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Cardiovascular risk management in people with type 1 diabetes: performance using three guidelines

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ABSTRACT

Introduction Cardiovascular disease (CVD) is the leading cause of mortality in individuals with type 1 diabetes mellitus (T1DM). Cardiovascular risk management is therefore essential in the management of individuals with T1DM. This study describes the performance of lipid and blood pressure management in individuals with T1DM using three guidelines.

Research design and methods Individuals ≥18 years with T1DM, treated with insulin for ≥1 year, visiting Diabeter or the University Medical Center Groningen between January 1, 2018 and December 31, 2018, were included. Lipid and blood pressure management were examined using the Dutch, American Diabetes Association (ADA) and National Institute for Health and Care Excellence (NICE) guidelines. Concordance of recommended and prescribed lipid-lowering (LLM) or antihypertensive medication (AHM) was assessed per guideline and 10-year age groups. Achievement of treatment targets was assessed for those prescribed medication.

Results A total of 1855 individuals with T1DM were included. LLM and AHM was prescribed in 19% and 17%, respectively. In individuals recommended LLM, this was prescribed in 22%–46% according to Dutch, ADA or NICE guideline recommendations. For individuals recommended AHM, this was prescribed in 52%–75%. Recommended and actual prescription of LLM and AHM increased over age for all three guidelines. However, discordance between treatment recommendation and medication prescribed was higher in younger, compared with older, age groups. Low-density lipoprotein-cholesterol targets were achieved by 50% (without CVD) and 31% (with CVD) of those prescribed LLM. The blood pressure target was achieved by 46% of those prescribed AHM.

Conclusion This study suggests that there is undertreatment of lipid and blood pressure according to guideline recommendations, particularly in younger age groups. Treatment targets are not met by most individuals prescribed medication, while guidelines recommendations differ considerably. We recommend to investigate the factors influencing undertreatment of lipid and blood pressure management in individuals with T1DM.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is a disproportionately higher incidence and prevalence of cardiovascular disease in individuals with type 1 diabetes.
⇒ Lipid-lowering medication and blood pressure management can improve cardiovascular outcomes.

WHAT THIS STUDY ADDS

⇒ There is substantial undertreatment of lipid levels and blood pressure.
⇒ There is a great discordance between guideline recommendations and medication prescription in younger age groups.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests undertreatment of cardiovascular management and suggests that research is needed to investigate factors influencing undertreatment to improve cardiovascular outcomes in individuals with type 1 diabetes and urges for harmonisation of international guidelines.

INTRODUCTION

The Diabetes Control and Complications trials demonstrated the importance of optimal glycemic control in the prevention of cardiovascular disease (CVD) in individuals with type 1 diabetes.[1] Advancements in blood glucose-lowering treatment strategies and cardiovascular risk management (CVRM) have led to a decreasing trend in CVD in the type 1 diabetes population,[2] yet an excess of CVD morbidity and mortality in type 1 diabetes still exists.[2 3]

CVRM in type 1 diabetes includes promoting exercise and a healthy diet, as well as the management of cardiovascular risk factors such as dyslipidemia and hypertension.[4 5] Multiple systematic reviews have shown that the lowering of total cholesterol and low-density lipoprotein (LDL)-cholesterol decreases the incidence of CVD.[6] The Heart Protection Study showed that the 5-year major vascular event rate among individuals with diabetes mellitus type 1 and 2, randomised to the simvastatin group was

lower compared with those who received placebo (20.2% vs 25.1%).[7] However, subanalysis in individuals with type 1 diabetes showed the 5-year major vascular event rate was not significantly lower (13.7% vs 17.5%).[7] Blood pressure management also plays a substantial role in CVD reduction. Hägg-Holmberg *et al* showed a linear relationship between blood pressure and the incidence of stroke in 4105 individuals with type 1 diabetes.[8] The HR for a stroke was 1.20 (95% CI 1.11 to 1.29) for every 10 mm Hg increased systolic blood pressure.[8] Evidence from these, and other studies, has led to the development of treatment targets in CVRM guidelines.

CVRM guideline recommendations for the identification of risk groups and treatment targets differ across countries. Specifically, for lipid management, no prospective clinical study on the effectiveness of lipid lowering has been conducted in a type 1 diabetes population. Consequently, evidence on the treatment criteria, optimal moment to start statin therapy, the target LDL-cholesterol and the resulting CVD risk reduction remain unclear.[9] As a result, CVRM guideline recommendations for individuals with type 1 diabetes are largely based on extrapolations from studies in people with type 2 diabetes. Differences in risk stratification and treatment goals are notable for lipid management.[5 10 11] For example, the 2018 American Diabetes Association (ADA) guideline for lipid management uses the minimum age of 40 years and classical risk factors to determine treatment recommendations.[12] In contrast, the Dutch guidelines use the presence of diabetes mellitus with end-organ damage, renal function and classical risk factors to determine an individual's risk.[5] The National Institute for Health and Care Excellence (NICE) guidelines recommend considering statins in all individuals with type 1 diabetes.[11] Less variation across guidelines/countries is seen in recommendations for blood pressure management where more evidence is available.[4 5 13]

In this study, we report the pharmacological lipid and blood pressure management of individuals with type 1 diabetes in two diabetes centres in the Netherlands. The aim of this study is to evaluate whether the study population is optimally treated, and how performance differs when using different guidelines. Using the Dutch (2018), ADA (2018) and NICE (2014) guidelines, we compare the recommended lipid and blood pressure management to the prescribed medication. Potential undertreatment or overtreatment will be described, as well as the degree of achieving treatment targets. By evaluating the use of management strategies overall, and in different age groups, we describe any undertreatment or overtreatment and potential areas of improvement.

METHODS

Study design/Participant selection

This is a cross-sectional record review. Data were collected from patients visiting Diabeter, a specialised type 1 diabetes treatment and research centre with five locations throughout the Netherlands, and the University Medical Center Groningen (UMCG) for annual diabetes complication screening between January 1, 2018 and December 31, 2018.

Individuals were included if they had a type 1 diabetes diagnosis, defined as having at least one of the ADA criteria for diabetes mellitus in combination with a clinical presentation of type 1 diabetes such as presenting with diabetic ketoacidosis or the presence of autoantibodies.[14] Furthermore, individuals were included if they were aged ≥18 years and had been treated with insulin therapy for ≥1 year. Individuals were excluded if total cholesterol, high-density lipoprotein (HDL)-cholesterol, LDL-cholesterol and triglycerides were not available.

Data extraction and variable definition

Pseudonymized data were extracted from electronic medical records (EMRs) from the annual diabetes complication screening visit, using text mining strategies. Data extracted included demographic data on sex, ethnicity or parent's country of birth, age in 2018 and smoking status. Diabetes-related complications extracted included coronary artery disease, cerebrovascular accidents or transient ischemic attacks and peripheral arterial disease. Furthermore, hypertension, dyslipidemia, height, weight, systolic and diastolic blood pressure and medication were extracted from the EMRs. Laboratory measurements were extracted from the annual screening. If no laboratory measurements had been made on the day of the screening, the closest measurement within a window of 1 year from the annual diabetes complication screening visit was used. Laboratory measurements extracted included hemoglobin A1c (HbA1c), total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, creatinine, urinary creatinine, urinary albumin and albumin:creatinine ratio. Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease-Epidemiology (CKD-EPI) formula.[15]

Individuals were positive for atherosclerotic CVD if they had a positive medical history of coronary artery disease, cerebrovascular accidents, transient ischemic attacks or peripheral arterial disease in their EMR. Dyslipidemia was defined as either the presence of a positive medical history for dyslipidemia, the use of lipid-lowering medication (LLM) or the presence of at least one of the following: an untreated total cholesterol >6 mmol/L, LDL-cholesterol >4 mmol/L, HDL-cholesterol <1 mmol/L or triglycerides >2 mmol/L.[16] Hypertension was defined as either the presence of a positive medical history for hypertension, the use of antihypertensive medication (AHM) or the presence of an untreated blood pressure measurement >140/90 mm Hg measured during an outpatient visit.[4 5]

Ethnicity was coded as either western European or non-western European. The non-western European group was not further specified as this group was heterogeneous and no nuanced grouping could be made. When data on ethnicity were absent, the parental countries of birth were

used as a proxy. If at least one parent was born outside of Europe or Northern America, the ethnicity was coded as non-western European.

Body mass index (BMI) was calculated as weight in kilograms divided by the height in metres squared. Individuals were categorised as either underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) or obese (≥30 kg/m^2).[17]

Medication prescribed was coded based on the generic name, and classified into medicinal groups (ie, statin, ACE inhibitor, diuretic). If combination medication was used, the individual was positive for both medicinal groups. Finally, classification was made according to working mechanism: LLM, AHM and antithrombotic medication. An individual was positive for one of these groups if at least one medication was prescribed per working mechanism. For example, an individual prescribed an angiotensin blocker and a calcium antagonist would be positive for AHM.

Guideline recommendations and treatment targets

For each individual, criteria from the 2018 Dutch, ADA and NICE guideline recommendations were applied to determine whether they would recommend LLM and AHM. These criteria were assessed based on the available data from the annual screening visit and were coded according to the guideline criteria (see online supplemental table 1).

For the Dutch guidelines, individuals were coded as: no LLM, consider LLM and start LLM. Applying the ADA lipid recommendations, individuals were coded as: no LLM, consider moderate LLM, moderate LLM, consider high-intensity LLM and start high-intensity LLM. Using the NICE lipid guideline, individuals were coded as: consider moderate LLM, offer LLM and start LLM. We used the class lables in agreement with the respective guidelines.

For the ADA and NICE blood pressure guidelines, individuals were coded as no AHM and start AHM. For the Dutch guidelines, individuals were coded into the groups no AHM, consider AHM and start AHM.

Achieving treatment targets is defined by the ADA and Dutch guidelines as achieving a treated LDL-cholesterol <2.6 mmol/L or <1.8 mmol/L for those without CVD and with CVD, respectively. The NICE guidelines do not use specific treatment targets but recommend aiming for a 40% reduction in non-HDL. Due to the cross-sectional study design, this target could not be assessed. Individuals prescribed AHM achieved targets if their blood pressure was <140/90 mm Hg.

Statistical analysis

This is a descriptive study; no inferential statistical tests were performed. Analyses were conducted using R Statistical Software, R Studio Software and R packages: dplyr, qwraps2 and ggplot2.[18–23] Participant characteristics are presented for the whole study population. Data shown are unadjusted means and SD, medians and IQR (25th, 75th percentile) or n with %s. Missing data are reported as n (%).

The frequency of each recommendation per guideline and the prescription of LLM and AHM for each recommendation are presented as n (%). Additionally, the frequency of recommendations per guideline and prescription of medication are presented for the age groups: 18 to <25, 25 to <30, 30 to <40, 40 to <50, 50 to <60, 60 to <70, and 70+ years. Lastly, achieving targets are given as percentages of those meeting treatment targets in those prescribed LLM and AHM.

RESULTS

In total, 1855 individuals with type 1 diabetes were included for analysis and 438 were excluded due to missing data. Individuals with missing data were more often non-Western European with slightly poorer renal function (online supplemental table 2). Characteristics of the study population can be found in table 1. Median age and diabetes duration were 27 (IQR 22, 43) years and 16 (IQR 10, 24) years, respectively. Half the study population was female, and the majority was western European. The mean HbA1c was 63 mmol/mol (7.9%).

CVD was present in 4.3% of the population. LLM was prescribed in 19% of the population and AHM was prescribed in 17% of the total study population.

Lipid guideline recommendation and medication prescription

Figure 1 shows the frequency of each guideline recommendation and the count and percentage of LLM prescribed per recommendation (for details see online supplemental table 3). The discrepancy between recommendations and prescription patterns are evident for all three guidelines. However, the biggest discrepancy can be seen when using the Dutch guidelines (figure 2A). More than half of the individuals recommended to start LLM are not prescribed it. Moreover, less than a quarter of the individuals recommended to consider LLM are prescribed LLM.

The gap observed between recommendation and prescription in figure 1 is further demonstrated per age group in figure 2. Recommendations to consider or start LLM are more frequent in the older age groups, and the number of prescriptions appears to increase accordingly with age. In comparison, in the younger age groups the recommendations to start and consider LLM are less frequent, however the prescription of LLM also appears to be less frequent. This pattern is most prominent in the Dutch guideline. As figure 2A illustrates, 18% of individuals with very high risk between ages 18 and 25 years were prescribed LLM in comparison to 70% with an age ≥70 years (online supplemental table 4). Similar patterns of medication prescription are shown when using the ADA (figure 2B) and NICE (figure 2C) guidelines (online supplemental tables 5 and 6).

Although the overall patterns in prescription are similar for all three guidelines, the heterogeneity in

Table 1 Population characteristics

Participant demographic and anthropometric measurements, n=1855	
Age, years	26.8 (22.3, 43.4)
Age group (years)	
18 to <25, n (%)	769 (41.5)
25 to <30, n (%)	339 (18.3)
30 to <40, n (%)	227 (12.2)
40 to <50, n (%)	173 (9.3)
50 to <60, n (%)	190 (10.2)
60 to <70, n (%)	115 (6.2)
≥70 years, n (%)	42 (2.3)
Female sex, n (%)	932 (50.2)
Ethnicity western European, n (%)	1754 (94.6)
Diabetes duration, years	15.7 (10.1, 23.8)
Smoking	
Current smoker, n (%)	250 (14.2)
Former smoker, n (%)	61 (3.5)
Never smoker, n (%)	1448 (82.3)
BMI, kg/m^2	25.6±4.4
Underweight, n (%)	25 (1.5)
Normal weight, n (%)	824 (49.2)
Overweight, n (%)	584 (34.8)
Obese, n (%)	243 (14.5)
Systolic blood pressure, mm Hg	131±13
Diastolic blood pressure, mm Hg	76±9
Laboratory measurements	
HbA1c, mmol/mol	63±17
HbA1c, %	7.9±1.5
Creatinine, µmol/L	70 (62, 80)
eGFR, mL/min/1.73 m^2	98 (82, 117)
Cholesterol, mmol/L	4.46±0.91
HDL-cholesterol, mmol/L	Male: 1.46±0.39 Female: 1.71±0.46
LDL-cholesterol, mmol/L	2.68±0.79
Triglycerides, mmol/L	1.00 (0.73, 1.40)
Diabetes-related complications	
Retinopathy, n (%)	270 (14.6)
Neuropathy, n (%)	153 (8.3)
Nephropathy, n (%)	116 (6.3)
Coronary artery disease, n (%)	59 (3.2)
Cerebrovascular disease, n (%)	14 (0.8)
Peripheral arterial disease, n (%)	31 (1.7)
Diabetic foot abnormalities, n (%)	87 (4.7)
Dyslipidemia, n (%)	662 (35.7)
Hypertension, n (%)	607 (35.0)
Cardiovascular disease, n (%)	80 (4.3)
Medication use	
Lipid-lowering medication, n (%)	358 (19.3)
Statin, n (%)	347 (18.7)
Ezetimibe, n (%)	37 (2.0)
Antihypertensive medication, n (%)	318 (17.1)
ACE inhibitor, n (%)	203 (10.9)
Angiotensin receptor blocker, n (%)	83 (4.5)
Dihydropyridines, n (%)	90 (4.9)
Diuretic, n (%)	103 (5.6)
Beta-blocker, n (%)	81 (4.4)
Antithrombotic medication, n (%)	103 (5.7)
Platelet aggregation inhibitor, n (%)	67 (3.6)
Anticoagulants, n (%)	21 (1.1)
Low molecular weight heparin, n (%)	28 (1.5)

Data presented as mean (±SD), median (Q1, Q3), n (%). N=1 missing: DM duration, retinopathy, neuropathy, nephropathy, coronary artery, CVA, dyslipidemia, CVD. N=2 missing: peripheral arterial disease. N=6 missing: HbA1c. N=9 missing: diabetic foot abnormalities. N=36 missing: creatinine and eGFR. N=96 missing: smoking. N=118 missing: hypertension. N=137 missing: systolic and diastolic blood pressure. N=179 missing: BMI.
BMI, body mass index; CVA, cerebrovascular accident; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

recommendations is more evident per age group across the three guidelines.

Blood pressure guideline recommendation and medication prescription

Figure 3 illustrates the frequency of recommendations and the prescription of AHM per guideline (for details see online supplemental tables 7 and 8). The percentage of individuals who were treated with AHM according to the guideline recommendations were 52% for the ADA and NICE guidelines, and 75% using the Dutch guidelines.

Similar to the LLM recommendations, both the recommendation and prescription of AHM increases in the older age groups, with a slight tapering in the age group 70+ years (figure 4). Again, despite guideline recommendations to start AHM, medication is prescribed less frequently in younger age groups in comparison to older age groups. This is visible in figure 4B and C, where in the age group 18–25 years, 12% of individuals who should be offered AHM were prescribed medication vs 72% in the age group 70+ years. Applying the Dutch guideline (figure 4A), a similar pattern is observed, where 64% of the age group 18–25 years recommended medication were prescribed AHM, in comparison to 83% in the 70+ years age group.

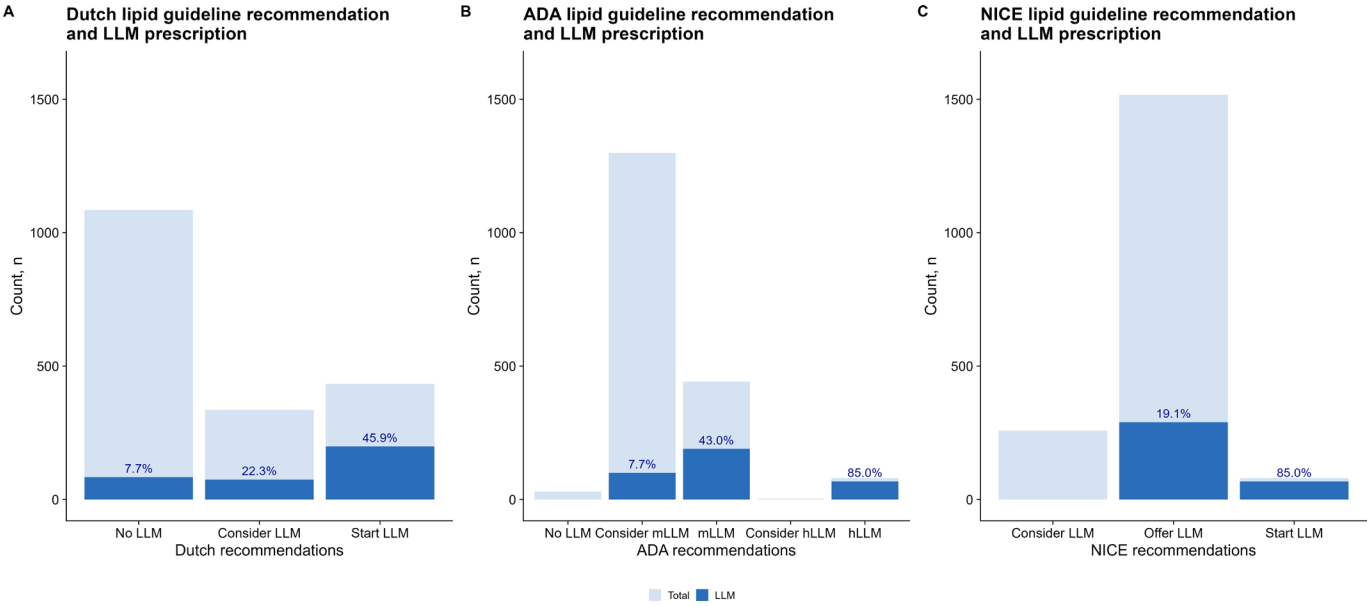

Figure 1 Frequency of lipid guideline recommendations in the study population based on the (A) Dutch, (B) American Diabetes Association (ADA) and (C) National Institute for Health and Care Excellence (NICE) guidelines and the prescription of lipid-lowering medication (LLM) for each recommendation group. Percentages presented are the percentage of LLM use per recommendation.

Achieving treatment targets: lipids and blood pressure

LLM was prescribed to 290 individuals without CVD and the target of LDL-cholesterol <2.6 mmol/L was achieved by 50%. LLM was also prescribed to 68 individuals with CVD, of whom 31% had achieved the target LDL-cholesterol of <1.8 mmol/L. Blood pressure measurements were available for 302 individuals using AHM, of which 46% had reached the target of <140/90 mm Hg (see online supplemental table 9).

DISCUSSION

In this study, we have described the pharmacological lipid and blood pressure management of individuals with type 1 diabetes in six diabetes centres in the Netherlands. As there is no uniform worldwide consensus, we have compared the results of three different guidelines. The data suggest that there may be undertreatment for the prevention of cardiovascular disease, for both lipid and blood pressure management. We also found that a

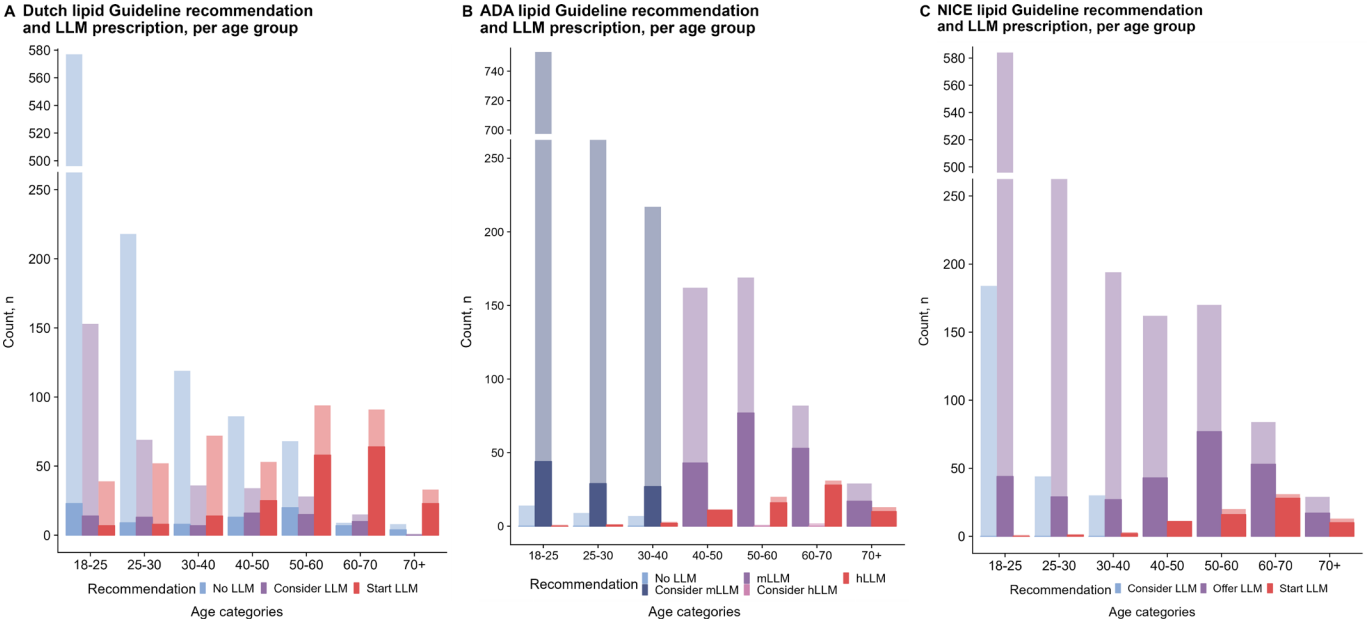

Figure 2 Frequency of lipid guideline recommendations per age category based on the (A) Dutch, (B) American Diabetes Association (ADA) and (C) National Institute for Health and Care Excellence (NICE) guidelines and the prescription of lipid-lowering medication (LLM) within each recommendation group.

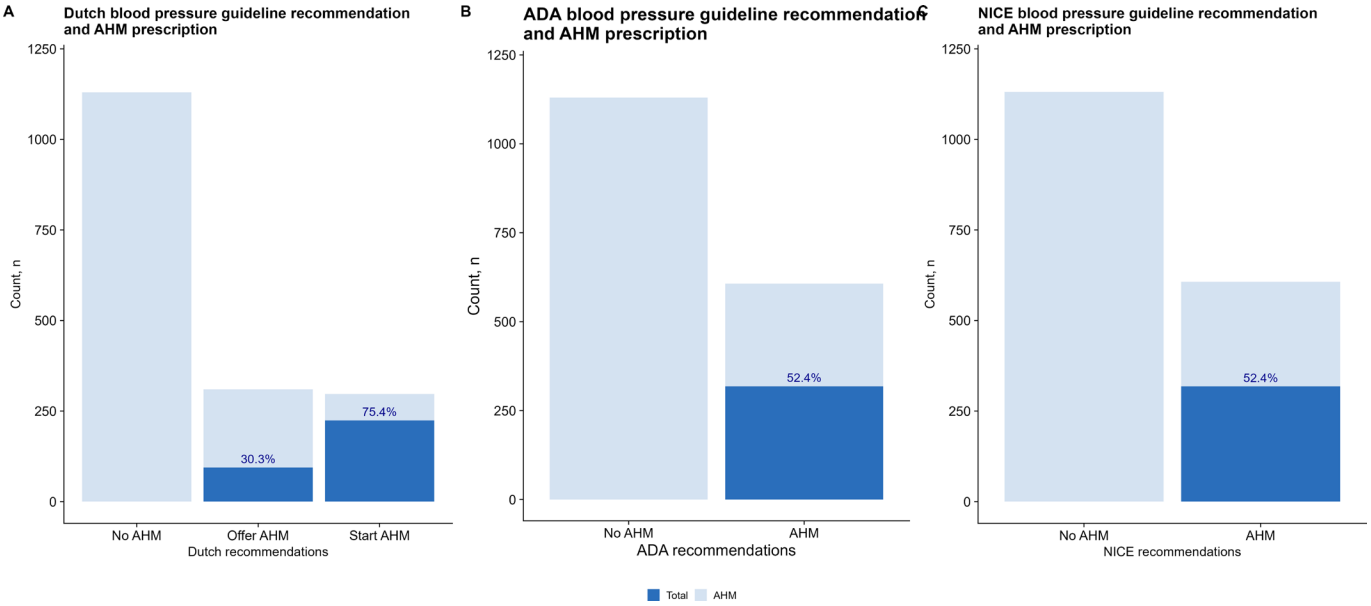

Figure 3 Frequency of blood pressure management recommendations in the study population based on the (A) Dutch, (B) American Diabetes Association (ADA) and (C) National Institute for Health and Care Excellence (NICE) guidelines and the prescription of antihypertensive medication (AHM) for each recommendation group. Percentages presented are the percentage of AHM use per recommendation.

large proportion of individuals, to whom medication was prescribed, were not achieving treatment targets. Age was an important factor in the undertreatment of lipid levels and blood pressure, as seen in the gap between recommendation and medication prescription. Regardless of guideline recommendations, younger individuals were prescribed less LLM and AHM.

To our knowledge, this study is the first to show undertreatment in the context of discrepancies between lipid and blood pressure guideline recommendations and prescription of medication in individuals with type 1 diabetes. Undertreatment of cardiovascular risk factors has previously been described in the type 1 diabetes exchange cohort (T1DX) and prospective diabetes follow-up registry (DPV).[9] Shah *et al* reported LLM use in 28% and 11% of the T1DX (28%) and DPV, respectively.[9] AHM use was reported in 28% and 15% of the T1DX and DPV, respectively.[9] Published over a decade ago, another study reported findings of undertreatment in individuals with type 1 and type 2 diabetes, with achievement of LDL-cholesterol and blood pressure targets in 47.2% and 57.3% of medication users, respectively.[24] Our findings are comparable to these studies and add to the evidence that, despite improvements in diabetes care, lipid and blood pressure undertreatment still exists among individuals with type 1 diabetes.

We further demonstrated that the discrepancies in recommendations and prescription practices were largest among the youngest age groups. This is particularly troubling as youth and young adults with type 1 diabetes have been demonstrated to have up to a 11-fold increased risk of cardiovascular mortality in comparison to age-matched

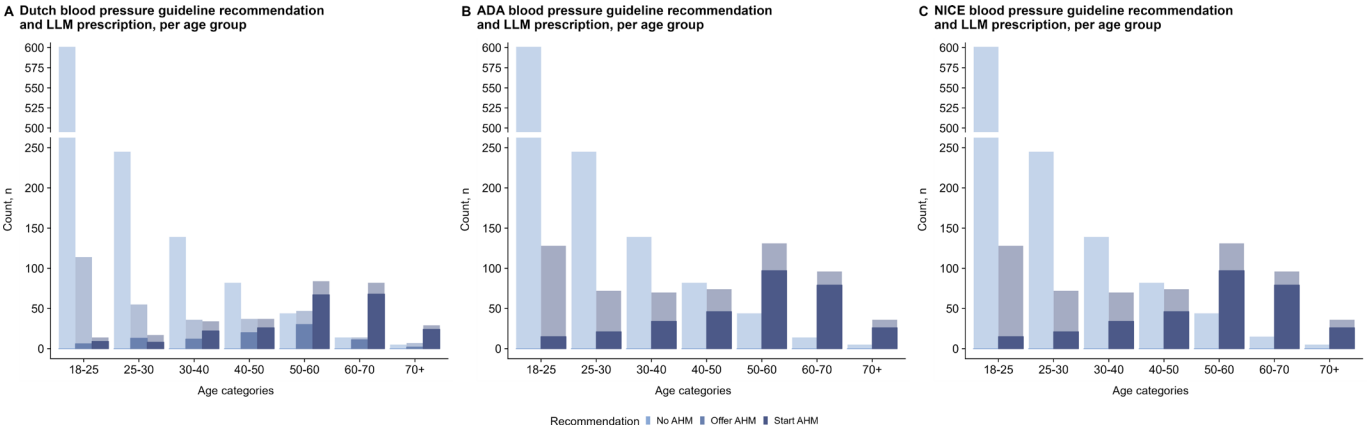

Figure 4 Frequency of blood pressure guideline recommendations per age category based on the (A) Dutch, (B) American Diabetes Association (ADA) and (C) National Institute for Health and Care Excellence (NICE) guidelines and the prescription of antihypertensive medication within each recommendation group. LLM, lipid-lowering medication.

and sex-matched controls.[25] Moreover, atherosclerosis has been observed as early as 6 years after type 1 diabetes onset,[26] and in youth and young adults.[27 28] Individuals with early onset type 1 diabetes are therefore exposed to risk factors for years before interventions take place.[29] The heterogeneity in recommendations across guidelines, particularly for the different age groups, cannot be overlooked as they lead to varying management strategies. The use of diabetes duration as a risk factor in the NICE guidelines helps to capture young individuals with type 1 diabetes in the prevention of CVD,[30] whereas the Dutch guideline uses presence of diabetes-related complications that may present before CVD. Alternatively, the ADA uses a cut-off of over or under 40 years of age, although recent guidelines recommend discussions between healthcare providers and individuals with type 1 diabetes already before the age of 40 years.[10] Each of these guidelines address the younger individual with type 1 diabetes differently. Nevertheless, regardless of which guideline was assessed, undertreatment of young individuals with type 1 diabetes is evident and warrants improvement.

To effectively address the problems of undertreatment of cardiovascular risk factors in individuals with type 1 diabetes, harmonisation of international guidelines may be beneficial. In addition, the barriers of starting LLM and AHM among individuals with type 1 diabetes need to be better understood in order to improve care. Deviations from recommendations could not be examined in this study, but there are many reasons for both physicians and individuals with type 1 diabetes to choose not to start LLM and AHM. Younger individuals may perceive their CVD risk differently and may therefore be less motivated to start medication.[31] Others may be dissuaded by side effects, and older individuals may prefer to stop certain preventive medication altogether as CVD prevention becomes less important. Other factors that may challenge healthcare providers are the competing outcomes, with glucose-related health issues taking priority, over other areas of diabetes management, within the limited time health professionals have per visit.[24] Although the favorable impact of early glycemic control on reduction of CVD incidence and protecting kidney function has been demonstrated repeatedly,[1 32] it could be hypothesized that early lipid and blood pressure interventions could do the same. Yet, without type 1 diabetes-specific empirical evidence of the added benefit of lipid and blood pressure management, decision making for both healthcare provider and individual with type 1 diabetes is difficult.

Strengths and limitations

Strengths of our study are (1) the use of real-world data from type 1 diabetes outpatient clinics; (2) the use of three guidelines to assess recommendation and performance (3) the relatively large study size.

Limitations include the cross-sectional design and the dependence on what the healthcare providers reported in the medical records. Cardiovascular risk management is a longitudinal process. As a result, a cross-sectional assessment of these data therefore may lead to underestimation or overestimation of treatment. For example, the group recommended no LLM in the Dutch guideline in the age group 60–70 years appear to use the most LLM. Individuals who have been treated for years with adequate LDL-cholesterol and blood pressure management have a lower risk of cardiovascular disease and will also have a low Systematic COronary Risk Evaluation.[5] These individuals may suggest that there is overtreatment, when in fact their low risk is a result of adequate CVRM. Furthermore, achievement of targets may be underestimated due to individuals who have not yet reached optimum dosages, who eventually may reach the suggested targets. Others with well-maintained LDL-cholesterol and blood pressure may also be measured less often. Missing lipid and blood pressure measurements may contribute to an overall overestimation of the degree of undertreatment.

The categorisation of individuals for different recommendations was conducted with data available from the data extraction, and therefore is limited by the information available in the medical records. Moreover, we could not identify why certain individuals were not using LLM and AHM. Some individuals may be intolerant to statins, and others may have refrained from pharmacological strategies and sought out over-the-counter products like red yeast rice as alternatives to prescription of LLM.[33] In young women who wish to conceive LLM are contraindicated, and this is a legitimate reason not to start LLM.[34] However, no differences were found when comparing LLM prescription by sex.

Finally, it is important to note that some individuals under the age of 25 years in this study were treated by pediatric endocrinologists who may be using the International Society for Paediatric and Adolescent Diabetes guidelines.[35]

Recommendations

Our study suggests that implementation of CVRM guidelines can be improved. The intrinsic differences of the available guidelines should be noted, as well as the challenges in choosing which guideline to implement. Harmonisation of international guidelines may be beneficial in the approach of CVRM for individuals with type 1 diabetes. More studies on CVRM strategies and cardiovascular outcomes are necessary in individuals with type 1 diabetes to reduce this ambiguity in guideline recommendations, to reduce hesitation and to help motivate individuals with type 1 diabetes to start CVRM interventions early. Investigating determinants of CVRM guideline implementation can help address undertreatment of individuals with type 1 diabetes.

CONCLUSION

In conclusion, this study shows that there is potential undertreatment of lipid and blood pressure management

in individuals with type 1 diabetes, as seen in the gap between guideline recommendations and medication prescription. Moreover, treatment targets are not met by most individuals using LLM and AHM. Younger age groups appear to be particularly vulnerable to undertreatment; however, further studies are needed to better understand the decisions and barriers in implementing guideline recommendations. Finally, higher-quality evidence specific to individuals with type 1 diabetes may be beneficial for robust evidence-based CVRM recommendations.

Contributors RDMV contributed to the design, data analysis and authored the paper. EB contributed to the design, interpretation of the results and supervised the work. CEV contributed to the data collection and interpretation of the results. HV contributed to the data collection and study design. DM and PRvD contributed to the design and interpretation of the results. MMvdK, BHRW and H-JA supervised the work and in that role contributed to the design, data interpretation and writing of the paper and acted as guarantor.

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Competing interests EB, DM, HV and H-JA are employed at Diabeter Netherlands, an independent clinic which was acquired by Medtronic. The research presented here was independently performed.

Patient consent for publication Not applicable.

Ethics approval The Medical Ethical Review Board of the UMCG, Groningen, the Netherlands declared that this study was not subject to the Dutch 'Medical Research Involving Human Subjects Act' (WMO) and a waiver was granted. The institutional review board approved the study protocol (research register number: 202000883).

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