



RESEARCH: EPIDEMIOLOGY

Undiagnosed diabetes: Prevalence and cardiovascular risk profile in a population-based study of 52,856 individuals. The HUNT Study, Norway

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ABSTRACT

Aims: We investigated the current extent of undiagnosed diabetes and prediabetes and their associated cardiovascular risk profile in a population-based study.

Methods: All residents aged ≥ 20 years in the Nord-Trøndelag region, Norway, were invited to the HUNT4 Survey in 2017–2019, and 54% attended. Diagnosed diabetes was self-reported, and in those reporting no diabetes HbA1c was used to classify undiagnosed diabetes (≥ 48 mmol/mol [6.5%]) and prediabetes (39–47 mmol/mol [5.7%–6.4%]). We estimated the age- and sex-standardized prevalence of these conditions and their age- and sex-adjusted associations with other cardiovascular risk factors.

Results: Among 52,856 participants, the prevalence of diabetes was 6.0% (95% CI 5.8, 6.2), of which 11.1% were previously undiagnosed (95% CI 10.1, 12.2). The prevalence of prediabetes was 6.4% (95% CI 6.2, 6.6). Among participants with undiagnosed diabetes, 58% had HbA1c of 48–53 mmol/mol (6.5%–7.0%), and only 14% (i.e., 0.1% of the total study population) had HbA1c > 64 mmol/mol (8.0%).

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Compared with normoglycaemic participants, those with undiagnosed diabetes or prediabetes had higher body mass index, waist circumference, systolic blood pressure, triglycerides and C-reactive protein but lower low-density lipoprotein cholesterol (all $p < 0.001$). Participants with undiagnosed diabetes had less favourable values for every measured risk factor compared with those with diagnosed diabetes.

Conclusions: The low prevalence of undiagnosed diabetes suggests that the current case-finding-based diagnostic practice is well-functioning. Few participants with undiagnosed diabetes had very high HbA1c levels indicating severe hyperglycaemia. Nonetheless, participants with undiagnosed diabetes had a poorer cardiovascular risk profile compared with participants with known or no diabetes.

KEYWORDS

diabetes mellitus, epidemiology, glycated haemoglobin A, heart disease risk factors, prediabetic state, prevalence, undiagnosed diseases

1 | INTRODUCTION

A challenge in diabetes care is the long-lasting asymptomatic diabetes stage during which vascular complications may develop unnoticed. Studies have suggested that 22%–25% of diabetes patients are undiagnosed in European countries,^{1–6} and the International Diabetes Federation (IDF) estimated this proportion to be as high as 41% in Europe in 2019.⁷ Such a large extent of undiagnosed diabetes could call for more systematic screening. However, most evidence on the extent of undiagnosed diabetes predates the establishment of glycated haemoglobin (HbA1c) as the routine diagnostic test,⁸ which may possibly have contributed to increased case-finding and a corresponding decrease in the proportion of undiagnosed cases. Elevated HbA1c levels below the diagnostic threshold for diabetes (prediabetes) also indicate increased risk of vascular diseases,^{9,10} and detecting this condition may be an opportunity to initiate lifestyle change, prevent diabetes and improve health outcomes.¹¹ To examine the current burden of undiagnosed diabetes and prediabetes in a general adult population, we estimated the prevalence of these hyperglycaemic conditions and their associated sociodemographic and cardiovascular characteristics in the population-based HUNT4 Survey in Norway.

2 | METHODS

2.1 | Participants

The Trøndelag Health Study (HUNT, <https://www.ntnu.edu/hunt>) is an ongoing population-based study in Norway that includes four comprehensive health

Novelty Statement

What is already known?

- Undiagnosed diabetes is assumed to be common, but there is limited data after HbA1c was established as the routine diagnostic test.

What has this study found?

- Among 52,856 participants in a population-based survey, 0.7% had HbA1c-detected undiagnosed diabetes (HbA1c ≥ 48 mmol/mol [6.5%]). Among these, 14% had HbA1c > 64 mmol/mol (8.0%).
- Of participants with diabetes, 11% were undiagnosed.
- Participants with undiagnosed diabetes had a more adverse cardiovascular risk profile compared with those with diagnosed diabetes.

What are the implications of the study?

- Low prevalence of undiagnosed diabetes reduces the rationale for systematic diabetes screening in this region.

surveys conducted at 10-year intervals during 1984–2019.^{12,13} We used data from HUNT4, conducted in August 2017–February 2019. The entire population of the Nord-Trøndelag region in Norway ≥ 20 years of age was invited, and 56,042 (54%) participated. The Nord-Trøndelag region has a demographic structure fairly representative to that

of Norway as a whole, except from lacking larger cities, and having an ethnically more homogenous population.

2.2 | Data collection

HUNT4 included extensive health and lifestyle questionnaires, clinical examinations, and non-fasting blood sampling, conducted by specially trained health personnel at field stations in each of the 23 municipalities in the region. From questionnaires that were mailed to participants and answered in hardcopy or online, we retrieved information on highest completed education level (≤ 10 , 11–13 or ≥ 14 years), family history of diabetes (first-degree relative; second, but no first-degree relative; or no relative with diabetes), history of cardiovascular disease (angina pectoris, myocardial infarction, atrial fibrillation or stroke), physical inactivity (leisure-time physical activity less than or equal to once per week on average), smoking (never, former or current daily smoking) and use of anti-hypertensive and lipid-lowering prescription drugs.

Height and weight were measured and body mass index (BMI, weight in kilograms divided by the squared value of height in meters) was calculated. Waist circumference was estimated by an InBody 770 body composition analyser using bioelectrical impedance, a technique that estimates various aspects of body composition based on the difference in water content and resistance of different body tissues. Waist circumference measured by bioelectrical impedance has been found to be valid compared with manual measurements.¹⁴ Blood pressure was measured three times, and we used the mean value of the second and third measurements, or either the second or third if one of them was missing. Non-fasting blood samples were collected and handled at the field stations according to appropriate standards, transferred to the HUNT biobank every evening in a cold chain, and delivered to the accredited laboratory at Levanger Hospital the following day for immediate analyses on an Abbott Architect ci8200. HbA1c was measured using an International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) standardized method where HbA1c and haemoglobin were measured in non-fasting whole blood samples using enzymatic methods (Reagent kit; 4P52-21 Haemoglobin A1c, Multigent, Abbott Laboratories, USA). Total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, C-reactive protein (CRP) and creatinine were measured in serum samples. We estimated low-density lipoprotein (LDL) cholesterol levels using the Sampson equation¹⁵ and glomerular filtration rate (eGFR) using the CKD-EPI equation.¹⁶ We calculated the Finnish Diabetes Risk Score (FINDRISC)¹⁷ using the same variables and scoring system as previously described,¹⁸ except that we used leisure

time physical activity >1 time/week (yes, 0; no, 2 points) as a proxy for the item 'daily physical activity of ≥ 30 min'.

2.3 | Classification of diabetes and prediabetes

History of diabetes was assessed with the question 'Have you had, or do you have any of the following diseases?', followed by a short list of diseases, including diabetes, and the alternatives of answering 'yes' or 'no'. We classified participants as having diagnosed diabetes (indicated by self report), undiagnosed diabetes (no self reported diabetes and having an HbA1c ≥ 48 mmol/mol [6.5%]), prediabetes (no self reported diabetes and having HbA1c 39–47 mmol/mol [5.7%–6.4%]),¹⁹ or normoglycaemia (no self reported diabetes and having HbA1c ≤ 38 mmol/mol [5.6%]). In additional analyses, we used an alternative definition for prediabetes: HbA1c 42–47 mmol/mol [6.0%–6.4%] and no self reported diabetes.²⁰

2.4 | Statistical analysis

Among 56,042 participants, we excluded 927 who did not answer the question on previous diabetes diagnosis in the HUNT4 questionnaire and 2259 with missing HbA1c values, leaving 52,856 participants for analysis. We estimated the prevalence of diagnosed, undiagnosed and total diabetes and prediabetes, and the proportion of diabetes that was previously undiagnosed. To account for the impact of differential participation by age and sex, we calculated age- and sex-standardized prevalence estimates using weights equal to the inverse probability of participation, calculated based on information on the adult population in Nord-Trøndelag in 2017, from Statistics Norway (<https://www.ssb.no/home>). We investigated whether participation in the previous HUNT survey (HUNT3, 2006–2008) could have influenced the estimates by comparing the proportion of undiagnosed diabetes and the prevalence of prediabetes between participants and nonparticipants of HUNT3.

To investigate differences in prevalence of diabetes and prediabetes according to established risk factors for diabetes, we used log-binomial regression to estimate age- and sex-adjusted (using 10-year age groups) prevalence ratios of each of the hyperglycaemic conditions according to age, sex, education level, family history of diabetes and BMI. Furthermore, to investigate the utility of the FINDRISC as a screening tool for undiagnosed diabetes and prediabetes, we used receiver operating characteristic (ROC) curve analysis to calculate the C-statistic, and we calculated the sensitivity, specificity and positive and negative predictive values for the recommended cut-off point of FINDRISC ≥ 15 out of 26.

To compare the cardiovascular risk factor profile in participants with diabetes or prediabetes to that of participants with normoglycaemia, we used linear regression to estimate age- and sex-adjusted mean differences in continuous risk factors and additive binomial regression to estimate differences in proportion for categorical risk factors. In cases when the additive binomial regression model failed to converge, we calculated differences in proportion for categorical risk factors based on predicted mean probabilities from a logistic regression model using Stata's `adjrr` command. Similarly, we estimated mean differences in cardiovascular risk factors between participants with undiagnosed and diagnosed diabetes, using diagnosed diabetes as the reference group. In the analyses of cardiovascular risk factors, participants aged ≥ 75 years were excluded because treatment intensity for prevention of cardiovascular disease in older patients to a larger degree will be individualized.

Analyses were performed using Stata software (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

2.5 | Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics and the Norwegian Data Protection Authority, and all participants gave informed consent. To ensure appropriate follow-up of participants with abnormal HbA1c measurements, those with undiagnosed diabetes were recommended to consult their general practitioner within 1 month, and participants < 65 years with HbA1c of 42–47 mmol/mol were recommended to consult their general practitioner within 6 months.

3 | RESULTS

3.1 | Prevalence of undiagnosed diabetes and prediabetes

Characteristics of the study population are presented in Table 1. Among 52,856 participants, 6.0% reported diagnosed diabetes, 0.7% had HbA1c-detected undiagnosed diabetes (HbA1c ≥ 48 mmol/mol [6.5%]) and 7.3% had prediabetes (HbA1c 39–47 mmol/mol [5.7%–6.4%], Table 2). The age- and sex-standardized prevalence estimates, accounting for differential participation by age and sex, were 5.3% (95% CI 5.1, 5.5) for diagnosed diabetes, 0.7% (95% CI 0.6, 0.7) for undiagnosed diabetes and 6.4% (95% CI 6.2, 6.6) for prediabetes. Among participants with undiagnosed diabetes, 58% had HbA1c ≤ 53 mmol/mol

(7.0%) and 14% (i.e., 0.1% of the total study population) had HbA1c > 64 mmol/mol (8.0%). Thirty-nine percent of participants with undiagnosed diabetes were ≥ 70 years of age (Table S1). In participants with diagnosed diabetes, the median duration since diabetes diagnosis, calculated from self-reported age at diagnosis, was 11.3 years (IQR 5.3, 18.6). When applying the alternative definition of prediabetes (HbA1c 42–47 mmol/mol [6.0%–6.4%]), its age- and sex-standardized prevalence was 1.9% (95% CI 1.8, 2.0, $n = 1132$).

For all hyperglycaemic conditions, the prevalence increased with advancing age (Figure 1), was higher in men than in women, increased with larger BMI, decreased with higher education level and was higher in participants with a first-degree relative with diabetes (Table 2). Of the total diabetes cases (diagnosed and undiagnosed), the proportion of undiagnosed diabetes was 10.8% (95% CI 9.8, 11.9), and when applying inverse probability weights, the age- and sex-standardized estimated proportion of undiagnosed diabetes was 11.1% (95% CI 10.1, 12.2). This proportion was slightly higher in men than in women, higher in those with no family history of diabetes compared with those with a first-degree family member with diabetes and similar across age groups and education levels (Table 2). The prevalence of prediabetes and the proportion of undiagnosed diabetes did not substantially differ by participation status in the 2006–2008 HUNT3 Survey (Table S2).

3.2 | FINDRISC for detecting undiagnosed diabetes and prediabetes

The C-statistic of the FINDRISC to detect undiagnosed diabetes was 83% (95% CI 80, 85), with sensitivity 61% (95% CI 55, 66), specificity 84% (95% CI 84, 84), positive predictive value 3% (95% CI 2, 3) and negative predictive value 99.7% (95% CI 99.6, 99.7) for FINDRISC ≥ 15 . For detection of undiagnosed diabetes or prediabetes the C-statistic was 77% (95% CI 76, 78), with sensitivity 45% (95% CI 43, 47), specificity 86% (95% CI 86, 87), positive predictive value 22% (95% CI 21, 23) and negative predictive value 95% (95% CI 95, 95) for FINDRISC ≥ 15 .

3.3 | Cardiovascular risk factors

Compared with normoglycaemic participants, those with diagnosed diabetes, undiagnosed diabetes and prediabetes had higher age- and sex-adjusted BMI (+3.0, +4.4 and +3.1 kg/m², respectively), wider waist circumference (+8.5, +13.1 and +9.3 cm), higher systolic blood pressure (+1.8, +5.6 and +2.9 mmHg), lower HDL cholesterol

TABLE 1 Demographic characteristics and HbA1c level by diabetes status

	Diagnosed diabetes	Undiagnosed diabetes ^a	Prediabetes ^b	Normoglycaemia
No. of participants, <i>n</i>	3170	385	3850	48,169
Age, years, median (IQR)	68 (59, 75)	67 (58, 74)	69 (61, 76)	53 (39, 66)
Sex, <i>n</i> (%)				
Women	1495 (47)	144 (37)	1771 (46)	25,538 (56)
Men	1675 (53)	241 (63)	2079 (54)	19,913 (44)
Education level, <i>n</i> (%)				
≤10 years completed	702 (22)	87 (23)	847 (22)	4377 (10)
11–13 years completed	1592 (51)	186 (49)	1983 (52)	22,155 (49)
≥14 years completed	837 (27)	105 (28)	973 (26)	18,544 (41)
Family history of diabetes, <i>n</i> (%)				
No first- or second-degree relative with diabetes	796 (25)	156 (41)	1839 (48)	24,864 (55)
First-degree relative	1946 (61)	168 (43)	1466 (38)	10,819 (24)
Second-degree, but no first-degree relative	428 (14)	61 (16)	545 (14)	9765 (21)
HbA1c, median (IQR)				
mmol/mol	50 (43, 58)	52 (49, 58)	40 (39, 42)	33 (31, 35)
%	6.7 (6.1, 7.5)	6.9 (6.6, 7.5)	5.8 (5.7, 6.0)	5.2 (5.0, 5.4)
HbA1c distribution within diabetes group, <i>n</i> (%)				
<48 mmol/mol (6.5%)	1315 (42)	-	-	-
48–53 mmol/mol (6.5–7.0%)	704 (22)	224 (58)	-	-
54–64 mmol/mol (7.1–8.0%)	747 (24)	106 (28)	-	-
>64 mmol/mol (8.0%)	404 (13)	55 (14)	-	-

Abbreviation: HbA1c, glycated haemoglobin.

^aUndiagnosed diabetes: HbA1c ≥48 mmol/mol (6.5%) and no self report of diabetes.

^bPrediabetes: HbA1c 39–47 mmol/mol (5.7%–6.4%) and no self report of diabetes.

(−0.2, −0.3 and −0.2 mmol/l), higher triglycerides (+0.5, +1.1 and +0.5 mmol/l) and higher CRP (+0.9, +2.7 and +1.2 mg/l), but lower LDL cholesterol (−0.8, −0.3 and −0.1 mmol/l, all $p < 0.001$, Figure 2 and Table S3). They were more likely to be prescribed anti-hypertensive or lipid-lowering drugs, to have a history of cardiovascular disease, and to be physically inactive (Table 3). Compared with those with diagnosed diabetes, participants with undiagnosed diabetes had more adverse values for every measured cardiovascular risk factor, but slightly higher eGFR, and they were more likely to surpass clinical treatment thresholds for systolic blood pressure and LDL cholesterol (Table S4).²¹

4 | DISCUSSION

In this large Norwegian population-based study, the prevalence of HbA1c-detected undiagnosed diabetes was 0.7%,

and only 0.1% of the study population had severe undetected hyperglycaemia with HbA1c >64 mmol/mol (8%). However, participants with undiagnosed diabetes had a less favourable cardiovascular risk profile compared with those with diagnosed diabetes.

The diabetes prevalence of 6.0% is comparable with or slightly lower than the prevalence in other Western European countries,^{1,2,5} whereas the 6.4% prevalence of prediabetes is low compared with previous prevalence estimates of 9%–28% in studies using the same definition as our study (HbA1c 39–47 mmol/mol [5.7%–6.4%]).^{1,23,26} The proportion of diabetes cases that were undiagnosed of 11% is low compared with previous reports of 22%–25%,^{1–6} and far lower than IDF estimates from 2019 of 41% undiagnosed diabetes in Europe.⁷ Nonetheless, several studies report declining proportions of undiagnosed diabetes,^{2,4,24,25} and two population-based studies from 2020 from Denmark and Greece found only 12% and 9% of patients with diabetes being undiagnosed, respectively.^{22,26}

TABLE 2 Prevalence and adjusted prevalence ratios of diabetes and prediabetes by sex, age, family history of diabetes, education level and body mass index

Demographic characteristic	Prediabetes ^a		Undiagnosed diabetes ^b		Diagnosed diabetes		Proportion undiagnosed ^c	
	Prevalence, % (95% CI)	Prevalence ratio (95% CI)	Prevalence, % (95% CI)	Prevalence ratio (95% CI)	Prevalence, % (95% CI)	Prevalence ratio (95% CI)	Proportion, % (95% CI)	Proportion, % (95% CI)
Overall	7.3 (7.1, 7.5)		0.7 (0.7, 0.8)		6.0 (5.8, 6.2)		10.8 (9.8, 11.9)	
Sex								
Women	6.1 (5.8, 6.4)	1 (reference)	0.5 (0.4, 0.6)	1 (reference)	5.2 (4.9, 5.4)	1 (reference)	8.8 (7.5, 10.3)	
Men	8.7 (8.3, 9.1)	1.4 (1.3, 1.4)	1.0 (0.9, 1.1)	2.0 (1.6, 2.4)	7.0 (6.7, 7.3)	1.3 (1.2, 1.4)	12.6 (11.1, 14.2)	
Age group, years								
20–29	0.3 (0.2, 0.5)	0.1 (0.1, 0.2)	0.02 (0.00, 0.1)	0.05 (0.01, 0.4)	0.9 (0.7, 1.2)	0.3 (0.3, 0.5)	1.8 (0.1, 9.7)	
30–39	0.8 (0.6, 1.1)	0.3 (0.2, 0.5)	0.2 (0.1, 0.3)	0.5 (0.3, 1.1)	1.8 (1.5, 2.2)	0.7 (0.5, 0.8)	9.5 (5.0, 16.1)	
40–49	2.5 (2.2, 2.8)	1 (reference)	0.4 (0.2, 0.5)	1 (reference)	2.7 (2.4, 3.1)	1 (reference)	11.5 (7.9, 15.9)	
50–59	6.0 (5.5, 6.4)	2.4 (2.0, 2.8)	0.8 (0.6, 1.0)	2.2 (1.4, 3.3)	4.7 (4.3, 5.2)	1.7 (1.5, 2.0)	14.0 (11.2, 17.1)	
60–69	11.3 (10.7, 11.9)	4.5 (3.9, 5.2)	1.0 (0.9, 1.2)	2.9 (2.0, 4.4)	8.6 (8.1, 9.2)	3.1 (2.7, 3.6)	10.7 (8.9, 12.7)	
70–79	14.4 (13.6, 15.2)	5.7 (4.9, 6.6)	1.2 (1.0, 1.5)	3.5 (2.3, 5.2)	12.0 (11.3, 12.7)	4.4 (3.8, 5.0)	9.2 (7.5, 11.1)	
80–89	19.0 (17.5, 20.5)	7.6 (6.5, 8.9)	1.8 (1.3, 2.3)	5.0 (3.2, 7.8)	13.0 (11.8, 14.3)	4.8 (4.1, 5.6)	11.8 (8.9, 15.4)	
≥90	20.0 (16.3, 24.1)	8.3 (6.6, 10.4)	1.9 (0.8, 3.6)	5.3 (2.4, 11.5)	11.9 (9.0, 15.3)	4.5 (3.3, 5.9)	13.4 (6.0, 25.0)	
Family history of diabetes								
No relative with diabetes	6.6 (6.4, 6.9)	1 (reference)	0.6 (0.5, 0.7)	1 (reference)	2.9 (2.7, 3.1)	1 (reference)	16.4 (14.1, 18.9)	
First-degree relative	10.2 (9.7, 10.7)	1.3 (1.2, 1.4)	1.2 (1.0, 1.4)	1.9 (1.5, 2.3)	13.5 (13.0, 14.1)	4.2 (3.9, 4.5)	8.0 (6.8, 9.2)	
Second-degree, but no first-degree relative	5.0 (4.6, 5.5)	1.0 (0.9, 1.1)	0.6 (0.4, 0.7)	1.3 (1.0, 1.7)	4.0 (3.6, 4.4)	1.7 (1.5, 1.9)	12.5 (9.7, 15.7)	
Education level, years completed								
≤10	14.1 (13.2, 15.0)	1.5 (1.4, 1.6)	1.4 (1.2, 1.8)	1.8 (1.3, 2.4)	11.7 (10.9, 12.5)	1.6 (1.5, 1.8)	11.0 (8.9, 13.4)	
11–13	7.7 (7.3, 8.0)	1.3 (1.2, 1.4)	0.7 (0.6, 0.8)	1.2 (0.9, 1.5)	6.1 (5.9, 6.4)	1.3 (1.2, 1.4)	10.5 (9.1, 12.0)	
≥14	4.7 (4.4, 5.0)	1 (reference)	0.5 (0.4, 0.6)	1 (reference)	4.1 (3.8, 4.4)	1 (reference)	11.2 (9.2, 13.3)	
Body mass index, kg/m ²								
<25	3.2 (2.9, 3.5)	1 (reference)	0.2 (0.1, 0.2)	1 (reference)	2.9 (2.6, 3.1)	1 (reference)	5.2 (3.5, 7.4)	
25–30	7.4 (7.0, 7.8)	1.8 (1.7, 2.0)	0.7 (0.6, 0.8)	3.2 (2.1, 4.8)	5.7 (5.4, 6.0)	1.6 (1.5, 1.8)	10.3 (8.8, 12.0)	
30–35	11.6 (10.9, 12.2)	3.0 (2.7, 3.3)	1.4 (1.2, 1.7)	7.1 (4.7, 10.7)	9.5 (8.9, 10.1)	2.8 (2.5, 3.1)	13.0 (11.0, 15.2)	
≥35	15.4 (14.2, 16.7)	4.6 (4.1, 5.1)	2.2 (1.7, 2.8)	13.1 (8.5, 20.2)	13.3 (12.2, 14.5)	4.4 (3.9, 5.0)	14.2 (11.3, 17.5)	

Note::: Prevalence ratios are adjusted for age and sex.

^aPrediabetes: HbA1c 39–47 mmol/mol (5.7%–6.4%) and no self report of diabetes.

^bUndiagnosed diabetes: HbA1c ≥48 mmol/mol (6.5%) and no self report of diabetes.

^cProportion undiagnosed: Proportion out of total diabetes cases (diagnosed and undiagnosed) that were undiagnosed.

FIGURE 1 Prevalence of total, diagnosed, and undiagnosed diabetes, prediabetes and total hyperglycaemia (diabetes and prediabetes), by age group

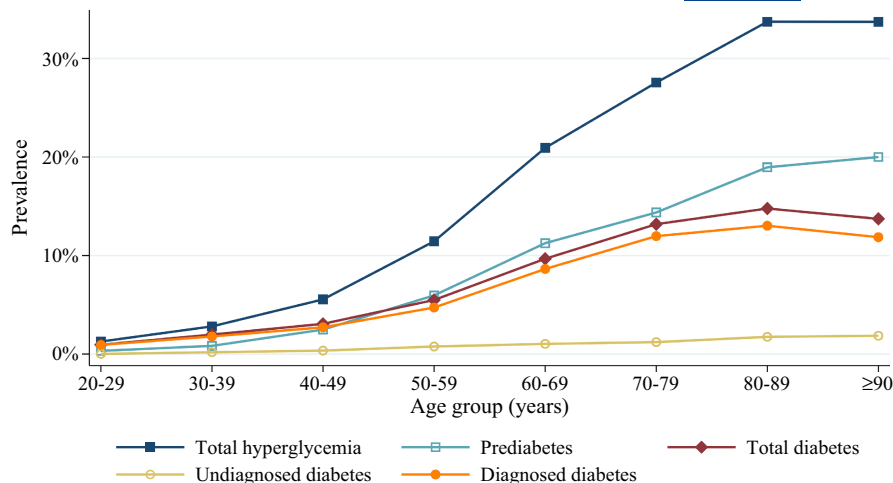


TABLE 3 Cardiovascular risk factors and patient characteristics in diabetes and prediabetes compared with normoglycaemia, in participants <75 years of age

	Proportion, % (95% CI)	Difference in percentage points (95% CI) from the normoglycaemia group		
		Prediabetes ^a	Undiagnosed diabetes ^b	Diagnosed diabetes
No. of participants, <i>n</i>	41,160	2757	300	2387
Prescribed anti-hypertensive drug	15 (15, 16)	+15 (13, 17)	+24 (18, 30)	+34 (32, 36)
Prescribed lipid-lowering drug	10 (10, 10)	+13 (11, 15)	+21 (15, 26)	+39 (37, 41)
History of cardiovascular disease	7 (7, 8)	+6 (4, 7)	+9 (5, 14)	+10 (9, 12)
Physical inactivity	35 (34, 35)	+11 (9, 13)	+17 (11, 23)	+10 (8, 13)
Current daily smoking	8 (8, 9)	+2 (0, 3)	+2 (0, 6)	+1 (0, 3)
Previous daily smoking	32 (32, 33)	+1 (-1, 3)	+4 (-2, 9)	+5 (3, 7)
Systolic blood pressure >140 mmHg	18 (17, 18)	+6 (4, 7)	+13 (7, 18)	+4 (2, 6)
Diastolic blood pressure >90 mmHg	5 (5, 6)	+1 (0, 2)	-1 (-3, 1)	-2 (-2, -1)
BMI ≥30 kg/m ²	22 (21, 22)	+26 (24, 28)	+38 (33, 44)	+25 (22, 27)
BMI ≥35 kg/m ²	5 (5, 6)	+12 (10, 13)	+19 (14, 24)	+11 (10, 13)
eGFR <60 ml/min/1.73 m ²	2 (2, 2)	+1 (0, 1)	+0 (-1, 1)	+3 (3, 4)

Note:: Adjusted for age and sex.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin.

^aPrediabetes: HbA1c 39-47 mmol/mol (5.9%-6.4%) and no self report of diabetes.

^bUndiagnosed diabetes: HbA1c ≥48 mmol/mol (6.5%) and no self report of diabetes.

In addition, a recent study from the UK Biobank found a similarly low prevalence of undiagnosed diabetes of 0.8%.²³

Contributing explanations for a decrease in the proportion of undiagnosed diabetes could be increased awareness and diagnosis, an increase in the prevalence of diagnosed diabetes due to better survival, and a decrease or stabilization of the incidence of diabetes, recently reported in Norway²⁷ and other high-income countries.²⁸ Furthermore, in 2012 HbA1c was introduced as the primary recommended diagnostic tool for diabetes in

Norway,²¹ following renewed recommendations from the World Health Organization.⁸ As HbA1c is a more convenient test compared with glucose measurements, due to not requiring fasting, it is possible that the rate of opportunistic screening for diabetes may have increased, leading to diabetes more often being diagnosed at an early stage.

Undiagnosed diabetes was associated with poorer values for all the measured cardiovascular risk factors compared with diagnosed diabetes. Closer follow-up and more intensive treatment of blood pressure and cholesterol in patients with diagnosed diabetes, as recommended

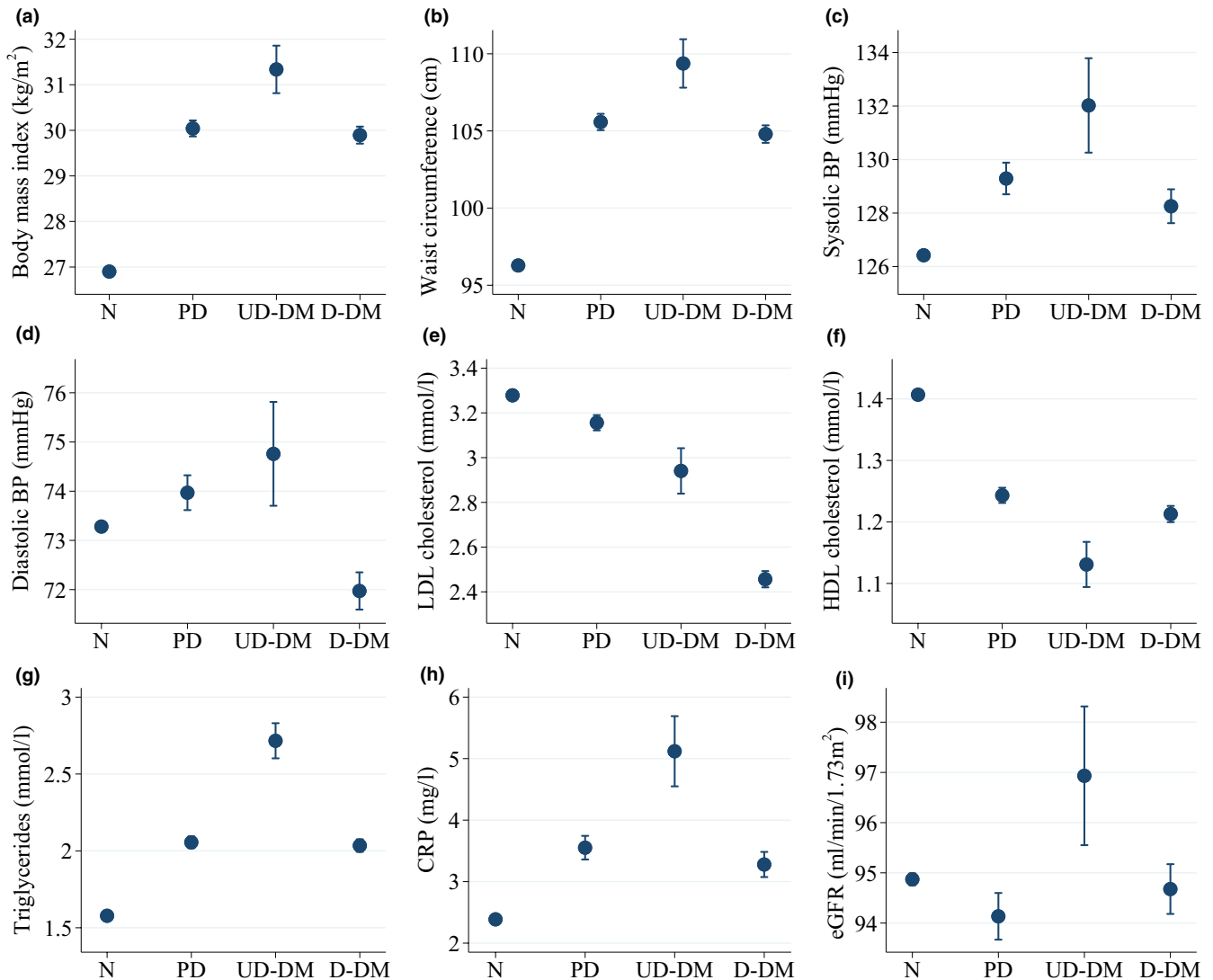


FIGURE 2 Estimated mean levels (with 95% CI) of cardiovascular risk factors adjusted for age and sex, by glycaemic group: normoglycaemia (N), prediabetes (PD), undiagnosed diabetes (UD-DM) and diagnosed diabetes (D-DM), in participants <75 years of age. BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate

by national guidelines²¹ might explain this difference. Although we cannot conclude on the direction of these associations, this finding might highlight some of the potential benefits of receiving a diabetes diagnosis. The lower LDL cholesterol observed in participants with diagnosed and undiagnosed diabetes and prediabetes compared with normoglycaemic participants, can probably be explained by their higher usage of lipid-lowering drugs. The slightly higher eGFR that we observed in participants with undiagnosed diabetes, could be due to transient glomerular hyperfiltration in the early stage of diabetes.²⁹

Norwegian national guidelines currently do not recommend systematic screening for diabetes in all adults, but recommend that the FINDRISC should be used for opportunistic screening in European-ancestry patients, and HbA1c measurements generally performed

in those with FINDRISC ≥ 15 .²¹ The 61% sensitivity of the FINDRISC in our study means that four out of ten cases would not be detected when using the recommended strategy, but the sensitivity could be higher in populations naïve to the use of the FINDRISC or similar screening tools. In practice, opportunistic screening is probably often performed with HbA1c measurements without prior FINDRISC scoring, which may be considered more time-efficient.³⁰

The low prevalence of undiagnosed diabetes found in this study indicates that the current practice of opportunistic screening for diabetes appears to be sufficient. Moreover, the very low prevalence of strong HbA1c elevations indicating severe hyperglycaemia suggests that there is little rationale for a population-based screening program. In addition, we did not detect any specific

demographic groups with a high proportion of undiagnosed diabetes that appear to need intensified opportunistic screening.

A limitation of our study is that we, as is common for most epidemiological studies, used a single HbA1c measurement to categorize the glycaemic status of participants. This leads to some overestimation of undiagnosed diabetes,³¹ compared with clinical practice where repeated elevated measurements of HbA1c are required for diabetes diagnosis in asymptomatic persons.²¹ Furthermore, although most of the recent studies on undiagnosed diabetes in Europe have used HbA1c as their screening test, including all the individual studies that we have compared our results to,^{1-5,22,23,26} it is important to take into consideration the poor concordance between HbA1c, fasting plasma glucose and oral glucose tolerance tests (OGTTs) in detecting diabetes, when comparing our results with previous studies. When using a single measurement, HbA1c has been shown to detect fewer patients than an OGTT. However, HbA1c displays less day-to-day variation, meaning that the probability that a follow-up measurement will confirm the diagnosis is higher. Thus, fewer of the HbA1c-detected individuals will be false positives. HbA1c measurements also have less pre-analytic variation, results show greater consistency between laboratories, and there is evidence that HbA1c might be better correlated with retinopathy and other microvascular complications compared with other diagnostic tests.^{32,33} Finally, the choice of HbA1c to detect diabetes in this study is consistent with clinical practice in Norway today, where HbA1c has been the primary recommended diagnostic tool for diabetes since 2012. It should be noted that HbA1c may be affected by factors such as ethnicity and certain haematological conditions, which were not investigated in this study.³² We did not classify the participants as having type 1 or type 2 diabetes, but most undiagnosed diabetes cases among adults will likely be type 2 diabetes. Self report of diabetes may cause misclassification but has previously been demonstrated to have high validity in HUNT (positive predictive value 96.4% and negative predictive value 99.7%).³⁴

Of the major strengths of this study are the large sample size and the population-based design, limiting the risk of selection bias. Furthermore, the 54% participation rate is high compared with other contemporary large-scale community-based studies. Nonetheless, nonparticipation in HUNT has been associated with diagnosed diabetes, cardiovascular disease, and lower education level,³⁵ suggesting that the prevalence of hyperglycaemic conditions could be underestimated in our study. In studies reporting higher proportions of undiagnosed diabetes, the participation rates were similar or lower to our study,^{1,2,5,23} and risks of selection bias were likely comparable or larger.

Although our results are likely generalizable to adult populations in similar Western countries with easy and generally free access to health care, our results may not be generalizable to populations with a different health care organization or to populations with a different ethnic composition.²³

In conclusion, in this large population-based study from 2017–2019, only 11% of participants with diabetes were undiagnosed, and few of these had very high HbA1c levels indicating severe hyperglycaemia. However, those with undiagnosed diabetes had more adverse values for cardiovascular risk factors compared with participants with known or no diabetes.

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CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

AUTHOR CONTRIBUTIONS

VVB, EBH, AL and BOÅ designed the study with contributions from the other authors. AL and BOÅ facilitated acquisition of data. VVB performed the statistical analyses and drafted the manuscript, with supervision from EBH, AL and BOÅ. All authors interpreted the data and critically revised the manuscript and provided final approval of the version to be published.

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