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DIABETES MELLITUS

Impact of time since last caloric intake on blood glucose levels

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Abstract Blood glucose (BG) is usually measured after a caloric restriction of at least 8 h; however evidence-based recommendations for the duration of a fasting status are missing. Here we analyze the effect of fasting duration on levels of BG to determine the minimal fasting duration to achieve comparable BG levels to conventional fasting measurements. We used data of a cross-sectional study on primary care patients, performed in October 2005. We included 28,024 individuals (age-range 18–99 years; 63% women) without known diabetes mellitus and without missing data for BG and fasting status. We computed general linear models, adjusting for age, sex, time of blood withdrawal, systolic blood pressure, waist circumference, total- and HDL-cholesterol, physical activity, smoking, intake of beta-blocker and alcohol. We tested the intra-individual variability with respect to fasting status. Overall, the mean BG differed only slightly between individuals fasting ≥8 h and those fasting <8 h (men: 5.1 ± 0.8 mmol/L versus 5.2 ± 1.2 mmol/L; women: 4.9 ± 0.7 mmol/L, 5.0 ± 1.0 mmol/L). After 3 h of fasting differences of BG diminished in men to −0.08 mmol/L (95%-CI: −0.15; −0.01 mmol/L), in women to −0.07 mmol/L (−0.12; −0.03 mmol/L) compared to individuals fasting ≥8 h. Noteworthy, age, time of day of blood withdrawal, physical activity, and intake of hard liquor influenced BG levels considerably. Our data challenge the necessity for a fasting duration of ≥8 h when measuring blood glucose, suggesting a random sampling or a fasting duration of 3 h as sufficient. Rather, our study indicates that essentially more effort on the assessment of additional external/internal factors on BG levels is necessary.

Keywords Blood glucose · Risk assessment · Nonfasting · Cross-sectional study

Abbreviations

ADA	American Diabetes Association
BG	Blood glucose
CVD	Cardiovascular disease
GEMCAS	GErman Metabolic and Cardiovascular riSk Project
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
oGTT	Oral glucose tolerance test
T-C	Total cholesterol
TG	Triacylglycerol

Introduction

The measurement of blood glucose is a well established procedure routinely used for many clinical and research purposes. In epidemiological studies blood glucose is an often measured parameter be it as a risk factor, mediator or confounder. Measuring blood glucose requires standardized procedures to minimize variability and bias, both in terms of required analytical methods and biological variability. Blood glucose levels are influenced by external factors, like caloric intake resulting in an increase of blood

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glucose or metabolic demands like muscle activity resulting in a decline of blood glucose. In an attempt to obtain unbiased blood glucose measurements one of the routinely requested basic requirements for pre-analytical blood sampling is the fasting state. However the fasting state is not well defined, i.e. the WHO recommends an 8–14 h (h) fast [1], the American Diabetes Association (ADA) defines fasting as "no caloric intake for at least 8 h" [2] or "an overnight 8- to 10-h fast" [3]. Moreover, evidence-based recommendations for the definition of the duration of the fasting status are missing—perhaps one reason, why blood glucose measurements in epidemiological and clinical studies are carried out inconsistently with regard to fasting duration. Pre-analytical blood sampling schemes range from overnight fast, fasting duration between 8 h and >12 h, ≥ 12 h, random sampling to even no information at all.

In the clinical as well as in the research environment, the required fasting status—however defined—is a challenging task. For clinicians and patients it would be much simpler if a blood sample could be taken at any time of the day, irrespective of the fasting duration. In studies, especially epidemiological studies, fasting requirement influences the study design, complicates the field work and increases the costs of the study. Moreover, and most important, it is not feasible to reliably control for the self-reported fasting status.

So far, few studies have examined the association between fasting duration and blood glucose comprehensively. Most of them studied only the dichotomous approach of fasting versus non-fasting, using various cut-points and not taking into account the course of blood glucose fluctuation according to duration of fasting status.

The aim of our study is to analyze the effect of fasting duration on levels of blood glucose to determine the minimal fasting duration to achieve comparable blood glucose levels to >8 h fasting measurements. For this purpose we use the dataset of GEMCAS (GErman Metabolic and Cardiovascular riSk Project), a recent nationwide study.

Methods

Study design and study participants

GEMCAS was conducted during 2 weeks in October 2005 at 1,511 randomly selected primary care physicians across Germany. Methods have been previously described in detail [4, 5]. Briefly, we included all eligible individuals aged 18–99 years visiting a general practitioner during these 2 weeks regardless of the reason of their visit and regardless of their fasting status. The study was planned and conducted according to the German guidelines for Good Epidemiology Practices (GEP) [6]. All participants gave their written informed consent and the study protocol was approved by the institutional ethics committee.

Data assessment

Data were collected on sociodemographic variables, antihypertensive, lipid-lowering and diabetic medication, smoking habits, physical activity and time of day of blood withdrawal. Self-reported physician diagnosed history of CVD and diabetes mellitus was filled in by the physician. Type and time of the last caloric intake (meals and drinks) were documented, waist circumference and blood pressure measured according to the study protocol. For blood sampling a two-step approach was performed [5]. First, all participants underwent a screening by using a blood glucose quick test from a capillary (finger stick) sample. Accordingly, it was possible to directly exclude or diagnose hyperglycaemia in those participants with a fasting duration of ≥ 8 h and a capillary blood glucose of <5.56 or >11.11 mmol/L. If the findings concerning fasting serum glucose were ambiguous (≥ 5.56 or ≤ 11.11 mmol/L) due to a meal in the previous 8 h, the participant was asked to come for a re-examination to give a fasting blood sample. Furthermore, a random sample (30%) of participants was asked to come for a second fasting blood sample, regardless of the result of the blood glucose quick test.

Laboratory analysis

For the main analysis a venous blood sample was collected from each participant, and shipped within 24 h to a central laboratory (Berlin, Germany) by an assigned courier service. Standardised enzymatic methods were used to determine total cholesterol (T-C), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triacylglycerol (TG) using Roche Hitachi MODULAR systems. Glucose levels from blood in natriumfluorid (NaF)-tubes were estimated by the glucose-6-phosphate dehydrogenase method (G6P-DH).

Quality assurance

We implemented a comprehensive quality assurance, performing a special monitoring concept, which included telephone-monitoring and random on-site visits, recently described in detail [5].

Diagnostic conventions and covariates

The fasting state was defined by a fasting duration of at least 8 h. Smoking was defined as current smoking or as a

history of cigarette smoking during the past year. Physical inactivity was set by <2 h/week. The time since last caloric intake was calculated by generating the difference between the time of blood withdrawal and time of last caloric intake (meal or drink) whereas missing data for one of the two variables was excluded.

Statistical analyses

Of the 35,869 study participants we excluded for the present analysis those with missing data for blood glucose (n = 1,236) and fasting status (n = 1,947) as well as those with a fasting status >35 h (n = 12). Since the impact of time of last caloric intake on blood glucose differed markedly between participants with and without known diabetes mellitus, we further excluded 4,650 participants with known diabetes mellitus, leaving a study sample of 28,024 (mean age 49.9 ± 15.9 years, 63% women). For analyses, where the exact time since last caloric intake was necessary, additional 2,489 participants were excluded (n = 25,535; mean age 49.5 ± 15.9 years, 62% women).

Differences in levels of glucose as a function of time since last caloric intake were tested with the Student *t* test between fasting levels (≥8 h) and the remaining 8 time points (t_0, …, t_7). Tests were corrected for multiple comparisons with the Bonferroni method. To investigate the relationship between duration of fasting and age on blood glucose in more detail, we conducted analysis of covariance. We used continuous blood glucose as the dependent variable, and time since last caloric intake as categorical covariate (t_{1h}, …, $t_{\geq 8h}$ as reference) adjusting for age. To account for possible influences of other covariates on blood glucose we used general linear models including the variables age, sex, time of day of blood withdrawal (dichotomized as morning, <12.00 a.m., and afternoon), systolic blood pressure, waist circumference, HDL-cholesterol, total cholesterol, intake of beta-blocker, physical activity, alcohol intake and smoking status. Because of the nonlinear relationship between day time of blood withdrawal and blood glucose a piecewise linear regression was conducted which fitted one slope for morning and one slope for afternoon appointments.

In sensitivity analysis we compared the intraindividual variance of blood glucose by computing age- and sex-adjusted differences between (random) first and fasting (second) blood glucose measurement stratified by the time of last caloric intake at the first. The (random) intra-individual variance was assessed by the standard deviation of the test–retest differences (SD_{diff}) of the means (measurement 1 minus measurement 2) with their 95% confidence intervals (CI) [7]. The SD_{diff} can easily be interpreted as 95% of the random test–rest differences will be less than $2*SD_{diff}$ [8]. All statistical analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC, USA).

Results

Characteristics of study population and duration of fasting status

Characteristics of the study population stratified by the duration of fasting status are shown in eTable 1. Striking differences according to fasting duration, independent from age, could not be observed. Figure 1 demonstrates a bimodal distribution of fasting duration on the survey day. About 50% of the participants reported a fasting duration of less then 4 h, 28% more than ≥8 h. Only very few participants had a fasting duration of 7 h or 8 h.

Especially in men the proportion of study participants with a fasting duration ≥8 h decreased with age (<36 years: 34%, 36–59 years: 30%, 60–80 years: 25%, >80 years: 19%; women resp. 26, 23, 21, 20%).

Blood glucose levels and fasting status

Overall, mean blood glucose levels differed only slightly between fasting and non-fasting individuals: 5.1 ± 0.8 mmol/L in fasting men, 5.2 ± 1.2 mmol/L in non-fasting men; resp. women 4.9 ± 0.7, 5.0 ± 1.0 mmol/L. Table 1 depicts an age-effect in men, with lowest differences between fasting and non-fasting men in the youngest age-group (+0,012 mmol/L) and highest differences in the oldest age-group ≥80 years (-0.302 mmol/L), reflecting a deteriorating effect of the glucose metabolism with increasing age. This age-effect is not observable in women, but like in men, the oldest women showed the highest blood glucose differences (-0.032 mmol/L), even though on a much lower mean blood glucose level.

Blood glucose levels and hours of last caloric intake

Figure 2 illustrates the course of age- and sex-adjusted mean blood glucose levels according to hours of last caloric intake. Blood glucose levels of individuals with less than 3 h of fasting were higher compared to blood glucose levels of individuals with a fasting duration of 8 to more than 18 h (t_{0h} = 5.3 mmol/L, t_{2h} = 5.2 mmol/L, t_{8h} = 5.0 mmol/L). However, after this time period blood glucose levels are even lower (t_{4h}, t_{5h}) or do not differ anymore ($t_{6h} - t_{7h}$).

Additionally, stratifying for sex and controlling for time of day did not influence the effect of duration since last caloric intake (eTable 2). Despite the well-known fact of a pronounced age effect on blood glucose levels, the above described time pattern of changes of blood glucose and

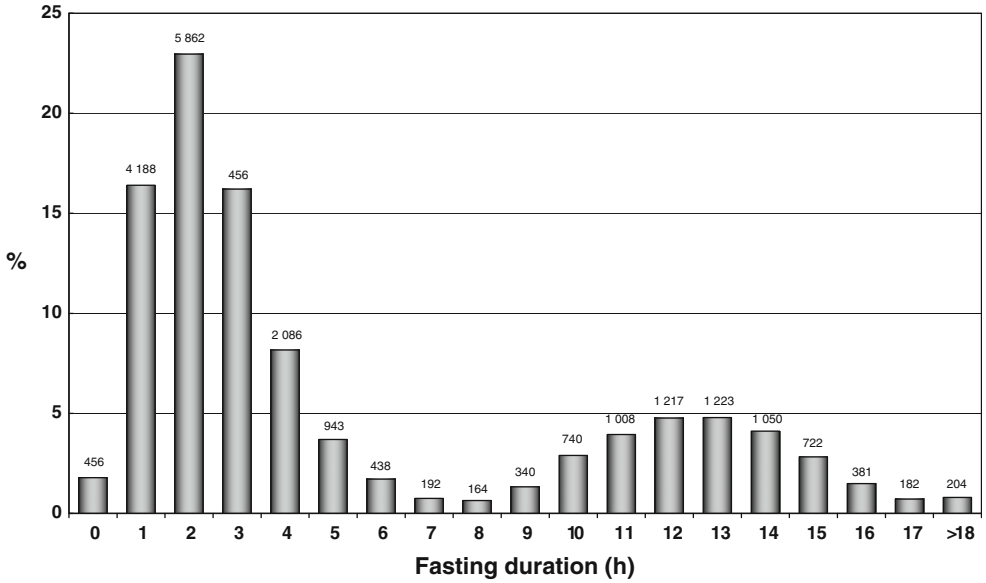

Fig. 1 Distribution of fasting duration on the survey day (n = 25,535)

Table 1 Difference of mean blood glucose levels (mmol/L) between fasting and non-fasting men and women

Age-groups	Fasting status				Difference[a]	
	Fasting (≥8 h)		Non-fasting (<8 h)			
(years)	n	Mean ± SD	n	Mean ± SD		*P* value*
Men						
<36	618	4.79 ± 0.61	1,206	4.78 ± 0.86	0.012	0.74
36–59	1,613	5.13 ± 0.86	3,785	5.21 ± 1.19	−0.082	0.0045
60–80	759	5.37 ± 0.84	2,242	5.50 ± 1.34	−0.128	0.0022
≥80	38	5.43 ± 0.65	167	5.73 ± 1.46	−0.302	0.0529
All	3,028	5.13 ± 0.83	7,400	5.24 ± 1.22	−0.115	<0.001
Women						
<36	924	4.57 ± 0.49	2,602	4.60 ± 0.69	−0.032	0.1272
36–59	2,196	4.91 ± 0.63	7,356	4.95 ± 0.92	−0.037	0.0303
60–80	868	5.21 ± 0.81	3,260	5.23 ± 1.09	−0.018	0.5864
≥80	79	5.27 ± 0.74	311	5.43 ± 1.14	−0.162	0.1261
All	4,067	4.90 ± 0.69	13,529	5.0 ± 0.96	−0.056	<0.001

Fasting: last caloric intake ≥8 h, non-fasting: last caloric intake <8 h

* *P* values refer to *t*-tests differences between fasting and nonfasting blood glucose in each age-and sex-specific group

[a] Difference = (last caloric intake ≥ 8 h) − (last caloric intake <8 h)

fasting duration is similar to all but very old participants >80 years (Fig. 3).

Control of external influence factors

Table 2 shows the sex-specific impact of fasting duration on blood glucose levels additionally adjusted for waist circumference, metabolic and lifestyle factors. With each additional hour of fasting the blood glucose decreases by about 0.024 mmol/L (≙0.4 mg/dL) in men and 0.009 mmol/L (≙0.2 mg/dL) in women. Theoretically, adding this up to 8 h (irrespective of day of blood sampling) this amounts to about 3 mg/dL in men and about 2 mg/dL in women, confirming the above reported results of marginal higher blood glucose levels comparing fasting and non-fasting blood glucose concentrations. In addition to the well known associations of blood glucose with CVD risk factors (lipids, blood pressure, obesity), we observed a strong association with time of day of blood sampling (Table 2). Notably this association was only observable when stratifying our analysis by sex,

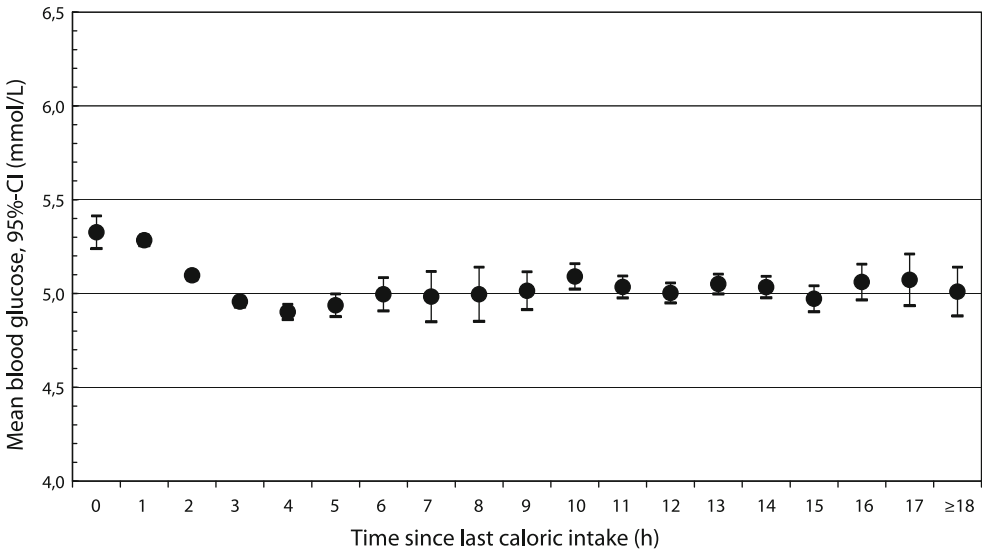

Fig. 2 Age- and sex-adjusted blood glucose levels by time since last caloric intake (n = 25,535)

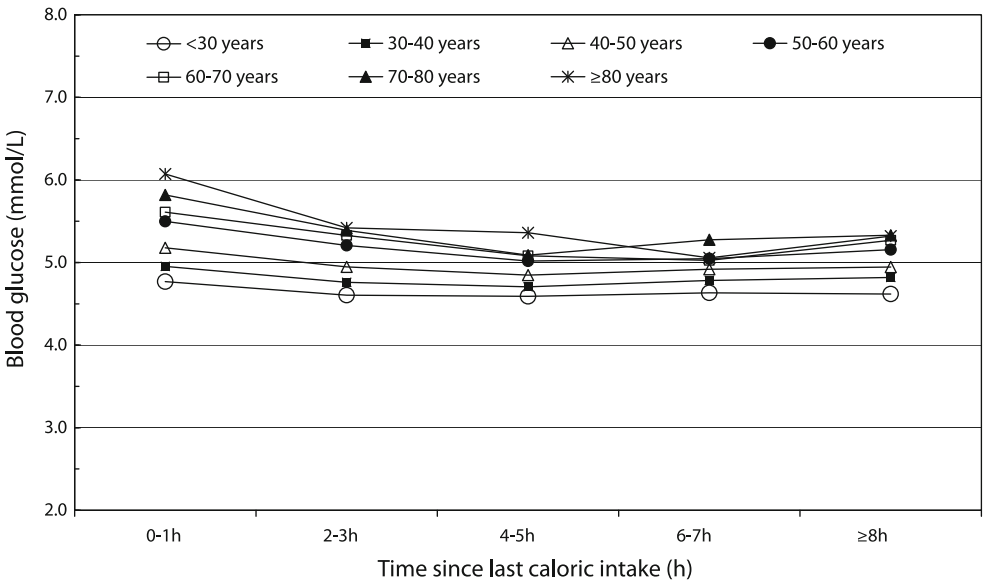

Fig. 3 Sex-adjusted blood glucose levels by time since last caloric intake stratified by age-groups

demonstrating a bidirectional trend between sampling in the morning and in the afternoon.

Sensitivity analyses

As expected, the intra-individual variability differed with regard to fasting status on two consecutive measurements. The spearman correlation coefficient was highest with a fasting status at both measurements, reaching 0.625 (eFigure 1). The coefficient diminished to 0.388 comparing a first random versus a second fasting measurement, which did not differ from two consecutive measurements both at random (0.386).

However, the mean age- and sex-adjusted difference between a first (random) and a second (fasting) blood glucose measurement, stratified by fasting duration at the first measurement (eFigure 2), shows the highest difference (+0.66 mmol/L) when fasting status is less than 1 h compared to the fasting blood glucose at the second measurement and no differences when fasting was ≥4 h, confirming the previous results. Restriction of this analysis to the random sample of participants did not change our results substantially.

Differences in blood glucose between first and second measurement were remarkable small regardless of fasting status of first and second measurement (fasting/fasting,

Table 2 Association between blood glucose and fasting duration, time of blood sampling and personal characteristics stratified by sex

	Men		Women	
	Change of blood glucose (mmol/L)		Change of blood glucose (mmol/L)	
	ß	95%-CI	ß	95%-CI
Age (years)	0.010	0.008; 0.011	0.010	0.009; 0.012
Fasting duration (h)	−0.024	−0.029; −0.018	−0.009	−0.013; −0.006
Time of day of blood sampling				
Morning (< 12.00 p.m.)	−0.052	−0.075; −0.029	−0.027	−0.042; −0.011
Afternoon (≥ 12.00 p.m.)	0.011	−0.015; 0.037	0.020	0.005; 0.035
HDL-cholesterol (mmol/L)	−0.120	−0.189; −0.050	−0.095	−0.132; −0.058
Total cholesterol (mmol/L)	−0.003	−0.026; 0.021	0.018	0.001; 0.034
Systole blood pressure (mmHg)	0.004	0.002; 0.005	0.002	0.002; 0.003
Intake of beta-blocker	0.160	0.100; 0.220	0.152	0.111; 0.193
Waist circumference (cm)	0.010	0.008; 0.012	0.008	0.006; 0.009
Smoking	0.048	−0.004; 0.100	0.022	−0.013; 0.056
Beverage				
Soft/fizzy drinks[a]	0.004	−0.054; 0.062	0.046	0.001; 0.089
Hard liquor[a]	0.234	0.053; 0.414	0.212	0.014; 0.409
Physical activity (ref. < 2 h/week)	−0.096	−0.150; −0.042	−0.034	−0.069; 0.001

[a] Reference for beverages = never and seldom

Table 3 Sex-specific intraindividual variability in blood glucose measured by two consecutive appointments according to fasting status

		$\Delta_{\text{measurement 1 – measurement 2}}$ (mmol/L)		
	n	Mean_{dif}	95%-CI	SD_{dif}
Men				
Fasting–fasting	612	0.047	−0.004; 0.099	0.653
Non fasting–fasting	3,099	0.344	0.301; 0.388	1.234
Fasting–nonfasting	64	−0.053	−0.274; 0.168	0.886
Nonfasting–nonfasting	425	0.024	−0.102; 0.150	1.320
Women				
Fasting–fasting	664	0.112	0.051; 0.172	0.794
Non fasting–fasting	4,472	0.275	0.247; 0.304	0.975
Fasting–nonfasting	94	−0.130	−0.313; 0.053	0.892
Nonfasting–nonfasting	729	0.153	0.072; 0.233	1.108

SD_{dif} standard deviation of the first and second measurement differences

Fasting ≥8 h, non-fasting < 8 h since last caloric intake, 95%-CI: 95% confidence interval

non-fasting/fasting, etc.), despite a lower variance—expressed as the standard deviation of the mean difference—in the fasting/fasting combination (Table 3).

At least we tested intra-individual changes of assignment to blood glucose-risk categories (*low*: < 5.6 mmol/L, *medium*: 5.6–7.0 mmol/L, *high* ≥ 7.0 mmol/L) at the repeated second fasting measurement compared to different fasting durations (≥8, > 0, ≥3 h) at first measurement. We found that 91.8% of those individuals with a low fasting blood glucose (≥8 h) at first measurement remained in the low category at the repeated measurement (Table 4). This proportion attenuated slightly comparing those with a random fasting (> 0 h) and a fasting status ≥3 h at first measurement (90.6%, resp. 89.3%). On the other hand, in only 22.2% of the individuals with a fasting duration ≥8 h, resp. 18.4% with a fasting duration ≥3 h and 11.3% with a random measurement, a high blood glucose level could be confirmed at the second measurement. Hence, transitions between the medium and high categories were high—independent of fasting duration at first and second measurement.

Discussion

In our study population of women and men, aged 18–99 years, the minimal fasting duration to achieve comparable blood glucose levels between fasting and non-fasting measurements was 3 h. Overall, mean blood glucose levels differed only marginally between fasting and non-fasting individuals. Although the variance of blood glucose was higher in men and older individuals, the results are independently from age and sex. This pattern persisted even when taking into account varying waist circumference, metabolic and lifestyle factors. Analyzing intraindividual changes between non-fasting and fasting measurements confirmed these results, underlining the robustness of our findings. Moreover, our data show strong associations between blood glucose levels and time of day of blood

Table 4 Intraindividual change of blood glucose categories at second (fasting) measurement compared to a fasting duration of ≥8 h, >0 h (random) and ≥3 h at first measurement

1. Measurement		2. Fasting measurement ≥ 8 h							
Fasting duration (h)	Blood glucose category[a]	Low		Medium		High		All	
		%	n	%	n	%	n	%	n
≥8	Low	91.8	938	7.9	81	0.3	3	80.2	1,022
>0 (random)		90.6	4,966	8.7	479	0.7	37	72.5	5,482
≥3		89.3	2,473	10.3	278	0.7	20	79.6	2,771
≥8	Medium	48.2	109	45.6	103	6.2	14	17.7	226
>0 (random)		77.0	1,220	21.6	343	1.4	22	21.0	1,585
≥3		67.0	382	30.9	176	2.1	12	21.0	1,101
≥8	High	40.7	11	37.0	10	22.2	6	2.1	27
>0 (random)		57.5	284	31.2	154	11.3	56	6.5	494
≥3		48.9	69	32.6	46	18.4	26	4.1	141
≥8	All	83.0	1,085	15.2	194	1.8	23	100	1,275
>0 (random)		85.6	6,470	12.9	976	1.5	115	100	7,561
≥3		84.0	2,924	14.4	500	1.7	58	100	3,482

[a] Categories defined as a low blood glucose <5.6 mmol/L, medium blood glucose 5.6–7.0 mmol/L, high blood glucose ≥7.1 mmol/L

withdrawal, regular physical activity or drinking of hard liquor.

Fasting versus non-fasting blood glucose measurements

To the best of our knowledge, evidence is missing demonstrating that blood glucose measurements with a fasting duration of more than 8 h do better than those with less than 8 h of fasting duration. The main argument for fasting glucose measurements is the rise in blood glucose levels seen after a caloric meal or drink, especially during an oral glucose tolerance test (oGTT) [9]. However, our data show higher mean blood glucose levels only in the first 3 h after a caloric intake. This observation is in line with an earlier study from the fifties [10] and the ADA in 2001, stating that in nondiabetic individuals, blood glucose levels return to preprandial levels within 2–3 h [11]. In the British Regional Heart Study, a cross-sectional study of 60–79 year old men [12], no difference of blood glucose levels between fasting <6 h versus ≥6 h were found (5.6 mmol/L resp. 5.7 mmol/L), which is in accordance to our results (Table 1). Further studies—mainly focussing on the effect of diurnal variations of blood glucose levels or postprandial glucose metabolism—report a decrease of blood glucose to normal blood glucose levels 2–3 h after an oral glucose tolerance test or test meal [9, 13–15], supporting our findings of small differences between fasting and non-fasting glucose levels.

To maintain glucose homeostasis, the human body is able to tightly regulate levels of circulating blood glucose by coupling nutrient-stimulated insulin secretion (insulin response) and the metabolic action of insulin to stimulate glucose disposal [16]. In individuals with diabetes the glucose homeostatis is disturbed. Diabetics not only exceed normal blood glucose levels, but also experience high blood glucose fluctuations, with a higher increase of blood glucose after caloric intake and a prolonged decrease to baseline levels compared to normal individuals. Thus we excluded participants with known diabetes mellitus from our analysis.

Increasing age is associated with increasing impairment of the glucose homeostasis, possibly due to a decreasing insulin secretory capacity or insulin action [17]. Our data show higher blood glucose differences between fasting and non-fasting participants in the oldest age-group, especially in men (Table 1). However, these differences are rather low and they seem to be no reason for a fasting duration of more than 3 h.

Blood glucose levels are influenced by analytical conditions [18] and (intra-individual) biologic variations [19–22]. The latter is dependent on a number of factors like time of day, medication intake prior exercise status or alcohol intake [22–25]. The observed maximum age- and sex-adjusted blood glucose increase in our study of 0.3 mmol/L (≙5.4 mg/dL) with regard to duration of last caloric intake is very like within the variation of these biologic factors.

Strengths and limitations

One strength of our study is the large sample size and the broad age-range, allowing us to study the influence of age

and sex in detail. A notable gain of our study is the repeated blood glucose measurement in a subsample of participants. Thus, we were able to determine in sensitivity analyses directly the intra-individual variability with respect to fasting status. Since time of last caloric intake was self-reported and therefore subject to error, participants not only were asked by the doctor for the exact time of last caloric intake, but additionally for the type of last meal and drink. Accordingly, participants more likely remember the right time, which in turn should reduce this potential recall bias. In any case, other methods to measure last caloric intake with less bias are apparently unacceptable for study participants or patients. Our participants were mostly white and recruited from different geographically located general practices across Germany. Thus our results may not apply to other ethnic groups. A detailed discussion of possible selection bias of our study is provided in [5]. Briefly, characteristics of this primary health care sample are comparable to other German population-based samples and to the German federal statistical data with regard to anthropometric measures, smoking status, marital status, schooling and unemployment rate (i.e. GEMCAS: 10.2%, Germany October 2005: 10.4%). This high conformance might be explained by the situation that 92% of adults in Germany consult a general practitioner during 1 year [26]. However, the proportion of participants with diabetes and CVD is higher than compared to population-based samples, but still lower than in real patient-based samples [5]. We found differences in demographic characteristics in fasting versus non-fasting individuals. To account for these differences we stratified by sex and age-groups and estimated adjusted associations; nonetheless residual confounding in this observational study might still be an issue. Overall, our results have to be interpreted in terms of the observational nature of our study.

Implications for blood sampling in clinical practice and research

Possible implications for blood sampling regimes depend on the intention of blood glucose measurements. In clinical practice blood glucose is basically measured in order to obtain information about the existence and extent (control and treatment of diabetes) of a disturbed glucose metabolism (diagnosis of diabetes mellitus). According to recommendations of international experts a diagnosis of diabetes mellitus is possible in different ways: random or fasting blood glucose measurement or oGTT. For the ADA a confirmation of the test on a subsequent day is mandatory in the absence of unequivocal hyperglycemia [27]. In this sense the recommendation of the WHO is even stricter stating "… the diagnosis of diabetes in an asymptomatic subject should *never* be made on the basis of a single abnormal blood glucose value. For the asymptomatic person, at least one additional plasma/blood glucose test result with a value in the diabetic range is essential, either fasting, from a random (casual) sample, or from the OGTT" [1]. The importance of a replicate test is supported by our data, showing high transition rates between medium and high blood glucose categories—independent of fasting duration. Thus, several methods for a diagnosis of diabetes are already available, allowing clinicians to apply the most advantageous method in their everyday practice and the most convenient method for their patients.

One argument in favour of recommending a fasting measurement might be the often concurrent determination of lipid profiles for CVD risk assessment. However, according to recent studies [28–32] and recommendations [33–36] fasting blood glucose measurements for clinical purposes are not necessary in the first place, even in combination with the determination of lipid profiles for CDV risk assessment.

Implications for research purposes depend on the study question to be studied. (1) Aetiological studies aiming to understand glucose metabolism or the development of diabetes mellitus certainly need highly standardized conditions concerning fasting status. Anyhow, our results confirm that —beyond the fasting status—a thorough control of a wide range of factors is necessary to achieve unbiased measurements. (2) In epidemiological studies blood glucose is often measured as risk factor, mediator or confounder. In this case, our results not only challenge the current need of a fasting duration of more than 8 h, but also suggest a random sampling accomplished by a detailed assessment of last caloric intake or—if feasible—a fasting duration of 3 h as sufficient. As discussed above, fasting measurements are not necessarily unbiased, as marked variations due to a wide range of external and internal influencing factors still occur.

In conclusion, our data challenge the necessity for a fasting duration of >8 h when measuring blood glucose. A random blood glucose sample or a fasting duration of 3 h seems sufficient for reliable blood glucose measurements. Rather, our study indicates that essentially more effort on the assessment of additional external/internal factors on blood glucose levels is necessary. Blood glucose assessment should be accomplished by a detailed assessment of last caloric meal and drink as well as a thorough assessment of alcohol consumption, medication intake, exercise status, and time of day of blood sampling. Further studies are warranted, systematically studying the effect of different fasting duration on blood glucose levels. In case of a confirmation of our results, this would simplify routines in clinical practices for both the clinicians and the patients and would facilitate the scheduling appointments at epidemiological studies with a considerable cost reducing effect.

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Conflict of interest None declared.

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