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ORIGINAL RESEARCH

Impact of Population-Based Screening for Diabetes and Prediabetes Among 67-Year-Olds Using Point-of-Care HbA1c on Healthcare Ultilisation, Results from the VISP Cohort

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Purpose: The present study aims to evaluate the changes in healthcare utilization following population-based screening for diabetes mellitus (DM) using point-of-care HbA1c measurement in the Viborg Screening Program (VISP) cohort, which invites all 67-year-olds in Viborg, Denmark, for cardiovascular disease (CVD) and DM screening.

Patients and Methods: We conducted a cohort study using data from VISP and Danish national health registers. The study included 2386 individuals invited to VISP from August 1, 2014, to May 31, 2017. Exclusion criteria were non-attenders, those with prior DM, and those with missing HbA1c measurements. Pre- and post-screening healthcare utilization was analyzed, stratified by HbA1c levels: <42 mmol/mol (normal), 42–48 mmol/mol (pre-DM), and ≥48 mmol/mol (DM). Statistical analyses were performed using Poisson and logistic regression models to compare ratios of healthcare utilization before and after screening.

Results: Of the participants, 16.5% had pre-DM, and 3.4% had DM. Screening resulted in increased general physician contacts across all HbA1c groups, the highest increase was seen in the DM group with a pre- vs post-screening odds ratio [OR] of 3.25 (95% CI: 1.06–9.95) and a relative odds ratio [ROR] of 2.70 (0.87–8.39). Also, in this group, the OR for having ≥1 HbA1c measurement one year pre- vs post-screening was 5.56 (2.77 −11.14) and 26.8% (17.6–37.9) started glucose-lowering treatment within two years post-screening. Despite expectations, healthcare utilization did not decrease among those with normal HbA1c levels.

Conclusion: Population-based screening for DM and CVD among 67-year-olds resulted in increased healthcare utilization, particularly among those with screen-detected DM and pre-DM. The anticipated reduction in healthcare utilization among individuals with normal HbA1c levels was not observed. These findings highlight the potential for screening to enhance disease management and underscore the need for strategies to optimize healthcare resource use following screening, especially for individuals without DM.

Trial Registration: NCT03395509.

Keywords: epidemiology, medication, general practice, Denmark, diabetes

Introduction

The International Diabetes Federation estimates that nearly half of individuals with diabetes mellitus (DM) worldwide are undiagnosed. This contrasts with early diagnostic efforts dating back to 1968, when population-based screening for DM and cardiovascular diseases (CVD) was first suggested.[1,2] The proportion of undiagnosed DM is higher in countries or regions with lower socioeconomic status and limited healthcare resources, possibly due to variations in the availability

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of testing and access to healthcare, leading to inequality between countries and regions.[2] Even in Denmark, a high-income Western European country with tax-funded general healthcare, approximately one-fourth to one-third of individuals with DM remain undiagnosed.[2–4] However, the benefit of screening for DM is continuously debated, and systematic population-based screening has not been introduced in most Western countries, including Denmark.

The high proportion of individuals with undiagnosed DM, together with its progressive nature, where the risk of complications increases with levels of haemoglobin A1c (HbA1c), makes screening for DM relevant.[5–7] Measuring the HbA1c level is simple, cheap and without any risks. HbA1c reflects long-term (8 to 12 weeks) plasma glucose levels and, although it can be influenced by conditions that affect erythrocyte turnover, it is a recommended tool for diagnosing and monitoring diabetes mellitus.[7,8] Additionally, the availability and continuous development of well-tolerated accessible treatments with known effects on complications and mortality underline that DM is a viable target for screening.[9] Simulations indicate improved public health and cost-effectiveness from screening for DM.[10] The US Preventive Services Task Force has recently updated their recommendations on population-based screening for DM and, in line with the simulations, suggest a moderate net benefit from screening when including and treating pre-DM.[11–13] However, larger real-world trials have yet to show an effect on all-cause or type-specific mortality with screening compared with standard care. Nevertheless, an effect is indicated, for instance, among those screened between 1990 and 1992 in the ELY cohort (Cambridgeshire, UK).[14,15] However, low participation rates and selection bias present limitations in these studies.[14–16]

The prevalence of unknown DM, the relevance of screening and the discrepancy between expectations and findings in studies on the effects of screening for DM highlight the need to further understand possible mechanisms facilitating the effect of population-based screening for DM. One possible way to address this is to study changes in healthcare utilization following screening, which represents a natural link from screening to effect. Only a limited number of studies have assessed such changes in healthcare utilisation, including consultations, medicine usage and laboratory testing.[17] Additionally, hardly any research has been conducted on these changes in screening programs using HbA1c without prior risk stratification.

Therefore, we wanted to describe the changes in healthcare utilisation following screening for DM using a point of care HbA1c measurement in the Viborg Screening Program (VISP) cohort. VISP invites all 67-year-olds from the rural municipality of Viborg in Denmark to participate in screening for DM and cardiovascular diseases. We reported absolute along with relative pre- and post-screening measures for consultations, medication usage and laboratory testing. The results were stratified based on the HbA1c value at screening. Based on earlier studies, we expected to identify a considerable proportion of individuals with unknown DM and pre-DM for whom we anticipated to find a post-screening increase in healthcare utilisation. Furthermore, we expected a relative decrease in healthcare utilisation among individuals without DM.[3,18]

Materials and Methods

Study Design and Setting

We designed a cohort study based on results from the VISP combined with data from Danish national health registers. VISP is an ongoing screening initiative implemented in the municipality of Viborg, Denmark.[19] The program was initiated in August 2014 and invites all citizens on their 67th birthday to undergo screening for CVD and DM. The age of 67 was selected based on the premise that the prevalence of DM and CVD is significant at this point, while minimizing the risk of encountering extensive irreversible complications. Approximately 1000 individuals are invited annually. The overall participation rate is 84%.[18] The screening involves measurements of blood pressure, distal blood pressure, ultrasound scan of the carotid arteries and the abdominal aorta, 12-point electrocardiography and a point-of-care HbA1c measurement. All conducted tests, including the HbA1c test, are conducted by trained nurses. HbA1c is measured using the Quo-Test analyzer (Quotient Diagnostics Ltd, West Molesey, UK), maintenance and calibration following recommendations from the manufacturer, including calibration using reference samples every month.[20] Individuals with HbA1c values ≥48 mmol/mol are advised to visit their GP for a follow-up measurement and, if necessary, initiate treatment under their GP's supervision.

Study Population

We included individuals invited to VISP during the period 01.08.2014 to 31.05.2017.[18] The invitation date was used as index date for follow-up. Individuals were followed until their death or the end of follow-up set to 31.12.2019, whichever came first. The date for end of follow-up was chosen to ensure a minimum of two years of follow-up on medication usage in the present dataset. We excluded screening non-attenders, individuals who for any reason did not have an available HbA1c measurement at screening and those who had a history of DM prior to screening. A history of DM was established when a prescription for an antidiabetic medication (ATC code: A10) was handed in during the year preceding screening.

Study Variables

Utilising the Danish Civil Registration Number, we merged data from the VISP with data from selected national registers containing information on baseline characteristics and the participants' healthcare utilisation. Selected registers and the corresponding variables with their coding are presented in the supplementary (Supplementary Table 1). All reported HbA1c values are mmol/mol. The intervals for the HbA1c groups were selected to reflect common clinical cutoffs. HbA1c <42, [42–48[and ≥48 mmol/mol correspond to normal, pre-DM and DM. Specific drug usage in the year preceding screening was used as a surrogate for the diagnosis of hypertension (HT) and DM, using the Anatomical Therapeutic Chemical (ATC) classification system. This was necessary because in Denmark, these conditions are mostly treated at the GP. Accordingly, they therefore cannot be identified through hospital diagnoses reported in The National Patient Register. Other comorbidities were reported based on A or B diagnoses obtained from hospital admissions in the 10 years preceding screening, in accordance with the International Classification of Diseases, tenth version (ICD-10).[21]

Main outcomes included the use of glucose-lowering, antiplatelet, lipid-lowering and antihypertensive medication, GP contacts and HbA1c laboratory measurements. Secondary analyses are reported in the supplementary material and included anticoagulant therapy, contacts with outpatient clinics specialised in endocrinology (EC) and measurement of LDL cholesterol and creatinine.

Missing Data

For baseline general characteristics, less than 5% of the data are missing owing to the high level of completeness of the screen data and the general nature of the Danish healthcare system, which operates a central system for medicine prescription, laboratory testing and has very limited private activity. We therefore find data from the used registers as complete and do not report any missing data for the category's comorbidities, medicine usage, use of laboratory measurements and healthcare contacts. Concerning laboratory findings, the proportion with at least one measurement is included in the results.

Statistical Analysis

Baseline characteristics were presented using descriptive statistics. Categorical variables were reported as absolute numbers together with the percentage of total within each group. Continuous variables were reported as means.

We used Poisson regression to calculate rates of contacts (IR) with GP/EC and relative contact rates (RIR) comparing periods before and after invitation to screening and comparing the development between the HbA1c groups. We used logistic regression to calculate odds ratios (OR) and relative odds ratios (ROR), again comparing periods before and after the invitation to screening along with the relative development between the groups for binary outcomes, ≥1 contact at GP, ≥1 measurement of HbA1c, use of medicine including glucose lowering, antiplatelet, lipid-lowering and antihypertension. All estimates are accompanied by 95% confidence intervals (CIs). For both the Poisson and the logistic regressions, robust CIs were reported to account for the non-independence of multiple observations of the same individual. The HbA1c < 42 group served as a reference, except for the variable glucose-lowering medicine as no one in the group used the medicine as a natural result of the inclusion criteria. Here, the HbA1c [42–48[group served as a reference.

The analyses were performed using the STATA 17 software.[22] All data storage and statistical analyses were conducted on the secured servers of Statistics Denmark.

Ethics

All participating individuals were adults and competent. Prior to their involvement in the screening, they provided verbal confirmation of their willingness to participate. This study including the process of informed verbal consent received approval from the Danish patient safety authority, with a designated registration number: 3–3013-2764/1 and was carried out in accordance with the declaration of Helsinki. The data collected for this research were securely stored and processed on the secured servers of Statistics Denmark in accordance with the protocols set forth by the local health authority in Region Midtjylland, Denmark, identified with the registration number: 1–16-02-232-15. All data were anonymised and presented in a manner that does not permit personal identification of any individual involved in the study.

Results

Among the 3078 invited for screening in the study period, 2613 (84.9%) attended, of these 220 (8.4%) were excluded due to known DM prior to screening and 7 (0.3%) due to missing HbA1c measurements at screening. This yielded a total study population of 2386 (Figure 1).

Baseline Data

Of the 2386 included, 16.5% (15.0–18.0) had pre-DM, and 3.4% (2.8–4.3) had DM. The baseline characteristics among HbA1c groups differed on several parameters, burdening those with higher HbA1c (Table 1). Compared to the HbA1c < 42 group, the HbA1c [42–48[and ≥48 groups had fewer individuals with medium-term or higher education, a lower proportion exercising ≥4 hours/week, more smokers, higher BMI and a wider waist circumference. The groups were similar concerning comorbidities. The proportion of individuals with the combined cardiovascular comorbidity was 8.0% (6.8–9.3), 11.7% (8.7–15.3) and 8.5% (3.5–16.8) among individuals with a HbA1c level of <42, [42–48[and ≥48, respectively. For all medications, a higher usage was reported among individuals with higher HbA1c values. For instance, the proportion of individuals on antiplatelet therapy was 13.9% (12.4–15.5), 21.6% (17.7–26.0) and 19.5% (11.6–29.7), respectively. The laboratory values and average follow-up time were similar among the groups.

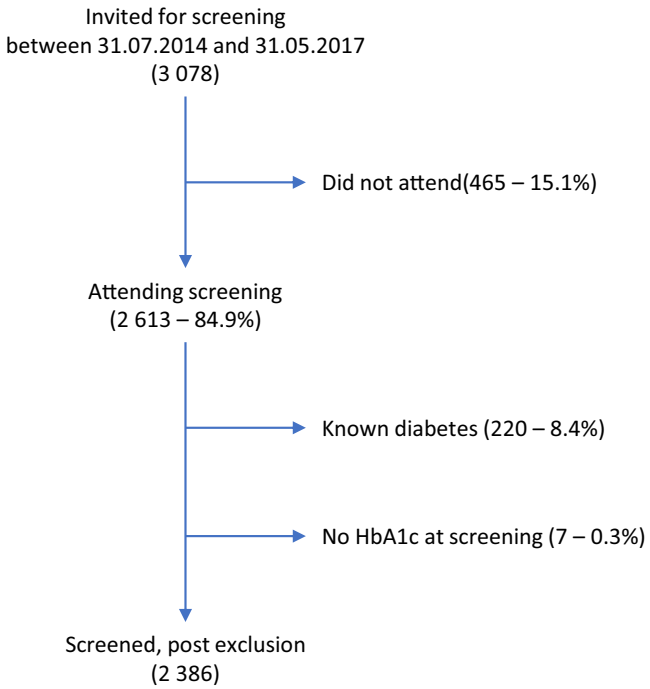

Figure 1 Selection.

Table 1 Baseline Characteristics, Total n = 2386

	HbA1c < 42		HbA1c [42–48[		HbA1c ≥ 48	
	n=1911	95% CI	n=393	95% CI	n=82	95% CI
Proportion of total, %	80.1	78.4–81.7	16.5	15.0–18.0	3.4	2.8–4.3
General, n (%)						
Age, years	67	n/a	67	n/a	67	n/a
Sex, female	997 (52.2)	49.9–54.4	179 (45.6)	40.6–50.6	37 (45.1)	34.1–56.5
Follow-up years, mean	3.93	3.89–3.97	3.97	3.88–4.06	3.70	3.47–3.93
Education, medium-term or higher	556 (29.1)	27.1–31.2	78 (19.9)	16.0–24.1	19 (23.2)	14.6–33.8
Ethnicity, immigrants, and decedents	36 (1.9)	1.3–2.6	10 (2.5)	1.2–4.6	≤ 3***	n/a
Marital status, married	1414 (74.0)	72.0–76.0	295 (75.1)	70.5–79.3	55 (67.1)	55.8–77.1
Current smokers	324 (17.0)	15.3–18.8	83 (21.1)	17.2–25.5	17 (20.7)	13.1–32.2
Exercise ≥ 4 hours/week	595 (31.1)	29.3–33.5	100 (25.5)	21.4–30.3	12 (14.6)	8.1–25.0
Waist Cm, mean	91.7	91.0–92.27	96.16	94.80–97.51	99.95	96.53–103.37
BMI kg/m^2, mean	26.12	25.92–26.31	27.92	27.41–28.42	28.83	27.57–30.09
Comorbidity, known n (%) *						
Hypertension	700 (36.6)	34.5–38.8	180 (45.8)	40.8–50.9	38 (46.3)	35.2–57.7
Atrial fibrillation	82 (4.3)	3.4–5.3	20 (5.1)	1.4–5.0	4 (4.9)	1.3–12.2
Acute myocardial infarction	39 (2.0)	1.5–2.8	11 (2.8)	0.2–2.2	≤ 3***	n/a
Ischaemic heart disease	99 (5.2)	4.2–6.3	24 (6.1)	4.0–9.0	5 (6.1)	2.0–13.7
Ischaemic stroke	39 (2.0)	1.5–2.8	15 (3.8)	2.2–6.2	≤ 3***	n/a
Peripheral arterial disease	6 (0.31)	0.12–0.68	≤ 3***	n/a	≤ 3***	n/a
Combined, AMI, IHD, IS & PAD	152 (8.0)	6.8–9.3	46 (11.7)	8.7–15.3	7 (8.5)	3.5–16.8
Medicine, n (%)						
Antiplatelet	265 (13.9)	12.4–15.5	85 (21.6)	17.7–26.0	16 (19.5)	11.6–29.7
Lipid-lowering drugs	484 (25.3)	23.4–27.3	143 (36.4)	31.6–41.4	28 (34.2)	24.0–45.6
Anticoagulant	91 (4.8)	3.9–5.8	24 (6.1)	4.0–9.0	6 (7.3)	2.7–15.3
Antihypertensive	700 (36.6)	34.5–38.8	180 (45.8)	40.8–50.9	38 (46.3)	353. – 57.7
Lab findings pre-screening, mean **						
Creatinine, µmol/L	78.2	77.1–79.4	78.4	76.2–80.7	77.9	72.2–83.5
Total Cholesterol, mmol/L	5.1	5.0–5.2	4.9	4.8–5.1	4.9	4.5–5.2
LDL cholesterol, mmol/L	3.0	2.9–3.0	2.9	2.8–3.0	2.8	2.5–3.0

Notes: * ICD10 diagnoses within 10 years pre-screening, except hypertension, which is based on prescribed medicine one year pre-screening. ** Latest result within a maximum of one year pre-screening. *** Due to the data-reporting rules and few numbers, we are not allowed to specify these.

Comparison of Pre- and Post-Screening Healthcare Utilization

The odds for having at least one contact with the GP during the year before screening were similar across the HbA1c groups. For all HbA1c groups, the odds rose after screening compared with before screening (Table 2). The pre- vs post-screening OR was 1.20 (95% CI: 1.01–1.43), 1.92 (95% CI: 1.25–2.94) and 3.25 (95% CI: 1.06–9.95) for the HbA1c <42, [42–48[and ≥48 group, respectively. Compared to the HbA1c < 42 group, the ROR was 1.59 (95% CI: 1.01–2.53) for the HbA1c [42–48[group and 2.70 (95% CI: 0.87–8.39) for the HbA1c ≥ 48 group, indicating a relatively higher increase in the odds for having at least one contact with the GP.

For the number of contacts with the GP, the same trend was found with a pre- vs post-screening IR of 1.05 (95% CI: 1.01–1.09), 1.11 (95% CI: 1.03–1.20), 1.36 (95% CI: 1.18–1.57) for the HbA1c <42, [42–48[and ≥48 groups, respectively. In the HbA1c ≥ 48 group, this represents an increase from 8.2 (6.4–10.1) to 11.2 (9.3–13.1). A RIR of 1.06 (95% CI: 0.97–1.16) and 1.30 (95% CI: 1.18–1.57) indicated a higher relative increase in the number of contacts in the HbA1c [42–48[and ≥48 groups. We similarly analysed contacts with an EC and found no differences, although the numbers were small (Supplementary Table 2).

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Table 2 Comparative Analyses of Healthcare Utilisation, Total n = 2386

Characteristics	HbA1c < 42		HbA1c [42–48[		HbA1c ≥ 48	
	n=1911	95% CI*	n=393	95% CI	n=82	95% CI
Use of the healthcare system						
Persons with ≥1 contact at GP, n (%)						
1 year pre-screening	1679 (87.9)	86.3–89.2	346 (88.0)	84.4–91.1	73 (89.0)	80.9–94.9
OR	1		1.02	0.73–1.42	1.12	0.55–2.27
1 year post-screening	1714 (89.7)	88.2–91.0	367 (93.4)	90.5–95.6	79 (96.3)	89.7–99.2
Pre- vs post-screening OR	1.20	1.01–1.43	1.92	1.25–2.94	3.25	1.06–9.95
ROR	1		1.59	1.01–2.53	2.70	0.87–8.39
Contacts with GP, n mean						
1 year pre-screening	8.0	7.7–8.4	8.7	7.8–9.7	8.2	6.4–10.1
IR	1		1.09	0.97–1.22	1.03	0.82–1.29
1 year post-screening	8.4	8.0–8.8	9.7	8.8–10.7	11.2	9.3–13.1
Pre- vs post-screening IR	1.05	1.01–1.09	1.11	1.03–1.20	1.36	1.18–1.57
RIR	1		1.06	0.97–1.16	1.30	1.18–1.57
Use of medicine						
Glucose lowering, n (%)**						
1 year post-screening	0 (0.0)	0.0–0.2	5 (1.3)	0.4–2.9	14 (17.0)	9.7–27.0
OR	n/a		1		15.98	5.57–45.85
2-year post-screening	0 (0.00)	0.00–0.2	8 (2.0)	0.9–3.7	22 (26.8)	17.6–37.8
Year 1 vs year 2 post-screening OR	n/a		1.61	0.94–2.78	1.78	1.21–2.62
ROR	n/a		1		1.10	0.57 −2.15
Antiplatelet, n (%)						
1 year pre-screening	265 (13.9)	12.4–15.5	85 (21.6)	17.7–26.0	16 (19.5)	11.6–29.7
OR	1		1.71	1.30–2.25	1.51	0.86–2.64
1 year post-screening	580 (30.4)	28.3–32.5	154 (39.2)	34.3–44.2	31 (37.8)	27.3–49.2
Pre- vs post-screening OR	2.71	2.42–3.03	2.33	1.91–2.85	2.51	1.57–4.01
ROR	1		0.86	0.69–1.08	0.93	0.57–1.50
Lipid-lowering drugs, n (%)						
1 year pre-screening	484 (25.3)	23.4–27.3	143 (36.4)	31.6–41.4	28 (34.2)	24.0–45.5
OR	1		1.69	1.34–2.12	1.53	0.96–2.44
1 year post-screening	758 (39.7)	37.5–41.9	197 (50.1)	45.1–55.2	39 (47.6)	36.4–58.9
Pre- vs post-screening OR	1.94	1.79–2.10	1.76	1.49–2.08	1.75	1.21–2.54
ROR	1		0.91	0.75–1.09	0.90	0.62–1.32
Antihypertension, n (%)						
1 year pre-screening	700 (36.6)	34.5–38.8	180 (45.8)	40.8–50.9	38 (46.3)	35.3–57.7
OR	1		1.46	1.17–1.82	1.49	0.96–2.33
1 year post-screening	768 (40.2)	38.0–42.4	200 (50.9)	45.8–55.9	44 (53.7)	42.3–64.8
Pre- vs post-screening OR	1.16	1.11–1.21	1.23	1.10–1.36	1.34	1.03–1.75
ROR	1		1.05	0.94–1.19	1.15	0.88–1.51
Use of lab-measurements						
Persons ≥1 measurement of HbA1c, n (%)						
1 year pre-screening	885 (46.3)	44.06–48.6	187 (47.6)	42.6–52.7	42 (51.2)	39.9–62.4
OR	1		1.05	0.85–1.31	1.22	0.78–1.89
1 year post-screening	897 (46.9)	44.7–49.2	266 (67.7)	62.8–72.3	70 (85.3)	75.8–92.2
Pre- vs post-screening OR	1.03	0.92–1.14	2.31	1.76–3.02	5.56	2.77–11.14
ROR	1		2.25	1.68–3.00	5.42	2.68–10.96

Notes: *95% CI for the comparative analyses OR and IRR are calculated using logarithmic analyses for binary outcomes (OR) and Poisson regression analyses for continuous outcomes (RR) - in both cases, robust intervals are reported. **Using antidiabetic medicine is part of our exclusion.

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In the first two years after screening, nobody started treatment with glucose-lowering medicine in the HbA1c < 42 group, while 2.0% (0.9–3.7) started in the HbA1c [42–48[group and 26.8% (17.6–37.8) in the HbA1c ≥ 48 group. The pre- vs post-screening OR of being on antiplatelet therapy was 2.71 (95% CI: 2.42–3.03), 2.33 (95% CI: 1.91–2.85), 2.51 (95% CI: 1.57–4.01) among individuals in the HbA1c of <42, [42–48[and ≥48 groups, respectively. The relative increase was similar between groups with RORs around one. The same trends were present for lipid-lowering and antihypertensive medicine.

The proportion of individuals with one or more HbA1c measurements in the year prior to screening was 46.3% (44.1–48.6), 47.6% (42.6–52.7) and 51.2 (39.9–62.4) for the HbA1c <42 [42–48[and ≥48 groups, respectively. The pre- vs post-screening OR was 2.31 (95% CI: 1.76–3.02) in the HbA1c [42–48[group and 5.56 (95% CI: 2.77–11.14) in the ≥48 group. Compared with the HbA1c < 42 group, the ROR was 2.25 (95% CI: 1.7–3.0) in the HbA1c [42–48[group and 5.42 (95% CI: 2.68–10.96) in the HbA1c ≥48 group, indicating a higher relative increase in the latter group. The trend was similar for measurements of creatinine and LDL, which is reported in the supplementary (Supplementary Table 2).

Discussion

We found increased healthcare utilisation among those with screen-detected DM or pre-DM following screening for DM and CVD in a population of 67-year-olds without known DM.

Among individuals with screen-detected DM, 96.3% had at least one contact with their GP in the year after screening, representing a pre- vs post-screening OR of 3.25 and with a ROR of 2.70 this increase was noticeably higher than for individuals without detected DM. The proportion starting glucose-lowering treatment among those with screen-detected DM increased from 17.1% in one year after screening to 26.8% after two years. Monitoring and laboratory testing increased in parallel, and 85.3% had at least one HbA1c measurement in the year after screening, representing a pre- vs post-screening OR of 5.56. With an ROR of 5.42, this increase was also markedly higher than for individuals without DM. Overall, the same trends were found among individuals with screen-detected pre-DM, with the exception that for glucose-lowering treatment were only 2.0% received treatment two years after screening.

Contrary to our expectations and representing a novel finding, we observed no decrease in healthcare utilisation, including consultations, medicine usage and laboratory testing among individuals without DM or pre-DM after screening compared with before screening.

Strength and Limitations

As only a negligible part of healthcare utilisation in Denmark is conducted outside the tax-funded setting, using the Danish national registers to collect pre- and post-screening data is a major strength and lowers the risk of selection bias.[23] We added to this strength by combining these data with data from our screening setup, which also had a high coverage with less than 5% missing data. For HbA1c measurement, we used a single state-of-the-art test-device to avoid measurement error. The present study also had a very high participation rate of 84.6%, and we performed biochemical testing of the included population without any pre-test selection tools. This further reduced selection bias and provides the possibility to describe a broad segment of the selected population.

After stratification, some categories, especially in the HbA1c ≥ 48 group, have relatively few numbers with broad CIs, which represents a weakness in our study. Also, our analyses are unadjusted, and are therefore subject to influence from confounders. Several potential confounders may be identified as the HbA1c groups differ on many variables. Many of these differences, such as smoking, exercise level and waist measure, are less likely to effect the individual's healthcare utilisation and hereby our results.[24] On the other hand, factors such as sex, education and marital status are often related to healthcare utilisation.[25] Some of the differences, especially for comorbidities, could represent causal pathways between a high HbA1c and healthcare utilisation. Moreover, given the proper power, adjusting should be carefully considered. Due to the descriptive nature of this study, the problem of confounding is of less importance. An elevated HbA1c is likely associated with other screening findings, and the observed increase in healthcare utilisation could therefore be fully or partly explained by such contemporaneous findings.[26] This effect is likely less pronounced for DM-specific medications and laboratory tests but would most certainly affect a variable such as the follow-up at the GP. As a result of the chosen stratification, we do not have sufficient power to adjust for these findings. However, in future

studies, this would be relevant along with adjustments for other baseline confounders, trying to isolate the effect of detected pre-DM or DM.

Comparison with Previous Studies

The baseline prevalence of known comorbidities seemed similar among the different HbA1c groups. This represents a contrast with other studies identifying individuals with an increased HbA1c, which find that they have an increased risk for several comorbidities. This disparity could be explained by the fact that we excluded those with known DM or it could be related to the selected age group.[27,28] Choices like these need to be taken into account when considering the application of our findings. Due to low participation rates and pre-screen selections, selection bias is a concern in other studies.[15,29] Despite a high participation rate and no pre-screen selection, the present study must consider the risk of selection bias. Hence, non-attenders could represent a different willingness to initiate treatment and follow-up than attenders. It is described how comorbidities among non-attenders often exceed attenders' comorbidities.[30] Whether non-attenders represent poorer adherence and willingness to follow-up is more uncertain. Sieben et al[31] found a similar adherence and belief in medication among screening responders and screening non-responders. As mentioned, the high attendance rate in the present study limits these risks compared with the risks encountered in other studies with lower attendance. In the Ely study, the attendance rates were 68% in the first round of screening in 1990–1992 and 45% in the second round in 2000–2003.[15] In the ADDITION study (Denmark), 18% attended their GP for a DM test.[14]

To understand the possible mechanisms behind the effect of population-based screening for DM, the proportion of participants who initiated glucose-lowering treatment is of special interest. To generate an effect from screening, initiation of medical treatment seems crucial.[32,33] We found that 17.0% of those with screen-detected DM received treatment after one year, a proportion we would have expected to be higher. A similar post-screening treatment proportion was reported by Simmons et al[16] who found that 20.8% started treatment in the first year of follow-up. We saw a further increase to 26.8 after two years. A similar, continuous increase was also reported by Simmons et al.[16] Whether the findings represent a patient- or a healthcare-provider-driven delay remains unclear. We are reporting on redeemed prescriptions; hence, the increase could reflect adherence. A review by Krass et al[34] evaluated adherence to antidiabetic treatment and found varying results, between 38.5% and 93.1%. The increase could also be explained by ongoing treatment involving lifestyle modification, which unfortunately does not present itself in the registers and could be an issue of great interest in future studies. Among those with screen-detected pre-DM, even fewer started medical treatment; and after two years, only 2.0% received treatment. Whether individuals with pre-DM should receive medical treatment remains contested, even though increasing evidence suggests that metformin and other newer agents reduce the risk of progression and this group most likely represents a high-risk population.[12,32,33] Most guidelines recommend lifestyle modifications with a focus on weight loss and metformin as first-line treatment based on the cost-effectiveness of this approach.[35–38] New medications with effects on obesity could further alter the balance between medical treatment and lifestyle modifications for weight loss; and along with new treatments, the identification of pre-DM could hence become increasingly important.[39,40] Irrespective of this, the initial low proportion in treatment among those with DM and pre-DM represents a possibility to further benefit from screening. The use of other cardioprotective medications also increased after screening, including antiplatelet, lipid-lowering and antihypertensive medications. The increase here was similar among the HbA1c groups as shown by RORs close to one. This increase could well be driven by contemporaneous screening findings, and the increase is similar to findings reported by Simmons et al.[16]

The low proportion in glucose-lowering treatment was at odds with the high proportion of follow-up contacts at the GP. However, despite a relative increase in these contacts among those with DM and pre-DM, the absolute increase was minor. This was due to a very high pre-screen level of control, with 89.0% of those with screen-detected DM and 88.0% of those with pre-DM having at least one contact with their GP in the year before screening, with mean numbers of contacts of 8.23 and 8.74, respectively. Other Danish studies on GP consultations have reported similar proportions of follow-up contacts.[23] We believe that the participation rates, the high baseline control, and the low initiation of DM-specific medication adds valuable information to our understanding of the mechanisms behind the missing effect of screening for DM reported in previous randomised controlled trials.[15,41]

The high proportion attending the GP was accompanied by a high proportion and an increase in biochemical testing. The pre- vs post-screening ORs for testing with HbA1c was 2.31 for the pre-DM group and 5.56 for the DM group. Compared with the no-DM group, RORs of 2.25 and 5.42 clearly indicated that the increased biochemical control after screening was selective for the Pre-DM and DM group. Contrary to our expectation, the amount of biochemical control in the group with normal HbA1c values at screening did not decrease post-screening levels. In a healthcare system with limited resources and a growing list of possible diseases and treatments, attention towards negative findings is of utmost importance. Hence, by optimising the use of negative findings at screening, we could reduce the need for future controls. In the present study, no individuals without DM or pre-DM at screening were medically treated for DM within the following two years. Yet, 46.9% had at least one HbA1c measurement during the first year after screening, and the number of contacts along with the proportion contacting the GP remained stationary. Other studies suggest that a normal HbA1c would be sufficient to postpone controls for as long as 3–5 years.[42,43] A normal HbA1c test result may be used to limit the population invited for subsequent testing by prescribing a "safety" period after screening.

Due to contemporaneous findings at screening and the confounding described in the limitations section, we cannot state causality between an elevated HbA1c at screening and an increase in healthcare utilisation since the reported changes could be attributable to the "overall screening". Nevertheless, we believe that the presented changes in healthcare utilisation would represent the expected changes in most screening setups, and most current evidence in the field represents similar conditions where screening for DM and CVD is combined.[44] This approach seems rational in a real-world setting as coexisting CVD and its treatment greatly influence the prognosis for individuals with DM.[45–47] It is also our belief that our findings are novel, mainly due to the setup, minimising selection bias, the use of bedside HbA1c and the inclusion of pre-DM.

Conclusion

Screening for CVD and detection of DM and pre-DM in a general population of 67-years-olds without known DM increased contacts with the GP, use of specific laboratory monitoring and use of glucose-lowering medical treatments. Among individuals with DM and pre-DM, fewer than expected initiated glucose-lowering medicine. Despite intensive follow-up at the GP, the absolute increase in contacts was small due to a high level of pre-screen monitoring. Unexpectedly, GP contacts and monitoring with targeted laboratory testing of those with normal HbA1c values at screening remained unchanged. These findings provide novel insights into the mechanisms underlying the effects of population-based screening for DM and pre-DM and identify possibilities for improving screening for DM in the future. Further research is required to determine whether this behavioral change translates into improved outcomes.

Data Sharing Statement

In accordance with Danish law and for data protection purposes, the datasets analysed for this study are not publicly available.

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Disclosure

The authors have no competing interest to declare.

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References

1. Wilson JM, Jungner YG. Principles and practice of mass screening for disease. *BolOficina SanitPanam*. 1968;65(4):281–393.
2. Magliano D, Boyko EJ. *IDF Diabetes Atlas*. 10th edition ed. International Diabetes Federation; 2021.

3. Andersen JW, Dahl M, Yderstraede KB, Hoegh A. Use of point-of-care HbA1c measurement to estimate the level of undiagnosed diabetes mellitus among 67-year-old participants in a cardiovascular screening programme in the municipality of Viborg, Denmark. *Diabet Med*. 2018;35(9):1197–1201. doi:10.1111/dme.13759
4. Jørgensen ME, Ellervik C, Ekholm O, Johansen NB, Carstensen B. Estimates of prediabetes and undiagnosed type 2 diabetes in Denmark: the end of an epidemic or a diagnostic artefact? *Scand J Public Health*. 2020;48(1):106–112. doi:10.1177/1403494818799606
5. Fonseca VA. Defining and characterizing the progression of type 2 diabetes. *Diabetes Care*. 2009;32(Suppl 2):S151–156. doi:10.2337/dc09-S301
6. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405–412. doi:10.1136/bmj.321.7258.405
7. World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. World Health Organization; 2011. http://www.ncbi.nlm.nih.gov/books/NBK304267/. Accessed May 23, 2022.
8. Nathan DM, Turgeon H, Regan S. Relationship between glycated haemoglobin levels and mean glucose levels over time. *Diabetologia*. 2007;50(11):2239–2244. doi:10.1007/s00125-007-0803-0
9. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. the multicenter metformin study group. *N Engl J Med*. 1995;333(9):541–549. doi:10.1056/NEJM199508313330902
10. Herman WH, Ye W, Griffin SJ, et al. Early detection and treatment of type 2 diabetes reduce cardiovascular morbidity and mortality: a simulation of the results of the Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION-Europe). *Diabetes Care*. 2015;38(8):1449–1455. doi:10.2337/dc14-2459
11. Davidson KW, Barry MJ, Mangione CM, et al.; US Preventive Services Task Force. Screening for prediabetes and type 2 diabetes: us preventive services task force recommendation statement. *JAMA*. 2021;326(8):736–743. doi:10.1001/jama.2021.12531
12. Lauritzen T, Sandbaek A, Carlsen AH, Borch-Johnsen K. All-cause mortality and pharmacological treatment intensity following a high risk screening program for diabetes. A 6.6 year follow-up of the ADDITION study, Denmark. *Prim Care Diabetes*. 2012;6(3):193–200. doi:10.1016/j.pcd.2012.04.005
13. Carris NW, Corvin JA. Prediabetes: an undiagnosed pandemic. *Endocr Pract*. 2022;28(2):231–232. doi:10.1016/j.eprac.2021.10.004
14. Simmons RK, Griffin SJ, Witte DR, Borch-Johnsen K, Lauritzen T, Sandbaek A. Effect of population screening for type 2 diabetes and cardiovascular risk factors on mortality rate and cardiovascular events: a controlled trial among 1,912,392 Danish adults. *Diabetologia*. 2017;60(11):2183–2191. doi:10.1007/s00125-017-4323-2
15. Simmons RK, Rahman M, Jakes RW, et al. Effect of population screening for type 2 diabetes on mortality: long-term follow-up of the Ely cohort. *Diabetologia*. 2011;54(2):312–319. doi:10.1007/s00125-010-1949-8
16. Simmons RK, Griffin SJ, Lauritzen T, Sandbaek A. Effect of screening for type 2 diabetes on risk of cardiovascular disease and mortality: a controlled trial among 139,075 individuals diagnosed with diabetes in Denmark between 2001 and 2009. *Diabetologia*. 2017;60(11):2192–2199. doi:10.1007/s00125-017-4299-y
17. Jonas DE, Crotty K, Yun JDY, et al. Screening for prediabetes and type 2 diabetes mellitus: an evidence review for the U.S. preventive services task force. Agency for Healthcare Research and Quality (US); 2021. Available from: http://www.ncbi.nlm.nih.gov/books/NBK574057/. Accessed April 11, 2022.
18. Dahl M, Lindholt J, Søgaard R, et al. Relevance of the Viborg population based screening programme (VISP) for cardiovascular conditions among 67 year olds: attendance rate, prevalence, and proportion of initiated cardiovascular medicines stratified by sex. *Eur J Vasc Endovasc Surg*. 2023;66(1):119–129. doi:10.1016/j.ejvs.2023.03.014
19. Høgh A, Lindholt JS, Søgaard R, et al. Protocol for a cohort study to evaluate the effectiveness and cost-effectiveness of general population screening for cardiovascular disease: the Viborg Screening Programme (VISP). *BMJ Open*. 2023;13(2):e063335. doi:10.1136/bmjopen-2022-063335
20. Report from the evaluation SKUP. 2012. Available from: www.skup.org. Accessed January 21, 2025.
21. World Health Organization. International statistical classification of diseases and related health problems. 10th revision. https://icd.who.int/browse10/2019/en. Accessed September 12, 2024.
22. StataCorp. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC; 2021.
23. Pedersen KM, Andersen JS, Søndergaard J. General practice and primary health care in Denmark. *J Am Board Fam Med*. 2012;25(Suppl 1):S34–38. doi:10.3122/jabfm.2012.02.110216
24. Hajek A, Bock JO, König HH. Which factors affect health care use among older Germans? Results of the German ageing survey. *BMC Health Serv Res*. 2017;17(1):30. doi:10.1186/s12913-017-1982-0
25. Babitsch B, Gohl D, von Lengerke T. Re-revisiting Andersen's behavioral model of health services use: a systematic review of studies from 1998-2011. *Psychosoc Med*. 2012;9:Doc11. doi:10.3205/psm000089
26. Sarwar N, Gao P; Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet*. 2010;375(9733):2215–2222. doi:10.1016/S0140-6736(10)60484-9
27. Morgan CL, Currie CJ, Peters JR. Relationship between diabetes and mortality: a population study using record linkage. *Diabetes Care*. 2000;23(8):1103–1107. doi:10.2337/diacare.23.8.1103
28. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. *Cardiovasc Diabetol*. 2018;17(1):83. doi:10.1186/s12933-018-0728-6
29. Lindholt JS, Frystyk J, Hallas J, Rasmussen LM, Diederichsen ACP. Feasibility study of advanced cardiovascular screening in middle-aged patients with diabetes. *Clin Epidemiol*. 2020;12:447–455. doi:10.2147/CLEP.S246636
30. Park BH, Lee BK, Ahn J, Kim NS, Park J, Kim Y. Association of participation in health check-ups with risk factors for cardiovascular diseases. *J Korean Med Sci*. 2021;36(3):e19. doi:10.3346/jkms.2021.36.e19
31. Sieben A, Bredie SJH, Luijten JCHBM, van Laarhoven CJHM, van Dulmen S, van Onzenoort H a W. Prior medication adherence of participants and non participants of a randomized controlled trial to improve patient adherence in cardiovascular risk management. *BMC Med Res Methodol*. 2019;19(1):95. doi:10.1186/s12874-019-0743-7
32. Davidson MB. How our current medical care system fails people with diabetes: lack of timely, appropriate clinical decisions. *Diabetes Care*. 2009;32(2):370–372. doi:10.2337/dc08-2046

33. Campbell JM, Bellman SM, Stephenson MD, Lisy K. Metformin reduces all-cause mortality and diseases of ageing independent of its effect on diabetes control: a systematic review and meta-analysis. *Ageing Res Rev*. 2017;40:31–44. doi:10.1016/j.arr.2017.08.003
34. Krass I, Schieback P, Dhippayom T. Adherence to diabetes medication: a systematic review. *Diabet Med*. 2015;32(6):725–737. doi:10.1111/dme.12651
35. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J*. 2020;41(2):255–323. doi:10.1093/eurheartj/ehz486
36. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 diabetes Management Algorithm - 2020 executive summary. *Endocr Pract*. 2020;26(1):107–139. doi:10.4158/CS-2019-0472
37. Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med*. 2005;142(5):323–332. doi:10.7326/0003-4819-142-5-200503010-00007
38. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*. 2022;65(12):1925–1966. doi:10.1007/s00125-022-05787-2
39. Sorli C, Harashima SI, Tsoukas GM, et al. Efficacy and safety of once-weekly semaglutide monotherapy versus placebo in patients with type 2 diabetes (SUSTAIN 1): a double-blind, randomised, placebo-controlled, parallel-group, multinational, multicentre phase 3a trial. *Lancet Diabetes Endocrinol*. 2017;5(4):251–260. doi:10.1016/S2213-8587(17)30013-X
40. ElSayed NA, Aleppo G, Aroda VR, et al. 3. prevention or delay of type 2 diabetes and associated comorbidities: standards of care in diabetes-2023. *Diabetes Care*. 2023;46(Suppl 1):S41–S48. doi:10.2337/dc23-S003
41. Simmons RK, Echouffo-Tcheugui JB, Sharp SJ, et al. Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial. *Lancet*. 2012;380(9855):1741–1748. doi:10.1016/S0140-6736(12)61422-6
42. Takahashi O, Farmer AJ, Shimbo T, Fukui T, Glasziou PP. A1C to detect diabetes in healthy adults: when should we recheck? *Diabetes Care*. 2010;33(9):2016–2017. doi:10.2337/dc10-0588
43. Kahn R, Alperin P, Eddy D, et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet*. 2010;375(9723):1365–1374. doi:10.1016/S0140-6736(09)62162-0
44. Dahl M, Frost L, Søgaard R, Klausen IC, Lorentzen V, Lindholt J. A population-based screening study for cardiovascular diseases and diabetes in Danish postmenopausal women: acceptability and prevalence. *BMC Cardiovasc Disord*. 2018;18(1):20. doi:10.1186/s12872-018-0758-8
45. Kelsey MD, Nelson AJ, Green JB, et al. Guidelines for cardiovascular risk reduction in patients with type 2 diabetes: JACC guideline comparison. *J Am Coll Cardiol*. 2022;79(18):1849–1857. doi:10.1016/j.jacc.2022.02.046
46. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med*. 2008;358(6):580–591. doi:10.1056/NEJMoa0706245
47. Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet*. 2011;378(9786):156–167. doi:10.1016/S0140-6736(11)60698-3