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SHORT COMMUNICATION

Socio-economic gradients in diagnosed and undiagnosed Type 2 diabetes and its related health complications

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Abstract *Background and aims:* Diagnosed and undiagnosed Type 2 Diabetes (T2D) remains a challenge in high-income countries. In addition, the presence of T2D can cause further disease burden because of its high susceptibility to complications. Nevertheless, there is limited evidence of socio-economic gradients in undiagnosed T2D and its complications in a large population cohort. We investigated this using the Dutch Lifelines Cohort Study (Lifelines).
Methods and results: Within Lifelines, baseline data of 102 163 adults aged 30 and above were collected from 2007 to 2013. The associations of Socio-Economic Status (SES), indicated by monthly household income, with the prevalence of T2D status and the number of T2D complications were assessed using multinomial Poisson and linear regressions with adjustments for age and sex. The prevalence of diagnosed and undiagnosed T2D was, respectively, 3.0% and 3.0% in the low SES group compared to 1.1% and 1.8% in the high SES group. Individuals with lower SES were at higher risk of having undiagnosed T2D (relative risk ratio (rrr) [95% CI]: 1.63 [1.47–1.81] for low SES and 1.16 [1.05–1.29] for middle SES) and diagnosed T2D, compared with those with high SES. Lower SES was positively associated with the number of T2D complications (low SES vs. high SES (ref); B [95% CI]: 0.15 [0.13–0.16]).
Conclusion: Complementing the known socio-economic gradients in diagnosed T2D, we document socio-economic gradients in undiagnosed T2D and T2D complications in a single, large general representative population. Furthermore, individuals with low SES with diagnosed or undiagnosed T2D were more susceptible to T2D complications.

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What is already known on this topic

While the socio-economic gradient in T2D is well established for high-income countries, commensurately little is known about the socio-economic gradients in either undiagnosed T2D or in T2D complications.

What this study adds

We document socio-economic gradients in undiagnosed T2D as well as T2D complications using the same study population.

How this study might affect research, practice or policy

Our results serve to inform health policy on the socio-economic gradient in T2D and its complications and highlight the need for focusing preventive and curative policy on reducing the burden of complications stemming from undiagnosed as well as diagnosed T2D, especially for individuals with a low SES.

1. Introduction

Type 2 Diabetes (T2D) is often followed by several health complications, such as cardiovascular disease (CVD), nephropathy, and diabetic foot [1]. Amongst other implications, these complications reduce the quality of life over and above the direct consequences of T2D [2] and additional healthcare costs [3].

While the socio-economic gradient in T2D in the Netherlands and other high-income countries is well documented, with lower socio-economic groups displaying a higher risks of prevalent and incident T2D [4,5], little is known about the gradient of T2D complications. Despite implementing public health interventions, no reduction in health inequalities has been observed in high-income countries, including the Netherlands [6]. We hypothesize that this scenario could be partially explained by the socio-economic gradient among the undiagnosed T2D group; presumably, this group is more likely to develop worse T2D complications if their T2D remains undetected and untreated [7–9]. Nevertheless, there is limited evidence of such a socio-economic gradient in undiagnosed T2D and its complications, as undiagnosed T2D in combination with its complications is typically not studied in a single large population cohort in the Netherlands. The unique data from the Lifelines Biobank and Cohort Study (Lifelines) allow us to study this.

Considering the direct and indirect health and financial consequences of T2D, identifying people with T2D at an early stage is essential for effective and efficient care, as early glucose control can prevent T2D complications [13]. However, for a variety of reasons, there is a group of people who remain undiagnosed with T2D. In fact, undiagnosed T2D remains a problem even in high-income countries with wide access to healthcare, including Germany [11] and the UK [12], where 2.9% and 2.0% of the study populations had undiagnosed T2D, respectively. Presumably, the Netherlands is not an exception in terms of undiagnosed T2D. Furthermore, T2D patients may already suffer from T2D complications at the point of diagnosis [7,8]. Indeed, undiagnosed T2D is also a higher risk for CVD and mortality compared with diagnosed T2D [9].

In this report, we investigated socio-economic inequalities in T2D status (diagnosed T2D, undiagnosed T2D, and non-T2D) and its complications (CVD, hypertension, stroke, dyslipidaemia, poor control of diabetes, need for hospitalization, and nephropathy) in the baseline assessment of Lifelines.

2. Methods

Lifelines is a large, population-based biobank and cohort study based in the northern part of the Netherlands. The Lifelines adult study population broadly represents the adult population in the north of the Netherlands [14,15]. Participants visited one of the Lifelines research sites for a physical examination, including extensive questionnaires about their demographics, health status, and Socio-Economic Status (SES). Blood samples were drawn at baselines and subsequently stored at −80 °C to allow for future measurements, including serum levels of glucose and HbA1c. Before study entry, a signed informed consent form was obtained from each participant. In total, 152,928 adults (age ≥18) were recruited at baseline from 2007 to 2013. Despite the slightly old baseline assessment, the unique nature of the Lifelines cohort in combining diagnosed as well as undiagnosed T2D and its complications should be highlighted. The Lifelines study was conducted according to the principles of the Declaration of Helsinki and approved by the Medical Ethics Committee of the Institutional Review Board of the University Medical Center Groningen, the Netherlands (2007/152).

Among the 152 928 adult participants recruited at Lifelines baseline, participants aged 30 years and above were selected because of their relatively stable SES. In total, 102 163 were aged 30 and above and had valid data on SES and T2D status (Figure S1). SES was defined according to self-reported household net income [1]: low − <2000 euro/month [2]; middle − 2000–3000 euro/month; and [3] high − >3000 euro/month. Detailed definitions of T2D status and T2D complications, as well as SES, are contained in detail in Methods S1. The number of T2D complications was calculated by scoring the presence of each T2D complication as 1 and then summing up the scores.

The prevalence of T2D complications were assessed across T2D status and SES, and the prevalence of T2D status and the number of its complications were presented across SES. The associations of SES with T2D status and single complications, as well as the total number of complications, were assessed using multinomial Poisson regression and linear regression, respectively, with adjustment for age and sex. Relative risk ratios (rrr) [95%

Table 1 Prevalence of Type 2 Type 2 Diabetes (T2D) complications across T2D status and Socio-Economic Status (SES) (a), and T2D status and the number of its complications across SES (b).

		Cardiovascular disease	Hypertension	Stroke	Dyslipidaemia	Poor control of diabetes	Need for hospitalization	Nephropathy
Diagnosed T2D (Case/population: 1874/102,163)	Low SES (n = 840)	218 (26.0%)	584 (69.5%)	26 (3.1%)	687 (82.8%)	311 (38.2%)	83 (15.7%)	43 (5.1%)
	Middle SES (n = 605)	131 (21.6%)	396 (65.5%)	12 (2.0%)	501 (83.5%)	231 (39.3%)	59 (14.4%)	28 (4.6%)
	High SES (n = 429)	85 (19.8%)	269 (62.7%)	12 (2.8%)	350 (82.7%)	162 (39.6%)	40 (14.4%)	17 (4.0%)
	Total (n = 1874)	434 (23.2%)	1249 (66.7%)	50 (2.7%)	1538 (83.1%)	704 (38.8%)	182 (14.9%)	88 (4.7%)
Undiagnosed T2D (Case/population: 2293/102,163)	Low SES (n = 861)	144 (16.7%)	324 (37.6%)	15 (1.7%)	449 (61.7%)	93 (13.2%)	71 (13.1%)	22 (2.6%)
	Middle SES (n = 765)	80 (10.5%)	250 (32.7%)	7 (0.9%)	393 (59.9%)	98 (15.8%)	53 (10.5%)	17 (2.2%)
	High SES (n = 667)	56 (8.4%)	178 (26.7%)	6 (0.9%)	281 (53.3%)	66 (13.1%)	28 (7.0%)	18 (2.7%)
	Total (n = 2293)	280 (12.2%)	752 (32.8%)	28 (1.2%)	1123 (58.8%)	257 (14.0%)	152 (10.5%)	57 (2.5%)
Non-T2D (Case/population: 97,996/102,163)	Low SES (n = 26,732)	1676 (6.3%)	5034 (18.8%)	203 (0.8%)	9937 (37.2%)	/	1772 (10.0%)	313 (1.2%)
	Middle SES (n = 34,419)	1641 (4.8%)	5317 (15.5%)	177 (0.5%)	11,964 (34.8%)	/	1995 (8.5%)	306 (0.9%)
	High SES (n = 36,845)	1330 (3.6%)	4643 (12.6%)	113 (0.3%)	11,672 (31.7%)	/	1891 (7.7%)	252 (0.7%)
	Total (n = 97,996)	4647 (4.7%)	14 994 (15.3%)	493 (0.5%)	33,573 (34.3%)	/	5658 (8.6%)	871 (0.9%)

	T2D status			The number of T2D complications[a]			
SES	Diagnosed T2D	Undiagnosed T2D	Non-T2D	0	1	2	≥3
Low SES (n = 28,433)	3%	3%	94%	46%	33.4%	13.4%	7.1%
Middle SES (n = 35,789)	1.7%	2.1%	96.2%	50%	34.5%	10.8%	4.7%
High SES (n = 37,941)	1.1%	1.8%	97.1%	54.7%	33.1%	8.9%	3.3%
Total (n = 102,163)	1.8%	2.2%	95.9%	50.6%	33.7%	10.8%	4.9%

[a] The number of T2D complications was calculated by scoring the presence of each T2D complication as 1 and then summing up the scores.

CI] and unstandardized beta-coefficients (B) [95% CI] were presented. All statistical analyzes were conducted using Stata 13.1 (StataCorp, Texas, USA).

3. Results

Overall, the prevalence of diagnosed and undiagnosed T2D was 1.8% and 2.2%, respectively, for the total sample population. Among individuals with lower SES, the prevalence of diagnosed and undiagnosed T2D was, respectively, 3.0% and 3.0%, compared to 1.1% and 1.8% among individuals with high SES. 7.1% and 3.3% of the participants in, respectively, low- and high-SES groups had three or more T2D complications (Table 1). The prevalence of T2D complications was elevated for the lower SES strata (Fig. 1 and Table S1) and among individuals with diagnosed and undiagnosed T2D. Among the T2D group, individuals with diagnosed T2D had the highest prevalence of complications (Table 1). Among diagnosed as well as undiagnosed T2D groups, socio-economic gradients in T2D complications were also observed, with individuals with low SES having a higher prevalence of T2D complications than individuals with middle or high SES. T2D complications were more prevalent among individuals with low SES in either the diagnosed or undiagnosed T2D groups compared to those with low SES but without T2D (Table 1).

Compared to individuals with high SES, individuals with lower SES were shown to have higher risks of diagnosed T2D (rrr [95% CI]: 2.03 [1.80–2.30], $p < 0.001$ for low SES and 1.29 [1.13–1.46], $p < 0.001$ for middle SES) and undiagnosed T2D (rrr [95% CI]: 1.63 [1.47–1.81], $p < 0.001$ for low SES and 1.16 [1.05–1.29], $p = 0.004$ for middle SES) (see Table 2). Furthermore, lower SES was also positively associated with the number of T2D complications (B [95% CI]: 0.15 [0.13–0.16], $p < 0.001$ for low SES and 0.06 [0.04–0.07], $p < 0.001$ for middle SES, with high SES as the reference, Table 2).

4. Discussion

4.1. Key results

In this general Dutch population, individuals with low SES were at higher risk of having diagnosed T2D and undiagnosed T2D compared to individuals with higher SES, which is consistent with previous studies conducted in populations from England [12] and Germany [11]. Complementing the reported SES inequalities in T2D complications in a systematic review [3], we found that the prevalence of T2D complications was higher among individuals with low SES and T2D (either diagnosed or undiagnosed), compared to individuals with high SES and without T2D.

4.2. Limitations

First, extra caution is needed when interpreting the prevalence of undiagnosed T2D because the blood sample

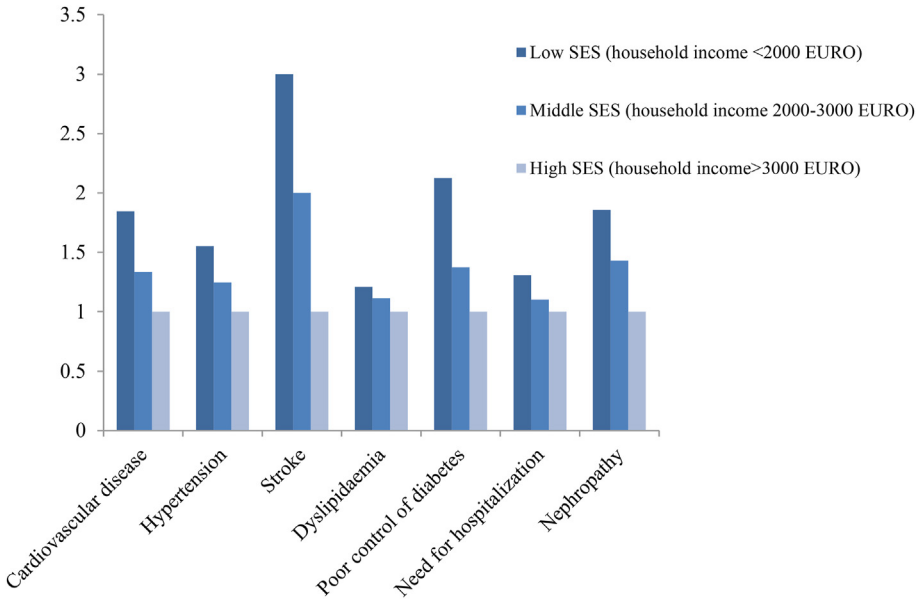

Figure 1 Relative prevalence of T2D complications across different Socio-Economic Status (SES) with high SES as the reference group.

collection and measurements were done over five consecutive years. Therefore, undiagnosed T2D in this study was partially interfered with incident T2D. Second, the baseline assessment used in this study is nearly a decade old, and investigations with more recent assessments are needed to validate the results. Third, reporting bias could occur as T2D complications were partially self-reported. Fourth, selection bias should be acknowledged as Lifelines is not a registration database, so the prevalence of T2D and complications could be influenced by the recruitment criteria. Finally, no causal inferences should be drawn from our findings, given the cross-sectional nature of our study.

4.3. Interpretation and generalization

While previously published studies on the associations between SES and undiagnosed T2D are limited and not consistent [10–12,16,17], our results highlight that SES might be a risk factor not only for diagnosed T2D and undiagnosed T2D but also for T2D complications. More importantly, individuals with low SES with diagnosed or undiagnosed T2D were found to be even more susceptible to T2D complications. This might hint at a mechanism whereby T2D only gets diagnosed once a complication has arisen. If people with lower SES and undiagnosed T2D are left undiagnosed and untreated, the double burden of low SES and undiagnosed T2D will result in worse quality of life as well as extra healthcare costs. Future research should identify the individual and societal risk factors associated with undiagnosed T2D compared to diagnosed T2D across different SES groups. It is worth mentioning that the multi-dimensional and multi-faceted nature of SES could also affect the SES gradients in T2D status and complications, as suggested by previous studies [4,18]. Thus, the interplay between different SES indicators needs to be addressed to tackle the SES gradients in T2D and its complications. Moreover, there is a need to dissect the role of an individual's lifestyle in these inequalities as lifestyle intervention is often advocated to prevent and manage

Table 2 Association of Socio-Economic Status (SES) with Type 2 Diabetes (T2D) status and the number of T2D complications, respectively.[a]

	T2D status Diagnosed T2D (Case/population: 1874/102,163)		Undiagnosed T2D (Case/population: 2293/102,163)		Non-T2D		The number of T2D complications[b]	
SES	rrr (95% CI)	p	rrr (95% CI)	p	rrr (95% CI)	p	B (95% CI)	p
Low SES	2.03 (1.80–2.30)	<0.001	1.63 (1.47–1.81)	<0.001		0.15 (0.13–0.16)	<0.001	
Middle SES	1.29 (1.13–1.46)	<0.001	1.16 (1.05–1.29)	0.004	Ref	0.06 (0.04–0.07)	<0.001	
High SES			Ref			Ref		

[a] Models were adjusted for age and sex. rrr: relative risk ratio; B: beta-coefficient; CI: confidence interval.
[b] The number of T2D complications was calculated by scoring the presence of each T2D complication as 1 and then summing up the scores. The higher the score, the presence of more T2D complications.

T2D. While we have focused on the Netherlands, future research should aim to understand whether the patterns that we have documented also hold in other countries.

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Declaration of competing interest

The authors have nothing to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2022.09.018.

References

[1] Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010;375(9733):2215–22.
[2] Arnold SV, Khunti K, Tang F, Chen H, Nicolucci A, Gomes MB, et al. Impact of micro- and macrovascular complications of type 2 diabetes on quality of life: insights from the DISCOVER prospective cohort study. Endocrinol Diabetes Metab 2022:e00321.
[3] Tatulashvili S, Fagherazzi G, Dow C, Cohen R, Fosse S, Bihan H. Socioeconomic inequalities and type 2 diabetes complications: a systematic review. Diabetes Metab 2020;46(2):89–99.
[4] Qi Y, Koster A, van Boxtel M, Köhler S, Schram M, Schaper N, et al. Adulthood socioeconomic position and type 2 diabetes mellitus-A comparison of education, occupation, income, and material deprivation: the maastricht study. Int J Environ Res Publ Health 2019; 16(8).
[5] Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. Int J Epidemiol 2011;40(3):804–18.
[6] Hu Y, van Lenthe FJ, Judge K, Lahelma E, Costa G, de Gelder R, et al. Did the English strategy reduce inequalities in health? A difference-in-difference analysis comparing England with three other European countries. BMC Publ Health 2016;16(1):865.
[7] Spijkerman AM, Dekker JM, Nijpels G, Adriaanse MC, Kostense PJ, Ruwaard D, et al. Microvascular complications at time of diagnosis of type 2 diabetes are similar among diabetic patients detected by targeted screening and patients newly diagnosed in general practice: the hoorn screening study. Diabetes Care 2003;26(9):2604–8.
[8] Khalil SA, Megallaa MH, Rohoma KH, Guindy MA, Zaki A, Hassanein M, et al. Prevalence of chronic diabetic complications in newly diagnosed versus known type 2 diabetic subjects in a sample of alexandria population, Egypt. Curr Diabetes Rev 2019;15(1): 74–83.
[9] Paprott R, Schaffrath Rosario A, Busch MA, Du Y, Thiele S, Scheidt-Nave C, et al. Association between hemoglobin A1c and all-cause mortality: results of the mortality follow-up of the German National Health Interview and Examination Survey 1998. Diabetes Care 2015;38(2):249–56.
[10] Zhang N, Yang X, Zhu X, Zhao B, Huang T, Ji Q. Type 2 diabetes mellitus unawareness, prevalence, trends and risk factors: national Health and Nutrition Examination Survey (NHANES) 1999-2010. J Int Med Res 2017;45(2):594–609.
[11] Du Y, Baumert J, Paprott R, Teti A, Heidemann C, Scheidt-Nave C. Factors associated with undiagnosed type 2 diabetes in Germany: results from German health interview and examination survey for adults 2008–2011. BMJ Open Diabetes Res Care 2020;8(1).
[12] Moody A, Cowley G, Ng Fat L, Mindell JS. Social inequalities in prevalence of diagnosed and undiagnosed diabetes and impaired glucose regulation in participants in the Health Surveys for England series. BMJ Open 2016;6(2).
[13] Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359(15):1577–89.
[14] Klijs B, Scholtens S, Mandemakers JJ, Snieder H, Stolk RP, Smidt N. Representativeness of the LifeLines cohort study. PLoS One 2015; 10(9):e0137203.
[15] van der Ende MY, Hartman MHT, Hagemeijer Y, Meems LMG, de Vries HS, Stolk RP, et al. The LifeLines Cohort Study: prevalence and treatment of cardiovascular disease and risk factors. Int J Cardiol 2017;228:495–500.
[16] Heltberg A, Andersen JS, Sandholdt H, Siersma V, Kragstrup J, Ellervik C. Predictors of undiagnosed prevalent type 2 diabetes - the Danish general suburban population study. Prim Care Diabetes 2018;12(1):13–22.
[17] Leahy S, AM OH, OL N, Healy M, McCormack M, Kenny RA, et al. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: findings from the Irish Longitudinal Study on Ageing (TILDA). Diabetes Res Clin Pract 2015;110(3):241–9.
[18] Allen K, McFarland M. How are income and education related to the prevention and management of diabetes? J Aging Health 2020; 32(9):1063–74.