-ID study started with a focus on physical activity and fitness, nutrition and nutritional state and mood and anxiety. A detailed description of the rationale and design of the baseline measurements can be found elsewhere [1]. After three and five years, follow-up measurements consisting of medical file research and questionnaires about the health of the participants were completed. New topics were included during this follow-up period: cardiovascular disease, frailty, mortality and causes of death [2].

The baseline results of the HA-ID study showed that older adults with ID had more health problems than their peers in the general population and that these problems occurred at younger ages [3, 4]. Older adults with ID became frail earlier and became more severely frail than their peers in the general population [5]. High prevalences of polypharmacy [6], multi-morbidity [6], sleep problems [7], major depressive disorders [8], dysphagia [9], obesity [10], suboptimal nutritional intake [11] and low physical activity and fitness levels were found [12-15].

Based on data from the 3 and 5-year follow-ups, frailty at baseline was predictive for the development of comorbidity [16], a decline in daily functioning and mobility [17], increased medication use [16], increased care intensity [18] and a higher mortality risk [19]. Also poor physical fitness was predictive for a decline in mobility [20], daily functioning [20, 21] and for a higher mortality risk [22]. Use of atypical antipsychotics, chronic kidney disease, abdominal obesity and histories of stroke and heart failure were predictive for developing cardiovascular disease (CVD) over a 3-year period [23]. These first results from the longitudinal data of the HA-ID study provided important insights for policy and care about how to contribute to a better health of older adults with ID. The results of the HA-ID study have been used in developing of diagnostic instruments and guidelines [3, 24, 25] and to illustrate the vulnerability and poor health situation of people with ID, resulting in changes to the Dutch legislation on long-term financing of support, care and treatment for people with ID.

Following the start of the HA-ID study, other research groups initiated longitudinal studies focusing on various aspects of health in adults with ID, such as the IDS-TILDA study in Ireland [26], the SAge-ID study in Australia [27] and a longitudinal cohort study about dementia and mortality in people with Down syndrome in the Netherlands

[28]. Despite these initiatives, epidemiological research into the health of adults with ID is still extremely limited. Too little is known about the health of this group as they age, or about changes in health status over time and early indicators for health problems. However, this knowledge is important for providing the evidence base for improving care and support of older adults with ID and guiding care providers in preparing for this growing group of elderly with ID. Longitudinal research makes it possible to make statements about causality, which contributes to e.g. identifying group-specific risk factors, groups at risk off specific diseases and other negative outcomes such as declining in independence. This knowledge can be used to reduce the occurrence of specific risk factors and identify, monitor and treating high-risk groups in good time. More longitudinal studies focusing on the health of this specific group are therefore urgently needed.

This article describes the design for the 10-year follow-up measurements of the HA-ID cohort. To learn more about changes in health status and indicators for health problems over time, a wide range of health data will be collected. Based on previous measurements and results, the focus will be on five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders (including sleep problems); 4) nutrition and nutritional state (including dysphagia); and 5) frailty. This article presents the design of the HA-ID cohort study and a summary of the main findings up to now, and provides an update of the planned measurements of the 10-year follow-up research themes.

METHODS AND ANALYSIS

STUDY COHORT

The HA-ID cohort consists of older adults with borderline to profound ID. All participants receive care or support from one of the care organisations of the HA-ID consortium. These organisations provide care to a wide spectrum of individuals with ID (in terms of the level of ID, residential status and mobility) in various settings (central residential settings, community-based homes, day activity centres and supported living) in both urban and rural areas in various regions in the Netherlands. At baseline, the care organisations provided care to approximately 10% of the total Dutch ID population receiving care or support from an ID care organisation [29]. At the start of the study, 10% of the individuals receiving care from the HA-ID care organisations was 50 or older, comparable to the total Dutch ID population receiving care or support from ID care organisations [29]. Based on these numbers, we concluded that the base population was representative for the total population of older adults with ID receiving care or support from ID care organisations in the Netherlands [1]. All individuals with ID within the consortium aged 50 or older by September 2008 were eligible to participate and received an invitation. Ultimately, 1,050 of the 2,322 (45.2%) invited individuals with ID participated in the baseline measurements. Table 1 presents the baseline characteristics of the participants, which were largely comparable to the overall group of invited individuals with ID and formed a near-representative study population for the total Dutch population of older adults with ID receiving formal support or care, with an underrepresentation of 80-to 84-year -olds, a slight overrepresentation of women and an underrepresentation of the more independent group. A more detailed description of the representativeness of the sample has been published elsewhere [1].

<<INSERT TABLE 1 ABOUT HERE>>

Figure 1 summarises the number of participants in the cohort over time. At baseline, measurements consisted of reviewing medical files, administering questionnaires, physical examinations with portable measuring equipment, fitness tests, observations, interviews, laboratory assessments and diaries [1]. At the 3-year follow-up, medical files were reviewed and professional caregivers completed questionnaires about the participant's health. Five years after the baseline measurements, causes of death were examined in the files of the deceased participants. The participants themselves were not actively involved in the data collection for these follow-up measurements. At the 3-year and 5-year follow-ups, the cohort consisted of 873 and 787 participants respectively.

All individuals with ID who participated in the baseline measurements and still receive care or support from one of the participating care organisations will be invited to participate in the 10-year follow-up measurements. There is one exclusion criterion: individuals are excluded from physical measurements if they are so seriously ill that participating in the study is not desirable. This decision is made based on shared decision making with caregivers and professionals.

<<INSERT FIGURE 1 ABOUT HERE>>

INFORMED CONSENT PROCEDURE

Because not all individuals with ID are mentally capable of giving informed consent, two separate consent procedures are followed. A behavioural scientist evaluates whether the individual is able to understand the specifically designed study information to let them make an informed decision about participation. If an individual is capable of making an informed decision, an easy-to-read information letter with supporting pictures and a consent form will be sent to this individual. If the behavioural scientist assesses the individual as being unable to make an informed decision about participation, an information letter and consent form will be sent to the legal representative of this individual. The professional caregiver of the individual with ID is informed about the study and the informed consent procedure to support the individual or legal representative in making their decision for participation. Inclusion of the participants started in July 2020 and the data collection in October 2020. Both the inclusion and the data collection are still ongoing.

RESEARCH THEMES

An outline is presented of the published results for each research theme, followed by a description of the data collection for the 10-year follow-up, with a specific focus on newly added measurements. In the 10-year follow-up, we also omitted measurements that turned out to be unfeasible, invalid or unreliable, based on the baseline measurements. For clarity, these measurements are not listed separately below. An overview of all measurements at baseline and the 3, 5 and 10-year follow-ups can be found in Table 2.

1. Cardiovascular disease

The HA-ID study provided many insights into the prevalence of CVD risk factors and the incidence of CVD in older adults with ID. The prevalences of hypertension (53.0%), diabetes (13.7%), metabolic syndrome (44.7%) and chronic kidney disease (15.3%) were similarly to those in the general population [30, 31]. However, the prevalence of peripheral arterial disease (20.7%) and obesity in women (25.6%) as measured by the Body Mass Index (BMI) was significantly higher than in the general population [10, 32]. The incidence of newly diagnosed CVD during a 3-year follow-up period was also examined. Incidence rates for myocardial infarction (2.8 per 1,000 person-years), stroke (3.2 per 1,000 person-years) and heart failure (12.8 per 1,000 person-years) were similar to the general population [23]. The use of atypical antipsychotics, chronic kidney disease, abdominal obesity and histories of stroke and heart failure turned out to be predictive for developing CVD during the 3-year follow-up period [23].

The baseline measurements revealed underdiagnosis of CVD risk factors in the HA-ID cohort. For example, 54% of the participants with diabetes had not been previously diagnosed with this condition. This was the case in 46% of the participants for hypercholsterolemia, in 50% for hypertension and in 94% for metabolic syndrome [30]. Atypical presentation of symptoms, limitations in communication, limited cooperation and resilience make diagnostics in people with ID more challenging [33]. This makes underdiagnosis a common problem in people with ID [4, 34]. The incidence of CVD described above is therefore also probably underestimated [23].

With increasing longevity and increased prevalence of some CVD risk factors, people with ID may be at higher risk of developing CVD. The 10-year follow-up of the HA-ID cohort provides opportunities to learn more about CVD risk factors and the development of CVD over time in older adults with ID. The planned measurements for the 10-year follow-up are summarised in Table 2. The presence of CVD risk factors, CVD and CVD treatments/interventions over the past ten years will be assessed by reviewing the medical files of all participants who participated in the baseline measurements, including the medical files of deceased participants.

Blood will be collected through venepuncture. Blood will be stored for 15 years at -80°C, allowing analyses of relevant biochemical markers now and in the future (Table 2).

The following measurements were added to the physical examination to gain more insight into the presence of CVD and its risk factors. Body composition will be studied with Bioelectrical Impedance Analysis (BIA) using the Tanita Body Composition Analyser (Tanita DC-430 MA, Tanita, Netherlands). An electrocardiogram will be performed to examine heart conditions. In addition, heart rate variability will be measured as a marker for the autonomic nervous system by wearing a heart rate monitor (Polar Vantage V HR H10, Polar Electro Oy, Finland) at rest for 5 minutes. Finally, various haemodynamic measurements (mean arterial pressure (mmHg), pulse pressure (mmHg), resting heart rate (bpm), stroke volume (mL), cardiac output (l/min), cardiac index (l/m*1/m), augmentation index (%), peripheral vascular resistance (s*mmHg/mL) and pulse wave velocity (m/s)) will be obtained with a non-invasive electronic blood pressure oscillometric monitoring system (Mobil-O-Graph 24h PWA Monitor, I.E.M. GmbH, Germany) [35]. Adding the Mobil-O-Graph provides a clearer picture of the presence of arterial stiffness and central systolic blood pressure, two important risk factors for CVD and morbidity [36].

2. Physical activity, fitness and musculoskeletal disorders

The HA-ID study yielded important results about physical activity and fitness. Older adults with ID had very low physical activity and fitness levels [12, 14]. In short, most participants were categorised as 'low active' (5,000-7,449 steps/day; 25.3%) or 'sedentary' (<5,000 steps/day; 38.5%). Only 36.2% of the participants walked ≥7,500 steps/day [12]. These results are likely to underestimate the problem because physical activity levels were only measured in participants who were physically able to walk at a sufficiently high speed for the pedometers to provide reliable measurements. In addition to these low physical activity levels, people with ID aged 50 and over had physical fitness levels comparable to or worse than people in the general population aged 70 and over [13, 14]. Data from the 3 and 5-year follow-ups showed that these low physical fitness levels at baseline were indicative of a decline in daily functioning and mobility over the 3-year follow-up period and a higher mortality risk over the 5-year follow-up period [20-22, 37]. Additionally, it was found that being fit is more important for survival than obesity. People who were unfit had a mortality risk four times higher than people who were fit, regardless of obesity [37]. Because of the importance of physical fitness, suitable fitness tests for this population are essential. Based on our previous research examining the reliability and feasibility of eight physical fitness tests in older adults with ID [38, 39] we developed the ID-fitscan to assess the physical fitness levels of adults with ID [24].

In the 10-year follow-up measurements, physical activity and fitness levels will be assessed again (see Table 2). Based on previous results and experiences, some changes were made to the measurements. Physical activity will be

measured using the ActiGraph (wGT3X-BT Accelerometer, ActiGraph, USA), an instrument that can make measurements at very low walking speeds and provides more detailed information about the physical activity levels of the participant. Complementary to this, we will use the International Physical Activity Questionnaire – Short Form (IPAQ-SF) to collect physical activity data [40]. The ID-fitscan [24], supplemented with the two-minute step test [41], will be used to assess physical fitness. Physical fitness tests that turned out to be less suitable at the baseline measurements are excluded [24].

The 10-year follow-up will also focus on musculoskeletal disorders, in particular osteoarthritis. Osteoarthritis is common in older people in the general population, leading to pain, joint instability, limitations in daily activities and decreased quality of life [42, 43]. Little is known about the prevalence of knee and hip osteoarthritis in people with ID. High prevalence is expected because many factors that have been associated with osteoarthritis (such as obesity, poor physical fitness levels, poor motor skills, gait abnormalities, musculoskeletal complications and developmental problems) are commoner in adults with ID than in the general population [14, 44-48].

Osteoarthritis of the hip and the knee will be assessed by applying the American College of Rheumatology (ACR) criteria for the diagnosis of osteoarthritis. These criteria cover clinical symptoms, consisting of pain and functional limitations of the joint and include radiological characteristics from X-rays as well [49]. The 10-year follow-up includes several tests to identify the presence of the ACR criteria, including physical examinations with pain observations (Rotterdam Elderly Pain Observation Scale (REPOS) filled out by the health professional performing the physical examination, supplemented by a Numeric Rating Scale observation filled out by the professional caregiver during the physical examination and a face-scale for self-report of pain [50]). The REPOS will also be used to assess pain during rest and daily activities that may provoke osteoarthritis complaints. Also, the Animated Activity Questionnaire (AAQ) will be used to identify whether the participants have complaints due to osteoarthritis during daily living activities, filled out by the professional caregivers of the participants [51]. Additional, data about gait characteristics that may be related to osteoarthritis will be collected through a structured observation. To signal pain, stiffness and range of motion the standardised questionnaires (the Hip disability and Osteoarthritis Outcome Score (HOOS) [52, 53] and the Knee disability and Osteoarthritis Outcome Score (KOOS) [54]) will be used.

3. Psychological problems and psychiatric disorders

At baseline, data were collected on the prevalence of depression and anxiety disorders. The prevalence of major depressive disorder was 7.6% [8], which is higher than in the general population (1.8% to 4.0%) [55]. Only 4.4% of the participants met the criteria for one of the anxiety disorders [8]. This was lower than expected and lower than the prevalence in the general population (10.2% to 11.6%) [56]. This may be explained by the fact that proxy reports had to be used in 78% of the participants. It is difficult for respondents such as professional caregivers to recognise symptoms of anxiety (e.g. pounding heart, worrying). This may have led to underestimation of the prevalence of anxiety disorders.

In the general population there is a strong association between sleep problems and anxiety- and mood disorders [57]. Data on sleep and sleep-wake rhythm were therefore also collected at baseline based on wrist-worn accelerometry

(Actiwatch AW7, Cambridge Technology Ltd, Cambridge, United Kingdom [49, 50]). It was found that 23.9% of the participants lay awake for more than one hour before falling asleep. In addition, 63.1% lay awake for more than 90 minutes after sleep onset and before final morning awakening, 20.9% slept less than 6 hours and 9.3% were already awake for more than 60 minutes before getting out of bed [58]. In total 72.1% of the participants were classified as having at least one of these sleep problems [58].

During the 10-year follow-up, data about anxiety disorders, depression and sleep will be collected again, with some changes and additions to the baseline data collection (see Table 2). The 10-year follow-up has been extended with data retrieval from the psychological files about the presence of mood disorders, autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders, personality disorders, psychotic disorders, post-traumatic stress disorder and cognitive disorders (including dementia). In older people with ID, there is an association between the presence of a mental health diagnosis and problem behaviour [59]. Data about problem behaviour will therefore also be collected within the 10-year follow-up using the Aberrant Behaviour Checklist (ABC) [60]. The ABC is a widely used behaviour rating scale and measures problem behaviour using five subscales: irritability, lethargy, stereotypy, hyperactivity and excessive speech. In addition, a potential objective biomarker for long-term stress in people with ID will be evaluated, which may help to future diagnostic assessment. Long-term stress over the recent months will be retrospectively examined with a hair cortisol measurement. Recently published studies in the general population indicate that there is a strong association between the level of hair cortisol, life events and symptoms of anxiety and depression [61-64].

Data on sleep and sleep-wake rhythm will still be collected with accelerometry; however, we will now use the GENEActiv (Original, Activinsights Ltd, UK). Data from the GENEActiv are comparable to data collected by the Actiwatch that was used at baseline [65]. Extra questions about sleep hygiene and sleep circumstances have been added to learn more about the influence of these factors on sleep in older adults with ID.

4. Nutritional intake and nutritional state

The baseline measurements of the HA-ID study yielded insights into the dietary intake and nutritional state of older adults with ID. Three-day dietary records completed by professional caregivers revealed inadequate dietary intake, with none of the participants meeting all Dutch recommendations for a healthy dietary intake. The food intake was too low in calories in 68.6% of the participants, too low in protein in 30.2%, too low in dietary fibre in 98.2% and too high in saturated fat in 89.5% of the participants [11]. Forty-two per cent of the participants had vitamin D deficiency, of which 9% had severe vitamin D deficiency [66]. Vitamin D supplement were routinely provided to 45% of the participants and this group had significantly higher mean vitamin D serum levels than those without supplement. This calls for more attention for prescribing vitamin D in older adults with ID [66]. These results also indicate that there is plenty of room for improvement in healthy nutrition.

Mealtime observations using the Dysphagia Disorder Survey (DDS) [67] showed moderate to severe dysphagia in 51.7% of the participants, which is comparable to the prevalence in nursing homes [9]. In 89.5% of the participants with dysphagia, this had not been previously diagnosed. The high degree of underdiagnosis illustrates the

importance of screening and diagnosing dysphagia to prevent complications in clinical practice. Greater age, Down syndrome, mobility impairment, needing help with feeding and use of benzodiazepines were positively and independently associated with dysphagia [9].

The prevalence of sarcopenia was also studied. Fourteen per cent of the participants were classified as having sarcopenia, which developed at a relatively young age compared to the general population. At a prevalence of 12.7%, sarcopenia was already significantly present in participants aged 50 to 64 [68]. Additionally, the bone quality was low in 43.9% of participants. Being female, greater age, more severe ID, mobility impairment and anticonvulsant drug use were positively associated with low bone quality [69]. Higher BMI was negatively associated with low bone quality [69]. These results suggest an approach for periodic screening of high-risk groups for low bone quality and target groups for prevention in clinical practice [69].

In the 10-year follow-up, the baseline measurements will be repeated (see Table 2). To gain a better picture of the degree of malnutrition among older adults with ID, the Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) will be added to the data collection. The SNAQRC is a screening instrument for early detection of undernutrition in nursing or residential home settings using a traffic light system in which BMI and four questions related to involuntary weight loss, loss of appetite and eating with help are combined [70]. The SNAQRC will be completed by professional caregivers.

At baseline, a short dental file examination provided some data on the dental condition of the participants. To get a fuller picture of the dental condition and dental hygiene of older adults with ID, the dental file review will be extended. Data will be collected about dental condition, premedication and sedation during check-up and treatment, dental prosthesis, enamel wear, the number of dentist and dental hygienist visits, the number of elements in the upper and lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis and periodontitis, mobile elements and loss of dental elements due to trauma.

5. Frailty

Frailty is a clinically recognisable state of increased vulnerability resulting from age-associated decline in reserves and functions across multiple physiological systems [71]. Frailty leads to deterioration of daily functioning and mobility, increased disability, development of comorbidity and increased care intensity [17, 72, 73]. As a result, signalling frailty could play a valuable role in care planning, potentially improving quality of life and increasing the life expectancy of frail people with ID. In the general population, frailty is usually measured by tools such as the frailty phenotype [74]. However, we theorised that the ID population might require a more specific approach than the available tools allow. Based on the baseline data, an ID-Frailty Index was created consisting of 51 items [3]. The ID-Frailty Index focuses on multiple aspects of daily functioning, opposed to a broader focus on physical frailty and mobility impairment [75]. As a result, the ID-Frailty Index could be applied to a larger proportion of the study population than the frailty phenotype and was deemed more suitable for measuring frailty in older adults with ID [75]. Furthermore, the ID-Frailty index showed a stronger relationship with mortality than the frailty phenotype [75]. The 3-year follow-up data showed that higher scores on the ID-Frailty Index resulted in a greater risk of death

[19]. Finally, the ID-Frailty Index was predictive for a decline in mobility and increases in disability, polypharmacy and care intensity [16-18].

In the 10-year follow-up all previous measurements that were used to create the ID-Frailty index will be repeated (see Table 2). This lets us investigate the characteristics of frailty over time. In an attempt to further increase the practical and clinical usability of the ID-Frailty Index, a shortened version was developed. During the 10-year follow-up, the utility of this short form of the ID-Frailty Index will be further investigated.

General health data

In addition to these five research themes, data on other health variables will also be collected such as data on other diseases, medication use, hospitalisation, mortality, activities of daily life, smoking and alcohol/drug use (Table 2, under the heading 'General health data').

PROCEDURE

To limit the burden and impact on participants and their professional caregivers, all measurements will be done in settings close to where the participants live. All measurements will be carried out by test administrators consisting of professionals working in the care organisations. All test administrators will be trained to ensure accurate administration and correct scoring of the measurements. All measurements for a specific participant will be scheduled within one week. This test week consists of a physical examination performed by medical staff, fitness tests supervised by movement therapists or physiotherapists, observations to assess pain during activities of daily life performed by trained healthcare professionals, a mealtime observation to screen for dysphagia performed by speech and language therapists and a maximum of two interviews by trained and qualified professionals aimed at screening and diagnosing anxiety and depression. The participant will wear portable measuring equipment on the wrist and hip for seven days to monitor physical activity and sleep-wake rhythm. If separate consent is provided, blood samples and a tuft of scalp hair will be collected. For logistical reasons, the hip and knee X-rays take place outside this test week. All measurements together require a maximum time investment of four hours for each participant. However, the time investment per participant will probably vary because not every participant can undergo all measurements. The study will not interfere with routine medical practice. In addition to measurements for which active involvement of the participants is needed, the professional caregiver will be asked to complete questionnaires about the participant's health and data will be collected from the medical, psychological and dental files. The medical file review is performed using the records of all participants who participated in the baseline measurements, including the medical files of deceased participants. A complete overview of all measurements within the HA-ID study can be found in Table 2. After the test week, the participant's physician and behavioural scientist receive a report with a summary of the results of the measurements.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not involved in the design of this study.

STATISTICAL ANALYSIS

In line with the previous measurements, the 10-year follow-up will provide cross-sectional and longitudinal data. Various statistical analyses will be applied. Descriptive statistics are used to answer questions about the prevalence and incidence of health conditions and possible risk factors. Multivariable regression analyses are used to answer questions about differences between subgroups and associations between variables, considering possible confounders and to adjust for these covariates. Survival analysis with Cox proportional hazard models will be used to investigate relationships between various factors (including age, sex, level of ID and comorbidity) and several health conditions and mortality over time. For repeated measurements, the dependency of measurements for the same participant will be adjusted by using generalised linear mixed-effects models (GLME).

IMPLICATIONS FOR PRACTICE

The HA-ID study so far has yielded knowledge of various health problems that are prevalent in older adults with ID, and how these compare to the general population. This knowledge suggested approaches for improving care for adults with ID. The 10-year follow-up will provide a deeper understanding of the course of health over time and risk factors for health problems in older adults with ID. Research into CVD risk factors in this population, for example, is still very limited. More knowledge about CVD risk factors and possible group-specific risk factors will give a better estimate of the cardiovascular risk profile of older adults with ID. The 10-year follow-up will also give a clearer picture of how frailty develops over time and whether there are certain groups of people with ID who are at higher risk for adverse outcomes.

What characterises the HA-ID study is that it is a prospective multicentre cohort study in which, compared to other ID studies, a relatively large (n=1,050) and heterogeneous group of older adults with ID is followed over time. The extensive measurements let us evaluate the health of older adults with ID from a broad perspective and investigate the interrelationships between medical domains such as cardiovascular disease, physical fitness, psychological problems and psychiatric disorders, nutrition and frailty. Looking across research themes is especially important because multi-morbidity is common in people with ID [4].

We know from experience that conducting epidemiological research into this field can be difficult and involves challenges in selecting suitable measuring instruments; some require certain levels of cognitive, physical or verbal ability that may not be compatible with those of the participants. To allow for optimal comparison between the general population and our cohort, we have aligned the measurements of the 10-year follow-up as much as possible to existing cohort studies of (specifically older) adults in the general population. However, feasibility, validity and reliability in older adults with ID were the leading criteria when selecting measuring instruments, using previously acquired knowledge and experience from the HA-ID study. How invasive and time-consuming instruments are was also considered, as were the feasibility for a large proportion of our population, the extent to which it is possible to do the measurement at the care organisations and the extent to which the instruments can be used by a large group of professionals without making concessions in terms of inter-rater reliability. In addition, the costs of the measuring instruments were considered, considering use in clinical practice. The HA-ID study is continuously searching for innovative and feasible measuring instruments that can be implemented for data collection.

A limitation of our study is that financial and feasibility reasons mean it has not been possible to perform follow-up measurements more regularly. Fortunately, the presence of routine registrations performed by the care organisations in medical, psychological and dental files lets us retrospectively collect data on the health of the participants over the past 10 years. Given the age of our study population and the length of follow-up, selection bias caused by the survival of healthier participants may distort our results. We are aware of this healthy survivor effect and address this when analysing and interpreting our results. It should be noted, that we do have access to the medical files of participants who have passed away. This lets us retrospectively collect data on the health of this group.

Results from the 10-year follow-up measurements are important for prioritising policy and care and underpinning clinical decision making about screening, prevention and treatment to improve healthy ageing of adults with ID. Longitudinal data collected in the 10-year follow-up of the HA-ID cohort therefore has high added value.

<<INSERT TABLE 2 ABOUT HERE>>

ETHICS AND DISSEMINATION

As for the previous parts of the HA-ID study (MEC-2008-234 and MEC-2011-309), ethical approval for the 10-year follow-up has been obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number NL8564) and follows the guidelines of the Declaration of Helsinki [76]. Local ethical committees and boards of individuals with ID and their representatives of the three involved care organisations were informed. Inclusion of the participants started in July 2020 and is ongoing.

ABBREVIATIONS

AAQ	Animated Activity Questionnaire
ABC	Aberrant Behaviour Checklist
ACR	American College of Rheumatology
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CVD	Cardiovascular disease
DDS	Dysphagia Disorder Survey
GLME	Generalised linear mixed-effects models
HA-ID	Healthy Ageing and Intellectual Disability
HOOS	Hip disability and Osteoarthritis Outcome Score
ID	Intellectual disabilities
IPAQ-SF	Physical Activity Questionnaire – Short Form
KOOS	Knee disability and Osteoarthritis Outcome Score
MEC	Medical Ethics Review Committee
NTR	Dutch Trial Register
REPOS	Rotterdam Elderly Pain Observation Scale
SNAQRC	Short Nutritional Assessment Questionnaire for Residential Care

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TABLE 1 Baseline characteristics of the HA-ID cohort (n=1,050) [1]

Characteristic		*n* (%)
Sex	Male	539 (51)
	Female	511 (49)
Age		60 (11, 50-93)*
Level of ID	Borderline	31 (3.0)
	Mild	223 (21.2)
	Moderate	506 (48.2)
	Severe	172 (16.4)
	Profound	91 (8.7)
	Unknown	27 (2.6)
Residential status	Central setting	557 (53.0)
	Community-based	432 (41.1)
	Independent with ambulatory support	43 (4.1)
	With relatives	7 (0.7)
	Unknown	11 (1.1)
Level of care (ZZP-scores)	Only day care indication	6 (0.6)
	Only indication ambulant care	37 (3.5)
	Residence with minimal support (1 VG)	12 (1.1)
	Residence with support (2 VG)	39 (3.7)
	Residence with support and care (3 VG)	138 (13.1)
	Residence with support and intensive care (4 VG)	207 (19.7)
	Residence with intensive support and intensive care (5 VG)	325 (31.0)
	Residence with intensive support, care and regulation of behaviour (6 VG)	93 (8.9)
	(Enclosed) residence with very intensive support, care and regulation of behaviour (7 VG)	142 (13.5)
	Mental Health Care ZZP scores	2 (0.2)
	Unknown	49 (4.7)

* Median (interquartile range, range)

ID = intellectual disability

ZZP = the Dutch classification of levels of support, care and/or treatment as a basis for long-term financing (Zorgzwaartepakket) [77]

VG = Dutch abbreviation for intellectual disability

TABLE 2 **Measurements within the HA-ID study: baseline, 3, 5 and 10-year follow-up per research theme***

Type	Outcome	Details	Moment of data collection			
			Baseline (2009-2010)	3-year follow-up (2012-2013)	5-year follow- up (2015)	10-year follow-up (2020-2022)
Demographics						
Medical file	Age	-	X		X	X
	Sex	-	X			
	Residential status	Central setting (with or without 24-hour support), community based (with or without 24-hour support), independent with ambulatory support (by appointment), with relatives, with partner, independent.	X			X
	Level of care	Care Intensity Packages (Dutch ZZP-scores) [77].	X			X
1. Cardiovascular disease						
Physical assessment	Brachial blood pressure*	Omron M7 (OMRON Healthcare, the Netherlands).	X			
	Central blood pressure and arterial stiffness	Mobil-O-Graph 24h PWA Monitor (IEM GmbH, Germany) including pulse wave velocity.				X
	Ankle-Arm-Index*	Omron M7 (OMRON Healthcare, the Netherlands) (arm). Boso classico and 8-MHz Doppler probe (Huntleigh MD II, United Kingdom) (ankle). Ankle-arm-index calculated: systolic blood pressure ankle divided by systolic blood pressure arm.	X			X
	Heart rate variability	Polar Vantage V HR H10 (Polar Electro Oy, Finland).				X
	Electrical activity of the heart	Electrocardiogram (ECG).				X
	Fat percentage	Formulas Durnin and Womersly [78] for calculating fat percentage from the sum of four skinfolds: triceps, biceps, subscapular and suprailiacal. Thickness of skinfolds measured with skinfold calliper (Harpenden, Baty International, United Kingdom).	X			X
		Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X
	Body composition	Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X

Venipuncture	Biochemical markers*	Fasting plasma levels: glucose, cholesterol (total/HDL*/LDL), haemoglobin (HB)*, haemoglobin A1c (HbA1c), triglyceride, C-reactive protein (CRP), interleukin 6 (IL-6), Tumour Necrosis Factor alpha (TNF alpha), albumin, vitamin D, calcium, creatinine, cystatin C, troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP) etc. The participants' blood is stored for 15 years at -80 degrees Celsius, in order to perform additional analyses afterwards.	X			X
Medical file	Cardiovascular disease*	Presence of CVD (heart failure, myocardial infarction, stroke, transient ischemic attack (TIA), cardiac arrhythmias, angina pectoris, aortic aneurysm, peripheral arterial disease (PAD), hypertension etc.), CVD risk factors (diabetes mellitus, central obesity, metabolic syndrome, rheumatoid arthritis, incriminating family history etc.) and treatments/ interventions (revascularisation of the coronary artery, pacemaker and implantable cardioverter-defibrillator (ICD)).	X			X
	Endocrine disorders*	Presence of endocrine disorders (such as diabetes mellitus*, hypercholesterolemia and metabolic syndrome).	X			X
2. Physical activity, fitness and musculoskeletal disorders						
Fitness assessment	Manual dexterity*	Box and block test [79].	X			X
	Reaction time	Auditive and visual reaction time test [80, 81].	X			
	Balance*	Berg Balance Scale [82].	X			
		Comfortable and maximum walking speed (5m) [24]*.	X			X
		Static balance test (for stances) [24].				X
	Grip strength*	Jamar Hand Dynamometer (#5030J1, Sammons Preston Rolyan, USA) [24].	X			X
	Muscle endurance	30s chair stand [24].	X			X
		5 times chair stand [24].				X
	Cardiorespiratory endurance	10m Incremental shuttle walking test [83]. Results of this test recalculated to VO2max [84].	X			
		2 minute step test [41], with heart rate monitor (Polar RS400, Polar Electro Oy, Finland).				X
	Flexibility	Extended version of Modified back saver sit and reach test [85, 86].	X			
Measurement at home	Physical activity	Pedometer NL-1000 (New Lifestyles, USA).	X			
		ActiGraph wGT3X-BT Accelerometer (ActiGraph, USA).				X
Questionnaires professional		Self-assembled questionnaire about the participants' habitual physical activity.	X			

caregiver		International Physical Activity Questionnaire – short version (IPAQ-s) [40].				X
	Activities of daily life/mobility	Animated Activity Questionnaire (AAQ) [51].				X
	Mobility*	Self-assembled questionnaire based on the Hauser Ambulation Index [87] and the characteristics of the Gross Motor Function Classification Scale [88].	X			X
	Falling	Self-assembled questionnaire about the number of falls in the last three months.				X
	Symptoms/ limitations related to (hip/knee) OA	Hip disability and OA Outcome Score (HOOS) [52, 53].				X
		Knee injury and OA Outcome Score (KOOS) [54].				X
	Use of lower extremity aids	Self-assembled questions about the presence/use of aids for extra support of the lower extremity (such as orthopaedic footwear, splints and braces).	X			X
Physical assessment	Clinical/ symptomatic OA	Physical examination to examine the ACR criteria for clinical osteoarthritis of the hip and the knee [89, 49]. The following tests will be performed [90]: palpable warmth of the knee joint, joint crepitus of the knee, bony enlargement of the knee joint, quadriceps wasting, bone margin tenderness, patellofemoral joint tenderness, anserine tenderness, tibiofemoral joint tenderness, bulge sign of the knee, range of motion flexion and extension of the knee, range of motion flexion and extension of the hip, range of motion endorotation and exorotation of the hip. In addition, the laxity of the joints will be tested [91] and the gait and the postural alignment will be observed [92].				X
Interview	Self-report pain	The participants undergo a comprehension test to test whether their self-reported pain on a face-scale is a valid measurement [50]. When they succeed they will be asked to grade their pain during examination of the joint tenderness, flexion of the joints and hip internal rotation on a face-scale.				X
Observation	Observed pain	The health care professional will perform the Rotterdam Elderly Pain Observation Scale (REPOS) to observe pain behaviour during the physical examination for OA. A NRS-obs will be asked from the professional caregiver as part of the REPOS observation [93].				X
Medical imaging	Radiographic hip/knee OA	X-rays of the hip and knee: anterior posterior (AP) view of both knees (if possible weight-bearing), lateral view of right and left knee, skyline view of the patellofemoral joint of right and left knee, AP view of pelvis, faux profile view of right and				X

		left hip (only made by participants who are able to stand up (with support)).				
Medical file	Musculoskeletal disorders*	Presence of musculoskeletal disorders in the medical file (such as OA, scoliosis*, spasticity and bone fractures).	X			X
3. Psychological problems and psychiatric disorders						
Measurement at home	Sleep-wake & circadian rhythm	Actiwatch AW7 (Cambridge Technology Ltd, United Kingdom).	X			
		GENEActiv Original (Activinsights Ltd, United Kingdom).				X
Interview	Self-report depression	Inventory of Depressive Symptomatology Self Report (IDS-SR) [94]. Phrasing of the questions adapted to people with ID.	X			X
	Self-report anxiety	Glasgow Anxiety Scale for people with an Intellectual Disability (GAS-ID) [95].	X			X
		Hospital Anxiety and Depression Scale (HADS) – anxiety subscale [96]. Phrasing of the questions adapted to people with ID.	X			
	Quality of life	Intellectual Disability Quality of Life (IDQOL-16) [97].	X			
	Diagnostic interview depression and/or anxiety	Participants with scores above the preset cut-off scores on one of the depression or anxiety questionnaires are further examined using the Psychiatric Assessment Schedule for Adults with Developmental Disability ICD-10 version (PAS-ADD-10). Interviews are conducted with the participant or his/her caregiver [98].	X			X
Questionnaires professional caregiver	Informant-report depression and anxiety*	Anxiety, Depression and Mood Scale (ADAMS) [99]*.	X			X
		Signaallijst Depressie Zwakzinnigen (SDZ) [100]*.	X			X
	Somatic complaints	Somatic complaints subscale of the Symptom Checklist-90 (SCL-90) [101].	X			
	Life-events	Self-assembled checklist about life events based on other checklists, earlier life event-studies and experience from professionals working with people with ID.	X			X
	Social outcome	Self-assembled checklist about number of contacts with family, friends and peers and visiting leisure-clubs.	X			
	Cognitive functioning*	Dementia questionnaire for people with intellectual disabilities (DMR) [102].	X			X
	Aberrant behaviour	Aberrant Behaviour Checklist (ABC) [60].				X
	Sleep problems	Self-assembled questions about sleep problems, including problems with falling asleep and waking up early.	X			X
	Sleep hygiene	Self-assembled questions about sleep hygiene (such as sleeping conditions, bedtimes, sleeping rituals, eating habits and use of				X

		TV, smartphone or tablet before going to bed and provided professional support).				
Psychological file	Psychological problems and psychiatric disorders	Baseline: level of intellectual disability, autism, depression, anxiety, dementia, psychoses, other psychiatric disorders and serious behavioural problems. 10-year follow-up: baseline variables + mood disorders, autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders, personality disorders, psychotic disorders, post-traumatic stress disorder, cognitive disorders (including dementia), traumatising and support or treatment received by the participant.	X			X
Medical file	Sleep disorders/sleep problems	Presence of sleep disorders/problems in the medical file (such as problems with falling asleep and waking up early).	X			X
Physical assessment	Cortisol concentration last month	A small hair sample of at least 1cm (length) will be taken from the posterior vertex close to the scalp [103].				X
4. Nutritional intake and nutritional state						
Physical assessment	Height*	-	X			X
	Weight*	-	X			X
	Body circumferences	Measuring tape for hip, calf* and upper arm circumference.	X			X
	Bone Quality*	Ultrasonometer (Lunar Achilles Insight, GE Healthcare, United States) for measuring bone stiffness calcaneus.	X			X
Diary	Food intake	Self-assembled 3-day food intake diary.	X			X
Meal time observation	Dysphagia*	Dysphagia Disorder Survey [67].	X			X
Questionnaires professional caregiver	Malnutrition*	Mini Nutritional Assessment (MNA) [104]*.	X			X
		Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) [70].				X
	Eating disorders*	Screening Tool of fEeding Problems (STEP) [105].	X			X
	Gastro-oesophageal reflux disease	GORD Questionnaire: self-assembled questionnaire consisting of 50 items involving risk factors and symptoms of gastro-oesophageal reflux disease.	X			
Dental file	Dental condition	Baseline: dental condition, premedication/sedation during check-up or treatment, dental prosthesis and enamel wear.	X			X

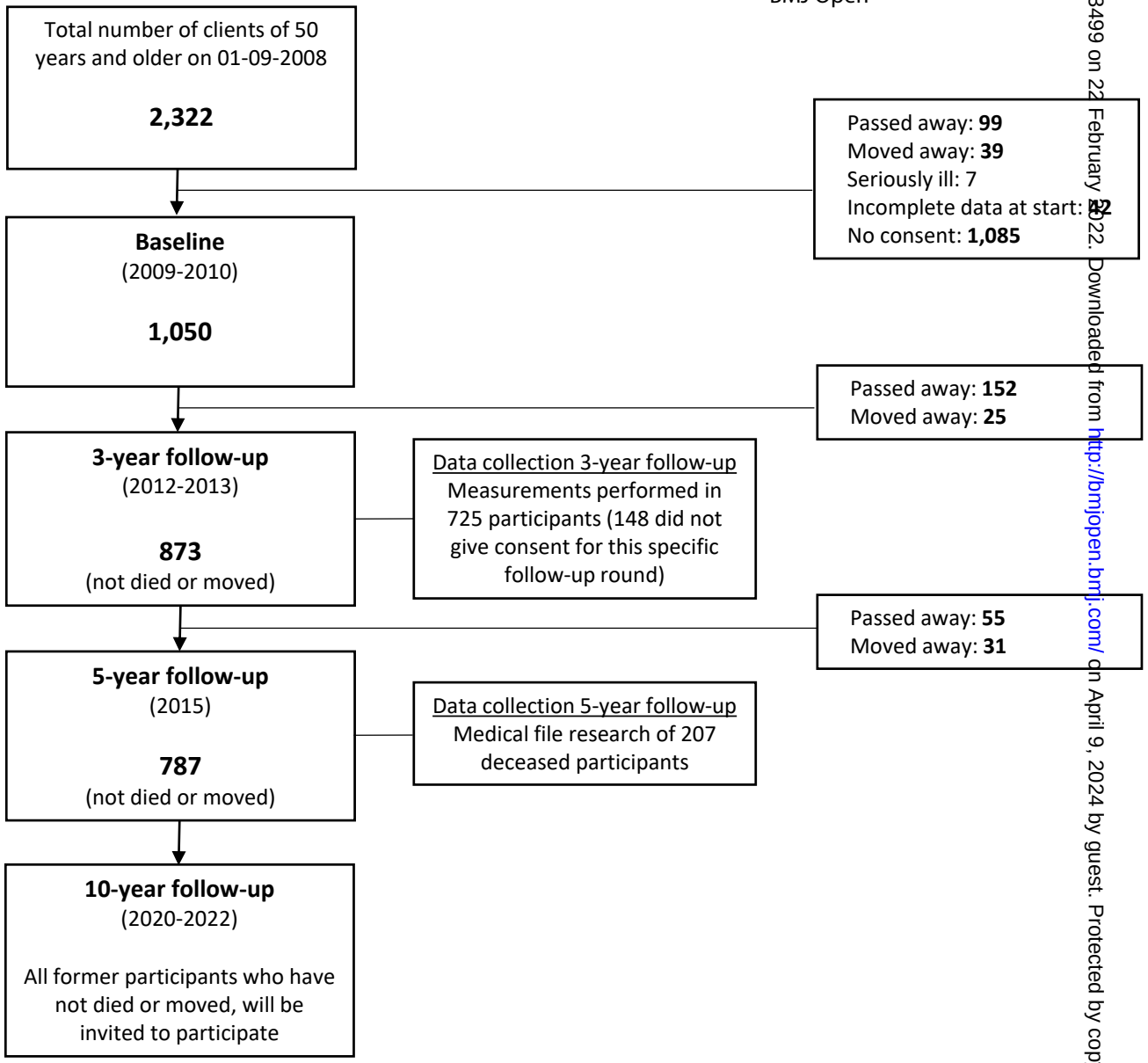
		10-year follow-up: baseline variables + number of dentist/dental hygienist visits, number of elements in the upper/lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis/periodontitis, mobile elements and loss of dental elements due to trauma.				
Medical file	Gastrointestinal diseases*	Presence of gastrointestinal disease in the medical file (such as gastroesophageal reflux disease*, gastric ulcer, constipation* and dysphagia*).	X			X
5. Frailty						
All outcomes / measurements with an asterisk* in this table are part of the overarching research theme 'Frailty'.						
General health data						
Medical file	Aetiology of intellectual disability	Presence of the aetiology of the intellectual disability in the medical file (such as a specific genetic syndrome).	X			X
	Malignancies*	Presence of malignancies in the medical file.	X			X
	Pulmonary diseases*	Presence of pulmonary disease in the medical file (such as asthma*, chronic obstructive pulmonary disease* and sleep apnoea syndrome).	X			X
	Neurological disorders	Presence of neurological disorders in the medical file (such as dementia, epilepsy and Parkinson's disease).	X			X
	Diseases of the genitourinary system	Presence of diseases of the genitourinary system in the medical file (such as urinary tract infections, incontinence and renal failure).	X			X
	Visual and hearing impairments*	Presence of visual and hearing impairments in the medical file.	X			X
	Medication use*	Medication use (medicament and dosage) as stated in the medical file.	X			X
	Hospitalisation*	Number of hospitalisations in the past period.				X
	Mortality	Date of death, as stated in the medical file.			X	X
	Cause of death	Cause of death, as stated in the medical file.			X	X
Questionnaires professional caregiver	Activities of daily life*	Barthel Index [106]*.	X			X
	Instrumental activities of daily life*	Questionnaire based on the Instrumental Activities of Daily Living of Lawton and Brody [107] and the Groningen Activities Restriction Scale [108].	X			X

	Daytime activities*	Self-assembled questions about daytime activities and/or work of the participant.	X			X
	Smoking	Self-assembled questions about the smoking habits of the participant (how many cigars, cigarettes and/or pipe per day + past smoking habits).	X			X
	Alcohol use	Self-assembled questions about the participant's alcohol consumption (alcohol use per day + alcohol use in the past).	X			X
	Drug use	Self-assembled questions about the drug use of the participant (use of cannabis and hard drugs per day + drug use in the past).				X
	Use of caffeinated drinks	Self-assembled questions about the use of caffeinated drinks (coffee, tea, Coke, energy drink and chocolate milk) by the participant.				X

FIGURE LEGENDS

Fig.1 Flow chart that shows the number of participants in the HA-ID cohort over time

Figure presents 1) the number of participants eligible for participation in the HA-ID cohort, 2) the number of participants who participated in measurements, 3) and the numbers of participants who dropped out the cohort



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Healthy Ageing and Intellectual Disability study: summary of findings and the protocol for the 10-year follow-up study

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Healthy Ageing and Intellectual Disability study: summary of findings and the protocol for the 10-year follow-up study

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DECLARATIONS

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests statement

The authors declare that they have no competing interests.

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Author contributions

We would like to justify the authors' contribution by describing their involvement in the different phases of the writing process: 1) devising and shaping the research project (AO, TH, DM), 2) drafting the study protocol (MdL, AO, RE, MK), 3) writing the first draft of the manuscript (MdL), 4) critically revising the manuscript (AO, RE, MK, MvM, MvB, TH, PB, DM) and 5) drafting the manuscript, tables and figures to their final version (MdL, AO, RE). All authors have critically reviewed the content of this paper and have approved the final version of the manuscript.

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ABSTRACT

Introduction

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study in the Netherlands that started in 2008, including 1,050 older adults (aged ≥50) with intellectual disabilities. The study is designed to learn more about the health and health risks of this group as they age. Compared to the amount of research in the general population, epidemiological research into the health of older adults with intellectual disabilities is still in its infancy. Longitudinal data about the health of this vulnerable and relatively unhealthy group are needed so that policy and care can be prioritised and for guiding clinical decision making about screening, prevention and treatment to improve healthy ageing.

Methods and analysis

This article presents a summary of the previous findings of the HA-ID study and describes the design of the 10-year follow-up in which a wide range of health data will be collected within five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders; 4) nutrition and nutritional state; and 5) frailty.

Ethics and dissemination

Ethical approval for the 10-year follow-up measurements of the HA-ID study has been obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number NL8564) and has been conducted according to the principles of the Declaration of Helsinki.

KEY WORDS

Intellectual disability, healthy ageing, elderly, cohort study, epidemiology.

ARTICLE SUMMARY

Strengths and limitations of this study

- This protocol outlines the design of the 10-year follow-up of the HA-ID study, a prospective multicentre cohort study in which a heterogeneous group of 1,050 older adults with intellectual disabilities is followed over time.
- The longitudinal design of the study makes it possible to make statements about causality and to study health progress and health indicators, which is important for prioritising policy and care and guiding clinical decision making about screening, prevention and treatment to improve healthy ageing.
- The comprehensive set of measurements makes it possible to evaluate the health of older adults with intellectual disabilities from a broad perspective and to investigate the interrelationships between medical domains.
- The data collection consists of measurements that have been shown to be feasible, valid and reliable in older adults with intellectual disabilities, based on previously acquired knowledge and experience within the HA-ID study.
- For financial and feasibility reasons, it has not been possible to perform follow-up measurements on a more regular basis.

INTRODUCTION

The Healthy Ageing and Intellectual Disability (HA-ID) study is a prospective multicentre cohort study including older adults with intellectual disabilities (ID) in the Netherlands. The study was designed in response to the increasing longevity of people with ID and the lack of epidemiological data about their health and health risks at older ages. The absence of this knowledge raised questions about how to organise care and support for this vulnerable and relatively unhealthy group [1]. Based on this need for knowledge, a consortium was established in 2006 consisting of three ID care organisations (Ipse de Bruggen, Amarant and Abrona) and the research group of Intellectual Disability Medicine of the Erasmus MC, University Medical Centre Rotterdam. The HA-ID consortium aims to 1) increase knowledge on healthy ageing in people with ID through scientific research; 2) strengthen the scientific attitude of care professionals through participation in research and continuous education; and 3) innovate care by implementing research outcomes. In 2008, the HA-ID study started with a focus on physical activity and fitness, nutrition and nutritional state and mood and anxiety. A detailed description of the rationale and design of the baseline measurements can be found elsewhere [1]. After three and five years, follow-up measurements consisting of medical file research and questionnaires about the health of the participants were completed. New topics were included during this follow-up period: cardiovascular disease, frailty, mortality and causes of death [2].

The baseline results of the HA-ID study showed that older adults with ID had more health problems than their peers in the general population and that these problems occurred at younger ages [3, 4]. Older adults with ID became frail earlier and became more severely frail than their peers in the general population [5]. High prevalences of polypharmacy [6], multi-morbidity [6], sleep problems [7], major depressive disorders [8], dysphagia [9], obesity [10], suboptimal nutritional intake [11] and low physical activity and fitness levels were found [12-15].

Based on data from the 3 and 5-year follow-ups, frailty at baseline was predictive for the development of comorbidity [16], a decline in daily functioning and mobility [17], increased medication use [16], increased care intensity [18] and a higher mortality risk [19]. Also poor physical fitness was predictive for a decline in mobility [20], daily functioning [20, 21] and for a higher mortality risk [22]. Use of atypical antipsychotics, chronic kidney disease, abdominal obesity and histories of stroke and heart failure were predictive for developing cardiovascular disease (CVD) over a 3-year period [23]. These first results from the longitudinal data of the HA-ID study provided important insights for policy and care about how to contribute to a better health of older adults with ID. The results of the HA-ID study have been used in developing of diagnostic instruments and guidelines [3, 24, 25] and to illustrate the vulnerability and poor health situation of people with ID, resulting in changes to the Dutch legislation on long-term financing of support, care and treatment for people with ID.

Following the start of the HA-ID study, other research groups initiated longitudinal studies focusing on various aspects of health in adults with ID, such as the IDS-TILDA study in Ireland [26], the SAge-ID study in Australia [27] and a longitudinal cohort study about dementia and mortality in people with Down syndrome in the Netherlands

[28]. Despite these initiatives, epidemiological research into the health of adults with ID is still extremely limited. Too little is known about the health of this group as they age, or about changes in health status over time and early indicators for health problems. However, this knowledge is important for providing the evidence base for improving care and support of older adults with ID and guiding care providers in preparing for this growing group of elderly with ID. Longitudinal research makes it possible to make statements about causality, which contributes to e.g. identifying group-specific risk factors, groups at risk of specific diseases and other negative outcomes such as declining in independence. This knowledge can be used to reduce the occurrence of specific risk factors and identify, monitor and treating high-risk groups in good time. More longitudinal studies focusing on the health of this specific group are therefore urgently needed.

This article describes the design for the 10-year follow-up measurements of the HA-ID cohort. To learn more about changes in health status and indicators for health problems over time, a wide range of health data will be collected. Based on previous measurements and results, the focus will be on five research themes: 1) cardiovascular disease; 2) physical activity, fitness and musculoskeletal disorders; 3) psychological problems and psychiatric disorders (including sleep problems); 4) nutrition and nutritional state (including dysphagia); and 5) frailty. This article presents the design of the HA-ID cohort study and a summary of the main findings up to now, and provides an update of the planned measurements of the 10-year follow-up research themes.

METHODS AND ANALYSIS

STUDY COHORT

The HA-ID cohort consists of older adults with borderline to profound ID. All participants receive care or support from one of the care organisations of the HA-ID consortium. These organisations provide care to a wide spectrum of individuals with ID (in terms of the level of ID, residential status and mobility) in various settings (central residential settings, community-based homes, day activity centres and supported living) in both urban and rural areas in various regions in the Netherlands. At baseline, the care organisations provided care to approximately 10% of the total Dutch ID population receiving care or support from an ID care organisation [29]. At the start of the study, 10% of the individuals receiving care from the HA-ID care organisations was 50 or older, comparable to the total Dutch ID population receiving care or support from ID care organisations [29]. Based on these numbers, we concluded that the base population was representative for the total population of older adults with ID receiving care or support from ID care organisations in the Netherlands [1]. All individuals with ID within the consortium aged 50 or older by September 2008 were eligible to participate and received an invitation. Ultimately, 1,050 of the 2,322 (45.2%) invited individuals with ID participated in the baseline measurements. Table 1 presents the baseline characteristics of the participants, which were largely comparable to the overall group of invited individuals with ID and formed a near-representative study population for the total Dutch population of older adults with ID receiving formal support or care, with an underrepresentation of 80-to 84-year -olds, a slight overrepresentation of women and an underrepresentation of the more independent group. A more detailed description of the representativeness of the sample has been published elsewhere [1].

<<INSERT TABLE 1 ABOUT HERE>>

Figure 1 summarises the number of participants in the cohort over time. At baseline, measurements consisted of reviewing medical files, administering questionnaires, physical examinations with portable measuring equipment, fitness tests, observations, interviews, laboratory assessments and diaries [1]. At the 3-year follow-up, medical files were reviewed and professional caregivers completed questionnaires about the participant's health. Five years after the baseline measurements, causes of death were examined in the files of the deceased participants. The participants themselves were not actively involved in the data collection for these follow-up measurements. At the 3-year and 5-year follow-ups, the cohort consisted of 873 and 787 participants respectively.

All individuals with ID who participated in the baseline measurements and still receive care or support from one of the participating care organisations will be invited to participate in the 10-year follow-up measurements. There is one exclusion criterion: individuals are excluded from physical measurements if they are so seriously ill that participating in the study is not desirable. This decision is made based on shared decision making with caregivers and professionals. Based on previous mortality rates and historical loss to follow-up, it is estimated that 424 participants from the HA-ID cohort could be invited to participate in the 10-year follow-up measurements. With a conservative inclusion rate estimate of 50%, approximately 212 participants are expected to actually participate in these measurements.

<<INSERT FIGURE 1 ABOUT HERE>>

INFORMED CONSENT PROCEDURE

Because not all individuals with ID are mentally capable of giving informed consent, two separate consent procedures are followed. A behavioural scientist evaluates whether the individual is able to understand the specifically designed study information to let them make an informed decision about participation. If an individual is capable of making an informed decision, an easy-to-read information letter with supporting pictures and a consent form will be sent to this individual. If the behavioural scientist assesses the individual as being unable to make an informed decision about participation, an information letter and consent form will be sent to the legal representative of this individual. The professional caregiver of the individual with ID is informed about the study and the informed consent procedure to support the individual or legal representative in making their decision for participation. Inclusion of the participants started in July 2020 and the data collection in October 2020. Both the inclusion and the data collection are still ongoing.

RESEARCH THEMES

An outline is presented of the published results for each research theme, followed by a description of the data collection for the 10-year follow-up, with a specific focus on newly added measurements. In the 10-year follow-up, we also omitted measurements that turned out to be unfeasible, invalid or unreliable, based on the baseline measurements. For clarity, these measurements are not listed separately below. An overview of all measurements at baseline and the 3, 5 and 10-year follow-ups can be found in Table 2.

1. Cardiovascular disease

The HA-ID study provided many insights into the prevalence of CVD risk factors and the incidence of CVD in older adults with ID. The prevalences of hypertension (53.0%), diabetes (13.7%), metabolic syndrome (44.7%) and chronic kidney disease (15.3%) were similarly to those in the general population [30, 31]. However, the prevalence of peripheral arterial disease (20.7%) and obesity in women (25.6%) as measured by the Body Mass Index (BMI) was significantly higher than in the general population [10, 32]. The incidence of newly diagnosed CVD during a 3-year follow-up period was also examined. Incidence rates for myocardial infarction (2.8 per 1,000 person-years), stroke (3.2 per 1,000 person-years) and heart failure (12.8 per 1,000 person-years) were similar to the general population [23]. The use of atypical antipsychotics, chronic kidney disease, abdominal obesity and histories of stroke and heart failure turned out to be predictive for developing CVD during the 3-year follow-up period [23].

The baseline measurements revealed underdiagnosis of CVD risk factors in the HA-ID cohort. For example, 54% of the participants with diabetes had not been previously diagnosed with this condition. This was the case in 46% of the participants for hypercholsterolemia, in 50% for hypertension and in 94% for metabolic syndrome [30]. Atypical presentation of symptoms, limitations in communication, limited cooperation and resilience make diagnostics in

people with ID more challenging [33]. This makes underdiagnosis a common problem in people with ID [4, 34]. The incidence of CVD described above is therefore also probably underestimated [23].

With increasing longevity and increased prevalence of some CVD risk factors, people with ID may be at higher risk of developing CVD. The 10-year follow-up of the HA-ID cohort provides opportunities to learn more about CVD risk factors and the development of CVD over time in older adults with ID. The planned measurements for the 10-year follow-up are summarised in Table 2. The presence of CVD risk factors, CVD and CVD treatments/interventions over the past ten years will be assessed by reviewing the medical files of all participants who participated in the baseline measurements, including the medical files of deceased participants.

Blood will be collected through venepuncture. Blood will be stored for 15 years at -80°C, allowing analyses of relevant biochemical markers now and in the future (Table 2).

The following measurements were added to the physical examination to gain more insight into the presence of CVD and its risk factors. Body composition will be studied with Bioelectrical Impedance Analysis (BIA) using the Tanita Body Composition Analyser (Tanita DC-430 MA, Tanita, Netherlands). An electrocardiogram will be performed to examine heart conditions. In addition, heart rate variability will be measured as a marker for the autonomic nervous system by wearing a heart rate monitor (Polar Vantage V HR H10, Polar Electro Oy, Finland) at rest for 5 minutes. Finally, various haemodynamic measurements (mean arterial pressure (mmHg), pulse pressure (mmHg), resting heart rate (bpm), stroke volume (mL), cardiac output (l/min), cardiac index (l/m*1/m), augmentation index (%), peripheral vascular resistance (s*mmHg/mL) and pulse wave velocity (m/s)) will be obtained with a non-invasive electronic blood pressure oscillometric monitoring system (Mobil-O-Graph 24h PWA Monitor, I.E.M. GmbH, Germany) [35]. Adding the Mobil-O-Graph provides a clearer picture of the presence of arterial stiffness and central systolic blood pressure, two important risk factors for CVD and morbidity [36].

2. Physical activity, fitness and musculoskeletal disorders

The HA-ID study yielded important results about physical activity and fitness. Older adults with ID had very low physical activity and fitness levels [12, 14]. In short, most participants were categorised as ‘low active’ (5,000-7,449 steps/day; 25.3%) or ‘sedentary’ (<5,000 steps/day; 38.5%). Only 36.2% of the participants walked ≥7,500 steps/day [12]. These results are likely to underestimate the problem because physical activity levels were only measured in participants who were physically able to walk at a sufficiently high speed for the pedometers to provide reliable measurements. In addition to these low physical activity levels, people with ID aged 50 and over had physical fitness levels comparable to or worse than people in the general population aged 70 and over [13, 14]. Data from the 3 and 5-year follow-ups showed that these low physical fitness levels at baseline were indicative of a decline in daily functioning and mobility over the 3-year follow-up period and a higher mortality risk over the 5-year follow-up period [20-22, 37]. Additionally, it was found that being fit is more important for survival than obesity. People who were unfit had a mortality risk four times higher than people who were fit, regardless of obesity [37]. Because of the importance of physical fitness, suitable fitness tests for this population are essential. Based on our previous research

examining the reliability and feasibility of eight physical fitness tests in older adults with ID [38, 39] we developed the ID-fitscan to assess the physical fitness levels of adults with ID [24].

In the 10-year follow-up measurements, physical activity and fitness levels will be assessed again (see Table 2). Based on previous results and experiences, some changes were made to the measurements. Physical activity will be measured using the ActiGraph (wGT3X-BT Accelerometer, ActiGraph, USA), an instrument that can make measurements at very low walking speeds and provides more detailed information about the physical activity levels of the participant. Complementary to this, we will use the International Physical Activity Questionnaire – Short Form (IPAQ-SF) to collect physical activity data [40]. The ID-fitscan [24], supplemented with the two-minute step test [41], will be used to assess physical fitness. Physical fitness tests that turned out to be less suitable at the baseline measurements are excluded [24].

The 10-year follow-up will also focus on musculoskeletal disorders, in particular osteoarthritis. Osteoarthritis is common in older people in the general population, leading to pain, joint instability, limitations in daily activities and decreased quality of life [42, 43]. Little is known about the prevalence of knee and hip osteoarthritis in people with ID. High prevalence is expected because many factors that have been associated with osteoarthritis (such as obesity, poor physical fitness levels, poor motor skills, gait abnormalities, musculoskeletal complications and developmental problems) are commoner in adults with ID than in the general population [14, 44-48].

Osteoarthritis of the hip and the knee will be assessed by applying the American College of Rheumatology (ACR) criteria for the diagnosis of osteoarthritis. These criteria cover clinical symptoms, consisting of pain and functional limitations of the joint and include radiological characteristics from X-rays as well [49]. The 10-year follow-up includes several tests to identify the presence of the ACR criteria, including physical examinations with pain observations (Rotterdam Elderly Pain Observation Scale (REPOS) filled out by the health professional performing the physical examination, supplemented by a Numeric Rating Scale observation filled out by the professional caregiver during the physical examination and a face-scale for self-report of pain [50]). The REPOS will also be used to assess pain during rest and daily activities that may provoke osteoarthritis complaints. Also, the Animated Activity Questionnaire (AAQ) will be used to identify whether the participants have complaints due to osteoarthritis during daily living activities, filled out by the professional caregivers of the participants [51]. Additional, data about gait characteristics that may be related to osteoarthritis will be collected through a structured observation. To signal pain, stiffness and range of motion the standardised questionnaires (the Hip disability and Osteoarthritis Outcome Score (HOOS) [52, 53] and the Knee disability and Osteoarthritis Outcome Score (KOOS) [54]) will be used.

3. Psychological problems and psychiatric disorders

At baseline, data were collected on the prevalence of depression and anxiety disorders. The prevalence of major depressive disorder was 7.6% [8], which is higher than in the general population (1.8% to 4.0%) [55]. Only 4.4% of the participants met the criteria for one of the anxiety disorders [8]. This was lower than expected and lower than the prevalence in the general population (10.2% to 11.6%) [56]. This may be explained by the fact that proxy reports had to be used in 78% of the participants. It is difficult for respondents such as professional caregivers to recognise

symptoms of anxiety (e.g. pounding heart, worrying). This may have led to underestimation of the prevalence of anxiety disorders.

In the general population there is a strong association between sleep problems and anxiety- and mood disorders [57]. Data on sleep and sleep-wake rhythm were therefore also collected at baseline based on wrist-worn accelerometry (Actiwatch AW7, Cambridge Technology Ltd, Cambridge, United Kingdom [49, 50]). It was found that 23.9% of the participants lay awake for more than one hour before falling asleep. In addition, 63.1% lay awake for more than 90 minutes after sleep onset and before final morning awakening, 20.9% slept less than 6 hours and 9.3% were already awake for more than 60 minutes before getting out of bed [58]. In total 72.1% of the participants were classified as having at least one of these sleep problems [58].

During the 10-year follow-up, data about anxiety disorders, depression and sleep will be collected again, with some changes and additions to the baseline data collection (see Table 2). The 10-year follow-up has been extended with data retrieval from the psychological files about the presence of mood disorders, autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders, personality disorders, psychotic disorders, post-traumatic stress disorder and cognitive disorders (including dementia). In older people with ID, there is an association between the presence of a mental health diagnosis and problem behaviour [59]. Data about problem behaviour will therefore also be collected within the 10-year follow-up using the Aberrant Behaviour Checklist (ABC) [60]. The ABC is a widely used behaviour rating scale and measures problem behaviour using five subscales: irritability, lethargy, stereotypy, hyperactivity and excessive speech. In addition, a potential objective biomarker for long-term stress in people with ID will be evaluated, which may help to future diagnostic assessment. Long-term stress over the recent months will be retrospectively examined with a hair cortisol measurement. Recently published studies in the general population indicate that there is a strong association between the level of hair cortisol, life events and symptoms of anxiety and depression [61-64].

Data on sleep and sleep-wake rhythm will still be collected with accelerometry; however, we will now use the GENEActiv (Original, Activinsights Ltd, UK). Data from the GENEActiv are comparable to data collected by the Actiwatch that was used at baseline [65]. Extra questions about sleep hygiene and sleep circumstances have been added to learn more about the influence of these factors on sleep in older adults with ID.

4. Nutritional intake and nutritional state

The baseline measurements of the HA-ID study yielded insights into the dietary intake and nutritional state of older adults with ID. Three-day dietary records completed by professional caregivers revealed inadequate dietary intake, with none of the participants meeting all Dutch recommendations for a healthy dietary intake. The food intake was too low in calories in 68.6% of the participants, too low in protein in 30.2%, too low in dietary fibre in 98.2% and too high in saturated fat in 89.5% of the participants [11]. Forty-two per cent of the participants had vitamin D deficiency, of which 9% had severe vitamin D deficiency [66]. Vitamin D supplement were routinely provided to 45% of the participants and this group had significantly higher mean vitamin D serum levels than those without

supplement. This calls for more attention for prescribing vitamin D in older adults with ID [66]. These results also indicate that there is plenty of room for improvement in healthy nutrition.

Mealtime observations using the Dysphagia Disorder Survey (DDS) [67] showed moderate to severe dysphagia in 51.7% of the participants, which is comparable to the prevalence in nursing homes [9]. In 89.5% of the participants with dysphagia, this had not been previously diagnosed. The high degree of underdiagnosis illustrates the importance of screening and diagnosing dysphagia to prevent complications in clinical practice. Greater age, Down syndrome, mobility impairment, needing help with feeding and use of benzodiazepines were positively and independently associated with dysphagia [9].

The prevalence of sarcopenia was also studied. Fourteen per cent of the participants were classified as having sarcopenia, which developed at a relatively young age compared to the general population. At a prevalence of 12.7%, sarcopenia was already significantly present in participants aged 50 to 64 [68]. Additionally, the bone quality was low in 43.9% of participants. Being female, greater age, more severe ID, mobility impairment and anticonvulsant drug use were positively associated with low bone quality [69]. Higher BMI was negatively associated with low bone quality [69]. These results suggest an approach for periodic screening of high-risk groups for low bone quality and target groups for prevention in clinical practice [69].

In the 10-year follow-up, the baseline measurements will be repeated (see Table 2). To gain a better picture of the degree of malnutrition among older adults with ID, the Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) will be added to the data collection. The SNAQRC is a screening instrument for early detection of undernutrition in nursing or residential home settings using a traffic light system in which BMI and four questions related to involuntary weight loss, loss of appetite and eating with help are combined [70]. The SNAQRC will be completed by professional caregivers.

At baseline, a short dental file examination provided some data on the dental condition of the participants. To get a fuller picture of the dental condition and dental hygiene of older adults with ID, the dental file review will be extended. Data will be collected about dental condition, premedication and sedation during check-up and treatment, dental prosthesis, enamel wear, the number of dentist and dental hygienist visits, the number of elements in the upper and lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis and periodontitis, mobile elements and loss of dental elements due to trauma.

5. Frailty

Frailty is a clinically recognisable state of increased vulnerability resulting from age-associated decline in reserves and functions across multiple physiological systems [71]. Frailty leads to deterioration of daily functioning and mobility, increased disability, development of comorbidity and increased care intensity [17, 72, 73]. As a result, signalling frailty could play a valuable role in care planning, potentially improving quality of life and increasing the life expectancy of frail people with ID. In the general population, frailty is usually measured by tools such as the frailty phenotype [74]. However, we theorised that the ID population might require a more specific approach than the available tools allow. Based on the baseline data, an ID-Frailty Index was created consisting of 51 items [3]. The

ID-Frailty Index focuses on multiple aspects of daily functioning, opposed to a broader focus on physical frailty and mobility impairment [75]. As a result, the ID-Frailty Index could be applied to a larger proportion of the study population than the frailty phenotype and was deemed more suitable for measuring frailty in older adults with ID [75]. Furthermore, the ID-Frailty index showed a stronger relationship with mortality than the frailty phenotype [75]. The 3-year follow-up data showed that higher scores on the ID-Frailty Index resulted in a greater risk of death [19]. Finally, the ID-Frailty Index was predictive for a decline in mobility and increases in disability, polypharmacy and care intensity [16-18].

In the 10-year follow-up all previous measurements that were used to create the ID-Frailty index will be repeated (see Table 2). This lets us investigate the characteristics of frailty over time. In an attempt to further increase the practical and clinical usability of the ID-Frailty Index, a shortened version was developed. During the 10-year follow-up, the utility of this short form of the ID-Frailty Index will be further investigated.

General health data

In addition to these five research themes, data on other health variables will also be collected such as data on other diseases, medication use, hospitalisation, mortality, activities of daily life, smoking and alcohol/drug use (Table 2, under the heading 'General health data').

PROCEDURE

To limit the burden and impact on participants and their professional caregivers, all measurements will be done in settings close to where the participants live. All measurements will be carried out by test administrators consisting of professionals working in the care organisations. All test administrators will be trained to ensure accurate administration and correct scoring of the measurements. All measurements for a specific participant will be scheduled within one week. This test week consists of a physical examination performed by medical staff, fitness tests supervised by movement therapists or physiotherapists, observations to assess pain during activities of daily life performed by trained healthcare professionals, a mealtime observation to screen for dysphagia performed by speech and language therapists and a maximum of two interviews by trained and qualified professionals aimed at screening and diagnosing anxiety and depression. The participant will wear portable measuring equipment on the wrist and hip for seven days to monitor physical activity and sleep-wake rhythm. If separate consent is provided, blood samples and a tuft of scalp hair will be collected. For logistical reasons, the hip and knee X-rays take place outside this test week. All measurements together require a maximum time investment of four hours for each participant. However, the time investment per participant will probably vary because not every participant can undergo all measurements. The study will not interfere with routine medical practice. In addition to measurements for which active involvement of the participants is needed, the professional caregiver will be asked to complete questionnaires about the participant's health and data will be collected from the medical, psychological and dental files. The medical file review is performed using the records of all participants who participated in the baseline measurements, including the medical files of deceased participants. A complete overview of all measurements

within the HA-ID study can be found in Table 2. After the test week, the participant's physician and behavioural scientist receive a report with a summary of the results of the measurements.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not involved in the design of this study.

STATISTICAL ANALYSIS

In line with the previous measurements, the 10-year follow-up will provide cross-sectional and longitudinal data. Various statistical analyses will be applied. Descriptive statistics are used to answer questions about the prevalence and incidence of health conditions and possible risk factors. Multivariable regression analyses are used to answer questions about differences between subgroups and associations between variables, considering possible confounders and to adjust for these covariates. Survival analysis with Cox proportional hazard models will be used to investigate relationships between various factors (including age, sex, level of ID and comorbidity) and several health conditions and mortality over time. For repeated measurements, the dependency of measurements for the same participant will be adjusted by using generalised linear mixed-effects models (GLME).

IMPLICATIONS FOR PRACTICE

The HA-ID study so far has yielded knowledge of various health problems that are prevalent in older adults with ID, and how these compare to the general population. This knowledge suggested approaches for improving care for adults with ID. The 10-year follow-up will provide a deeper understanding of the course of health over time and risk factors for health problems in older adults with ID. Research into CVD risk factors in this population, for example, is still very limited. More knowledge about CVD risk factors and possible group-specific risk factors will give a better estimate of the cardiovascular risk profile of older adults with ID. The 10-year follow-up will also give a clearer picture of how frailty develops over time and whether there are certain groups of people with ID who are at higher risk for adverse outcomes.

What characterises the HA-ID study is that it is a prospective multicentre cohort study in which, compared to other ID studies, a relatively large (n=1,050) and heterogeneous group of older adults with ID is followed over time. The extensive measurements let us evaluate the health of older adults with ID from a broad perspective and investigate the interrelationships between medical domains such as cardiovascular disease, physical fitness, psychological problems and psychiatric disorders, nutrition and frailty. Looking across research themes is especially important because multi-morbidity is common in people with ID [4].

We know from experience that conducting epidemiological research into this field can be difficult and involves challenges in selecting suitable measuring instruments; some require certain levels of cognitive, physical or verbal ability that may not be compatible with those of the participants. To allow for optimal comparison between the general population and our cohort, we have aligned the measurements of the 10-year follow-up as much as possible to existing cohort studies of (specifically older) adults in the general population. However, feasibility, validity and reliability in older adults with ID were the leading criteria when selecting measuring instruments, using previously acquired knowledge and experience from the HA-ID study. How invasive and time-consuming instruments are was also considered, as were the feasibility for a large proportion of our population, the extent to which it is possible to do the measurement at the care organisations and the extent to which the instruments can be used by a large group of professionals without making concessions in terms of inter-rater reliability. In addition, the costs of the measuring instruments were examined, considering use in clinical practice. The HA-ID study is continuously searching for innovative and feasible measuring instruments that can be implemented for data collection.

A limitation of our study is that financial and feasibility reasons mean it has not been possible to perform follow-up measurements more regularly. Fortunately, the presence of routine registrations performed by the care organisations in medical, psychological and dental files lets us retrospectively collect data on the health of the participants over the past 10 years. Given the age of our study population and the length of follow-up, selection bias caused by the survival of healthier participants may distort our results. We are aware of this healthy survivor effect and address this when analysing and interpreting our results. It should be noted, that we do have access to the medical files of participants who have passed away. This lets us retrospectively collect data on the health of this group.

Results from the 10-year follow-up measurements are important for prioritising policy and care and underpinning clinical decision making about screening, prevention and treatment to improve healthy ageing of adults with ID. Longitudinal data collected in the 10-year follow-up of the HA-ID cohort therefore has high added value.

<<INSERT TABLE 2 ABOUT HERE>>

ETHICS AND DISSEMINATION

As for the previous parts of the HA-ID study (MEC-2008-234 and MEC-2011-309), ethical approval for the 10-year follow-up has been obtained from the Medical Ethics Review Committee of the Erasmus MC, University Medical Centre Rotterdam (MEC-2019-0562). This cohort study is registered in the Dutch Trial Register (NTR number NL8564) and follows the guidelines of the Declaration of Helsinki [76]. Local ethical committees and boards of individuals with ID and their representatives of the three involved care organisations were informed. Inclusion of the participants started in July 2020 and is ongoing.

ABBREVIATIONS

AAQ	Animated Activity Questionnaire
ABC	Aberrant Behaviour Checklist
ACR	American College of Rheumatology
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CVD	Cardiovascular disease
DDS	Dysphagia Disorder Survey
GLME	Generalised linear mixed-effects models
HA-ID	Healthy Ageing and Intellectual Disability
HOOS	Hip disability and Osteoarthritis Outcome Score
ID	Intellectual disabilities
IPAQ-SF	Physical Activity Questionnaire – Short Form
KOOS	Knee disability and Osteoarthritis Outcome Score
MEC	Medical Ethics Review Committee
NTR	Dutch Trial Register
REPOS	Rotterdam Elderly Pain Observation Scale
SNAQRC	Short Nutritional Assessment Questionnaire for Residential Care

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TABLE 1 Baseline characteristics of the HA-ID cohort (n=1,050) [1]

Characteristic		*n* (%)
Sex	Male	539 (51)
	Female	511 (49)
Age		60 (11, 50-93)*
Level of ID	Borderline	31 (3.0)
	Mild	223 (21.2)
	Moderate	506 (48.2)
	Severe	172 (16.4)
	Profound	91 (8.7)
	Unknown	27 (2.6)
Residential status	Central setting	557 (53.0)
	Community-based	432 (41.1)
	Independent with ambulatory support	43 (4.1)
	With relatives	7 (0.7)
	Unknown	11 (1.1)
Level of care (ZZP-scores)	Only day care indication	6 (0.6)
	Only indication ambulant care	37 (3.5)
	Residence with minimal support (1 VG)	12 (1.1)
	Residence with support (2 VG)	39 (3.7)
	Residence with support and care (3 VG)	138 (13.1)
	Residence with support and intensive care (4 VG)	207 (19.7)
	Residence with intensive support and intensive care (5 VG)	325 (31.0)
	Residence with intensive support, care and regulation of behaviour (6 VG)	93 (8.9)
	(Enclosed) residence with very intensive support, care and regulation of behaviour (7 VG)	142 (13.5)
	Mental Health Care ZZP scores	2 (0.2)
	Unknown	49 (4.7)

* Median (interquartile range, range)

ID = intellectual disability

ZZP = the Dutch classification of levels of support, care and/or treatment as a basis for long-term financing (Zorgzwaartepakket) [77]

VG = Dutch abbreviation for intellectual disability

TABLE 2 **Measurements within the HA-ID study: baseline, 3, 5 and 10-year follow-up per research theme***

Type	Outcome	Details	Moment of data collection			
			Baseline (2009-2010)	3-year follow-up (2012-2013)	5-year follow- up (2015)	10-year follow-up (2020-2022)
Demographics						
Medical file	Age	-	X		X	X
	Sex	-	X			
	Residential status	Central setting (with or without 24-hour support), community based (with or without 24-hour support), independent with ambulatory support (by appointment), with relatives, with partner, independent.	X			X
	Level of care	Care Intensity Packages (Dutch ZZP-scores) [77].	X			X
1. Cardiovascular disease						
Physical assessment	Brachial blood pressure*	Omron M7 (OMRON Healthcare, the Netherlands).	X			
	Central blood pressure and arterial stiffness	Mobil-O-Graph 24h PWA Monitor (IEM GmbH, Germany) including pulse wave velocity.				X
	Ankle-Arm-Index*	Omron M7 (OMRON Healthcare, the Netherlands) (arm). Boso classico and 8-MHz Doppler probe (Huntleigh MD II, United Kingdom) (ankle). Ankle-arm-index calculated: systolic blood pressure ankle divided by systolic blood pressure arm.	X			X
	Heart rate variability	Polar Vantage V HR H10 (Polar Electro Oy, Finland).				X
	Electrical activity of the heart	Electrocardiogram (ECG).				X
	Fat percentage	Formulas Durnin and Womersly [78] for calculating fat percentage from the sum of four skinfolds: triceps, biceps, subscapular and suprailiacal. Thickness of skinfolds measured with skinfold calliper (Harpenden, Baty International, United Kingdom).	X			X
		Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X
	Body composition	Tanita Body Composition Analyser DC-430 MA (Tanita, the Netherlands).				X

Venipuncture	Biochemical markers*	Fasting plasma levels: glucose, cholesterol (total/HDL*/LDL), haemoglobin (HB)*, haemoglobin A1c (HbA1c), triglyceride, C-reactive protein (CRP), interleukin 6 (IL-6), Tumour Necrosis Factor alpha (TNF alpha), albumin, vitamin D, calcium, creatinine, cystatin C, troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP) etc. The participants' blood is stored for 15 years at -80 degrees Celsius, in order to perform additional analyses afterwards.	X			X
Medical file	Cardiovascular disease*	Presence of CVD (heart failure, myocardial infarction, stroke, transient ischemic attack (TIA), cardiac arrhythmias, angina pectoris, aortic aneurysm, peripheral arterial disease (PAD), hypertension etc.), CVD risk factors (diabetes mellitus, central obesity, metabolic syndrome, rheumatoid arthritis, incriminating family history etc.) and treatments/ interventions (revascularisation of the coronary artery, pacemaker and implantable cardioverter-defibrillator (ICD)).	X			X
	Endocrine disorders*	Presence of endocrine disorders (such as diabetes mellitus*, hypercholesterolemia and metabolic syndrome).	X			X
2. Physical activity, fitness and musculoskeletal disorders						
Fitness assessment	Manual dexterity*	Box and block test [79].	X			X
	Reaction time	Auditive and visual reaction time test [80, 81].	X			
	Balance*	Berg Balance Scale [82].	X			
		Comfortable and maximum walking speed (5m) [24]*.	X			X
		Static balance test (for stances) [24].				X
	Grip strength*	Jamar Hand Dynamometer (#5030J1, Sammons Preston Rolyan, USA) [24].	X			X
	Muscle endurance	30s chair stand [24].	X			X
		5 times chair stand [24].				X
	Cardiorespiratory endurance	10m Incremental shuttle walking test [83]. Results of this test recalculated to VO2max [84].	X			
		2 minute step test [41], with heart rate monitor (Polar RS400, Polar Electro Oy, Finland).				X
	Flexibility	Extended version of Modified back saver sit and reach test [85, 86].	X			
Measurement at home	Physical activity	Pedometer NL-1000 (New Lifestyles, USA).	X			
		ActiGraph wGT3X-BT Accelerometer (ActiGraph, USA).				X
Questionnaires professional		Self-assembled questionnaire about the participants' habitual physical activity.	X			

caregiver		International Physical Activity Questionnaire – short version (IPAQ-s) [40].				X
	Activities of daily life/mobility	Animated Activity Questionnaire (AAQ) [51].				X
	Mobility*	Self-assembled questionnaire based on the Hauser Ambulation Index [87] and the characteristics of the Gross Motor Function Classification Scale [88].	X			X
	Falling	Self-assembled questionnaire about the number of falls in the last three months.				X
	Symptoms/ limitations related to (hip/knee) OA	Hip disability and OA Outcome Score (HOOS) [52, 53].				X
		Knee injury and OA Outcome Score (KOOS) [54].				X
	Use of lower extremity aids	Self-assembled questions about the presence/use of aids for extra support of the lower extremity (such as orthopaedic footwear, splints and braces).	X			X
Physical assessment	Clinical/ symptomatic OA	Physical examination to examine the ACR criteria for clinical osteoarthritis of the hip and the knee [89, 49]. The following tests will be performed [90]: palpable warmth of the knee joint, joint crepitus of the knee, bony enlargement of the knee joint, quadriceps wasting, bone margin tenderness, patellofemoral joint tenderness, anserine tenderness, tibiofemoral joint tenderness, bulge sign of the knee, range of motion flexion and extension of the knee, range of motion flexion and extension of the hip, range of motion endorotation and exorotation of the hip. In addition, the laxity of the joints will be tested [91] and the gait and the postural alignment will be observed [92].				X
Interview	Self-report pain	The participants undergo a comprehension test to test whether their self-reported pain on a face-scale is a valid measurement [50]. When they succeed they will be asked to grade their pain during examination of the joint tenderness, flexion of the joints and hip internal rotation on a face-scale.				X
Observation	Observed pain	The health care professional will perform the Rotterdam Elderly Pain Observation Scale (REPOS) to observe pain behaviour during the physical examination for OA. A NRS-obs will be asked from the professional caregiver as part of the REPOS observation [93].				X
Medical imaging	Radiographic hip/knee OA	X-rays of the hip and knee: anterior posterior (AP) view of both knees (if possible weight-bearing), lateral view of right and left knee, skyline view of the patellofemoral joint of right and left knee, AP view of pelvis, faux profile view of right and				X

		left hip (only made by participants who are able to stand up (with support)).				
Medical file	Musculoskeletal disorders*	Presence of musculoskeletal disorders in the medical file (such as OA, scoliosis*, spasticity and bone fractures).	X			X
3. Psychological problems and psychiatric disorders						
Measurement at home	Sleep-wake & circadian rhythm	Actiwatch AW7 (Cambridge Technology Ltd, United Kingdom).	X			
		GENEActiv Original (Activinsights Ltd, United Kingdom).				X
Interview	Self-report depression	Inventory of Depressive Symptomatology Self Report (IDS-SR) [94]. Phrasing of the questions adapted to people with ID.	X			X
	Self-report anxiety	Glasgow Anxiety Scale for people with an Intellectual Disability (GAS-ID) [95].	X			X
		Hospital Anxiety and Depression Scale (HADS) – anxiety subscale [96]. Phrasing of the questions adapted to people with ID.	X			
	Quality of life	Intellectual Disability Quality of Life (IDQOL-16) [97].	X			
	Diagnostic interview depression and/or anxiety	Participants with scores above the preset cut-off scores on one of the depression or anxiety questionnaires are further examined using the Psychiatric Assessment Schedule for Adults with Developmental Disability ICD-10 version (PAS-ADD-10). Interviews are conducted with the participant or his/her caregiver [98].	X			X
Questionnaires professional caregiver	Informant-report depression and anxiety*	Anxiety, Depression and Mood Scale (ADAMS) [99]*.	X			X
		Signaallijst Depressie Zwakzinnigen (SDZ) [100]*.	X			X
	Somatic complaints	Somatic complaints subscale of the Symptom Checklist-90 (SCL-90) [101].	X			
	Life-events	Self-assembled checklist about life events based on other checklists, earlier life event-studies and experience from professionals working with people with ID.	X			X
	Social outcome	Self-assembled checklist about number of contacts with family, friends and peers and visiting leisure-clubs.	X			
	Cognitive functioning*	Dementia questionnaire for people with intellectual disabilities (DMR) [102].	X			X
	Aberrant behaviour	Aberrant Behaviour Checklist (ABC) [60].				X
	Sleep problems	Self-assembled questions about sleep problems, including problems with falling asleep and waking up early.	X			X
	Sleep hygiene	Self-assembled questions about sleep hygiene (such as sleeping conditions, bedtimes, sleeping rituals, eating habits and use of				X

		TV, smartphone or tablet before going to bed and provided professional support).				
Psychological file	Psychological problems and psychiatric disorders	Baseline: level of intellectual disability, autism, depression, anxiety, dementia, psychoses, other psychiatric disorders and serious behavioural problems. 10-year follow-up: baseline variables + mood disorders, autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, attachment disorders, personality disorders, psychotic disorders, post-traumatic stress disorder, cognitive disorders (including dementia), traumatising and support or treatment received by the participant.	X			X
Medical file	Sleep disorders/sleep problems	Presence of sleep disorders/problems in the medical file (such as problems with falling asleep and waking up early).	X			X
Physical assessment	Cortisol concentration last month	A small hair sample of at least 1cm (length) will be taken from the posterior vertex close to the scalp [103].				X
4. Nutritional intake and nutritional state						
Physical assessment	Height*	-	X			X
	Weight*	-	X			X
	Body circumferences	Measuring tape for hip, calf* and upper arm circumference.	X			X
	Bone Quality*	Ultrasonometer (Lunar Achilles Insight, GE Healthcare, United States) for measuring bone stiffness calcaneus.	X			X
Diary	Food intake	Self-assembled 3-day food intake diary.	X			X
Meal time observation	Dysphagia*	Dysphagia Disorder Survey [67].	X			X
Questionnaires professional caregiver	Malnutrition*	Mini Nutritional Assessment (MNA) [104]*.	X			X
		Short Nutritional Assessment Questionnaire for Residential Care (SNAQRC) [70].				X
	Eating disorders*	Screening Tool of fEeding Problems (STEP) [105].	X			X
	Gastro-oesophageal reflux disease	GORD Questionnaire: self-assembled questionnaire consisting of 50 items involving risk factors and symptoms of gastro-oesophageal reflux disease.	X			
Dental file	Dental condition	Baseline: dental condition, premedication/sedation during check-up or treatment, dental prosthesis and enamel wear.	X			X

		10-year follow-up: baseline variables + number of dentist/dental hygienist visits, number of elements in the upper/lower jaw, dental wear, dental caries, plastic restorations, crowns and bridges, implants, gingivitis/periodontitis, mobile elements and loss of dental elements due to trauma.				
Medical file	Gastrointestinal diseases*	Presence of gastrointestinal disease in the medical file (such as gastroesophageal reflux disease*, gastric ulcer, constipation* and dysphagia*).	X			X
5. Frailty						
All outcomes / measurements with an asterisk* in this table are part of the overarching research theme 'Frailty'.						
General health data						
Medical file	Aetiology of intellectual disability	Presence of the aetiology of the intellectual disability in the medical file (such as a specific genetic syndrome).	X			X
	Malignancies*	Presence of malignancies in the medical file.	X			X
	Pulmonary diseases*	Presence of pulmonary disease in the medical file (such as asthma*, chronic obstructive pulmonary disease* and sleep apnoea syndrome).	X			X
	Neurological disorders	Presence of neurological disorders in the medical file (such as dementia, epilepsy and Parkinson's disease).	X			X
	Diseases of the genitourinary system	Presence of diseases of the genitourinary system in the medical file (such as urinary tract infections, incontinence and renal failure).	X			X
	Visual and hearing impairments*	Presence of visual and hearing impairments in the medical file.	X			X
	Medication use*	Medication use (medicament and dosage) as stated in the medical file.	X			X
	Hospitalisation*	Number of hospitalisations in the past period.				X
	Mortality	Date of death, as stated in the medical file.			X	X
	Cause of death	Cause of death, as stated in the medical file.			X	X
Questionnaires professional caregiver	Activities of daily life*	Barthel Index [106]*.	X			X
	Instrumental activities of daily life*	Questionnaire based on the Instrumental Activities of Daily Living of Lawton and Brody [107] and the Groningen Activities Restriction Scale [108].	X			X

	Daytime activities*	Self-assembled questions about daytime activities and/or work of the participant.	X			X
	Smoking	Self-assembled questions about the smoking habits of the participant (how many cigars, cigarettes and/or pipe per day + past smoking habits).	X			X
	Alcohol use	Self-assembled questions about the participant's alcohol consumption (alcohol use per day + alcohol use in the past).	X			X
	Drug use	Self-assembled questions about the drug use of the participant (use of cannabis and hard drugs per day + drug use in the past).				X
	Use of caffeinated drinks	Self-assembled questions about the use of caffeinated drinks (coffee, tea, Coke, energy drink and chocolate milk) by the participant.				X

FIGURE LEGENDS

Fig.1 Flow chart that shows the number of participants in the HA-ID cohort over time

Figure presents 1) the number of participants eligible for participation in the HA-ID cohort, 2) the number of participants who participated in measurements, 3) and the numbers of participants who dropped out the cohort