Does abdominal obesity have a similar impact on cardiovascular disease and diabetes? A study of 91,246 ambulant patients in 27 European Countries

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Aims
Differences in cardiovascular risk factors across Europe provide an opportunity to examine the impact of adiposity on the frequency of diabetes and cardiovascular disease (CVD).

Methods and results
The International Day for Evaluation of Abdominal obesity (IDEA) study evaluated the prevalence of abdominal obesity, elevated body mass index (BMI), and other cardiometabolic risk factors among primary care patients. Abdominal obesity predicted increased diabetes risk, despite socio-economic, demographic, and risk factor differences. Cardiovascular disease was at least two-fold more frequent in Eastern Europe vs. Northwest Europe ($P<0.0001$) and 2.5-fold more vs. Southern Europe ($P<0.0001$). Waist circumference (WC) predicted increased ($P<0.0001$) age- and BMI-adjusted risks of CVD and diabetes. In women, odds ratios (95% confidence intervals) for CVD per 1 SD increase in WC were: Northwest Europe 1.28 (1.18–1.40); Southern Europe 1.26 (1.16–1.37); and Eastern Europe 1.10 (1.03–1.18). Values for diabetes were 1.72 (1.58–1.88), 1.45 (1.35–1.56), and 1.59 (1.46–1.73), with similar findings in men.

Conclusion
Abdominal obesity impacted similarly on the frequency of diabetes across Europe, despite regional differences in cardiovascular risk factors and CVD rates. Increasing abdominal obesity may offset future declines in CVD, even where CVD rates are lower.

Keywords
Cardiovascular disease • Diabetes • Risk factors • Abdominal obesity

Introduction
It is uncertain how socio-demographic and economic changes may influence the development of diabetes and cardiovascular disease (CVD) within Europe, particularly in Eastern Europe.¹⁻⁵ There are major regional differences in the prevalence of cardiovascular risk factors and CVD incidence in Europe.⁶⁻¹² and the prevalence of CVD in Eastern Europe is higher than elsewhere in Europe.⁸⁻¹¹,¹³ Adiposity has emerged in recent years as a key risk factor for both diabetes and CVD, and elevated waist circumference (WC) predicts risk beyond that of total adiposity as reflected by body mass index (BMI).¹⁴⁻²³ The substantial regional differences in ‘classical’ cardiovascular risk factors across Europe provide a unique opportunity to examine the incremental impact of adiposity on diabetes and on CVD.

The International Day for Evaluation of Abdominal obesity (IDEA) study was a large, non-interventional, cross-sectional study that evaluated the prevalence of abdominal obesity and the relationship between anthropometric measures (WC and BMI) and cardio-metabolic risk factors in a primary care setting.²⁴

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A graded increase in risk of CVD and diabetes with both increasing BMI and WC for both genders was demonstrated, with a stronger relationship for WC.\(^2\,^5\)

We report the findings in 91,246 patients from three European regions. Across these regions, the prevalence of CVD differs by more than three-fold. In particular, we have examined the consistency of impact of abdominal obesity on CVD and diabetes across European regions, in the context of substantial socio-economic, demographic, lifestyle, and risk factor disparities and variations in the proportion of risk attributable to individual factors.

**Methods**

**Study design**

IDEA was an international, non-interventional, cross-sectional study of patients who consulted a primary care physician (PCP). It was not designed to reflect the prevalence of risk factors among communities who remain independent of primary care contact. The rationale and design of the study have been described previously.\(^2\,^4\) Briefly, an exhaustive list of active PCPs was prepared for each country and each physician was assigned a unique random number. Countries were divided into commonly used administrative regions and physicians selected in the order of their randomly assigned number; selection was weighted according to the percentage of PCPs practising in different regions. Selection continued until the number of PCPs agreeing to participate in the study reached the level needed to recruit the required number of patients. All patients, aged 18–80 years consulting their PCP for any reason, were invited to participate on 2 half-days (between 9 May and 6 July 2005), pre-defined for each country. Women known to be pregnant were excluded.

Age, gender, level of education, professional activity, smoking status, and presence of known CVD (coronary heart disease, stroke, or prior revascularization), diabetes (type 1 or type 2), dyslipidaemia, or hypertension were recorded according to a written, standardized protocol. After appropriate training, a tape measure was used to determine WC midway between the lowest rib and the iliac crest. Weight and height were measured and BMI calculated.

All participating patients provided written, informed consent. Ethics Committee approval was obtained for each participating site.

**Sample size estimate**

Sample sizes were determined for each country according to the estimated frequency of abdominal obesity in primary care practice. Assuming an expected frequency of abdominal obesity of \(\sim 50\%\), we calculated that 1100–9600 patients were needed in each country to estimate the frequency with a precision of 1–3%.

**Statistics**

The SAS statistical package [version 8.2 (SAS Institute Inc., Cary, NC, USA)] was used.

European countries were grouped into three geographical regions: Northwest Europe (Austria, Belgium, Denmark, Finland, France, Germany, Ireland, The Netherlands, Norway, Sweden, and Switzerland), Southern Europe (Greece, Italy, Portugal, Spain, and Turkey), and Eastern Europe (Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Russia, Slovakia, Slovenia, and Ukraine).

Regional frequencies of CVD and diabetes were age-adjusted. For analyses of frequencies of CVD (overall and non-diabetic populations) and diabetes by gender-specific tertiles of WC and BMI categories, data were adjusted by age, region, smoking status, and presence of hypertension (CVD only). Odds ratios (OR) and their 95% confidence intervals (CI) for CVD and diabetes were calculated for an increase of 1 standard deviation (SD) in WC and BMI, and using multiple logistic regression model adjusted for age, linearity was tested by adding a squared terms. To study the independence of either factor, WC was adjusted for BMI and BMI was adjusted for WC.

The population attributable risk (PAR) of CVD and diabetes for abdominal obesity were calculated using the formula: 
\[
\text{PAR} = \frac{pd(1/R)}{RR}
\]

where \(pd\) is the proportion of cases (CVD or diabetes) exposed to abdominal obesity and \(RR\) the age-adjusted relative risk between abdominal obesity and CVD or diabetes.\(^2\,^6\) Confidence intervals of PAR were estimated using bootstrap estimators. Abdominal obesity was defined as WC > 102 cm for males and >88 cm for females.\(^2\,^7\)

**Results**

**Study population**

The study population comprised 37,437 men and 53,809 women from 27 countries (97% of eligible patients agreed to participate). The most marked difference between patients in each region was a lower prevalence of hypertension in Northwest Europe and a substantially higher prevalence in Eastern Europe (Table 1). There were also differences in the prevalence of physician-reported dyslipidaemia and in patient-reported smoking. Patients from Southern Europe had the highest WC on average; BMI measurements were similar in Southern Europe and in Eastern Europe, and in both instances were higher than in Northwest Europe.

**Frequencies of cardiovascular disease and diabetes**

The frequency of CVD (Table 1) was higher in males than in females in both Northwest Europe (19.2 vs. 10.8%) and Southern Europe (17.3 vs. 9.7%). However, CVD was substantially more frequent in Eastern Europe in both males (27.9%) and females (26.3%) compared with other regions. The risk of CVD in Eastern European women was substantially higher than that in females or males elsewhere in Europe (Figure 1).

Populations differed by age across the regions. The age-adjusted frequency of CVD (Figure 1) was substantially higher in Eastern Europe compared with Southern Europe and Northwest Europe (\(P < 0.0001\)). In contrast, the frequency of diabetes was similar across the three regions, irrespective of adjustment for age (Table 1 and Figure 1).

**Diabetes: impact of waist circumference and body mass index**

Increasing WC was associated with a greater risk of diabetes, irrespective of gender. In each geographic region, a 1 SD change in WC or BMI was associated with a highly significant increase in the frequency of diabetes (Table 2). The association remained significant even when WC was corrected for BMI (OR ranging from 1.3 to 1.5 in men and from 1.5 to 1.8 in women) or when BMI was corrected for WC (OR ranging from 1.2 to 1.4 in men and 1.3 in women). A logistic regression plot of the frequency of diabetes according to WC demonstrated a strikingly similar association in
Northwest Europe, Southern Europe, and Eastern Europe for both men and women (Figure 2).

**Cardiovascular disease: impact of waist circumference and body mass index**

Irrespective of geographical region, the adjusted OR for CVD was strongly associated with increased WC and with increased BMI (Table 2). Waist circumference remained independently associated with CVD, even after correction for BMI (OR ranging from 1.2 to 1.3 among men and from 1.1 to 1.3 among women) (Table 2).

Cardiovascular disease was more frequent in Eastern Europe for any given WC, irrespective of gender (Figure 3). Indeed, whereas the relationship between abdominal obesity and CVD was similar for Northwest Europe and Southern Europe, the curves were displaced for Eastern Europe (Figure 3): for any given level of abdominal obesity, the frequency of CVD was higher, in both males and females, compared with Northwest Europe and Southern Europe.

Body mass index was also independently associated with CVD after correction for WC, but this association was most evident in Eastern Europe (OR 1.22 in men and 1.43 in women). The interaction term between region and BMI was significant with a P-value, 0.001 for both males and females. The frequency of CVD across Europe adjusted for age, region, smoking status, and presence of hypertension is shown in Table 3: irrespective of the presence or absence of diabetes, patients in the highest tertile of BMI had higher rates of CVD for each category of WC. A similar relationship was observed for BMI, WC, and rates of diabetes (Figure 4 and Table 4).

**Proportion of risk attributable to increased waist circumference**

The age-adjusted PAR of CVD for abdominal obesity was higher in Eastern Europe than in the other regions [PAR for males was 10.2% (95% CI 8.2–12.0) in Eastern Europe, 6.3% (95% CI 4.7–7.8) in Northwest Europe, and 7.0% (95% CI 5.7–8.4) in Southern Europe]. The corresponding PAR in females was 11.8% (95% CI...
10.1–13.2) in Eastern Europe, 4.9% (95% CI 3.9–6.0) in Northwest Europe, and 3.7% (95% CI 2.6–4.7) in Southern Europe. Overall, however, the PARs were low, suggesting that the frequency of CVD would be reduced by 10% if abdominal obesity were eliminated. There was no clear difference between regions in the PAR of diabetes for abdominal obesity in women but a trend for a lower PAR in men in Southern Europe. The PAR for males was 11.8% (95% CI 10.3–13.4) in Eastern Europe, 12.1% (95% CI 10.7–13.5) in Northwest Europe, and 7.3% (95% CI 6.0–8.7) in Southern Europe. The corresponding PAR in females was 10.3% (95% CI 9.3–11.3) in Eastern Europe, 10.8% (95% CI 9.8–11.8) in Northwest Europe, and 10.8% (95% CI 9.8–11.9) in Southern Europe. The data

Table 2 Age-adjusted odds ratios (95% confidence interval) for cardiovascular disease and diabetes according to waist circumference and body mass index, by region

<table>
<thead>
<tr>
<th>Age-adjusted OR (95% CI) for CVD for a 1 SD change in WC or BMI</th>
<th>Northwest Europe</th>
<th>Southern Europe</th>
<th>Eastern Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men WC adjusted for BMI</td>
<td>1.17 (1.08–1.27), P = 0.0001</td>
<td>1.29 (1.20–1.39), P = 0.0001</td>
<td>1.20 (1.10–1.31), P &lt; 0.0001</td>
</tr>
<tr>
<td>Men BMI adjusted for WC</td>
<td>1.12 (1.04–1.22), P = 0.004</td>
<td>1.02 (0.95–1.09)</td>
<td>1.22 (1.12–1.33), P &lt; 0.0001</td>
</tr>
<tr>
<td>Women WC adjusted for BMI</td>
<td>1.28 (1.18–1.40), P &lt; 0.0001</td>
<td>1.26 (1.16–1.37), P &lt; 0.0001</td>
<td>1.10 (1.03–1.18), P = 0.0052</td>
</tr>
<tr>
<td>Women BMI adjusted for WC</td>
<td>1.08 (1.00–1.18)</td>
<td>1.04 (0.96–1.12)</td>
<td>1.43 (1.34–1.52), P &lt; 0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age-adjusted OR (95% CI) for diabetes for a 1 SD change in WC or BMI</th>
<th>Northwest Europe</th>
<th>Southern Europe</th>
<th>Eastern Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men WC adjusted for BMI</td>
<td>1.35 (1.24–1.48), P &lt; 0.0001</td>
<td>1.29 (1.20–1.39), P &lt; 0.0001</td>
<td>1.46 (1.32–1.63), P &lt; 0.0001</td>
</tr>
<tr>
<td>Men BMI adjusted for WC</td>
<td>1.37 (1.26–1.49), P &lt; 0.0001</td>
<td>1.17 (1.09–1.25), P &lt; 0.0001</td>
<td>1.30 (1.17–1.43), P &lt; 0.0001</td>
</tr>
<tr>
<td>Women WC adjusted for BMI</td>
<td>1.72 (1.58–1.88), P &lt; 0.0001</td>
<td>1.45 (1.35–1.56), P &lt; 0.0001</td>
<td>1.59 (1.46–1.73), P &lt; 0.0001</td>
</tr>
<tr>
<td>Women BMI adjusted for WC</td>
<td>1.32 (1.21–1.43), P &lt; 0.0001</td>
<td>1.30 (1.22–1.39), P &lt; 0.0001</td>
<td>1.31 (1.21–1.41), P &lt; 0.0001</td>
</tr>
</tbody>
</table>

Figure 1 Age-adjusted frequency of cardiovascular disease and diabetes in Northwest (NW), Southern (S), and Eastern (E) Europe. Mean values with 95% confidence intervals: males dark columns and grey highlight, females light columns and no highlight.
suggest that frequency of diabetes could therefore be reduced by ~10% by eliminating abdominal obesity, but this may underestimate the longer term impact.

**Discussion**

We studied an ambulant population in primary care because such patients could have access to appropriate dietary, lifestyle, and therapeutic interventions. Our very large cross-sectional study of ambulant patients attending a PCP demonstrated a striking discordance in the frequency of both CVD and diabetes across major geographic regions. The impact of a 1 SD increase in WC (or BMI) on the frequency of diabetes was similar across geographic regions even after age adjustment. The impact of adiposity on diabetes was strikingly similar across the different regions of Europe, despite socio-economic, demographic, and risk factor differences. This lack of regional differences suggests that abdominal obesity has a major influence on the development of diabetes. In contrast, although there was a tight relationship between adiposity and CVD in individual regions of Europe, there were marked regional differences in disease frequency. In both men and women, the rate of CVD in Eastern Europe was substantially higher for any given level of abdominal adiposity compared with Northwest or Southern Europe [two-fold higher than Northwest Europe ($P < 0.0001$) and 2.5-fold higher than Southern Europe ($P < 0.0001$)]. These findings suggest that adiposity adds a consistent incremental adverse influence to the background cardiovascular risk profile. Diabetes itself is a well recognized and potent factor driving the development of CVD and any ‘direct’ effect of adiposity on cardiovascular events is likely to be amplified by the resulting increase in diabetes after a variable time period. Hence, the PAR at the time of the study may underestimate the eventual impact on diabetes and CVD.

The finding that WC is a predictor of CVD irrespective of regional differences in the background CVD prevalence confirms and extends the findings of previous studies showing that abdominal obesity is an independent risk factor for CVD events irrespective.
Table 3  Frequency of cardiovascular disease across Europe adjusted for age, region, smoking status, and presence of hypertension by gender-specific waist circumference tertiles and body mass index categories

<table>
<thead>
<tr>
<th>Overall population</th>
<th>Patients without diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male WC tertile</strong></td>
<td><strong>&lt; 92</strong></td>
</tr>
<tr>
<td>BMI &lt; 25</td>
<td>13.6 (12.7–14.5) (n = 8365)</td>
</tr>
<tr>
<td>BMI ≥ 25 – &lt; 30</td>
<td>11.9 (10.6–13.3) (n = 3035)</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>17.3 (12.1–24.1) (n = 186)</td>
</tr>
<tr>
<td><strong>Female WC tertile</strong></td>
<td><strong>&lt; 82</strong></td>
</tr>
<tr>
<td>BMI &lt; 25</td>
<td>7.7 (7.1–8.3) (n = 1488)</td>
</tr>
<tr>
<td>BMI ≥ 25 – &lt; 30</td>
<td>9.4 (8.2–10.7) (n = 2259)</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>11.1 (7.0–17.3) (n = 160)</td>
</tr>
</tbody>
</table>

n, number of patients in each category of waist circumference. 95% confidence intervals are given in brackets.
Limitations of our study include the use of self-reported risk factors (e.g., smoking), which may be under-reported, and physician-reported observations (e.g., hypertension and dyslipidaemia), which may underestimate the true prevalence. The threshold for seeking medical attention may differ by geographic region. As a result, our findings may underestimate the strength of the relationship between risk factors and the disease conditions. Despite these cautions, our findings provide the basis for future studies, including those that will aim to determine a mechanism of these observations as well as to examine the link between diabetes development and cardiovascular outcome.

Our findings demonstrated that increased WC predicted an increased frequency of diabetes and CVD irrespective of gender and across the geographic regions of Europe. The findings have important implications. The growth in abdominal and generalized obesity is not limited to specific regions or subgroups of the population. The high frequency of abdominal obesity presents a major challenge irrespective of the different socio-demographic characteristics across Europe and the impact on diabetes may offset future declines in CVD prevalence, even in regions with lower rates of CVD. Population-wide policies are required across Europe at the pre-clinical stage of disease, to target the drivers of cardiovascular risk and to tackle the impact of socio-economic inequality. The high levels of compliance with dietary, exercise, smoking cessation, and pharmacologic therapy achieved in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial of patients with stable angina demonstrate that ambulant populations can be amenable to...
change. However, thus far, initiatives in the broader medical community and in populations have been less successful. The impressive impact of smoking cessation legislation on cardiovascular health provides an encouraging example of what can be achieved, but much remains to be done if we are to prevent a rise in the future burden of cardiometabolic disease.

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The interpretations of the data and the decision to submit the manuscript were made by members of the Steering Committee of the study, independently of the funding source. The authors participated in the conduct of the study and have seen and approved the final version of this manuscript. K.A.A.F. led the interpretation of the data and wrote the manuscript. J.E.D. and J.-P.D. made a substantial contribution to the analysis and interpretation of the data and the drafting of the manuscript. A.-J.R. and S.B. contributed to the analysis of the data.

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Conflict of interest:

A.-J.R. is an employee of sanofi-aventis; other authors have provided consultancy services to sanofi-aventis. K.A.A.F. has received grant funding and honoraria from sanofi-aventis, BMS, and GSK. J.-P.D. has received research grants from GlaxoSmithKline and sanofi aventis, has served as a consultant for MSD and sanofi aventis, and has served on the speakers’ bureau for abbott, AstraZeneca, Solvay Pharma, Glaxo-SmithKline, Pfizer and sanofi aventis.

Appendix

Members of the IDEA Steering Committee (“Executive Steering Committee Members”) were: Beverley Balkau (France), J.-P.D. (Canada), Steven Haffner (USA), Phil Barter (Australia), Jean-Pierre Bassand (France), J.E.D. (UK), K.A.A.F. (UK), Luc Van Gaal (Belgium), Christine Massin (France), A.-J.R. (France), Sydney Smith (USA), Chee-Eng Tan (Singapore), and Hans-Ulrich Wittchen (Germany).

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References


CARDIOVASCULAR FLASHLIGHT

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Cardiac magnetic resonance characterization of atrial pseudo-mass in Erdheim-Chester disease

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A 70-year-old man with end-stage renal failure due to Erdheim-Chester disease was admitted for dyspnoea. Cardiac auscultation revealed diminished heart tones. Transthoracic echocardiography showed an irregular thickening of the right atrium and a circumferential moderate-to-severe pericardial effusion. Thus, the patient was referred for further evaluation by cardiac magnetic resonance (CMR). Steady-state free-precession (SSFP) cine CMR images confirmed a pericardial effusion (asterisk on Panels A, B, and E) and showed a massive thickening (pseudo-mass) of the right atrium wall, which appeared hypointense to the normal myocardium (white arrows on Panels A and B); both on T1-weighted fast spin-echo (FSE) axial image without (Panel D) and with fat suppression (Panel E); the atrial pseudo-mass was hypointense (white arrows) to normal myocardium. As showed on parasagittal section by cine CMR (Panel E), the pseudo-mass causes obstruction (white arrows) of right atrial inflow through superior and inferior caval vein (SVC and IVC, respectively). Erdheim-Chester disease is a rare histiocytic disorder of unknown cause which frequently involves the appendicular skeleton and retroperitoneum. The diagnosis is based on the immunohistochemistry analysis (CD68+, CD1a–).

Cardiac pseudo-masses in Erdheim-Chester disease have largely been described previously. However, to our knowledge, this is the first case of severe limitation to the right atrial inflow due to the atrial pseudo-mass. We believe that CMR is a precious tool to diagnose cardiac involvement in Erdheim-Chester disease and quantifying the haemodynamics consequences.

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