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# Cohort profile: The Obesity and Disease Development Sweden (ODDS) study, a pooled cohort

Marisa da Silva<sup>1</sup>, Josef Fritz<sup>1,2</sup>, Innocent B. Mboya<sup>1</sup>, Ming Sun<sup>1</sup>, Jens Wahlström<sup>3</sup>, Bethany van Guelpen<sup>4</sup>, Carl Michaëlsson<sup>5</sup>, Patrik K. E. Magnusson<sup>6</sup>, Olle Melander<sup>7</sup>, Sven Sandin<sup>6,8</sup>, Weiyao Yin<sup>6</sup>, Ylva Trolle Lagerros<sup>9,10</sup>, Bright Nwaru<sup>11,12</sup>, Jerzy Leppert<sup>13</sup>, Abbas Chabok<sup>13</sup>, Nancy L. Pedersen<sup>6</sup>, Sölve Elmståhl<sup>7</sup>, Karolin Isaksson<sup>14,15</sup>, Christian Ingvar<sup>14</sup>, Linnea Hedman<sup>3</sup>, Helena Backman<sup>3</sup>, Christel Häggström<sup>16</sup>, Tanja Stocks<sup>1</sup>

<sup>&</sup>lt;sup>1</sup>Department of Translational Medicine, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>2</sup>Institute of Medical Statistics and Informatics, Medical University of Innsbruck, Innsbruck, Austria

<sup>&</sup>lt;sup>3</sup>Section of Sustainable Health, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>4</sup>Department of Diagnostics and Intervention, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>5</sup>Department of Surgical Sciences, Medical Epidemiology, Uppsala University, Uppsala, Sweden

<sup>&</sup>lt;sup>6</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>7</sup>Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>8</sup>Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA

<sup>&</sup>lt;sup>9</sup>Division of Clinical Epidemiology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>10</sup>Center for Obesity, Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden

<sup>&</sup>lt;sup>11</sup>Krefting Research Centre, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>12</sup>Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>13</sup>Center for Clinical Research, Uppsala University, Västmanland Hospital, Västerås, Sweden

<sup>&</sup>lt;sup>14</sup>Department of Clinical Sciences Lund, Lund University, Lund, Sweden

<sup>&</sup>lt;sup>15</sup>Department of Surgery, Kristianstad Hospital, Kristianstad, Sweden

<sup>&</sup>lt;sup>16</sup>Northern Registry Centre, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Correspondence to Marisa da Silva, <u>marisa\_da.silva@med.lu.se</u>, and Tanja Stocks, tanja.stocks@med.lu.se.



#### **Abstract**

<u>Purpose:</u> The Obesity and Disease Development Sweden (ODDS) study was designed to create a large cohort to study body mass index (BMI), waist circumference (WC), and changes in weight and WC, in relation to morbidity and mortality.

Participants: ODDS includes 4,295,859 individuals, 2,165,048 men and 2,130,811 women, in Swedish cohorts and national registers with information on weight assessed once (2,555,098 individuals) or more (1,740,761 individuals), in total constituting 7,733,901 weight assessments at the age of 17-103 years in 1963-2020 (recalled weight as of 1911). Information on WC is available in 152,089 men and 212,658 women, out of whom 108,795 have repeated information on WC (in total 512,273 assessments). Information on morbidity and mortality was retrieved from national registers, with follow-up until the end of 2019-2021, varying between the registers.

Findings to date: Amongst all weight assessments (of which 85% are objectively measured), the median year, age, and BMI (interquartile range, IQR) is 1985 (1977-1994) in men and 2001 (1991-2010) in women, age 19 (18-40) years in men and 30 (26-36) years in women, and BMI 22.9 (20.9-25.4) kg/m² in men and 23.2 (21.2-26.1) kg/m² in women. Normal weight (BMI 18.5-24.9 kg/m²) is present in 67% of assessments in men and 64% in women, and obesity (BMI ≥30 kg/m²) in 5% of assessments in men and 10% in women. The median (IQR) follow-up time from the first objectively measured or self-reported current weight assessment until emigration, death, or end of follow-up is 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women. During follow-up, 283,244 men and 123,457 women died.

<u>Future plans:</u> The large sample size and long follow-up of the ODDS study will provide robust results on anthropometric measures in relation to risk of common diseases and causes of deaths, and novel findings in subgroups and rarer outcomes.

- The Obesity and Disease Development Sweden (ODDS) study is a large, pooled cohort of men and women in Sweden with information on weight, height, and waist circumference assessed once or more between 1963 and 2020.
- The unique personal identity number of inhabitants of Sweden enables tracking of individuals across ODDS cohorts, thus identifying a large number of individuals with repeated assessments from one or more cohort/-s, used to compute changes of weight and waist circumference in adulthood.
- The large sample size and long follow-up in national registers for information on morbidity and mortality outcomes ensure high statistical power and enables investigation of anthropometric measures also in relation to rarer outcomes.
- Additional important information retrieved from national registers include sociodemographic characteristics, comorbidities, and prescribed drugs.
- Limitations are incomplete information on smoking habits, and no information on dietary intake, physical activity, and other potential disease-specific confounders.



#### Introduction

The prevalence of obesity has risen to pandemic proportions during the last decades, reaching an estimated global prevalence of around 14% in men and 18% in women in 2020<sup>1</sup> (projected from NCD-RisC<sup>2</sup>), generally with a higher prevalence in high income countries but with an accelerating prevalence in low- and middle-income countries<sup>2</sup>. The negative impact of obesity on public health is enormous, for example with disability-adjusted life years, i.e. years lost in full health, due to obesity projected to increase by 40% from 2020 to 2030<sup>3</sup>. The large negative public health impact of obesity is both attributed to its high prevalence and to the established association of obesity with many common diseases, including cardiovascular diseases (CVD)<sup>4</sup> and several cancers<sup>5</sup>, as well as with all-cause mortality and cause-specific death due to CVD and cancer<sup>6</sup>. Less is known about the association of obesity with rarer diseases, which, in a prospective cohort setting, requires a larger population size and/or a longer follow-up for investigation. Furthermore, body size including obesity has mostly been assessed using a onetime measure of body mass index (BMI, kg/m<sup>2</sup>) in relation to disease risk. Studies based on measures of central obesity, such as waist circumference (WC), and of changes in body size across life on the risk of morbidity and mortality, have been much fewer and smaller<sup>57</sup>. Such investigations could reveal for example if a particular timing of weight changes or a cumulative high life-time exposure to obesity, poses a particularly high risk.

The long history, high coverage, and good quality of many Swedish nationwide registers, together with the unique personal identity number of inhabitants of Sweden enabling individual linkage to national healthcare registers<sup>8</sup>, is a major advantage for epidemiological research in the country<sup>9</sup>. For example, the Swedish Cause of Death Register<sup>10</sup> and the Cancer Register<sup>11 12</sup> are based on mandatory reporting of deaths and cancer diagnoses of the population since 1952 and 1958, respectively, enabling long and close to complete tracking of individuals for epidemiological studies. The personal identity number further facilitates cross-identification of individuals between different cohorts in pooled studies, which avoids duplicate contribution of an individual included in more than one cohort. It also enables the use of repeated individual assessments between cohorts to enlarge the sample size for the investigation of factors such as longitudinal changes of anthropometrics.

The pooled Obesity and Disease Development Sweden (ODDS) study was created to form a large population to investigate the association of anthropometric measures (BMI, WC, and changes in weight and WC) with the risk of morbidity and mortality. The large sample size and

long follow-up ensures high statistical power in investigations. Herein, we describe the ODDS study population, and provide an overview of the information retrieved from national registers linked to individuals in ODDS.

## **Cohort description**

#### Study population

 Swedish cohorts for research and national registers with individual-level information on weight and height were identified for inclusion in ODDS. The included registers with weight and height information are hereafter denoted "cohorts" when referring to the study population. We included individuals with a weight assessment at a minimum age of 17 years, which was the lower age limit of the largest male cohort (military conscripts). We further required a recorded date for the assessment (year as a minimum, with any missing month and/or day replaced with June and/or day 15), and a valid personal identification number in the Swedish Total Population Register. Information on date, weight, and if available, height, WC, and smoking habits, were included from each assessment. The availability of height was not used as an inclusion criterion for each individual assessment as it could be derived from repeated assessments, and because other factors, such as sociodemographic factors, were regarded to be equally important as height in studies of changes in weight and WC. Hence, completeness of these factors as potential inclusion criteria was left for later decision according to relevance for individual studies.

The characteristics of the included cohorts forming the ODDS study population of 4,295,859 individuals with 7,733,901 weight assessments are described in Table 1. Cohort overlap, i.e. individuals participating in more than one cohort, is not considered in the table. Weight in these cohorts was assessed between 1963 and 2020, at an age of 17-103 years. The two largest cohorts are the Swedish Military Conscription Register and the Medical Birth Register, both nationwide and further described below. Other cohorts have local, regional, or nationwide coverage of included individuals (Table 1). Some of them were designed for research purposes and others were designed as general or disease-specific health checkups, from which the information was later made available for research.

### Weight assessments and completeness of the two largest cohorts

Data from military conscripts make up the majority of the male population (1,771,429 men with 1,779,681 weight assessments) and the Medical Birth Register makes up the majority of the female population (1,855,606 women with 3,208,127 weight assessments). In Sweden,

 conscription, i.e. enrolment for military service, was mandatory for men at around 18 years of age until June 30, 2010, and was thereafter voluntary until 2017<sup>14</sup>. For young women, conscription has been voluntary since the 1980s. The coverage in the Military Conscription Register of the Swedish male birth cohorts of 1951-88 (corresponding to conscription between 1969 and 2006) is 90%. Weight is missing for at most 5% of conscript examinations before year 2000. No information on WC is available in the Military Conscription Register.

The Medical Birth Register includes information on around 98% of all births in Sweden. Since 1982, information is recorded at the first antenatal visit of pregnancy, generally taking place between 8-10 weeks of gestation<sup>13</sup>, i.e. before any appreciable pregnancy-related weight gain has occurred<sup>37</sup>. Weight of pregnant women were recorded in the register in 1982-89 and from 1992 onwards, and has a coverage of more than 85% since 1992. In 1982-89, early pregnancy weight was estimated by subtracting pregnancy weight gain from weight at delivery, and since 1992, weight was measured at the first antenatal visit. Due to this change in weight recording, weight in 1982-89 was much lower than expected compared to measurements from 1992 onwards, as also observed in other studies<sup>38 39</sup>. Therefore, we corrected weight assessments in 1982-89 in the Medical Birth Register. For illustration purposes, we let *j* represent the calendar years 1982-1989 for an individual i. We first regressed weight  $(W_i)$  on the year  $(Y_i)$  at baseline examination (i.e., first antenatal care visit) to obtain the average weight change over time (constant,  $b_0$ ) and slope  $(b_1)$ . Using these values, we predicted the average weight for each calendar year j (1982-1989) as  $W_i = b_0 + b_1 \times Y_i$ . We then obtained the difference of the observed average weight from the predicted average weight between 1982-1989, then added this factor to the original weight value and obtained a more linear weight change, as also reported elsewhere<sup>38</sup>. These corrected weights were used in the herein pooled analysis and will be used in original ODDS studies. Additionally, pregnancy will be accounted for in all pooled analyses by inclusion of a binary variable (Medical Birth Register, yes/no) in the statistical regression or other models. No information on WC is available in the Medical Birth Register.

#### Weight and waist circumference assessments in other cohorts

Other cohorts than the two largest include 972,974 individuals (includes overlap with the military conscription and the Medical Birth Register); 594,690 men and 378,284 women with 2,225,946 assessments of current weight. In several of these cohorts, information on recalled weight was collected simultaneously with that of objectively measured or self-reported current weight (see footnote of Table 1). A total of 225,331 individuals reported 500,219 recalled

weights, mostly for age 20 years (139,936 [28%] of assessments), but also for 18, 25, 30, 40, 50, 60, 70 and 80 years of age, from the year 1911 or later. These assessments will primarily be used in ODDS studies of weight changes. In the pooled ODDS study population, recalled weight is counted as a distinct weight assessment. In total 364,747 individuals have information from 512,273 assessments of WC in 1981-2020, assessed at an age of 17-103 years.

### **Smoking information**

The questions asked regarding smoking habits and the completeness of smoking information varies considerably between ODDS cohorts. To increase the completeness of smoking status in individuals with repeated weight assessments with missing and non-missing smoking information, we performed imputation by carrying information forwards or backwards prioritising previous records over later records for never/former/current smoking status, but not for current smoking (yes/no). After imputation, never/former/current smoking information is available in 2,856,160 (37%) assessments, and current smoking (yes/no) information in 5,061,903 (65%) assessments. In total 828,763 individuals (19%) have at least one weight assessment with never/former/current smoking information available, and the proportion is larger for individuals with WC assessments (330,775 individuals, 91%). To increase the coverage of smoking information, more advanced imputation based on all available data may be considered in single ODDS studies. Furthermore, studies dependent on the coverage of registers with a later start, such as the Patient Register (for information on CVD and Charlson comorbidity index<sup>40</sup>) or the Swedish Social Insurance Agency for studies on sick-leave, will include only later years' measurements of weight, which have a markedly higher coverage of smoking information.

### Register linkages

By use of the unique personal identity number assigned to each resident of Sweden, individuals in ODDS were linked to a range of Swedish national registers from inception to the last possible follow-up date, varying between 2019 and 2021 depending on the specific register. Birth date was retrieved from the Total Population Register; however, due to Swedish legislation protecting individual integrity, date of birth was obtained only for the year and quarter of a year, resulting in a recorded birth date with day 15 and the middle month of the quarter in addition to the birth year.

 Table 2 gives an overview of the registers and the type of information retrieved. This includes information on outcomes: all-cause and cause-specific mortality by use of the Cause of Death Register; specific cancers in the Cancer Register; prostate cancer in detailed diagnostic risk categories by use of information from the National Prostate Cancer Register; CVD, hypertension and type 2 diabetes by use of the Patient Register and National Diabetes Register; and sick-leave by use of information from the Swedish Social Insurance Agency. Register information will also be used to study anthropometric measures jointly with e.g. CVD, hypertension, diabetes, and prescribed drugs as exposures, in relation to outcomes. Furthermore, sociodemographic information of relevance for all ODDS studies, such as education, income, marital status, and birth country, is retrieved from several national registers. Further linkages for example to clinical registers of specific cancers, to the Prescribed Drug Register for information on further types of prescribed drugs, and to the Cancer and Cause of Death Registers for extended follow-up, is planned for the next few years.

### Patient and public involvement

Study participants and/or the general public were not involved in the planning, design, or conduct of the study.

#### Findings to date

The characteristics of all 7,733,901 weight assessments in the 4,295,859 individuals in ODDS is shown in Table 3 and the cumulative number of ODDS participants by year of assessment of the first recorded current weight and WC, respectively, is shown in Figure 1. Most weight assessments were objectively measured (85%), and 4,066,876 individuals (95%) have information from at least one objectively measured weight assessment. Out of 1,740,761 individuals with two or more weight assessments, the median number of assessments is 3 (IQR 2-5) in men and 2 (IQR 2-3) in women. The median (IQR) year and age of weight assessment is 1985 (1977-94) in men and 2001 (1991-2010) in women, and age 19 (IQR 18-40) years in men and 30 (IQR 26-36) years in women. Normal weight (BMI 18.5-24.9 kg/m²) is present in 67% of assessments in men and 64% in women, and obesity (BMI  $\geq$ 30 kg/m²) in 5% of assessments in men and 10% in women. The low proportion of obesity in men is likely due to the, on average, young age and early calendar year at weight assessment. Information on WC is available in 152,089 men with 209,473 WC assessments and in 212,658 women with 302,800 WC assessments; 52% of these were objectively measured and 63% of individuals have at least one objectively measured WC assessment. The median (IQR) year of the 512,273 WC

assessments is later than that of weight, year 2007 (1997-2012) for men and 2003 (1997-2010) for women, and the median age is higher, 57 (49-66) years in men and 51 (43-62) years in women.

The follow-up time from the first recorded current weight until emigration, death or end of follow-up for death (31 Dec. 2020) is up to 58 years, with a median (IQR) of 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women, and a median (IQR) from the first WC assessment of 13.4 (8.0-23.2) years in men and 17.1 (9.6-25.0) years in women. The total time at risk for mortality is 66.3 million person-years for men and 42.0 million person-years for women, during which 280,537 men and 121,635 women died. Of these, 98,796 men and 35,198 women died from CVD as the primary death cause, and 78,178 men and 45,744 women died from cancer. Furthermore, during follow-up, 133,073 men and 62,245 women with repeated weight assessments died, 37,155 men and 35,951 women with at least one WC assessment died, and 9890 men and 8664 women with repeated WC assessments died.

Amongst morbidity outcomes, cancer has a higher priority in the ODDS working group. During follow-up, 197,168 men and 144,413 women were diagnosed with cancer, of which 31,862 were colorectal cancer, 62,027 prostate cancer, and 50,732 female breast cancer. The numbers of some of the rarer cancers are 1523 small intestine cancers, 658 penile cancers, and 742 vulvar cancers. Furthermore, during follow-up, 84,205 men and 70,697 women with two or more weight assessments were diagnosed with cancer, and the numbers for men and women with information on WC are 26,619 and 28,296, respectively, and 6407 and 7321 for men and women with repeated WC assessments.

Further information about ODDS can be found at https://odds.blogg.lu.se.

#### Strengths and limitations

 The ODDS study has several strengths. Firstly, the population is very large and has a nationwide coverage of Swedish cohorts, which generally have a high representativeness of their background population. Furthermore, the unique personal identity number of Swedish inhabitants enables cross identification of individuals between ODDS cohorts as well as tracking of individuals in Swedish nationwide registers. Loss to follow-up is negligible in those registers, and the objective, harmonized information on outcomes as well as on sociodemographic factors by use of national registers, is an additional major strength. The

 combination of anthropometric measures in the pooled population and register information further enables investigation of the combined exposure of anthropometric measures and, for example, CVD and medications on outcomes. Lastly, the long follow-up time together with the large sample size has accumulated many events resulting in overall high statistical power and the possibility to investigate subgroups and rarer outcomes.

The study also has some limitations. The large heterogeneity of the study population in terms of geographical region, age, and year of weight assessment, enables subgroup investigation; however, this heterogeneity may also hamper the investigation of certain smaller subgroups, for example of older age individuals. The study is further limited in that information on smoking habits, an important confounder for mortality and many diseases, is missing in a large part of the population and, apart from sociodemographic information, the ODDS database has no information on potential confounders such as diet, physical activity, and other disease-specific confounders.

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#### **Contributors**

MdS, JF, IBM, MS, CH and TS were involved in the conception and design of the study. JW, BvG, CM, PKEM, OM, SS, WY, YTL, BN, JL, AC, NLP, SE, KI, CI, LH and HB contributed original cohort data. MdS harmonized the cohort data. IBM calculated corrected weights in the Medical Birth Register. MdS, JF, MS and TS harmonized register data. TS organized the

collection of cohort and register data, analysed data, and drafted the manuscript. MdS, JF, IBM, MS, JW, PKEM, OM, SS, YTL, JL, NLP, CI, LH, HB and CH revised the manuscript. All authors made significant contributions to the manuscript and have read and approved the final version.

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### **Competing interests**

None declared.

#### **Ethics** approval

This study was approved by the Swedish Ethical Review Authority (no: 2020-03846).

#### **Data sharing statement**

All data are located on Statistics Sweden's Microdata Online Access (MONA) server and may only be accessed from countries in the European Union or the European Economic Area. Data access for questions covered by the ethical approval will be considered in agreement with the principal investigator of ODDS, Tanja Stocks, and upon approval from relevant register holders and steering committees of ODDS cohorts.

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 Table 1. Characteristics of cohorts of the Obesity and Disease Development Sweden (ODDS) study<sup>a</sup>

		N individ-	N assess-	Yeargo	Age in	N (%) individuals with at least one assessment of:		
Cohort Description		uals (% ments (% male)		, (lange) ω π	years, median (range)	Objectively measured weight	Smoking status <sup>b</sup>	Waist circum- ference
Swedish Medical Birth Register <sup>13</sup>	Includes ~98% of all births in Sweden. The mother's weight is measured at the first antenatal care visit, commonly at 8-10 gestational weeks. Since 1992, weight is missing for <15%	1,855,606 (0)	3,208,127 (0)	2003 7995 (1982-20 <b>9</b> 95	<b>R</b> (17-54)	1,855,606 (100)	94,555 (5)	0 (0)
Swedish Military Conscription Register <sup>14</sup>	In Sweden, conscription was mandatory for men aged ~18 years until 2010 and was then voluntary until 2017. The male birth cohorts of 1951-88 cover 90% of the target population, with ≤5% missing weight before 2000	1,790,751 (99)	1,799,609 (99)	1987 <b>&amp; 3</b> (1969-20 <b>3</b> 4 <b>%</b>	18 (17-58)	1,790,751 (100)	190,197 (11)	0 (0)
Construction Workers Cohort <sup>15</sup>	Construction workers were invited on a regular basis to a health checkup through a collective agreement that concerned almost all construction workers in Sweden. Attendance: ≥80%	387,545 (95)	1,149,722 (96)	1981 X 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	37 0 (17-82)	387,545 (100)	333,100 (86)	0 (0)
NSHDS <sup>16</sup>	Population-based cohorts in the northernmost counties of Sweden: Norrbotten and Västerbotten	138,379 (47)	254,441 (40)	2002 <b>5.0</b> (1985-20 <b>2</b> 0)		132,369 (96)	131,734 (95)	97,061 (70)
VIP <sup>17</sup>	All residents of Västerbotten county are invited to a health checkup at 40, 50, and 60 years of age (and 30 years until 1996). Attendance: 48-67%	124,200 (49)	194,650 (49)	2005 20 20 20 20 20 20 20 20 20 20 20 20 20	<b>=</b> (19-70)	124,200 (100)	123,216 (99)	87,538 (70)
MONICA <sup>18</sup>	Seven health screenings aimed for research were performed in random selections (within specific ages) of residents of Norrbotten and Västerbotten counties. Attendance: 67-81% in 1986-2009	12,260 (49)	16,097 (49)	1999 <b>5</b> (1986-20 <b>4</b> 4)	51 (24-79)	12,260 (100)	12,245 (>99)	12,235 (>99)
MSP <sup>19</sup>	A questionnaire aimed for research was filled in in connection with mammography screening offered every 2-3 years to women aged ~50-70 years in Västerbotten county. Attendance: ~85%	25,836 (0)	43,694 (0)	1999 <b>=</b> (1995-20 <b>2</b> 6)	58 (18-82)	0 (0)	20,026 (78)	0 (0)
SIMPLER <sup>20</sup>	Population-based cohorts in counties of southeastern Sweden: Uppsala, Västmanland, and Örebro	106,391 (43)	237,966 (39)	1997 <b>5</b> (1987-20 <b>7</b> 9)	64 (38-103)	0 (0)	89,598 (84)	81,462 (77)
SMC	All women born 1914/1917-1948, residing in Västmanland and Uppsala counties were invited to mammography screening that included a questionnaire aimed for research, with subsequent follow-ups. Attendance at baseline: 70%	60,709 (0)	145,234 (0)	1997 <b>a</b> (1987-20 <b><u>4</u>9)</b>	62 (38-103)	0 (0)	44,121 (73)	40,338 (66)
COSM	All men born 1918-52 residing in Västmanland and Örebro counties were invited to fill in a research-based questionnaire, with subsequent follow-ups. Attendance at baseline: 49%	45,682 (100)	92,732 (100)	0	67 (42-101)	0 (0)	45,477 (>99)	41,124 (90)
Swedish Twin Registry <sup>21 22</sup>	Research-based register on mono- and dizygotic twins across all of Sweden	97,533 (46)	154,666 (45)		48 (17-99)	12,360 (13)	90,182 (92)	12,328 (13)
Q63, 67, 70	All same-sex twins born 1886-1925 were invited to fill in a questionnaire (not including weight) in 1960. Follow-up questionnaires were sent out thrice during the subsequent 10 years (Q63, 67 and 70)	20,312 (44)	42,347 (41)	1967 <b>0</b> (1963-19 <b>6</b> 0)	53 (37-84)	0 (0)	17,986 (89)	0 (0)
Q73	All same-sex twins born 1926-58 were invited to fill in a questionnaire in 1973.  Attendance: ~83%	27,595 (48)	27,595 (48)	1973 <b>*</b> (1973-1973)	29 (17-47)	0 (0)	27,507 (>99)	0 (0)
SALT	All twins born 1944-58 were invited to a phone interview. Attendance: ~65%	42,754 (47)	42,754 (47)	2000 (1998-2003)	56 6 (41-99)	0 (0)	42,234 (99)	0 (0)
TwinGene	Twin pairs in SALT were invited to a follow-up investigation. Attendance: ~65%	12,360 (45)	12,360 (45)	2006 (2002-2009)	<b>B</b> 64 <b>c</b> (47-93)	12,360 (100)	12,237 (99)	12,328 (>99)
STAGE	All twin pairs born 1958-85 were invited to a web-based survey. Attendance: ~60%	23,448 (44)	23,448 (44)	2005 (2004-2006)	<b>5</b> 34 (19-47)	0 (0)	23,230 (99)	0 (0)

					<del></del>			
YATSS	All twin pairs born 1986-92 were invited to a web-based survey. Attendance: ~42%	6162 (40)	6162 (40)	2013 <b>2</b> (2013-20 <b>5</b> 4)	24 3 (20-28)	0 (0)	1988 (32)	0 (0)
Malmö cohorts	Population-based cohorts in Malmö city in southern Sweden (MPP and MDCS) and offspring of MDCS participants (MOS)	54,876 (53)	124,442 (54)	1995 <b>5</b>	56 (18-85)	54,860 (>99)	48,392 (88)	36,170 (66)
MPP <sup>23 24</sup>	All residents of Malmö city, born in certain years, 1921-49, were invited for screening for CVD and alcohol abuse, with subsequent follow-ups of all or a selected population. Attendance at baseline: ~71%	33,337 (67)	59,427 (70)	1983 (1974-20 <b>6</b> 6)n	53 (26-85)	33,337 (100)	28,294 (85)	4506 (14)
MDCS <sup>25</sup>	All residents of Malmö city, born in certain years, 1926-50, were invited to.a health examination aimed for research on diet and cancer, with subsequent follow-ups of all or a selected population. Attendance at baseline: ~41%	30,415 (40)	60,792 (39)	1997 reich (1991-20 de	_	30,390 (>99)	29,280 (96)	30,373 (>99)
MOS <sup>26</sup>	Children and grandchildren of a random sample of MDCS participants were invited to a health examination for research purposes	4223 (48)	4223 (48)	2016 <b>2.3</b> (2013-20 <b>3</b> 9 <b>3</b>	Q 44 <b>Q</b> (18-73)	4223 (100)	3799 (90)	4202 (>99)
Women's Lifestyle and Health <sup>27</sup>	Randomly selected women born 1943-62 residing in Uppsala county were invited to fill in a questionnaire aimed for research on lifestyle and cancer and CVD, and to one subsequent follow-up. Attendance at baseline: 51%	48,720 (0)	82,140 (0)	1992 <b>4 Sup</b> (1991-20 <b>04)</b>	nl 44 (27-61)	0 (0)	40,840 (84)	43,132 (89)
Swedish National March Cohort <sup>28</sup>	In 1997, a fund-raising event for the Swedish Cancer Society took place in ~3600 places across Sweden. Participants were requested to fill in a questionnaire aimed for research on lifestyle and chronic diseases	41,710 (36)	41,710 (36)	1997-1997)	52 (17-93)	0 (0)	35,801 (86)	31,893 (76)
West Sweden Asthma Study <sup>29</sup>	In 2008 and 2016, random selections of residents of western Sweden were invited to fill in a questionnaire aimed for research on asthma and respiratory diseases. Attendance: 62% and 50%, respectively	41,276 (46)	53,231 (45)	2016 <b>3.6</b> (2008-20 <b>36</b> )	51 (17-83)	0 (0)	40,506 (98)	0 (0)
WICTORY <sup>30</sup>	Residents of Västmanland county, born 1940-59, were invited to a health checkup at age ~40 or 50 years, aimed for CVD prevention. Attendance: ~60%	33,892 (48)	33,892 (48)	1994 <b>©</b> (1989-20 <b>)</b>	49 (35-55)	33,892 (100)	33,579 (99)	33,860 (>99)
LifeGene <sup>31</sup>	Residents across Sweden were invited through randomization (~44%) or volunteering to a health examination and a web-based survey for research	30,039 (41)	30,039 (41)	2011 <del>4</del> (2009-20 <b>2</b> 8)	33 (17-96)	28,861 (96)	16,407 (55)	28,861 (96)
EpiHealth <sup>32 33</sup>	Randomly selected ~45-75-year-old residents of Uppsala and Malmö city were invited to a health examination and a web-based survey for research on genediet interactions and diseases. Attendance: ~20%	25,337 (44)	25,337 (44)	2014 <b>n</b> (2011-2018)	61 (35-78)	25,337 (100)	18,416 (73)	25,337 (100)
Melanoma in Southern Sweden <sup>34</sup>	Randomly selected women with no prior cancer, ~25-64 years, residing in Southern Sweden, were in 1990-92 invited to fill in a questionnaire (not including weight) aimed for research on malignant melanoma and female cancers. A follow-up questionnaire included weight. Attendance at baseline: 74%	22,974 (0)	22,974 (0)	2001 <b>s</b> (1999-20 <b>5</b> 4)	54 9 (35-76)	0 (0)	2399 (10)	0 (0)
Obstructive Lung Disease in Northern Sweden <sup>35 36</sup>	In separate surveys (five in ODDS), randomly selected adults of specific ages, residing in Norrbotten county, were invited to a health examination and follow-ups, or to fill in a questionnaire (2016), aimed for research on asthma and respiratory diseases. Attendance at baseline: 66-91%	12,395 (49)	15,386 (49)		53 (19-85)	5853 (47)	12,241 (99)	0 (0)

NSHDS, Northern Sweden Health and Disease Study; VIP, Västerbotten Intervention Programme; MONICA, Monitoring of Trends of Cardiovas Bular Risease study in Northern Sweden; MSP, Mammography Screening Project; SIMPLER, Swedish Infrastructure for Medical Population-Based Life-Course and Environmental Research; Strong Across the Lifespan Twin Study; STAGE, Study of Twin Adults: Genes and Environment; YATSS, Young Adult Twins in Sweden Study; MPP, Malmö Preventive Project; CVD, cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Diet and Cancer Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Diet and Cancer Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Diet and Cancer Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, MoS, MoS, MoS, MoS, MoS, MoS, MoS, <sup>a</sup>The numbers include overlap of individuals between cohorts, and only objectively measured or self-reported current weight. Recalled weight is available in 225,331 individuals with 500,219 recalled

weights in: SIMPLER, Swedish Twin Registry (Q67 and Q70), MDCS, MOS, Women's Lifestyle and Health, Swedish National March Cohort, EpiHearth, and Melanoma in Southern Sweden, included

bNever/former/current smoking. To optimise smoking information, we imputed smoking information based on other assessments, also from other OD cohorts. Imputation generally makes up a small percentage of smoking information, except in the Medical Birth Register and the Military Conscription Register.

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Table 2. Information on Swedish national registers with linkage to the Obesity and Disease Development Sweden (ODDS) study population

Swedish register	Description	Type of information retrieved	covered in	Coverage of target population
The Cancer Register <sup>11 12</sup>	Contains information on histologically, cytologically or clinically diagnosed, or by autopsy verified (excluding death certificate only) malignant tumours, and certain benign, premalignant and borderline tumours, in Sweden	Date and type of cancer diagnosis, including International Classification of Diseases topography code, histopathology (Swedish SNOMED and PAD codes), and TNM status and trecorded since 2004)	1958-2019	96% in the year 1998 <sup>11</sup> , which appears to be stable over time
The Cause of Death Register <sup>10</sup>	Contains information on deaths and death causes in Sweden, in electronic form since 1952. The death cause is usually determined by the treating physician or the physician last seeing the patient before death	Date of death and underlying and contributing of the death causes according to International Classification of Diseases codes	1952-2020	>99%, and 96% of the underlying cause of death (>99% of deaths in ODDS)
The Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA)41	Contains information from a range of sources on education, occupation, income and employment in all residents of Sweden aged ≥16 years (≥15 years since 2010)	Highest attained education. Occupation, income and main source of income (recorded since mining mining).	1990-2019	>99% overall, 98% for education in 25-64 year old individuals
The National Diabetes Register <sup>42</sup>	Contains information on diabetes diagnoses (all types) and other information, such as complications and treatment, of diabetes patients aged ≥18 years in outpatient specialist clinics and in primary healthcare in Sweden	Date and type of diabetes diagnosis and treatment	1996-2020	Increased coverage over time; ~90% of Swedish adults with diabetes in 2015
The National Prostate Cancer Register <sup>44 45</sup>	Contains information on biopsy-confirmed prostate cancer diagnoses, tumour characteristics, and primary treatment of prostate cancer patients in Sweden	Date, TNM status, prostate-specific antigen level, and Gleason score at diagnosis, and the main reason for detection (recorded since 2004). Primary treatment, date of radical prostatection (recorded since 2007), and T status, Gleason score and positive margins (yes/no) after radical prostatectomy	1998-2021 (June)	98% of prostate cancer diagnoses in the National Cancer Register in 1998-2012
The Patient Register <sup>46 47</sup>	Contains information on diagnoses of inpatient care in Sweden, recorded since 1987, and of specialist outpatient care, recorded since 1997 for surgical care and since 2001 for other outpatient care	Date and type of diagnosis according to the Swedish International Classification of Disectors codes in inpatient and outpatient care. Information was obtained for cardiovascular diseases, hypertension, diabetes, and diagnose of the Charlson Comorbidity index <sup>40</sup>	1987-2020	Since 1987, >99% of inpatient care, and in 2001-2006, 71% of outpatient somatic care
The Population and Housing Census <sup>41</sup>	Contains sociodemographic information through self- reported questionnaires mailed to the full Swedish population aged ≥16 years, with mandatory response	Highest attained education, county of residence, and marital status	Every five years in 1960-1990	≥99% in 1960-1985, 97.5% in 1990 <sup>a</sup>

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The Prescribed Drug Register <sup>48</sup>	Contains information on all prescribed drugs dispensed at pharmacies in Sweden. Excludes over-the-counter drugs	Date of prescribing and dispensing, type of (e.g. ATC code and product name), dispensed amount and dosage, of antidiabetic, antihypertensive, and antilipidemic drugs		>95% of all utilised drugs in Sweden, excluding over-the-counter drugs
The Total Population Register <sup>49</sup>	Contains basic demographic information on all residents of Sweden	Birth date (year and quarter of year), country of birth for the individual and parents (four categories, see Table 2), county of residence, see marital status, and date/-s of immigration and categories.	1968-2020	>99% of births and deaths, 95% of immigrations, 91% of emigrations, resulting in a slight over-coverage
The Swedish Social Insurance Agency <sup>50</sup>	Contains information on sick leave for periods exceeding 14 days, and of disability pension, for individuals in Sweden with income from work or unemployment benefits, which qualify and apply for sickness absence or disability pension benefits. The first 14 days of sick leave is compensated by the employer and is not recorded by the Social Insurance Agency	Date, length, and type of sick-leave according to the leave according to according to a leave	1994-2021	No data available <sup>b</sup>

<sup>&</sup>lt;sup>a</sup>Personal communication with Beatrice Kalnins, Statistics Sweden.

<sup>&</sup>lt;sup>b</sup>Personal communication with Charlotte Limé, the Swedish Social Insurance Agency.

Table 3. Characteristics of all assessments in the Obesity and Disease Development Sweden (ODDS) study, in total and separately in 2,165,048 men and 2,130,811 women

Characteristic	Total (N assess- ments=7,733,901)	Men (N assess- ments=3,530,952)	Women (N assess- ments=4,202,949)
Assessments, median no. (IQR)	1 (1-2)	1 (1-1)	2 (1-2)
Assessments, median no. (IQR) in	2 (2-3)	3 (2-5)	2 (2-3)
individuals with ≥2 assessments	2 (2-0)	J (Z-J)	2 (2-3)
Year			
Median (IQR)	1993 (1983-2005)	1985 (1977-1994)	2001 (1991-2010)
N (%)			
1911-1959 <sup>a</sup>	102,331 (1)	49,817 (1)	52,514 (1)
1960-1969	159,059 (2)	70,493 (2)	88,566 (2)
1970-1979	1,118,503 (15)	1,011,194 (29)	107,309 (2)
1980-1989	1,866,055 (24)	1,128,163 (32)	737,892 (18)
1990-1999	1,775,421 (23)	780,028 (22)	995,393 (24)
2000-2009	1,470,566 (19)	365,475 (10)	1,105,091 (26)
≥2010	1,241,966 (16)	125,782 (4)	1,116,184 (27)
Age (years)			
Median (IQR)	28 (19-37)	19 (18-40)	30 (26-36)
N (%)			
17-19	1,941,872 (25)	1,780,928 (50)	160,944 (4)
20-29	2,222,093 (29)	417,774 (12)	1,804,319 (43)
30-39	1,858,853 (24)	373,384 (11)	1,485,469 (35)
40-49	661,048 (9)	375,880 (11)	285,168 (7)
50-59	570,068 (7)	337,970 (9)	232,098 (5)
60-69	324,381 (4)	174,004 (5)	150,377 (4)
≥70	155,586 (2)	71,012 (2)	84,574 (2)
Weight (kg), median (IQR)	68 (61-77)	73 (66-81)	64 (58-72)
Form of weight assessment, N (%)	00 (01 11)	70 (00 01)	01(0072)
Objectively measured	6,579,779 (85)	3,097,486 (88)	3,482,293 (83)
Self-reported current weight	653,903 (8)	207,579 (6)	446,324 (11)
Self-reported current weight	500,219 (7)	225,887 (6)	274,332 (6)
Height (cm), median (IQR)	171 (165-178)	178 (174-183)	166 (162-170)
Body mass index (kg/m²)	171 (103-170)	170 (174-100)	100 (102-170)
Median (IQR)	23.1 (21.0-25.7)	22.9 (20.9-25.4)	23.2 (21.2-26.1)
N (%) <sup>b</sup>	23.1 (21.0-23.1)	22.3 (20.3-23.4)	20.2 (21.2-20.1)
Underweight (<18.5)	305,069 (4)	160,666 (5)	144,403 (3)
Normal weight (18.5-24.9)	5,040,375 (65)	2,378,070 (67)	2,662,305 (63)
Overweight (25-29.9)	1,792,975 (23)	826,610 (23)	966,365 (23)
Obesity class I (30-34.9)	429,028 (6)	137,401 (4)	291,627 (7)
Obesity class I (30-34.9) Obesity class II and III (≥35)	129,392 (2)	23,465 (1)	105,927 (3)
Missing	37,062 (<1)	4740 (<1)	
Waist circumference (cm)	37,002 (~1)	4740 (<1)	32,322 (1)
	88 (79-97)	06 (90 103)	92 (75 00)
Median (IQR)	00 (19-91)	96 (89-103)	82 (75-90)
N (%) <sup>b</sup> Low (men, <94; women, <80)	240 490 (2)	96.436.(3)	124 062 (2)
	210,489 (3)	86,426 (2)	124,063 (3)
Medium (men, 94-101.9; women, 80-87.9)	143,891 (2)	64,225 (2)	79,666 (2)
High (men, ≥102; women, ≥88)	157,893 (2)	58,822 (2)	99,071 (2)
Missing	7,221,628 (93)	3,321,479 (94)	3,900,149 (93)
Smoking status, N (%)	1 224 560 (17)	704 267 (22)	E40 202 (42)
Never	1,334,569 (17)	794,267 (23)	540,302 (13)
Former	679,222 (9)	432,751 (12)	246,471 (6)
Current	842,369 (11)	613,139 (17)	229,230 (5)
Missing	4,877,741 (63)	1,690,795 (48)	3,186,946 (76)
Marital status, N (%) <sup>c</sup>	4 000 000 (50)	0.007.400.(05)	4.705.400.440
Unmarried	4,092,269 (53)	2,297,106 (65)	1,795,163 (43)
Married	3,102,435 (40)	1,048,593 (30)	2,053,842 (49)
Divorced	349,667 (5)	117,091 (3)	232,576 (5)
Widow/-er	88,954 (1)	23,535 (1)	65,419 (2)
Missing	100,576 (1)	44,627 (1)	55,949 (1)
County of residence, N (%) <sup>c</sup>			
Stockholm	1,253,881 (16)	481,693 (14)	772,188 (18)
Västra Götaland	1,136,238 (15)	521,656 (15)	614,582 (15)
Skåne	993,581 (13)	451,103 (13)	542,478 (13)

Västmanland	467,638 (6)	219,591 (6)	248,047 (6)
Västerbotten	439,512 (5)	203,544 (6)	235,968 (6)
Uppsala	382,360 (5)	102,044 (3)	280,316 (7)
Other counties	3,060,691 (39)	1,502,928 (42)	1,449,729 (34)
Missing	108,034 (1)	48,393 (1)	59,641 (1)
Highest achieved education (one assessment per individual), N (%) <sup>d</sup>			
Pre-upper secondary school <9 years	280,244 (7)	167,940 (8)	112,304 (5)
Pre-upper secondary school 9 years	366,211 (9)	215,953 (10)	150,258 (7)
Upper secondary school max. 2 years	1,030,829 (24)	578,620 (27)	452,209 (21)
Upper secondary school 3 years	880,747 (20)	455,344 (21)	425,403 (20)
Post-upper secondary school <3 years	613,421 (14)	299,872 (14)	313,549 (15)
Post-upper secondary school ≥3 years	1,020,461 (24)	393,934 (18)	626,527 (30)
PhD degree	52,219 (1)	28,056 (1)	24,163 (1)
Missing	51,727 (1)	25,329 (1)	26,398 (1)
Country of birth (one assessment per individual), N (%) <sup>e</sup>			
Born in Sweden, both parents born in Sweden	3,367,487 (78)	1,842,225 (85)	1,525,262 (72)
Born in Sweden, one parent born in Sweden	295,156 (7)	156,744 (7)	138,412 (6)
Born in Sweden, both parents born abroad	121,237 (3)	58,840 (3)	62,397 (3)
Born abroad	511,469 (12)	107,147 (5)	404,322 (19)
Missing	510 (<1)	92 (<1)	418 (<1)
OR interquartile range			

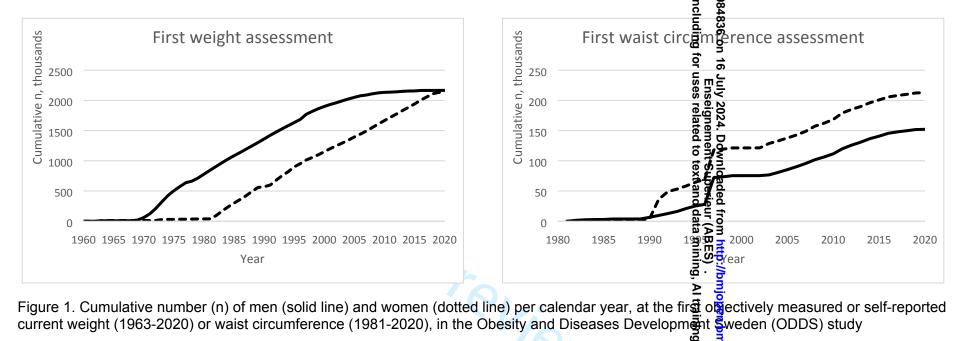
IQR, interquartile range.

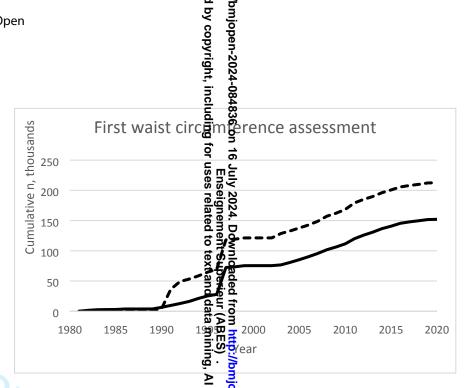
<sup>&</sup>lt;sup>a</sup>Includes only recalled weight assessments.

<sup>&</sup>lt;sup>b</sup>Categories according to the World Health Organization<sup>51 52</sup>.

From the Population and Housing Census in 1960 and 1965, and from the Register of the Total Population in 1968 onwards. Married, divorced and widow/-er also include registered partners, recorded as of 1998. Fifteen "other counties" each made up <5% of the total.

delighest achieved education through follow-up, retrieved from the Population and Housing Census in 1970, and from the Longitudinal Integration Database for Health Insurance and Labour Market Studies in 1990 onwards. From the Register of the Total Population.





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# **BMJ Open**

# Cohort profile: The Obesity and Disease Development Sweden (ODDS) study, a pooled cohort

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# Cohort profile: The Obesity and Disease Development Sweden (ODDS) study, a pooled cohort

Marisa da Silva<sup>1</sup>, Josef Fritz<sup>1,2</sup>, Innocent B. Mboya<sup>1</sup>, Ming Sun<sup>1</sup>, Jens Wahlström<sup>3</sup>, Bethany van Guelpen<sup>4</sup>, Carl Michaëlsson<sup>5</sup>, Patrik K. E. Magnusson<sup>6</sup>, Olle Melander<sup>7</sup>, Sven Sandin<sup>6,8</sup>, Weiyao Yin<sup>6</sup>, Ylva Trolle Lagerros<sup>9,10</sup>, Bright Nwaru<sup>11,12</sup>, Jerzy Leppert<sup>13</sup>, Abbas Chabok<sup>13</sup>, Nancy L. Pedersen<sup>6</sup>, Sölve Elmståhl<sup>7</sup>, Karolin Isaksson<sup>14,15</sup>, Christian Ingvar<sup>14</sup>, Linnea Hedman<sup>3</sup>, Helena Backman<sup>3</sup>, Christel Häggström<sup>16</sup>, Tanja Stocks<sup>1</sup>

<sup>&</sup>lt;sup>1</sup>Department of Translational Medicine, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>2</sup>Institute of Medical Statistics and Informatics, Medical University of Innsbruck, Innsbruck, Austria

<sup>&</sup>lt;sup>3</sup>Section of Sustainable Health, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>4</sup>Department of Diagnostics and Intervention, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>5</sup>Department of Surgical Sciences, Medical Epidemiology, Uppsala University, Uppsala, Sweden

<sup>&</sup>lt;sup>6</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>7</sup>Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>8</sup>Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA

<sup>&</sup>lt;sup>9</sup>Division of Clinical Epidemiology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>10</sup>Center for Obesity, Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden

<sup>&</sup>lt;sup>11</sup>Krefting Research Centre, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>12</sup>Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>13</sup>Center for Clinical Research, Uppsala University, Västmanland Hospital, Västerås, Sweden

<sup>&</sup>lt;sup>14</sup>Department of Clinical Sciences Lund, Lund University, Lund, Sweden

<sup>&</sup>lt;sup>15</sup>Department of Surgery, Kristianstad Hospital, Kristianstad, Sweden

<sup>&</sup>lt;sup>16</sup>Northern Registry Centre, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Correspondence to Marisa da Silva, <u>marisa\_da.silva@med.lu.se</u>, and Tanja Stocks, tanja.stocks@med.lu.se.



#### **Abstract**

<u>Purpose:</u> The Obesity and Disease Development Sweden (ODDS) study was designed to create a large cohort to study body mass index (BMI), waist circumference (WC), and changes in weight and WC, in relation to morbidity and mortality.

Participants: ODDS includes 4,295,859 individuals, 2,165,048 men and 2,130,811 women, in Swedish cohorts and national registers with information on weight assessed once (2,555,098 individuals) or more (1,740,761 individuals), in total constituting 7,733,901 weight assessments at the age of 17-103 years in 1963-2020 (recalled weight as of 1911). Information on WC is available in 152,089 men and 212,658 women, out of whom 108,795 have repeated information on WC (in total 512,273 assessments). Information on morbidity and mortality was retrieved from national registers, with follow-up until the end of 2019-2021, varying between the registers.

Findings to date: Amongst all weight assessments (of which 85% are objectively measured), the median year, age, and BMI (interquartile range, IQR) is 1985 (1977-1994) in men and 2001 (1991-2010) in women, age 19 (18-40) years in men and 30 (26-36) years in women, and BMI 22.9 (20.9-25.4) kg/m² in men and 23.2 (21.2-26.1) kg/m² in women. Normal weight (BMI 18.5-24.9 kg/m²) is present in 67% of assessments in men and 64% in women, and obesity (BMI ≥30 kg/m²) in 5% of assessments in men and 10% in women. The median (IQR) follow-up time from the first objectively measured or self-reported current weight assessment until emigration, death, or end of follow-up is 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women. During follow-up, 283,244 men and 123,457 women died.

<u>Future plans:</u> The large sample size and long follow-up of the ODDS study will provide robust results on anthropometric measures in relation to risk of common diseases and causes of deaths, and novel findings in subgroups and rarer outcomes.

- The Obesity and Disease Development Sweden (ODDS) study is a large, pooled cohort of men and women in Sweden with information on weight, height, and waist circumference assessed once or more between 1963 and 2020.
- The unique personal identity number of inhabitants of Sweden enables tracking of individuals across ODDS cohorts, thus identifying a large number of individuals with repeated assessments from one or more cohort/-s, used to compute changes of weight and waist circumference in adulthood.
- The large sample size and long follow-up in national registers for information on morbidity and mortality outcomes ensure high statistical power and enables investigation of anthropometric measures also in relation to rarer outcomes.
- Additional important information retrieved from national registers include sociodemographic characteristics, comorbidities, and prescribed drugs.
- Limitations are incomplete information on smoking habits, and no information on dietary intake, physical activity, and other potential disease-specific confounders.

#### Introduction

The prevalence of obesity has risen to pandemic proportions during the last decades, reaching an estimated global prevalence of around 14% in men and 18% in women in 2020<sup>1</sup> (projected from NCD-RisC<sup>2</sup>), generally with a higher prevalence in high income countries but with an accelerating prevalence in low- and middle-income countries<sup>2</sup>. The negative impact of obesity on public health is large, for example with disability-adjusted life years, i.e. years lost in full health, due to obesity projected to increase by 40% from 2020 to 2030<sup>3</sup>. The large negative public health impact of obesity is both attributed to its high prevalence and to the established association of obesity with many common diseases, including cardiovascular diseases (CVD)<sup>4</sup> and several cancers<sup>5</sup>, as well as with all-cause mortality and cause-specific death due to CVD and cancer<sup>6</sup>. Less is known about the association of obesity with rarer diseases, which, in a prospective cohort setting, requires a larger population size and/or a longer follow-up for investigation. Furthermore, body size including obesity has mostly been assessed using a onetime measure of body mass index (BMI, kg/m<sup>2</sup>) in relation to disease risk. Studies based on measures of central obesity, such as waist circumference (WC), and of changes in body size across life on the risk of morbidity and mortality, have been much fewer and smaller<sup>5</sup> <sup>7</sup>. For example, to our knowledge, the largest study to date on BMI and mortality had 367,512 deaths during follow-up<sup>6</sup>, whereas recent meta-analyses of studies on weight changes in middle-age<sup>8</sup> and older age<sup>9</sup> included 34,038 and 69,255 deaths, respectively, for all studies combined. Moreover, most studies of weight changes on outcomes were based on only two weight assessments prone to measurement error. To explore whether particular ages of weight gain rather than cumulative life-time exposure to obesity poses a particularly high risk, different ages of weight assessments are needed in the studied population to enable prediction of age-specific individual weight changes<sup>10</sup>. Such sensitive ages to obesity have been shown important for example for the development of hypertension and breast cancer<sup>11</sup>. Last, weight fluctuations, i.e. large variation in weight, is commonly believed to, but not concluded to, result in negative physiological changes, such as less muscle mass and a lower metabolic rate<sup>12</sup>. The association of weight fluctuations on disease risk and mortality has been studied to some extent, but large studies with many repeated weight assessments are limited<sup>13</sup>.

The long history, high coverage, and good quality of many Swedish nationwide registers, together with the unique personal identity number of inhabitants of Sweden enabling individual linkage to national healthcare registers<sup>14</sup>, is a major advantage for epidemiological research in the country<sup>15</sup>. For example, the Swedish Cause of Death Register<sup>16</sup> and the Cancer Register<sup>17</sup> 18

are based on mandatory reporting of deaths and cancer diagnoses of the population since 1952 and 1958, respectively, enabling long and close to complete tracking of individuals for epidemiological studies. The personal identity number further facilitates cross-identification of individuals between different cohorts in pooled studies, which avoids duplicate contribution of an individual included in more than one cohort. It also enables the use of repeated individual assessments between cohorts to enlarge the sample size for the investigation of factors such as longitudinal changes of anthropometrics.

The pooled Obesity and Disease Development Sweden (ODDS) study was created to form a large population to investigate the association of anthropometric measures (BMI, WC, and changes in weight and WC) with the risk of morbidity and mortality. The large sample size and long follow-up ensures high statistical power in investigations. Herein, we describe the ODDS study population, and provide an overview of the information retrieved from national registers linked to individuals in ODDS.

## **Cohort description**

### Study population

 Swedish cohorts for research and national registers with individual-level information on weight and height were identified for inclusion in ODDS. The included registers with weight and height information are hereafter denoted "cohorts" when referring to the study population. We included individuals with a weight assessment at a minimum age of 17 years, which was the lower age limit of the largest male cohort (military conscripts). We further required a recorded date for the assessment (year as a minimum, with any missing month and/or day replaced with June and/or day 15), and a valid personal identification number in the Swedish Total Population Register. Information on date, weight, and if available, height, WC, and smoking habits, were included from each assessment. The availability of height was not used as an inclusion criterion for each individual assessment as it could often be derived from repeated assessments, and because other factors, such as sociodemographic factors, were regarded to be equally important as height in studies of changes in weight and WC. Hence, completeness of these factors as potential inclusion criteria was left for later decision according to relevance for individual studies.

The characteristics of the included cohorts forming the ODDS study population of 4,295,859 unique individuals with 7,733,901 weight assessments are described in Table 1. Each cohort is

 presented separately in the table so individuals participating in more than one cohort are counted in each of these cohorts. Weight in the cohorts was assessed between 1963 and 2020, at an age of 17-103 years. The two largest cohorts are the Swedish Military Conscription Register and the Medical Birth Register, both nationwide and further described below. Other cohorts have local, regional, or nationwide coverage of included individuals (Table 1). Some of them were designed for research purposes and others were designed as general or disease-specific health checkups, from which the information was later made available for research.

# Weight assessments, completeness, and population coverage of the two largest cohorts

Data from military conscripts make up the majority of the male population (1,771,429 men with 1,779,681 weight assessments) and the Medical Birth Register makes up the majority of the female population (1,855,606 women with 3,208,127 weight assessments). In Sweden, conscription, i.e. enrolment for military service, was mandatory for men at around 18 years of age until June 30, 2010, and was thereafter voluntary until 2017<sup>20</sup>. For young women, conscription has been voluntary since the 1980s. The coverage in the Military Conscription Register of the Swedish male birth cohorts of 1951-88 (corresponding to conscription between 1969 and 2006) is 90%. Weight is missing for at most 5% of conscript examinations before year 2000. No information on WC is available in the Military Conscription Register.

The Medical Birth Register includes information on around 98% of all births in Sweden. Since 1982, information is recorded at the first antenatal visit of pregnancy, generally taking place between 8-10 weeks of gestation<sup>19</sup>. A large population-based study in Sweden showed that weight gain in pregnancy was minimal during the first 15 weeks of gestation, for example with a median weight gain in normal weight women of 0.7 kg between gestational week six and ten<sup>43</sup>. Weight of pregnant women were recorded in the Medical Birth Register in 1982-89 and from 1992 onwards, and has a coverage of more than 85% since 1992. In 1982-89, early pregnancy weight was estimated by subtracting pregnancy weight gain from weight at delivery, and since 1992, weight was measured at the first antenatal visit. Due to this change in weight recording, weight in 1982-89 was much lower than expected compared to measurements from 1992 onwards, as also observed in other studies<sup>44</sup> <sup>45</sup>. Therefore, we corrected weight assessments in 1982-89 in the Medical Birth Register using a linear regression model of weight and calendar year from 1992 onwards. For illustration purposes, we let j represent the calendar years 1982-1989 for an individual i. We first regressed weight  $(W_i)$  on the year  $(Y_i)$  at baseline examination (i.e., first antenatal care visit) to obtain the average weight change over time

# Weight and waist circumference assessments in other cohorts

Other cohorts than the two largest include 972,974 individuals with 2,225,946 objectively measured or self-reported current weight assessments, of which objectively measured or selfreported WC is available in 364,747 individuals with 512,273 assessments. Self-reported current weight has shown very high validity in western populations with a correlation coefficient with objectively measured weight of over 0.95<sup>46</sup> <sup>47</sup>. High validity has also been shown for self-reported WC in western populations, showing correlation coefficients with objectively measured WC of over 0.85 when instructions were provided on how to measure WC<sup>46</sup> <sup>47</sup>, and only slightly lower when no instructions were provided<sup>48</sup>. In ODDS, the SIMPLER cohorts and the National March Cohort collected self-reported WC information from questionnaires without further instructions, and in Women's Lifestyle and Health, a picture indicated where to place the tape measure. WC in the other cohorts were objectively measured. In several cohorts, information on recalled weight was collected simultaneously with that of current weight (see footnote of Table 1). A total of 225,331 individuals reported 500,219 recalled weights, mostly for age 20 years (139,936 [28%] of assessments), but also for 18, 25, 30, 40, 50, 60, 70 and 80 years of age, from the year 1911 or later. These assessments will primarily be used in ODDS studies of weight changes, and a sensitivity analysis excluding these measures will always be performed. In the pooled ODDS study population, recalled weight is counted as a distinct weight assessment with the date set to that of the age for the recalled weight.

# Smoking information

 The questions asked regarding smoking habits and the completeness of smoking information varies considerably between ODDS cohorts. To increase the completeness of smoking status in individuals with repeated weight assessments with missing and non-missing smoking

 information, we performed single imputation by carrying information forwards or backwards within and between cohorts, prioritising previous records over later records for never/former/current smoking status, but not for current smoking (yes/no). After imputation, never/former/current smoking information is available in 2,856,160 (37%) assessments, and current smoking (yes/no) information in 5,061,903 (65%) assessments. In total 828,763 individuals (19%) have at least one weight assessment with never/former/current smoking information available, and the proportion is larger for individuals with WC assessments (330,775 individuals, 91%). To increase the coverage of smoking information, multiple imputation<sup>49</sup> based on all available data may be considered in single ODDS studies. Furthermore, studies dependent on the coverage of registers with a later start, such as the Patient Register (for information on CVD and Charlson comorbidity index<sup>50</sup>) or the Swedish Social Insurance Agency for studies on sick-leave, will include only later years' measurements of weight, which have a markedly higher coverage of smoking information.

# Register linkages

By use of the unique personal identity number assigned to each resident of Sweden, individuals in ODDS were linked to a range of Swedish national registers from inception to the last possible follow-up date, varying between 2019 and 2021 depending on the specific register. Birth date was retrieved from the Total Population Register; however, due to Swedish legislation protecting individual integrity, date of birth was obtained only for the year and quarter of a year, resulting in a recorded birth date with day 15 and the middle month of the quarter, e.g. February for the first quarter, in addition to the birth year.

Table 2 gives an overview of the registers and the type of information retrieved. This includes information on outcomes: all-cause and cause-specific mortality by use of the Cause of Death Register; specific cancers in the Cancer Register; prostate cancer in detailed diagnostic risk categories by use of information from the National Prostate Cancer Register; CVD, hypertension and type 2 diabetes by use of the Patient Register and National Diabetes Register; and sick-leave by use of information from the Swedish Social Insurance Agency. Sociodemographic information of relevance for all ODDS studies, such as education, income, marital status, and birth country, was retrieved from several national registers.

#### Patient and public involvement

Study participants and/or the general public were not involved in the planning, design, or conduct of the study.

# Findings to date

# Characteristics of all weight and waist circumference assessments

The characteristics of all 7,733,901 weight assessments in the 4,295,859 individuals in ODDS is shown in Table 3 and the cumulative number of ODDS participants by year of assessment of the first recorded current weight and WC, respectively, is shown in Figure 1. Most weight assessments were objectively measured (85%), and 4,066,876 individuals (95%) have information from at least one objectively measured weight assessment. The median (IQR) year and age of weight assessment is lower in men than in women; year 1985 (1977-94) vs. 2001 (1991-2010), and 19 (18-40) vs. 30 (26-36) years of age. Normal weight (BMI 18.5-24.9 kg/m<sup>2</sup>) is present in 67% of assessments in men and 64% in women, and obesity (BMI ≥30 kg/m²) in 5% of assessments in men and 10% in women. The low proportion of obesity in men is likely due to the, on average, young age and early calendar year at weight assessment. Information on WC is available in 152,089 men with 209,473 WC assessments and in 212,658 women with 302,800 WC assessments; 52% of these were objectively measured and 63% of individuals have at least one objectively measured WC assessment. The median (IQR) year of the 512,273 WC assessments is later than that of weight, year 2007 (1997-2012) for men and 2003 (1997-2010) for women, and the median age is higher, 57 (49-66) years in men and 51 (43-62) years in women.

#### Characteristics of repeated weight and waist circumference assessments

Individuals with two or more assessments of weight or WC, respectively, will be eligible for inclusion in studies of change of these factors, on outcomes. In these studies, we will utilise all assessments in an individual, i.e. allowing assessments to take place in different cohorts. For each assessment, age, form of assessment (objectively measured/self-reported current/self-reported recalled) and, in women, a pregnancy indicator (Medical Birth Register, yes/no) will be included as predictor variables to model weight and WC trajectories in mixed effects models<sup>10</sup>.

Out of 477,705 men and 1,263,056 women with two or more weight assessments, totaling 1,843,609 assessments in men and 3,335,194 in women, the median number of assessments is 3 (IQR 2-5) in men and 2 (IQR 2-3) in women. Of these, the by far largest number of

 assessments in men originate from the Construction Workers Cohort (n=1,036,968) followed by the Cohort of Swedish Men (n=268,408) and the Military Conscription Register (n=216,585), and the by far most assessments in women are from the Medical Birth Register (n=2,435,226) followed by the Swedish Mammography Cohort (n=273,717) and Women's Lifestyle and Health (n=127,384). Out of 41,669 men and 67,126 women with two or more WC assessments, totaling 99,053 assessments in men and 157,268 in women, the median number of assessments is 2 (IQR 2-3) in men and 2 (IQR 2-2) in women. Of these, the largest number of WC assessments in men originate from the Cohort of Swedish Men (n=59,863) and the Västerbotten Intervention Programme (n=19,549), and in women from the Swedish Mammography Cohort (n=56,222) and Women's Lifestyle and Health (n=51,696).

# Follow-up time and events

The follow-up time from the first recorded current weight until emigration, death or end of follow-up for death (31 Dec. 2020) is up to 58 years, with a median (IQR) of 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women, and a median (IQR) from the first WC assessment of 13.4 (8.0-23.2) years in men and 17.1 (9.6-25.0) years in women. The total time at risk for mortality is 66.3 million person-years for men and 42.0 million person-years for women, during which 280,537 men and 121,635 women died. Amongst morbidity outcomes, cancer is of main focus in the ODDS working group. Information on the number of deaths (all-cause and cause-specific) and incident cancers (all and some site-specific) during follow-up in the full ODDS population, in individuals with two or more weight assessments for studies of weight change, and in individuals with one and two or more WC assessments, respectively, is shown in Table 4.

#### Ongoing and planned studies

Several ODDS studies are ongoing or planned to start shortly on BMI, WC, and changes in weight and WC, in relation to the risk of outcomes (currently mortality and cancer). Changes in weight and WC include the investigation of changes across adulthood, and in age-spans of young, middle, and late adulthood. We further plan to investigate: i) weight fluctuations in individuals with many repeated weight assessments in relation to outcomes, ii) anthropometric measures in interaction with, and mediated through, cardiometabolic diseases (CVD, hypertension, and type 2 diabetes) on non-CVD outcomes, iii) anthropometric measures jointly with prescribed drugs (using retrieved data and after additional register linkages) on outcomes, and iv) anthropometric measures in relation to specific cancers with detailed diagnostic

information, after additional linkages to national quality registers of cancer. ODDS enables a range of further possible investigations to be done in the obesity field, based on already collected data or after additional register linkages. Further information about ODDS can be found at <a href="https://odds.blogg.lu.se">https://odds.blogg.lu.se</a>.

#### Strengths and limitations

The ODDS study has several strengths. Firstly, the population is very large and has a nationwide coverage of Swedish cohorts, which, although not completely population-based, generally have a high representativeness of their background population. Furthermore, the unique personal identity number of Swedish inhabitants enables cross identification of individuals between ODDS cohorts as well as tracking of individuals in Swedish nationwide registers. Loss to follow-up is negligible in those registers, and the objective, harmonized information on outcomes as well as on sociodemographic factors by use of national registers, is an additional major strength. The combination of anthropometric measures in the pooled population with, for example, cardiometabolic diseases and medications retrieved from national registers, enables the investigation of various risk factors jointly with anthropometrics. Lastly, the long follow-up time together with the large sample size has accumulated many events resulting in overall high statistical power and the possibility to investigate subgroups and rarer outcomes.

The study also has some limitations. The large heterogeneity of the study population in terms of geographical region, age, and year of weight assessment, enables subgroup investigation; however, certain subgroups, for example older age individuals, will be too small for a separate investigation. The study is further limited in that information on smoking habits, an important confounder for mortality and many diseases, is missing in a large part of the population and, apart from sociodemographic information, the ODDS database has no information on potential confounders such as diet, physical activity, and other disease-specific confounders.

#### Collaboration

The ODDS collaboration conducts research in accordance with the ethical approval of the ODDS cohort as well as approvals from the steering committee of each subcohort. New research ideas will require new approvals. Researchers interested in collaboration can contact the ODDS Principal Investigator, Tanja Stocks, for further information and discussion.

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#### **Contributors**

MdS, JF, IBM, MS, CH and TS were involved in the conception and design of the study. JW, BvG, CM, PKEM, OM, SS, WY, YTL, BN, JL, AC, NLP, SE, KI, CI, LH and HB contributed original cohort data. MdS harmonized the cohort data. IBM calculated corrected weights in the Medical Birth Register. MdS, JF, MS and TS harmonized register data. TS organized the collection of cohort and register data, analysed data, and drafted the manuscript. MdS, JF, IBM, MS, JW, PKEM, OM, SS, YTL, JL, NLP, CI, LH, HB and CH revised the manuscript. All authors made significant contributions to the manuscript and have read and approved the final version.

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# **Competing interests**

None declared.

# **Ethics approval**

# Data sharing statement

 All data are located on Statistics Sweden's Microdata Online Access (MONA) server and may only be accessed from countries in the European Union or the European Economic Area. Data access for questions covered by the ethical approval will be considered in agreement with the principal investigator of ODDS, Tanja Stocks, and upon approval from relevant register holders and steering committees of ODDS cohorts.

# Figure caption

Figure 1. Cumulative number (n) of men (solid line) and women (dotted line) per calendar year, at the first objectively measured or self-reported current weight (1963-2020) or waist circumference (1981-2020), in the Obesity and Diseases Development Sweden (ODDS) study

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	acteristics of cohorts of the Obesity and Disease Developmen	N individ-	N assess-	udy <sup>a</sup> <u>Cl</u> <u>di</u> Year <u>,</u>	Age in years,	as	duals with at sessment of:	
Cohort	Description	uals (% male)	ments (% male)	(range)	(range) 6 median	Objectively measured weight	Smoking status	Waist circum-ference
Swedish Medical Birth Register <sup>19</sup>	Includes ~98% of all births in Sweden. The mother's weight is measured at the first antenatal care visit, commonly at 8-10 gestational weeks. Since 1992, weight is missing for <15%	1,855,606 (0)	3,208,127 (0)	2003 n. 6 (1982-20 <b>996</b>	29 (17-54)	1,855,606 (100)	94,555 (5)	0 (0)
Swedish Military Conscription Register <sup>20</sup>	In Sweden, conscription was mandatory for men aged ~18 years until 2010 and was then voluntary until 2017. The male birth cohorts of 1951-88 cover 90% of the target population, with ≤5% missing weight before 2000	1,790,751 (99)	1,799,609 (99)	1987 <b>6.39</b> (1969-20 <b>5</b> 4 <b>9</b>	18 (17-58)	1,790,751 (100)	190,197 (11)	0 (0)
Construction Workers Cohort <sup>21</sup>	Construction workers were invited on a regular basis to a health checkup through a collective agreement that concerned almost all construction workers in Sweden. Attendance: ≥80%	387,545 (95)	1,149,722 (96)	1981 <b>X UD</b> (1971-19 <b>9</b> 3 <b>6</b>	<b>E</b> (17-82)	387,545 (100)	333,100 (86)	0 (0)
NSHDS <sup>22</sup>	Population-based cohorts in the northernmost counties of Sweden: Norrbotten and Västerbotten	138,379 (47)	254,441 (40)	2002	50 (18-82)	132,369 (96)	131,734 (95)	97,061 (70)
VIP <sup>23</sup>	All residents of Västerbotten county are invited to a health checkup at 40, 50, and 60 years of age (and 30 years until 1996). Attendance: 48-67%	124,200 (49)	194,650 (49)	2005 D (1985-20 <b>2</b> 0 <b>7</b>	<b>B</b> 49	124,200 (100)	123,216 (99)	87,538 (70)
MONICA <sup>24</sup>	Seven health screenings aimed for research were performed in random selections (within specific ages) of residents of Norrbotten and Västerbotten counties. Attendance: 67-81% in 1986-2009	12,260 (49)	16,097 (49)	1999 11.05		12,260 (100)	12,245 (>99)	12,235 (>99)
MSP <sup>25</sup>	A questionnaire aimed for research was filled in in connection with mammography screening offered every 2-3 years to women aged ~50-70 years in Västerbotten county. Attendance: ~85%	25,836 (0)	43,694 (0)		58 (18-82)	0 (0)	20,026 (78)	0 (0)
SIMPLER <sup>26</sup>	Population-based cohorts in counties of southeastern Sweden: Uppsala, Västmanland, and Örebro	106,391 (43)	237,966 (39)	1997 <b>5</b> (1987-20 <del>1</del> 9)	64 (38-103)	0 (0)	89,598 (84)	81,462 (77)
SMC	All women born 1914/1917-1948, residing in Västmanland and Uppsala counties were invited to mammography screening that included a questionnaire aimed for research, with subsequent follow-ups. Attendance at baseline: 70%	60,709 (0)	145,234 (0)	1997	62 (38-103)	0 (0)	44,121 (73)	40,338 (66)
COSM	All men born 1918-52 residing in Västmanland and Örebro counties were invited to fill in a research-based questionnaire, with subsequent follow-ups. Attendance at baseline: 49%	45,682 (100)	92,732 (100)		67 (42-101)	0 (0)	45,477 (>99)	41,124 (90)
Swedish Twin Registry <sup>27 28</sup>	Research-based register on mono- and dizygotic twins across all of Sweden	97,533 (46)	154,666 (45)	1999 <b>5</b> (1963-20 <b>3</b> 4)	48 (17-99)	12,360 (13)	90,182 (92)	12,328 (13)
Q63, 67, 70	All same-sex twins born 1886-1925 were invited to fill in a questionnaire (not including weight) in 1960. Follow-up questionnaires were sent out thrice during the subsequent 10 years (Q63, 67 and 70)	20,312 (44)	42,347 (41)	1007	53 (37-84)	0 (0)	17,986 (89)	0 (0)
Q73	All same-sex twins born 1926-58 were invited to fill in a questionnaire in 1973.  Attendance: ~83%	27,595 (48)	27,595 (48)	1973 (1973-1973)	29 (17-47)	0 (0)	27,507 (>99)	0 (0)
SALT	All twins born 1944-58 were invited to a phone interview. Attendance: ~65%	42,754 (47)	42,754 (47)	2000 (1998-2003)	<b>5</b> 6	0 (0)	42,234 (99)	0 (0)
TwinGene	Twin pairs in SALT were invited to a follow-up investigation. Attendance: ~65%	12,360 (45)	12,360 (45)	2006 (2002-2009)	<b>55</b> 64	12,360 (100)	12,237 (99)	12,328 (>99)
STAGE	All twin pairs born 1958-85 were invited to a web-based survey. Attendance: ~60%	23,448 (44)	23,448 (44)	2005	<b>5</b> (47-33) <b>6</b> (19-47)	0 (0)	23,230 (99)	0 (0)

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YATSS	All twin pairs born 1986-92 were invited to a web-based survey. Attendance: ~42%	6162 (40)	6162 (40)	2013 <b>2</b> (2013-20 <b>5</b> 4)	24 (20-28)	0 (0)	1988 (32)	0 (0)
Malmö cohorts	Population-based cohorts in Malmö city in southern Sweden (MPP and MDCS) and offspring of MDCS participants (MOS)	54,876 (53)	124,442 (54)	1995 <b>5</b>	56 56 5 (18-85)	54,860 (>99)	48,392 (88)	36,170 (66)
MPP <sup>29 30</sup>	All residents of Malmö city, born in certain years, 1921-49, were invited for screening for CVD and alcohol abuse, with subsequent follow-ups of all or a selected population. Attendance at baseline: ~71%	33,337 (67)	59,427 (70)	1983 (1974-20 <b>4</b> 6 <b>m</b>	53 (26-85)	33,337 (100)	28,294 (85)	4506 (14)
MDCS <sup>31</sup>	All residents of Malmö city, born in certain years, 1926-50, were invited to.a health examination aimed for research on diet and cancer, with subsequent follow-ups of all or a selected population. Attendance at baseline: ~41%	30,415 (40)	60,792 (39)	1997 <b>9</b> . (1991-20 <b>5</b> 2)	_	30,390 (>99)	29,280 (96)	30,373 (>99)
MOS <sup>32</sup>	Children and grandchildren of a random sample of MDCS participants were invited to a health examination for research purposes	4223 (48)	4223 (48)	2016 <b>2 3</b> (2013-20 <b>3</b> 9 <b>3</b>	<b>44 2</b> (18-73)	4223 (100)	3799 (90)	4202 (>99)
Women's Lifestyle and Health <sup>33</sup>	Randomly selected women born 1943-62 residing in Uppsala county were invited to fill in a questionnaire aimed for research on lifestyle and cancer and CVD, and to one subsequent follow-up. Attendance at baseline: 51%	48,720 (0)	82,140 (0)	1992 <b>6 %</b> (1991-20 <del>04</del>	44 (27-61)	0 (0)	40,840 (84)	43,132 (89)
Swedish National March Cohort <sup>34</sup>	In 1997, a fund-raising event for the Swedish Cancer Society took place in ~3600 places across Sweden. Participants were requested to fill in a questionnaire aimed for research on lifestyle and chronic diseases	41,710 (36)	41,710 (36)	1997 <b>a a</b>	52 (17-93)	0 (0)	35,801 (86)	31,893 (76)
West Sweden Asthma Study <sup>35</sup>	In 2008 and 2016, random selections of residents of western Sweden were invited to fill in a questionnaire aimed for research on asthma and respiratory diseases. Attendance: 62% and 50%, respectively	41,276 (46)	53,231 (45)	2016 <b>3 8</b> (2008-20 <b>3 6 9</b>	51 (17-83)	0 (0)	40,506 (98)	0 (0)
WICTORY <sup>36</sup>	Residents of Västmanland county, born 1940-59, were invited to a health checkup at age ~40 or 50 years, aimed for CVD prevention. Attendance: ~60%	33,892 (48)	33,892 (48)	1994 <b>9</b> (1989-20 <b>)</b>	49 (35-55)	33,892 (100)	33,579 (99)	33,860 (>99)
LifeGene <sup>37</sup>	Residents across Sweden were invited through randomization (~44%), or in other ways, e.g. shared household with the one invited, or volunteering, to a health examination and a web-based survey for research purposes	30,039 (41)	30,039 (41)	2011 <b>5</b> (2009-20 <b>5</b> 8)	33 (17-96)	28,861 (96)	16,407 (55)	28,861 (96)
EpiHealth <sup>38 39</sup>	Randomly selected ~45-75-year-old residents of Uppsala and Malmö city were invited to a health examination and a web-based survey for research on genediet interactions and diseases. Attendance: ~20%	25,337 (44)	25,337 (44)	2014 <u>-</u> (2011-20 <b>3</b> 8)	61 (35-78)	25,337 (100)	18,416 (73)	25,337 (100)
Melanoma in Southern Sweden <sup>40</sup>	Randomly selected women with no prior cancer, ~25-64 years, residing in Southern Sweden, were in 1990-92 invited to fill in a questionnaire (not including weight) aimed for research on malignant melanoma and female cancers. A follow-up questionnaire included weight. Attendance at baseline: 74%	22,974 (0)	22,974 (0)	2001 <b>m</b> (1999-20 <b>m</b>	54 (35-76)	0 (0)	2399 (10)	0 (0)
Obstructive Lung Disease in Northern Sweden <sup>41 42</sup>	In separate surveys (five in ODDS), randomly selected adults of specific ages, residing in Norrbotten county, were invited to a health examination and follow-ups, or to fill in a questionnaire (2016), aimed for research on asthma and respiratory diseases. Attendance at baseline: 66-91%	12,395 (49)	15,386 (49)	<u> </u>	53 (19-85)	5853 (47)	12,241 (99)	0 (0)

NSHDS, Northern Sweden Health and Disease Study; VIP, Västerbotten Intervention Programme; MONICA, Monitoring of Trends of Cardiovas under the Swedish Infrastructure for Medical Population-Based Life-Course and Environmental Research; MC, Swedish Mammography Cohort; COSM, Cohort of Swedish Men; SALT, Screening Across the Lifespan Twin Study; STAGE, Study of Twin Adults: Genes and Environment; YATSS, Young Adult The Institute of Swedish Men; SALT, Screening Across the Lifespan Twin Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular Risk Factors Study.

The numbers include overlap of individuals between cohorts, and only objectively measured or self-reported current weight. Recalled weight is available in 225,331 individuals with 500,219 recalled

weights in: SIMPLER, Swedish Twin Registry (Q67 and Q70), MDCS, MOS, Women's Lifestyle and Health, Swedish National March Cohort, EpiHeath, and Melanoma in Southern Sweden, included in Table 3.

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Table 2. Information on Swedish national registers with linkage to the Obesity and Disease Development's wedge (ODDS) study population

Swedish register	Description	Type of information retrieved g for 1	Years covered in ODDS	Coverage of target population
The Cancer Register <sup>17 18</sup>	Contains information on histologically, cytologically or clinically diagnosed, or by autopsy verified (excluding death certificate only) malignant tumours, and certain benign, premalignant and borderline tumours, in Sweden	Date and type of cancer diagnosis, including International Classification of Diseases topography code, histopathology (Swedish SNOMED and PAD codes), and TNM status (recorded since 2004)	1958-2019	96% in the year 1998 <sup>17</sup> , which appears to be stable over time
The Cause of Death Register <sup>16</sup>	Contains information on deaths and death causes in Sweden, in electronic form since 1952. The death cause is usually determined by the treating physician or the physician last seeing the patient before death	Date of death and underlying and contributing and death causes according to International Classification of Diseases codes	1952-2020	>99%, and 96% of the underlying cause of death (>99% of deaths in ODDS)
The Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) <sup>51</sup>	Contains information from a range of sources on education, occupation, income and employment in all residents of Sweden aged ≥16 years (≥15 years since 2010)	Highest attained education. Occupation, income ABES)  Highest attained education. Occupation, income ABES  1993)	1990-2019	>99% overall, 98% for education in 25-64 year old individuals
The National Diabetes Register <sup>52</sup>	Contains information on diabetes diagnoses (all types) and other information, such as complications and treatment, of diabetes patients aged ≥18 years in outpatient specialist clinics and in primary healthcare in Sweden	Date and type of diabetes diagnosis and treatment	1996-2020	Increased coverage over time; ~90% of Swedish adults with diabetes in 2015
The National Prostate Cancer Register <sup>54 55</sup>	Contains information on biopsy-confirmed prostate cancer diagnoses, tumour characteristics, and primary treatment of prostate cancer patients in Sweden	Date, TNM status, prostate-specific antigen level, and Gleason score at diagnosis, and the main reason for detection (recorded since 2004). Primary treatment, date of radical prostatection (recorded since 2007), and T status, Gleason score and positive margins (yes/no) after radical prostatectomy	1998-2021 (June)	98% of prostate cancer diagnoses in the National Cancer Register in 1998-2012
The Patient Register <sup>56 57</sup>	Contains information on diagnoses of inpatient care in Sweden, recorded since 1987, and of specialist outpatient care, recorded since 1997 for surgical care and since 2001 for other outpatient care	Date and type of diagnosis according to the Swedish International Classification of Diseases codes in inpatient and outpatient care.  Information was obtained for cardiovascular diseases, hypertension, diabetes, and diagnoses of the Charlson Comorbidity index <sup>50</sup>	1987-2020	Since 1987, >99% of inpatient care, and in 2001-2006, 71% of outpatient somatic care
The Population and Housing Census <sup>51</sup>	Contains sociodemographic information through self- reported questionnaires mailed to the full Swedish population aged ≥16 years, with mandatory response	Highest attained education, county of residence, and marital status	Every five years in 1960-1990	≥99% in 1960-1985, 97.5% in 1990 <sup>a</sup>

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The Prescribed Drug Register <sup>58</sup>	Contains information on all prescribed drugs dispensed at pharmacies in Sweden. Excludes over-the-counter drugs	Date of prescribing and dispensing, type of (e.g. ATC code and product name), dispensed amount and dosage, of antidiabetic, antihypertensive, and antilipidemic drugs	>95% of all utilised drugs in Sweden, excluding over-the-counter drugs
The Total Population Register <sup>59</sup>	Contains basic demographic information on all residents of Sweden	Birth date (year and quarter of year), country of birth for the individual and parents (four categories, see Table 2), county of residence marital status, and date/-s of immigration and emigration	>99% of births and deaths, 95% of immigrations, 91% of emigrations, resulting in a slight over-coverage
The Swedish Social Insurance Agency <sup>60</sup>	Contains information on sick leave for periods exceeding 14 days, and of disability pension, for individuals in Sweden with income from work or unemployment benefits, which qualify and apply for sickness absence or disability pension benefits. The first 14 days of sick leave is compensated by the employer and is not recorded by the Social Insurance Agency	Downloaded from Downloaded from the periods lasting more than 14 days, and obtained disability pension	No data available <sup>b</sup>

<sup>&</sup>lt;sup>a</sup>Personal communication with Beatrice Kalnins, Statistics Sweden.

<sup>&</sup>lt;sup>b</sup>Personal communication with Charlotte Limé, the Swedish Social Insurance Agency.

Table 3. Characteristics of all assessments in the Obesity and Disease Development Sweden (ODDS) study, in a total of 4,295,859 unique individuals and separately in 2,165,048 men and 2,130,811 women

Characteristic	Total (N assess- ments=7,733,901)	Men (N assess- ments=3,530,952)	Women (N assess- ments=4,202,949)
Assessments, median no. (IQR) Year	1 (1-2)	1 (1-1)	2 (1-2)
Median (IQR)	1993 (1983-2005)	1985 (1977-1994)	2001 (1991-2010)
N (%)	1999 (1909-2009)	1905 (1911-1994)	2001 (1331-2010)
1911-1959 <sup>a</sup>	102,331 (1)	49,817 (1)	52,514 (1)
1960-1969	159,059 (2)	70,493 (2)	88,566 (2)
1970-1979	1,118,503 (15)	1,011,194 (29)	107,309 (2)
1980-1989	1,866,055 (24)	1,128,163 (32)	737,892 (18)
1990-1999	1,775,421 (23)	780,028 (22)	995,393 (24)
2000-2009	1,470,566 (19)	365,475 (10)	1,105,091 (26)
≥2010	1,241,966 (16)	125,782 (4)	1,116,184 (27)
Age (years)	1,241,300 (10)	125,762 (4)	1,110,104 (21)
Median (IQR)	28 (19-37)	19 (18-40)	30 (26-36)
N (%)	20 (13-37)	19 (10-40)	30 (20-30)
17-19	1,941,872 (25)	1,780,928 (50)	160,944 (4)
20-29	2,222,093 (29)	417,774 (12)	1,804,319 (43)
30-39	1,858,853 (24)	373,384 (11)	1,485,469 (35)
40-49	661,048 (9)	375,880 (11)	285,168 (7)
50-59	570,068 (7)	337,970 (9)	232,098 (5)
60-69	324,381 (4)	174,004 (5)	150,377 (4)
≥70	155,586 (2)	71,012 (2)	84,574 (2)
Weight (kg), median (IQR)	68 (61-77)	73 (66-81)	64 (58-72)
Form of weight assessment, N (%)	00 (01-77)	73 (00-01)	04 (30-72)
Objectively measured	6,579,779 (85)	3,097,486 (88)	3,482,293 (83)
Self-reported current weight	653,903 (8)	207,579 (6)	446,324 (11)
Self-reported current weight	500,219 (7)	225,887 (6)	274,332 (6)
Height (cm), median (IQR)	171 (165-178)	178 (174-183)	166 (162-170)
Body mass index (kg/m²)	171 (103-170)	170 (174-100)	100 (102-170)
Median (IQR)	23.1 (21.0-25.7)	22.9 (20.9-25.4)	23.2 (21.2-26.1)
N (%) <sup>b</sup>	23.1 (21.0-23.1)	22.9 (20.9-25.4)	25.2 (21.2-20.1)
Underweight (<18.5)	305,069 (4)	160,666 (5)	144,403 (3)
Normal weight (18.5-24.9)	5,040,375 (65)	2,378,070 (67)	2,662,305 (63)
Overweight (25-29.9)	1,792,975 (23)	826,610 (23)	966,365 (23)
Obesity class I (30-34.9)	429,028 (6)	137,401 (4)	291,627 (7)
Obesity class I (30-34.3)  Obesity class II and III (≥35)	129,392 (2)	23,465 (1)	105,927 (3)
Missing	37,062 (<1)	4740 (<1)	32,322 (1)
Waist circumference (cm)	37,002 (11)	7770 (*1)	32,322 (1)
Median (IQR)	88 (79-97)	96 (89-103)	82 (75-90)
N (%) <sup>b</sup>	00 (13-31)	30 (03-103)	02 (13-30)
Low (men, <94; women, <80)	210,489 (3)	86,426 (2)	124,063 (3)
Medium (men, 94-101.9; women, 80-87.9)	143,891 (2)	64,225 (2)	79,666 (2)
High (men, ≥102; women, ≥88)	157,893 (2)	58,822 (2)	99,071 (2)
Missing	7,221,628 (93)	3,321,479 (94)	3,900,149 (93)
Smoking status, N (%)	1,221,020 (33)	3,321,473 (34)	3,300,143 (33)
Never	1,334,569 (17)	794,267 (23)	540,302 (13)
Former	679,222 (9)	432,751 (12)	246,471 (6)
Current	842,369 (11)	613,139 (17)	229,230 (5)
Missing	4,877,741 (63)	1,690,795 (48)	3,186,946 (76)
Marital status, N (%) <sup>c</sup>	4,011,141 (00)	1,000,700 (40)	0,100,540 (10)
Unmarried	4,092,269 (53)	2,297,106 (65)	1,795,163 (43)
Married	3,102,435 (40)	1,048,593 (30)	2,053,842 (49)
Divorced	349,667 (5)	117,091 (3)	232,576 (5)
Widow/-er	88,954 (1)	23,535 (1)	65,419 (2)
Missing	100,576 (1)	44,627 (1)	55,949 (1)
County of residence, N (%)°	100,570 (1)	<del>14</del> ,02 <i>l</i> (1)	55,348 (1)
Stockholm	1,253,881 (16)	481,693 (14)	772 100 (10)
			772,188 (18) 614,582 (15)
Västra Götaland	1,136,238 (15)	521,656 (15)	611 600 /151

Västmanland	467,638 (6)	219,591 (6)	248,047 (6)
Västerbotten	439,512 (5)	203,544 (6)	235,968 (6)
Uppsala	382,360 (5)	102,044 (3)	280,316 (7)
Other counties	3,060,691 (39)	1,502,928 (42)	1,449,729 (34)
Missing	108,034 (1)	48,393 (1)	59,641 (1)
Highest achieved education (one			
assessment per individual), N (%)d			
Pre-upper secondary school <9 years	280,244 (7)	167,940 (8)	112,304 (5)
Pre-upper secondary school 9 years	366,211 (9)	215,953 (10)	150,258 (7)
Upper secondary school max. 2 years	1,030,829 (24)	578,620 (27)	452,209 (21)
Upper secondary school 3 years	880,747 (20)	455,344 (21)	425,403 (20)
Post-upper secondary school <3 years	613,421 (14)	299,872 (14)	313,549 (15)
Post-upper secondary school ≥3 years	1,020,461 (24)	393,934 (18)	626,527 (30)
PhD degree	52,219 (1)	28,056 (1)	24,163 (1)
Missing	51,727 (1)	25,329 (1)	26,398 (1)
Country of birth (one assessment per individual), N (%)e			
Born in Sweden, both parents born in Sweden	3,367,487 (78)	1,842,225 (85)	1,525,262 (72)
Born in Sweden, one parent born in Sweden	295,156 (7)	156,744 (7)	138,412 (6)
Born in Sweden, both parents born abroad	121,237 (3)	58,840 (3)	62,397 (3)
Born abroad	511,469 (12)	107,147 (5)	404,322 (19)
Missing	510 (<1)	92 (<1)	418 (<1)

IQR, interquartile range.

<sup>&</sup>lt;sup>a</sup>Includes only recalled weight assessments.

<sup>&</sup>lt;sup>b</sup>Categories according to the World Health Organization<sup>61 62</sup>.

<sup>°</sup>From the Population and Housing Census in 1960 and 1965, and from the Register of the Total Population in 1968 onwards. Married, divorced and widow/-er also include registered partners, recorded as of 1998. Fifteen "other counties" each made up <5% of the total.

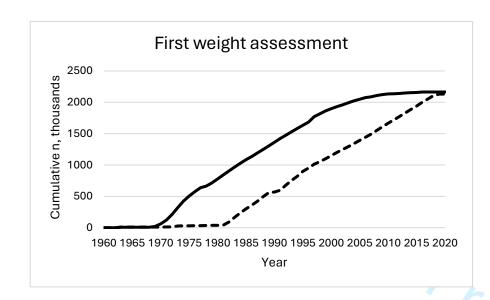
dHighest achieved education through follow-up, retrieved from the Population and Housing Census in 1970, and from the Longitudinal Integration Database for Health Insurance and Labour Market Studies in 1990 onwards. 
eFrom the Register of the Total Population.

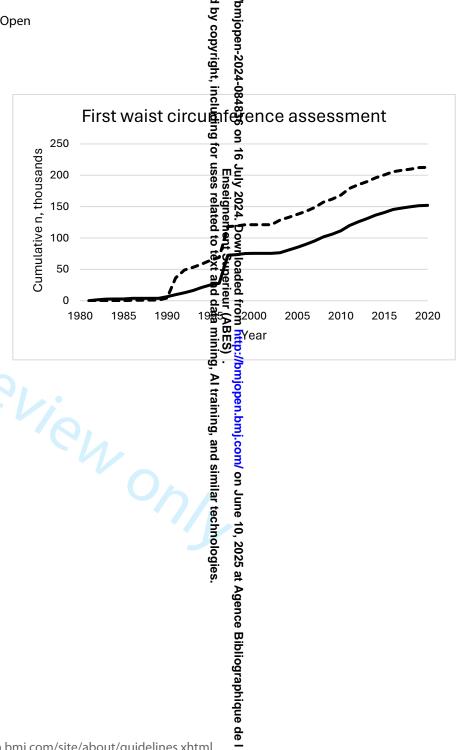
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Table 4. Number of individuals, deaths, and incident cancers during follow-up according to anthropometric measure in the Obesity and Disease Development Sweden (ODDS) study

	, ,				<b>5</b>		
Anthropometric measure	N indi	viduals	N deaths		N incident cancers		
Antinopometric measure	Men	Women	Men	Women	₽ 6 Men	Women	
Weight (full population)			280,537 all-cause	121,635 all-cause	# m12-7,168 all cancer	144,413 all cancer	
			98,796 CVD	35,198 CVD	<b>2</b> 2,027 prostate	50,732 breast	
	2,165,048	2,130,811	78,178 cancer	45,744 cancer	<b>♣ 9</b> . <b>≥</b> 11,448 colon	7920 colon	
			15,325 respiratory	7174 respiratory	20.811,448 colon 20.83 small intestine	530 small intestine	
			system	system	658 penis	742 vulva	
≥2 weight assessments	477,705	1,263,056	133,073 all-cause	62,245 all-cause	3 94,205 all cancer	70,697 all cancer	
Waist circumference	152,089	212,658	37,155 all-cause	35,951 all-cause	£ 26,619 all cancer	28,296 all cancer	
≥2 waist circumference assessments	41,669	67,126	9890 all-cause	8664 all-cause	20 20 407 all cancer	7321 all cancer	

CVD, cardiovascular diseases.





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# Cohort profile: The Obesity and Disease Development Sweden (ODDS) study, a pooled cohort

Marisa da Silva<sup>1</sup>, Josef Fritz<sup>1,2</sup>, Innocent B. Mboya<sup>1</sup>, Ming Sun<sup>1</sup>, Jens Wahlström<sup>3</sup>, Bethany van Guelpen<sup>4</sup>, Carl Michaëlsson<sup>5</sup>, Patrik K. E. Magnusson<sup>6</sup>, Olle Melander<sup>7</sup>, Sven Sandin<sup>6,8</sup>, Weiyao Yin<sup>6</sup>, Ylva Trolle Lagerros<sup>9,10</sup>, Bright Nwaru<sup>11,12</sup>, Jerzy Leppert<sup>13</sup>, Abbas Chabok<sup>13</sup>, Nancy L. Pedersen<sup>6</sup>, Sölve Elmståhl<sup>7</sup>, Karolin Isaksson<sup>14,15</sup>, Christian Ingvar<sup>14</sup>, Linnea Hedman<sup>3</sup>, Helena Backman<sup>3</sup>, Christel Häggström<sup>16</sup>, Tanja Stocks<sup>1</sup>

<sup>&</sup>lt;sup>1</sup>Department of Translational Medicine, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>2</sup>Institute of Medical Statistics and Informatics, Medical University of Innsbruck, Innsbruck, Austria

<sup>&</sup>lt;sup>3</sup>Section of Sustainable Health, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>4</sup>Department of Diagnostics and Intervention, Umeå University, Umeå, Sweden

<sup>&</sup>lt;sup>5</sup>Department of Surgical Sciences, Medical Epidemiology, Uppsala University, Uppsala, Sweden

<sup>&</sup>lt;sup>6</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>7</sup>Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden

<sup>&</sup>lt;sup>8</sup>Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA

<sup>&</sup>lt;sup>9</sup>Division of Clinical Epidemiology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden

<sup>&</sup>lt;sup>10</sup>Center for Obesity, Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden

<sup>&</sup>lt;sup>11</sup>Krefting Research Centre, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>12</sup>Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

<sup>&</sup>lt;sup>13</sup>Center for Clinical Research, Uppsala University, Västmanland Hospital, Västerås, Sweden

<sup>&</sup>lt;sup>14</sup>Department of Clinical Sciences Lund, Lund University, Lund, Sweden

<sup>&</sup>lt;sup>15</sup>Department of Surgery, Kristianstad Hospital, Kristianstad, Sweden

<sup>&</sup>lt;sup>16</sup>Northern Registry Centre, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Correspondence to Marisa da Silva, <u>marisa\_da.silva@med.lu.se</u>, and Tanja Stocks, tanja.stocks@med.lu.se.



#### **Abstract**

<u>Purpose:</u> The Obesity and Disease Development Sweden (ODDS) study was designed to create a large cohort to study body mass index (BMI), waist circumference (WC), and changes in weight and WC, in relation to morbidity and mortality.

Participants: ODDS includes 4,295,859 individuals, 2,165,048 men and 2,130,811 women, in Swedish cohorts and national registers with information on weight assessed once (2,555,098 individuals) or more (1,740,761 individuals), in total constituting 7,733,901 weight assessments at the age of 17-103 years in 1963-2020 (recalled weight as of 1911). Information on WC is available in 152,089 men and 212,658 women, out of whom 108,795 have repeated information on WC (in total 512,273 assessments). Information on morbidity and mortality was retrieved from national registers, with follow-up until the end of 2019-2021, varying between the registers.

Findings to date: Amongst all weight assessments (of which 85% are objectively measured), the median year, age, and BMI (interquartile range, IQR) is 1985 (1977-1994) in men and 2001 (1991-2010) in women, age 19 (18-40) years in men and 30 (26-36) years in women, and BMI 22.9 (20.9-25.4) kg/m² in men and 23.2 (21.2-26.1) kg/m² in women. Normal weight (BMI 18.5-24.9 kg/m²) is present in 67% of assessments in men and 64% in women, and obesity (BMI ≥30 kg/m²) in 5% of assessments in men and 10% in women. The median (IQR) follow-up time from the first objectively measured or self-reported current weight assessment until emigration, death, or end of follow-up is 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women. During follow-up, 283,244 men and 123,457 women died.

<u>Future plans:</u> The large sample size and long follow-up of the ODDS study will provide robust results on anthropometric measures in relation to risk of common diseases and causes of deaths, and novel findings in subgroups and rarer outcomes.

- The Obesity and Disease Development Sweden (ODDS) study is a large, pooled cohort of men and women in Sweden with information on weight, height, and waist circumference assessed once or more between 1963 and 2020.
- The unique personal identity number of inhabitants of Sweden enables tracking of individuals across ODDS cohorts, thus identifying a large number of individuals with repeated assessments from one or more cohort/-s, used to compute changes of weight and waist circumference in adulthood.
- The large sample size and long follow-up in national registers for information on morbidity and mortality outcomes ensure high statistical power and enables investigation of anthropometric measures also in relation to rarer outcomes.
- Additional important information retrieved from national registers include sociodemographic characteristics, comorbidities, and prescribed drugs.
- Limitations are incomplete information on smoking habits, and no information on dietary intake, physical activity, and other potential disease-specific confounders.



#### Introduction

The prevalence of obesity has risen to pandemic proportions during the last decades, reaching an estimated global prevalence of around 14% in men and 18% in women in 2020<sup>1</sup> (projected from NCD-RisC<sup>2</sup>), generally with a higher prevalence in high income countries but with an accelerating prevalence in low- and middle-income countries<sup>2</sup>. The negative impact of obesity on public health is large, for example with disability-adjusted life years, i.e. years lost in full health, due to obesity projected to increase by 40% from 2020 to 2030<sup>3</sup>. The large negative public health impact of obesity is both attributed to its high prevalence and to the established association of obesity with many common diseases, including cardiovascular diseases (CVD)<sup>4</sup> and several cancers<sup>5</sup>, as well as with all-cause mortality and cause-specific death due to CVD and cancer<sup>6</sup>. Less is known about the association of obesity with rarer diseases, which, in a prospective cohort setting, requires a larger population size and/or a longer follow-up for investigation. Furthermore, body size including obesity has mostly been assessed using a onetime measure of body mass index (BMI, kg/m<sup>2</sup>) in relation to disease risk. Studies based on measures of central obesity, such as waist circumference (WC), and of changes in body size across life on the risk of morbidity and mortality, have been much fewer and smaller<sup>5</sup> <sup>7</sup>. For example, to our knowledge, the largest study to date on BMI and mortality had 367,512 deaths during follow-up<sup>6</sup>, whereas recent meta-analyses of studies on weight changes in middle-age<sup>8</sup> and older age<sup>9</sup> included 34,038 and 69,255 deaths, respectively, for all studies combined. Moreover, most studies of weight changes on outcomes were based on only two weight assessments prone to measurement error. To explore whether particular ages of weight gain rather than cumulative life-time exposure to obesity poses a particularly high risk, different ages of weight assessments are needed in the studied population to enable prediction of age-specific individual weight changes<sup>10</sup>. Such sensitive ages to obesity have been shown important for example for the development of hypertension and breast cancer<sup>11</sup>. Last, weight fluctuations, i.e. large variation in weight, is commonly believed to, but not concluded to, result in negative physiological changes, such as less muscle mass and a lower metabolic rate<sup>12</sup>. The association of weight fluctuations on disease risk and mortality has been studied to some extent, but large studies with many repeated weight assessments are limited<sup>13</sup>.

The long history, high coverage, and good quality of many Swedish nationwide registers, together with the unique personal identity number of inhabitants of Sweden enabling individual linkage to national healthcare registers<sup>14</sup>, is a major advantage for epidemiological research in the country<sup>15</sup>. For example, the Swedish Cause of Death Register<sup>16</sup> and the Cancer Register<sup>17</sup> 18

are based on mandatory reporting of deaths and cancer diagnoses of the population since 1952 and 1958, respectively, enabling long and close to complete tracking of individuals for epidemiological studies. The personal identity number further facilitates cross-identification of individuals between different cohorts in pooled studies, which avoids duplicate contribution of an individual included in more than one cohort. It also enables the use of repeated individual assessments between cohorts to enlarge the sample size for the investigation of factors such as longitudinal changes of anthropometrics.

The pooled Obesity and Disease Development Sweden (ODDS) study was created to form a large population to investigate the association of anthropometric measures (BMI, WC, and changes in weight and WC) with the risk of morbidity and mortality. The large sample size and long follow-up ensures high statistical power in investigations. Herein, we describe the ODDS study population, and provide an overview of the information retrieved from national registers linked to individuals in ODDS.

# **Cohort description**

# Study population

 Swedish cohorts for research and national registers with individual-level information on weight and height were identified for inclusion in ODDS. The included registers with weight and height information are hereafter denoted "cohorts" when referring to the study population. We included individuals with a weight assessment at a minimum age of 17 years, which was the lower age limit of the largest male cohort (military conscripts). We further required a recorded date for the assessment (year as a minimum, with any missing month and/or day replaced with June and/or day 15), and a valid personal identification number in the Swedish Total Population Register. Information on date, weight, and if available, height, WC, and smoking habits, were included from each assessment. The availability of height was not used as an inclusion criterion for each individual assessment as it could often be derived from repeated assessments, and because other factors, such as sociodemographic factors, were regarded to be equally important as height in studies of changes in weight and WC. Hence, completeness of these factors as potential inclusion criteria was left for later decision according to relevance for individual studies.

The characteristics of the included cohorts forming the ODDS study population of 4,295,859 unique individuals with 7,733,901 weight assessments are described in Table 1. Each cohort is

 presented separately in the table so individuals participating in more than one cohort are counted in each of these cohorts. Weight in the cohorts was assessed between 1963 and 2020, at an age of 17-103 years. The two largest cohorts are the Swedish Military Conscription Register and the Medical Birth Register, both nationwide and further described below. Other cohorts have local, regional, or nationwide coverage of included individuals (Table 1). Some of them were designed for research purposes and others were designed as general or disease-specific health checkups, from which the information was later made available for research.

# Weight assessments, completeness, and population coverage of the two largest cohorts

Data from military conscripts make up the majority of the male population (1,771,429 men with 1,779,681 weight assessments) and the Medical Birth Register makes up the majority of the female population (1,855,606 women with 3,208,127 weight assessments). In Sweden, conscription, i.e. enrolment for military service, was mandatory for men at around 18 years of age until June 30, 2010, and was thereafter voluntary until 2017<sup>20</sup>. For young women, conscription has been voluntary since the 1980s. The coverage in the Military Conscription Register of the Swedish male birth cohorts of 1951-88 (corresponding to conscription between 1969 and 2006) is 90%. Weight is missing for at most 5% of conscript examinations before year 2000. No information on WC is available in the Military Conscription Register.

The Medical Birth Register includes information on around 98% of all births in Sweden. Since 1982, information is recorded at the first antenatal visit of pregnancy, generally taking place between 8-10 weeks of gestation<sup>19</sup>. A large population-based study in Sweden showed that weight gain in pregnancy was minimal during the first 15 weeks of gestation, for example with a median weight gain in normal weight women of 0.7 kg between gestational week six and ten<sup>43</sup>. Weight of pregnant women were recorded in the Medical Birth Register in 1982-89 and from 1992 onwards, and has a coverage of more than 85% since 1992. In 1982-89, early pregnancy weight was estimated by subtracting pregnancy weight gain from weight at delivery, and since 1992, weight was measured at the first antenatal visit. Due to this change in weight recording, weight in 1982-89 was much lower than expected compared to measurements from 1992 onwards, as also observed in other studies<sup>44</sup> <sup>45</sup>. Therefore, we corrected weight and calendar year from 1992 onwards. For illustration purposes, we let *j* represent the calendar years 1982-1989 for an individual *i*. We first regressed weight  $(W_i)$  on the year  $(Y_i)$  at baseline examination (i.e., first antenatal care visit) to obtain the average weight change over time

(constant,  $b_0$ ) and slope ( $b_1$ ). Using these coefficients, we predicted the average weight for each calendar year j (1982-1989) as  $W_j = b_0 + b_1 \times Y_j$ . We then obtained the difference of the observed average weight from the predicted average weight between 1982-1989, then added this factor to the original weight value and obtained a more linear weight change, as also reported elsewhere<sup>44</sup>. These corrected weights were used in the herein pooled analysis and will be used in original ODDS studies. Additionally, pregnancy will be accounted for in all pooled analyses by inclusion of a binary variable (Medical Birth Register, yes/no) in the statistical regression or other models. No information on WC is available in the Medical Birth Register.

# Weight and waist circumference assessments in other cohorts

Other cohorts than the two largest include 972,974 individuals with 2,225,946 objectively measured or self-reported current weight assessments, of which objectively measured or selfreported WC is available in 364,747 individuals with 512,273 assessments. Self-reported current weight has shown very high validity in western populations with a correlation coefficient with objectively measured weight of over 0.95<sup>46</sup> <sup>47</sup>. High validity has also been shown for self-reported WC in western populations, showing correlation coefficients with objectively measured WC of over 0.85 when instructions were provided on how to measure WC<sup>46</sup> <sup>47</sup>, and only slightly lower when no instructions were provided<sup>48</sup>. In ODDS, the SIMPLER cohorts and the National March Cohort collected self-reported WC information from questionnaires without further instructions, and in Women's Lifestyle and Health, a picture indicated where to place the tape measure. WC in the other cohorts were objectively measured. In several cohorts, information on recalled weight was collected simultaneously with that of current weight (see footnote of Table 1). A total of 225,331 individuals reported 500,219 recalled weights, mostly for age 20 years (139,936 [28%] of assessments), but also for 18, 25, 30, 40, 50, 60, 70 and 80 years of age, from the year 1911 or later. These assessments will primarily be used in ODDS studies of weight changes, and a sensitivity analysis excluding these measures will always be performed. In the pooled ODDS study population, recalled weight is counted as a distinct weight assessment with the date set to that of the age for the recalled weight.

# **Smoking information**

 The questions asked regarding smoking habits and the completeness of smoking information varies considerably between ODDS cohorts. To increase the completeness of smoking status in individuals with repeated weight assessments with missing and non-missing smoking

 information, we performed single imputation by carrying information forwards or backwards within and between cohorts, prioritising previous records over later records for never/former/current smoking status, but not for current smoking (yes/no). After imputation, never/former/current smoking information is available in 2,856,160 (37%) assessments, and current smoking (yes/no) information in 5,061,903 (65%) assessments. In total 828,763 individuals (19%) have at least one weight assessment with never/former/current smoking information available, and the proportion is larger for individuals with WC assessments (330,775 individuals, 91%). To increase the coverage of smoking information, multiple imputation<sup>49</sup> based on all available data may be considered in single ODDS studies. Furthermore, studies dependent on the coverage of registers with a later start, such as the Patient Register (for information on CVD and Charlson comorbidity index<sup>50</sup>) or the Swedish Social Insurance Agency for studies on sick-leave, will include only later years' measurements of weight, which have a markedly higher coverage of smoking information.

# Register linkages

By use of the unique personal identity number assigned to each resident of Sweden, individuals in ODDS were linked to a range of Swedish national registers from inception to the last possible follow-up date, varying between 2019 and 2021 depending on the specific register. Birth date was retrieved from the Total Population Register; however, due to Swedish legislation protecting individual integrity, date of birth was obtained only for the year and quarter of the year, so we imputed the missing date by the mean value of possible dates, e.g. Feb 15 for the first quarter of the year.

Table 2 gives an overview of the registers and the type of information retrieved. This includes information on outcomes: all-cause and cause-specific mortality by use of the Cause of Death Register; specific cancers in the Cancer Register; prostate cancer in detailed diagnostic risk categories by use of information from the National Prostate Cancer Register; CVD, hypertension and type 2 diabetes by use of the Patient Register and National Diabetes Register; and sick-leave by use of information from the Swedish Social Insurance Agency. Sociodemographic information of relevance for all ODDS studies, such as education, income, marital status, and birth country, was retrieved from several national registers.

#### Patient and public involvement

Study participants and/or the general public were not involved in the planning, design, or conduct of the study.

# Findings to date

# Characteristics of all weight and waist circumference assessments

The characteristics of all 7,733,901 weight assessments in the 4,295,859 individuals in ODDS is shown in Table 3 and the cumulative number of ODDS participants by year of assessment of the first recorded current weight and WC, respectively, is shown in Figure 1. Most weight assessments were objectively measured (85%), and 4,066,876 individuals (95%) have information from at least one objectively measured weight assessment. The median (IQR) year and age of weight assessment is lower in men than in women; year 1985 (1977-94) vs. 2001 (1991-2010), and 19 (18-40) vs. 30 (26-36) years of age. Normal weight (BMI 18.5-24.9 kg/m<sup>2</sup>) is present in 67% of assessments in men and 64% in women, and obesity (BMI ≥30 kg/m²) in 5% of assessments in men and 10% in women. The low proportion of obesity in men is likely due to the, on average, young age and early calendar year at weight assessment. Information on WC is available in 152,089 men with 209,473 WC assessments and in 212,658 women with 302,800 WC assessments; 52% of these were objectively measured and 63% of individuals have at least one objectively measured WC assessment. The median (IQR) year of the 512,273 WC assessments is later than that of weight, year 2007 (1997-2012) for men and 2003 (1997-2010) for women, and the median age is higher, 57 (49-66) years in men and 51 (43-62) years in women.

#### Characteristics of repeated weight and waist circumference assessments

Individuals with two or more assessments of weight or WC, respectively, will be eligible for inclusion in studies of change of these factors, on outcomes. In these studies, we will utilise all assessments in an individual, i.e. allowing assessments to take place in different cohorts. For each assessment, age, form of assessment (objectively measured/self-reported current/self-reported recalled) and, in women, a pregnancy indicator (Medical Birth Register, yes/no) will be included as predictor variables to model weight and WC trajectories in mixed effects models<sup>10</sup>.

Out of 477,705 men and 1,263,056 women with two or more weight assessments, totaling 1,843,609 assessments in men and 3,335,194 in women, the median number of assessments is 3 (IQR 2-5) in men and 2 (IQR 2-3) in women. The much smaller number of assessments in

 men than in women is due to the lack of repeated weight assessments in the Military Conscription Register as opposed to the many assessments in the Medical Birth Register. In individuals with two or more weight assessments, the by far largest number of assessments in men originate from the Construction Workers Cohort (n=1,036,968) followed by the Cohort of Swedish Men (n=268,408) and the Military Conscription Register (n=216,585), and the by far most assessments in women are from the Medical Birth Register (n=2,435,226) followed by the Swedish Mammography Cohort (n=273,717) and Women's Lifestyle and Health (n=127,384). Out of 41,669 men and 67,126 women with two or more WC assessments, totaling 99,053 assessments in men and 157,268 in women, the median number of assessments is 2 (IQR 2-3) in men and 2 (IQR 2-2) in women. Of these, the largest number of WC assessments in men originate from the Cohort of Swedish Men (n=59,863) and the Västerbotten Intervention Programme (n=19,549), and in women from the Swedish Mammography Cohort (n=56,222) and Women's Lifestyle and Health (n=51,696).

# Follow-up time and events

The follow-up time from the first recorded current weight until emigration, death or end of follow-up for death (31 Dec. 2020) is up to 58 years, with a median (IQR) of 31.4 (21.8-40.8) years in men and 19.6 (9.3-29.0) years in women, and a median (IQR) from the first WC assessment of 13.4 (8.0-23.2) years in men and 17.1 (9.6-25.0) years in women. The total time at risk for mortality is 66.3 million person-years for men and 42.0 million person-years for women, during which 280,537 men and 121,635 women died. Amongst morbidity outcomes, cancer is of main focus in the ODDS working group. Information on the number of deaths (all-cause and cause-specific) and incident cancers (all and some site-specific) during follow-up in the full ODDS population, in individuals with two or more weight assessments for studies of weight change, and in individuals with one and two or more WC assessments, respectively, is shown in Table 4.

# Ongoing and planned studies

Several ODDS studies are ongoing or planned to start shortly on BMI, WC, and changes in weight and WC, in relation to the risk of outcomes (currently mortality and cancer). Changes in weight and WC include the investigation of changes across adulthood, and in age-spans of young, middle, and late adulthood. We further plan to investigate: i) weight fluctuations in individuals with many repeated weight assessments in relation to outcomes, ii) anthropometric measures in interaction with, and mediated through, cardiometabolic diseases (CVD,

hypertension, and type 2 diabetes) on non-CVD outcomes, iii) anthropometric measures jointly with prescribed drugs (using retrieved data and after additional register linkages) on outcomes, and iv) anthropometric measures in relation to specific cancers with detailed diagnostic information, after additional linkages to national quality registers of cancer. ODDS enables a range of further possible investigations to be done in the obesity field, based on already collected data or after additional register linkages. Further information about ODDS can be found at <a href="https://odds.blogg.lu.se">https://odds.blogg.lu.se</a>.

#### Strengths and limitations

The ODDS study has several strengths. Firstly, the population is very large and has a nationwide coverage of Swedish cohorts, which, although not completely population-based, generally have a high representativeness of their background population. Furthermore, the unique personal identity number of Swedish inhabitants enables cross identification of individuals between ODDS cohorts as well as tracking of individuals in Swedish nationwide registers. Loss to follow-up is negligible in those registers, and the objective, harmonized information on outcomes as well as on sociodemographic factors by use of national registers, is an additional major strength. The combination of anthropometric measures in the pooled population with, for example, cardiometabolic diseases and medications retrieved from national registers, enables the investigation of various risk factors jointly with anthropometrics. Lastly, the long follow-up time together with the large sample size has accumulated many events resulting in overall high statistical power and the possibility to investigate subgroups and rarer outcomes.

The study also has some limitations. Because repeated weight measurements were not performed in military conscripts, which make up the largest male cohort in ODDS, only 22% of men have repeated measurements on weight. In contrast, almost 60% of women have two or more weight measurements. Furthermore, the large heterogeneity of the study population in terms of geographical region, age, and year of weight assessment, enforces subgroup investigation, to examine whether associations differ between subgroups. The study is further limited in that information on smoking habits, an important confounder for mortality and many diseases, is missing in a large part of the population and, apart from sociodemographic information, the ODDS database has no information on potential confounders such as diet, physical activity, and other disease-specific confounders.

#### Collaboration

 The ODDS collaboration conducts research in accordance with the ethical approval of the ODDS cohort as well as approvals from the steering committee of each subcohort. New research ideas will require new approvals. Researchers interested in collaboration can contact the ODDS Principal Investigator, Tanja Stocks, for further information and discussion.

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#### **Contributors**

MdS, JF, IBM, MS, CH and TS were involved in the conception and design of the study. JW, BvG, CM, PKEM, OM, SS, WY, YTL, BN, JL, AC, NLP, SE, KI, CI, LH and HB contributed original cohort data. MdS harmonized the cohort data. IBM calculated corrected weights in the Medical Birth Register. MdS, JF, MS and TS harmonized register data. TS organized the collection of cohort and register data, analysed data, and drafted the manuscript. MdS, JF, IBM, MS, JW, PKEM, OM, SS, YTL, JL, NLP, CI, LH, HB and CH revised the manuscript. All authors made significant contributions to the manuscript and have read and approved the final version.

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#### **Competing interests**

None declared.

# **Ethics approval**

This study was approved by the Swedish Ethical Review Authority (no: 2020-03846).

# Data sharing statement

All data are located on Statistics Sweden's Microdata Online Access (MONA) server and may only be accessed from countries in the European Union or the European Economic Area. Data access for questions covered by the ethical approval will be considered in agreement with the principal investigator of ODDS, Tanja Stocks, and upon approval from relevant register holders and steering committees of ODDS cohorts.

# Figure caption

Figure 1. Cumulative number (n) of men (solid line) and women (dotted line) per calendar year, at the first objectively measured or self-reported current weight (1963-2020) or waist circumference (1981-2020), in the Obesity and Diseases Development Sweden (ODDS) study

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Table 1. Characteristics of cohorts of the Obesity and Disease Development Sweden (ODDS) study<sup>a</sup>

		N individ-	N assess-	Year 💆	6 Age in	N (%) individuals with at least one assessment of:		
Cohort	Description	uals (% male)	ments (% male)	mediag (range <u>r</u> ග	j years, median (range)	Objectively measured weight	Smoking status	Waist circum-ference
Swedish Medical Birth Register <sup>19</sup>	Includes ~98% of all births in Sweden. The mother's weight is measured at the first antenatal care visit, commonly at 8-10 gestational weeks. Since 1992, weight is missing for <15%	1,855,606 (0)	3,208,127 (0)	2003 <b>9</b> (1982-20 <b>9</b>	nseign 29 (17-54)	1,855,606 (100)	94,555 (5)	0 (0)
Swedish Military Conscription Register <sup>20</sup>	In Sweden, conscription was mandatory for men aged ~18 years until 2010 and was then voluntary until 2017. The male birth cohorts of 1951-88 cover 90% of the target population, with ≤5% missing weight before 2000	1,790,751 (99)	1,799,609 (99)	1987 <b>5.</b> (1969-20 <b>5</b> 4	18 <b>2</b> (17-58)	1,790,751 (100)	190,197 (11)	0 (0)
Construction Workers Cohort <sup>21</sup>	Construction workers were invited on a regular basis to a health checkup through a collective agreement that concerned almost all construction workers in Sweden. Attendance: ≥80%	387,545 (95)	1,149,722 (96)	1981 (1971-19 <u>9</u> 3	0 37 6 (17-82)	387,545 (100)	333,100 (86)	0 (0)
NSHDS <sup>22</sup>	Population-based cohorts in the northernmost counties of Sweden: Norrbotten and Västerbotten	138,379 (47)	254,441 (40)	2002 - (1985-20 <b>2</b> 0	50 (18-82)	132,369 (96)	131,734 (95)	97,061 (70)
VIP <sup>23</sup>	All residents of Västerbotten county are invited to a health checkup at 40, 50, and 60 years of age (and 30 years until 1996). Attendance: 48-67%	124,200 (49)	194,650 (49)	2005 <b>5</b> (1985-20 <b>3</b> 0	累 🙀 (19-70)	124,200 (100)	123,216 (99)	87,538 (70)
MONICA <sup>24</sup>	Seven health screenings aimed for research were performed in random selections (within specific ages) of residents of Norrbotten and Västerbotten counties. Attendance: 67-81% in 1986-2009	12,260 (49)	16,097 (49)	1999 <b>5</b> (1986-2 <b>0</b>	51 (24-79)	12,260 (100)	12,245 (>99)	12,235 (>99)
MSP <sup>25</sup>	A questionnaire aimed for research was filled in in connection with mammography screening offered every 2-3 years to women aged ~50-70 years in Västerbotten county. Attendance: ~85%	25,836 (0)	43,694 (0)	1999 = (1995-20 <b>2)</b>	58 (18-82)	0 (0)	20,026 (78)	0 (0)
SIMPLER <sup>26</sup>	Population-based cohorts in counties of southeastern Sweden: Uppsala, Västmanland, and Örebro	106,391 (43)	237,966 (39)	1997 <b>5</b> (1987-20-19	64 (38-103)	0 (0)	89,598 (84)	81,462 (77)
SMC	All women born 1914/1917-1948, residing in Västmanland and Uppsala counties were invited to mammography screening that included a questionnaire aimed for research, with subsequent follow-ups. Attendance at baseline: 70%	60,709 (0)	145,234 (0)	1997 <b>d</b> (1987-20 <b>d</b> )	62 (38-103)	0 (0)	44,121 (73)	40,338 (66)
COSM	All men born 1918-52 residing in Västmanland and Örebro counties were invited to fill in a research-based questionnaire, with subsequent follow-ups. Attendance at baseline: 49%	45,682 (100)	92,732 (100)	2008 ai (1997-20 <b>1</b> 5	67 (42-101)	0 (0)	45,477 (>99)	41,124 (90)
Swedish Twin Registry <sup>27 28</sup>	Research-based register on mono- and dizygotic twins across all of Sweden	97,533 (46)	154,666 (45)	1999 <b>5</b> (1963-20 <b>5</b> 4	48 (17-99)	12,360 (13)	90,182 (92)	12,328 (13)
Q63, 67, 70	All same-sex twins born 1886-1925 were invited to fill in a questionnaire (not including weight) in 1960. Follow-up questionnaires were sent out thrice during the subsequent 10 years (Q63, 67 and 70)	20,312 (44)	42,347 (41)	1967 <b>.5</b> (1963-19 <b>5</b>	53 (37-84)	0 (0)	17,986 (89)	0 (0)
Q73	All same-sex twins born 1926-58 were invited to fill in a questionnaire in 1973.  Attendance: ~83%	27,595 (48)	27,595 (48)	1973 <b>**</b> (1973-1973	29 (17-47)	0 (0)	27,507 (>99)	(0)
SALT	All twins born 1944-58 were invited to a phone interview. Attendance: ~65%	42,754 (47)	42,754 (47)	2000 (1998-2003	56 (41-99)	0 (0)	42,234 (99)	0 (0)
TwinGene	Twin pairs in SALT were invited to a follow-up investigation. Attendance: ~65%	12,360 (45)	12,360 (45)	2006 (2002-2009		12,360 (100)	12,237 (99)	12,328 (>99)
STAGE	All twin pairs born 1958-85 were invited to a web-based survey. Attendance: ~60%	23,448 (44)	23,448 (44)	2005 (2004-2006	<b>5</b> 34 (19-47)	0 (0)	23,230 (99)	0 (0)

					<u> </u>			
YATSS	All twin pairs born 1986-92 were invited to a web-based survey. Attendance:	6162	6162	2013 <u>2</u>	24 3 (20-28)	0	1988	0
17100	~42%	(40)	(40)	(2013-20 <b><u></u>5</b> 4)	සූ (20-28)	(0)	(32)	(0)
Malmö cohorts	Population-based cohorts in Malmö city in southern Sweden (MPP and MDCS)	54,876	124,442	1995 <b>5</b>	56	54,860	48,392	36,170
	and offspring of MDCS participants (MOS)	(53)	(54)	(1974-20 <u>9</u> 9)	<b>5</b> (18-85)	(>99)	(88)	(66)
	All residents of Malmö city, born in certain years, 1921-49, were invited for	33,337	59,427	1983	<b>6</b> 53	33,337	28,294	4506
MPP <sup>29 30</sup>	screening for CVD and alcohol abuse, with subsequent follow-ups of all or a	(67)	(70)	(1974-20 <b>4</b> 6 <del>)</del> m	00	(100)	(85)	(14)
	selected population. Attendance at baseline: ~71%	(01)	(10)	(1974-20 <b>G</b> O)	E (20-03)	(100)	(00)	(14)
	All residents of Malmö city, born in certain years, 1926-50, were invited to.a	30,415	60,792	1997 7 0	<b>S</b> 61	30,390	29,280	30,373
MDCS <sup>31</sup>	health examination aimed for research on diet and cancer, with subsequent	(40)	(39)	1997 <b>9.</b> (1991-20 <b>5</b> 2)	8 (44-85)	(>99)	(96)	(>99)
	follow-ups of all or a selected population. Attendance at baseline: ~41%	. ,	` ′	(1991-20025	<b>2</b> (44-05)	. ,	` '	` ′
MOS <sup>32</sup>	Children and grandchildren of a random sample of MDCS participants were	4223	4223	2016	<b>D</b> 44	4223	3799	4202
	invited to a health examination for research purposes	(48)	(48)	(2013-20 <b>3</b> 9 <b>3</b>	<b>2</b> (18-73)	(100)	(90)	(>99)
Women's	Randomly selected women born 1943-62 residing in Uppsala county were invited	48,720	82,140	1992 💆 🕏	<u> </u>	0	40,840	43,132
Lifestyle and	to fill in a questionnaire aimed for research on lifestyle and cancer and CVD, and	(0)	(0)	(1991-20 <del>0</del> 4	<b>p</b> 77 (27-61)	(0)	(84)	(89)
Health <sup>33</sup>	to one subsequent follow-up. Attendance at baseline: 51%	(0)	(0)	1992 <b>e 0</b> (1991-20 <del>0</del> 4 <b>b</b>	(27-01)	(0)	(04)	(09)
Swedish	In 1997, a fund-raising event for the Swedish Cancer Society took place in	41.710	41.710	1997 de cu (1997-1987)	52	0	35,801	31,893
National March	~3600 places across Sweden. Participants were requested to fill in a	(36)	(36)	(1997-1987	(17-93)	(0)	(86)	(76)
Cohort <sup>34</sup>	questionnaire aimed for research on lifestyle and chronic diseases	(50)	(50)	(1007-100)	B (17-33)	(0)	(00)	(70)
West Sweden	In 2008 and 2016, random selections of residents of western Sweden were	41,276	53,231	20163 🛱	51	0	40,506	0
Asthma Study <sup>35</sup>	invited to fill in a questionnaire aimed for research on asthma and respiratory	(46)	(45)	(2008-20 <b>36</b> )		(0)	(98)	(0)
7 totilila Otady	diseases. Attendance: 62% and 50%, respectively	. ,	` ,	3			` ′	` '
WICTORY <sup>36</sup>	Residents of Västmanland county, born 1940-59, were invited to a health	33,892	33,892	1994🚾 •	49	33,892	33,579	33,860
WIOTOKI	checkup at age ~40 or 50 years, aimed for CVD prevention. Attendance: ~60%	(48)	(48)	(1989-20 <b>2</b> 0)	(35-55)	(100)	(99)	(>99)
	Residents across Sweden were invited through randomization (~44%), or in	30,039	30,039	2011 <b>ត្ត</b>	33	28,861	16,407	28,861
LifeGene <sup>37</sup>	other ways, e.g. shared household with the one invited, or volunteering, to a	(41)	(41)	(2009-20 <b>5</b> 8)	(17-96)	(96)	(55)	(96)
	health examination and a web-based survey for research purposes	(41)	(+1)	(2003-2030)	(17-30)	(50)	(55)	(30)
	Randomly selected ~45-75-year-old residents of Uppsala and Malmö city were	25,337	25,337	<b>ق</b> ب <sub>2014</sub>	61	25,337	18,416	25,337
EpiHealth <sup>38 39</sup>	invited to a health examination and a web-based survey for research on gene-	(44)	(44)	(2011-20 <b>3</b> 8)	(35-78)	(100)	(73)	(100)
	diet interactions and diseases. Attendance: ~20%	(1-1)	()	(2011 2050)	(00 70)	(100)	(10)	(100)
Melanoma in	Randomly selected women with no prior cancer, ~25-64 years, residing in			<u>v</u>	<u> </u>			
Southern	Southern Sweden, were in 1990-92 invited to fill in a questionnaire (not including	22,974	22,974	2001 =	54 (35-76)	0	2399	0
Sweden <sup>40</sup>	weight) aimed for research on malignant melanoma and female cancers. A	(0)	(0)	(1999-20 <del>13</del> 4)	<b>(</b> 35-76)	(0)	(10)	(0)
	follow-up questionnaire included weight. Attendance at baseline: 74%				5			
Obstructive	In separate surveys (five in ODDS), randomly selected adults of specific ages,			ec ec	D			
Lung Disease in	residing in Norrbotten county, were invited to a health examination and follow-	12,395	15,386	2004	53	5853	12,241	0
Northern	ups, or to fill in a questionnaire (2016), aimed for research on asthma and	(49)	(49)	(1986-20 <b>3</b> 6)	53 (19-85)	(47)	(99)	(0)
Sweden <sup>41 42</sup>	respiratory diseases. Attendance at baseline: 66-91%			9	02.			

NSHDS, Northern Sweden Health and Disease Study; VIP, Västerbotten Intervention Programme; MONICA, Monitoring of Trends of Cardiovas plan disease study in Northern Sweden; MSP, Mammography Screening Project; SIMPLER, Swedish Infrastructure for Medical Population-Based Life-Course and Environmental Research; MC, Swedish Mammography Cohort; COSM, Cohort of Swedish Men; SALT, Screening Across the Lifespan Twin Study; STAGE, Study of Twin Adults: Genes and Environment; YATSS, Young Adult Tyns in Sweden Study; MPP, Malmö Preventive Project; CVD, cardiovascular disease; MDCS, Malmö Diet and Cancer Study; MOS, Malmö Offspring Study; WICTORY, Westmannia Cardiovascular Risk Factors Study.

aThe numbers include overlap of individuals between cohorts, and only objectively measured or self-reported current weight. Recalled weight is available in 225,331 individuals with 500,219 recalled weights in: SIMPLER, Swedish Twin Registry (Q67 and Q70), MDCS, MOS, Women's Lifestyle and Health, Swedish National March Cohort, EpiHealth, and Melanoma in Southern Sweden, included

in Table 3.

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Table 2. Information on Swedish national registers with linkage to the Obesity and Disease Development Sweden (ODDS) study population

Swedish register	Description	Type of information retrieved 56 on 5	Years covered in ODDS	Coverage of target population
The Cancer Register <sup>17 18</sup>	Contains information on histologically, cytologically or clinically diagnosed, or by autopsy verified (excluding death certificate only) malignant tumours, and certain benign, premalignant and borderline tumours, in Sweden	Date and type of cancer diagnosis, including international Classification of Diseases topography code, histopathology (Swedish SNOMED and PAD codes), and TNM status (recorded since 2004)	1958-2019	96% in the year 1998 <sup>17</sup> , which appears to be stable over time
The Cause of Death Register <sup>16</sup>	Contains information on deaths and death causes in Sweden, in electronic form since 1952. The death cause is usually determined by the treating physician or the physician last seeing the patient before death	Date of death and underlying and contributing of countributing and contributing of countributing of countrib		>99%, and 96% of the underlying cause of death (>99% of deaths in ODDS)
The Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) <sup>51</sup>	Contains information from a range of sources on education, occupation, income and employment in all residents of Sweden aged ≥16 years (≥15 years since 2010)	Highest attained education. Occupation, income and main source of income (recorded since mining).	1990-2019	>99% overall, 98% for education in 25-64 year old individuals
The National Diabetes Register <sup>52</sup>	Contains information on diabetes diagnoses (all types) and other information, such as complications and treatment, of diabetes patients aged ≥18 years in outpatient specialist clinics and in primary healthcare in Sweden	Date and type of diabetes diagnosis and treatment	1996-2020	Increased coverage over time; ~90% of Swedish adults with diabetes in 2015
The National Prostate Cancer Register <sup>54 55</sup>	Contains information on biopsy-confirmed prostate cancer diagnoses, tumour characteristics, and primary treatment of prostate cancer patients in Sweden	Date, TNM status, prostate-specific antigen level, and Gleason score at diagnosis, and the main reason for detection (recorded since 2004). Primary treatment, date of radical prostatection (recorded since 2007), and T status, Gleason score and positive margins (yes/no) after radical prostatectomy	1998-2021 (June)	98% of prostate cancer diagnoses in the National Cancer Register in 1998-2012
The Patient Register <sup>56 57</sup>	Contains information on diagnoses of inpatient care in Sweden, recorded since 1987, and of specialist outpatient care, recorded since 1997 for surgical care and since 2001 for other outpatient care	Date and type of diagnosis according to the object of the Charlson Comorbidity index <sup>50</sup>	1987-2020	Since 1987, >99% of inpatient care, and in 2001-2006, 71% of outpatient somatic care
The Population and Housing Census <sup>51</sup>	Contains sociodemographic information through self- reported questionnaires mailed to the full Swedish population aged ≥16 years, with mandatory response	Highest attained education, county of residence, and marital status	Every five years in 1960-1990	≥99% in 1960-1985, 97.5% in 1990 <sup>a</sup>

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The Prescribed Drug Register <sup>58</sup>	Contains information on all prescribed drugs dispensed at pharmacies in Sweden. Excludes over-the-counter drugs	Date of prescribing and dispensing, type of aug (e.g. ATC code and product name), dispensed amount and dosage, of antidiabetic, antihypertensive, and antilipidemic drugs		>95% of all utilised drugs in Sweden, excluding over-the-counter drugs
The Total Population Register <sup>59</sup>	Contains basic demographic information on all residents of Sweden	Birth date (year and quarter of year), country of birth for the individual and parents (four categories, see Table 2), county of residence, marital status, and date/-s of immigration and emigration	1968-2020	>99% of births and deaths, 95% of immigrations, 91% of emigrations, resulting in a slight over-coverage
The Swedish Social Insurance Agency <sup>60</sup>	Contains information on sick leave for periods exceeding 14 days, and of disability pension, for individuals in Sweden with income from work or unemployment benefits, which qualify and apply for sickness absence or disability pension benefits. The first 14 days of sick leave is compensated by the employer and is not recorded by the Social Insurance Agency	Date, length, and type of sick-leave according to the length of the leave according to the	1994-2021	No data available <sup>b</sup>

<sup>&</sup>lt;sup>a</sup>Personal communication with Beatrice Kalnins, Statistics Sweden.

<sup>&</sup>lt;sup>b</sup>Personal communication with Charlotte Limé, the Swedish Social Insurance Agency.

Table 3. Characteristics of all assessments in the Obesity and Disease Development Sweden (ODDS) study, in a total of 4,295,859 unique individuals and separately in 2,165,048 men and 2,130,811 women

Characteristic	Total (N assess- ments=7,733,901)	Men (N assess- ments=3,530,952)	Women (N assess- ments=4,202,949)
Assessments, median no. (IQR)	1 (1-2)	1 (1-1)	2 (1-2)
Year	1 (1 2)	1 (1 1)	2(12)
Median (IQR)	1993 (1983-2005)	1985 (1977-1994)	2001 (1991-2010)
N (%)	1000 (1000 2000)	1000 (1011 1001)	2001 (1001 2010)
1911-1959 <sup>a</sup>	102,331 (1)	49,817 (1)	52,514 (1)
1960-1969	159,059 (2)	70,493 (2)	88,566 (2)
1970-1979	1,118,503 (15)	1,011,194 (29)	107,309 (2)
1980-1989	1,866,055 (24)	1,128,163 (32)	737,892 (18)
1990-1999	1,775,421 (23)	780,028 (22)	995,393 (24)
2000-2009	1,470,566 (19)	365,475 (10)	1,105,091 (26)
≥2010	1,241,966 (16)	125,782 (4)	1,116,184 (27)
Age (years)	, ,		
Median (IQR)	28 (19-37)	19 (18-40)	30 (26-36)
N (%)	, ,		
17-19	1,941,872 (25)	1,780,928 (50)	160,944 (4)
20-29	2,222,093 (29)	417,774 (12)	1,804,319 (43)
30-39	1,858,853 (24)	373,384 (11)	1,485,469 (35)
40-49	661,048 (9)	375,880 (11)	285,168 (7)
50-59	570,068 (7)	337,970 (9)	232,098 (5)
60-69	324,381 (4)	174,004 (5)	150,377 (4)
≥70	155,586 (2)	71,012 (2)	84,574 (2)
Weight (kg), median (IQR)	68 (61-77)	73 (66-81)	64 (58-72)
Form of weight assessment, N (%)			
Objectively measured	6,579,779 (85)	3,097,486 (88)	3,482,293 (83)
Self-reported current weight	653,903 (8)	207,579 (6)	446,324 (11)
Self-reported recalled weight	500,219 (7)	225,887 (6)	274,332 (6)
Height (cm), median (IQR)	171 (165-178)	178 (174-183)	166 (162-170)
Body mass index (kg/m²)		,	
Median (IQR)	23.1 (21.0-25.7)	22.9 (20.9-25.4)	23.2 (21.2-26.1)
N (%) <sup>b</sup>			
Underweight (<18.5)	305,069 (4)	160,666 (5)	144,403 (3)
Normal weight (18.5-24.9)	5,040,375 (65)	2,378,070 (67)	2,662,305 (63)
Overweight (25-29.9)	1,792,975 (23)	826,610 (23)	966,365 (23)
Obesity class I (30-34.9)	429,028 (6)	137,401 (4)	291,627 (7)
Obesity class II and III (≥35)	129,392 (2)	23,465 (1)	105,927 (3)
Missing	37,062 (<1)	4740 (<1)	32,322 (1)
Waist circumference (cm)	, ,		
Median (IQR)	88 (79-97)	96 (89-103)	82 (75-90)
N (%) <sup>b</sup>			
Low (men, <94; women, <80)	210,489 (3)	86,426 (2)	124,063 (3)
Medium (men, 94-101.9; women, 80-87.9)	143,891 (2)	64,225 (2)	79,666 (2)
High (men, ≥102; women, ≥88)	157,893 (2)	58,822 (2)	99,071 (2)
Missing	7,221,628 (93)	3,321,479 (94)	3,900,149 (93)
Smoking status, N (%)			
Never	1,334,569 (17)	794,267 (23)	540,302 (13)
Former	679,222 (9)	432,751 (12)	246,471 (6)
Current	842,369 (11)	613,139 (17)	229,230 (5)
Missing	4,877,741 (63)	1,690,795 (48)	3,186,946 (76)
Marital status, N (%) <sup>c</sup>			
Unmarried	4,092,269 (53)	2,297,106 (65)	1,795,163 (43)
Married	3,102,435 (40)	1,048,593 (30)	2,053,842 (49)
Divorced	349,667 (5)	117,091 (3)	232,576 (5)
Widow/-er	88,954 (1)	23,535 (1)	65,419 (2)
Missing	100,576 (1)	44,627 (1)	55,949 (1)
County of residence, N (%)°	, - \ /	, , ,	, - , ,
Stockholm	1,253,881 (16)	481,693 (14)	772,188 (18)
Västra Götaland	1,136,238 (15)	521,656 (15)	614,582 (15)
Skåne	993,581 (13)	451,103 (13)	542,478 (13)

Västmanland	467,638 (6)	219,591 (6)	248,047 (6)
Västerbotten	439,512 (5)	203,544 (6)	235,968 (6)
Uppsala	382,360 (5)	102,044 (3)	280,316 (7)
Other counties	3,060,691 (39)	1,502,928 (42)	1,449,729 (34)
Missing	108,034 (1)	48,393 (1)	59,641 (1)
Highest achieved education (one assessment per individual), N (%) <sup>d</sup>			
Pre-upper secondary school <9 years	280,244 (7)	167,940 (8)	112,304 (5)
Pre-upper secondary school 9 years	366,211 (9)	215,953 (10)	150,258 (7)
Upper secondary school max. 2 years	1,030,829 (24)	578,620 (27)	452,209 (21)
Upper secondary school 3 years	880,747 (20)	455,344 (21)	425,403 (20)
Post-upper secondary school <3 years	613,421 (14)	299,872 (14)	313,549 (15)
Post-upper secondary school ≥3 years	1,020,461 (24)	393,934 (18)	626,527 (30)
PhD degree	52,219 (1)	28,056 (1)	24,163 (1)
Missing	51,727 (1)	25,329 (1)	26,398 (1)
Country of birth (one assessment per individual), N (%) <sup>e</sup>			
Born in Sweden, both parents born in Sweden	3,367,487 (78)	1,842,225 (85)	1,525,262 (72)
Born in Sweden, one parent born in Sweden	295,156 (7)	156,744 (7)	138,412 (6)
Born in Sweden, both parents born abroad	121,237 (3)	58,840 (3)	62,397 (3)
Born abroad	511,469 (12)	107,147 (5)	404,322 (19)
Missing	510 (<1)	92 (<1)	418 (<1)
QR, interquartile range.			

<sup>&</sup>lt;sup>a</sup>Includes only recalled weight assessments.

<sup>&</sup>lt;sup>b</sup>Categories according to the World Health Organization<sup>61 62</sup>.

<sup>&</sup>lt;sup>c</sup>From the Population and Housing Census in 1960 and 1965, and from the Register of the Total Population in 1968 onwards. Married, divorced and widow/-er also include registered partners, recorded as of 1998. Fifteen "other counties" each made up <5% of the total.

dHighest achieved education through follow-up, retrieved from the Population and Housing Census in 1970, and from the Longitudinal Integration Database for Health Insurance and Labour Market Studies in 1990 onwards. eFrom the Register of the Total Population.

Table 4. Number of individuals, deaths, and incident cancers during follow-up according to anthropometric measure in the Obesity and Disease Development Sweden (ODDS) study

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Anthropometric measure	N individuals		N de	eaths	N incident cancers		
Anthropometric measure	Men	Women	Men	Women	<del>മ</del> ് 6 Men	Women	
Weight (full population)			280,537 all-cause	121,635 all-cause	<b>წ <sub>ლ</sub>19</b> 7,168 all cancer	144,413 all cancer	
			98,796 CVD	35,198 CVD	<b>♀ ;; ₹</b> 2,027 prostate	50,732 breast	
	2,165,048	2,130,811	78,178 cancer	45,744 cancer	କ୍ରି ଓ 11,448 colon କୁ ଲୁଞ୍ଜୁ small intestine	7920 colon	
			15,325 respiratory	7174 respiratory	क्र डु9 <b>§</b> 3 small intestine	530 small intestine	
			system	system	658 penis	742 vulva	
≥2 weight assessments	477,705	1,263,056	133,073 all-cause	62,245 all-cause	₹ <b>9 %</b> 4,205 all cancer	70,697 all cancer	
Waist circumference	152,089	212,658	37,155 all-cause	35,951 all-cause	± 26,619 all cancer	28,296 all cancer	
≥2 waist circumference assessments	41,669	67,126	9890 all-cause		25 20 20 20 20 20 20 20 20 20 20 20 20 20	7321 all cancer	

CVD, cardiovascular diseases.

