

# Sex Disparities in the Quality of Diabetes Care: Biological and Cultural Factors May Play a Different Role for Different Outcomes

A cross-sectional observational study from the AMD Annals initiative

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**OBJECTIVE**—To investigate the quality of type 2 diabetes care according to sex.

**RESEARCH DESIGN AND METHODS**—Clinical data collected during the year 2009 were extracted from electronic medical records; quality-of-care indicators were evaluated. Multilevel logistic regression analysis was applied to estimate the likelihood of women versus men to be monitored for selected parameters, to reach clinical outcomes, and to be treated with specific classes of drugs. The intercenter variability in the proportion of men and women achieving the targets was also investigated.

**RESULTS**—Overall, 415,294 patients from 236 diabetes outpatient centers were evaluated, of whom 188,125 (45.3%) were women and 227,169 (54.7%) were men. Women were 14% more likely than men to have HbA<sub>1c</sub> >9.0% in spite of insulin treatment (odds ratio 1.14 [95% CI 1.10–1.17]), 42% more likely to have LDL cholesterol (LDL-C) ≥130 mg/dL (1.42 [1.38–1.46]) in spite of lipid-lowering treatment, and 50% more likely to have BMI ≥30 kg/m<sup>2</sup> (1.50 [1.50–1.54]). Women were less likely to be monitored for foot and eye complications. In 99% of centers, the percentage of men reaching the LDL-C target was higher than in women, the proportion of patients reaching the HbA<sub>1c</sub> target was in favor of men in 80% of the centers, and no differences emerged for blood pressure.

**CONCLUSIONS**—Women show a poorer quality of diabetes care than men. The attainment of the LDL-C target seems to be mainly related to pathophysiological factors, whereas patient and physician attitudes can play an important role in other process measures and outcomes.

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\*A complete list of the members of the AMD Annals Study Group can be found in the Supplementary Data online.

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Gender medicine integrates aspects of biology, sociology, ethnicity, and culture responsible for different responses to care in women and men (1). Gender medicine applied to the field of diabetes care is particularly relevant because women with diabetes, regardless of menopausal status, have a four- to six-fold increase in the risk of developing coronary artery disease, whereas men with diabetes have a two- to threefold increase in risk (2). Women with diabetes have a poorer prognosis after myocardial infarction and a higher risk of death overall from cardiovascular disease than men with diabetes (3,4).

This greater excess coronary risk may be explained by more adverse cardiovascular risk profiles among women with diabetes (5). Compared with men, women with diabetes have higher prevalent abdominal obesity, increased risk of hypertension, and a more severe type of dyslipidemia (low levels of HDL cholesterol [HDL-C], small particle size of LDL cholesterol [LDL-C], and high levels of triglycerides). Furthermore, polycystic ovary syndrome is an important correlate of insulin resistance and metabolic syndrome (2).

Besides innate differences in sex physiology, disparities between sexes in the treatment of major cardiovascular risk factors also still exist, attributed to an underestimation of patient risk (6,7). Documenting these disparities and identifying their determinants in a specific health care setting can help caregivers provide higher standards of care and apply evidence-based therapies for diabetes care and prevention of cardiovascular disease (8–11).

In Italy, a continuous improvement effort implemented by a network of diabetes clinics has been promoted since 2006 (12,13). The initiative, which involves approximately one-third of all the diabetes outpatient clinics operating within the national health care system,

allows the monitoring of a large set of process and outcome indicators and the use of specific classes of drugs, with the aim of examining strengths and limitations of the current diabetes care.

We used the data of the Italian Association of Clinical Diabetologists (Associazione Medici Diabetologi [AMD] Annals to 1) evaluate whether sex differences in pharmacological and nonpharmacological treatment of diabetes exist in Italy and 2) investigate the role of biological and cultural factors in determining different outcomes for men and women.

## RESEARCH DESIGN AND METHODS

### The AMD Annals initiative

Since 2006, the AMD has promoted a continuous quality improvement initiative called AMD Annals. In this context, AMD identified a set of indicators to be used for benchmarking activities (9,10). Quality indicators include process measures evaluating diagnostic, preventive, and therapeutic procedures performed by the participating centers and outcome indicators measuring favorable and unfavorable modifications in patient health status. Furthermore, the use of antidiabetic, antihypertensive, and lipid-lowering drugs is evaluated. Centers share the same software for data extraction from electronic medical records. Data are collected annually in a standardized format (AMD data file) and centrally analyzed anonymously. The entire project is conducted without allocation of extra resources or financial incentives but simply through a physician-led effort, made possible by the commitment of the specialists involved.

### Quality-of-care indicators

Process measures are expressed as percentages of patients monitored at least once during the previous 12 months for the following parameters: HbA<sub>1c</sub>, blood pressure (BP), lipid profile (LDL-C or total and HDL-C and triglycerides), renal function, foot examination, and eye examination.

Intermediate outcome measures include the proportion of patients with satisfactory values as well as the percentage of those with unacceptably high values. Outcomes are considered satisfactory if HbA<sub>1c</sub> levels are  $\leq 7.0\%$  ( $\leq 53$  mmol/mol), BP values are  $< 130/80$  mmHg, LDL-C levels are  $< 100$  mg/dL, and BMI is  $< 27$  kg/m<sup>2</sup>.

Unsatisfactory outcomes include HbA<sub>1c</sub> levels  $> 8.0\%$ , BP values  $\geq 140/90$  mmHg, LDL-C levels  $\geq 130$  mg/dL, BMI  $\geq 30$  kg/m<sup>2</sup>, presence of micro/macroalbuminuria, and glomerular filtration rate (GFR)  $\leq 60$  mL/min. Seven indicators of treatment intensity/appropriateness were also measured to take into consideration the use of pharmacological treatments in relation to the achievement of the targets: no insulin despite HbA<sub>1c</sub>  $> 9.0\%$  ( $> 75$  mmol/mol), no lipid-lowering agents despite LDL-C  $\geq 130$  mg/dL, no antihypertensive treatments despite BP  $\geq 140/90$  mmHg, no ACE-I and/or angiotensin receptor blockers (ARBs) despite micro/macroalbuminuria, HbA<sub>1c</sub>  $> 9.0\%$  ( $> 75$  mmol/mol) in spite of insulin treatment, LDL-C  $\geq 130$  mg/dL in spite of lipid-lowering treatment, and BP  $\geq 140/90$  mmHg in spite of antihypertensive treatment.

Finally, a quality-of-care summary score (Q score) was calculated. The Q score has been developed and validated in two previous studies (14,15). It is based on a combination of process and outcome indicators relative to HbA<sub>1c</sub>, BP, LDL-C, and microalbuminuria. The score ranges between 0 and 40; the higher the score, the better the quality of care. Previous studies (14,15) documented that the risk of developing a new cardiovascular event was 80% higher in patients with a score  $< 15$  and 20% higher in those with a score between 15 and 25, as compared with those with a score  $> 25$ .

### Sample selection and data analyses

Clinical data collected during the year 2009 were extracted from electronic medical records. Only patients with a diagnosis of type 2 diabetes were selected. In cases of multiple records collected during the year for the same patient, the last available value was included in the quality-of-care profiling. The denominators for the different quality indicators vary according to the availability of the information in the index year (Fig. 1). No missing imputation was performed.

Because normal ranges for glycated hemoglobin varied among the different centers, to allow direct comparison, the percentage change with respect to the upper normal value (actual value/upper normal limit) was estimated and multiplied by 6.0. LDL-C was estimated by the Friedewald equation. Microalbuminuria was defined as albumin excretion rate  $\geq 20$   $\mu$ g/min, albumin-creatinine ratio  $> 2.5$  (men) or  $> 3.5$  (women) mg/mmol, or microalbuminuria  $> 30$  mg/L. GFR

was calculated with the Modification of Diet in Renal Disease (MDRD) formula (16).

### Statistical analyses

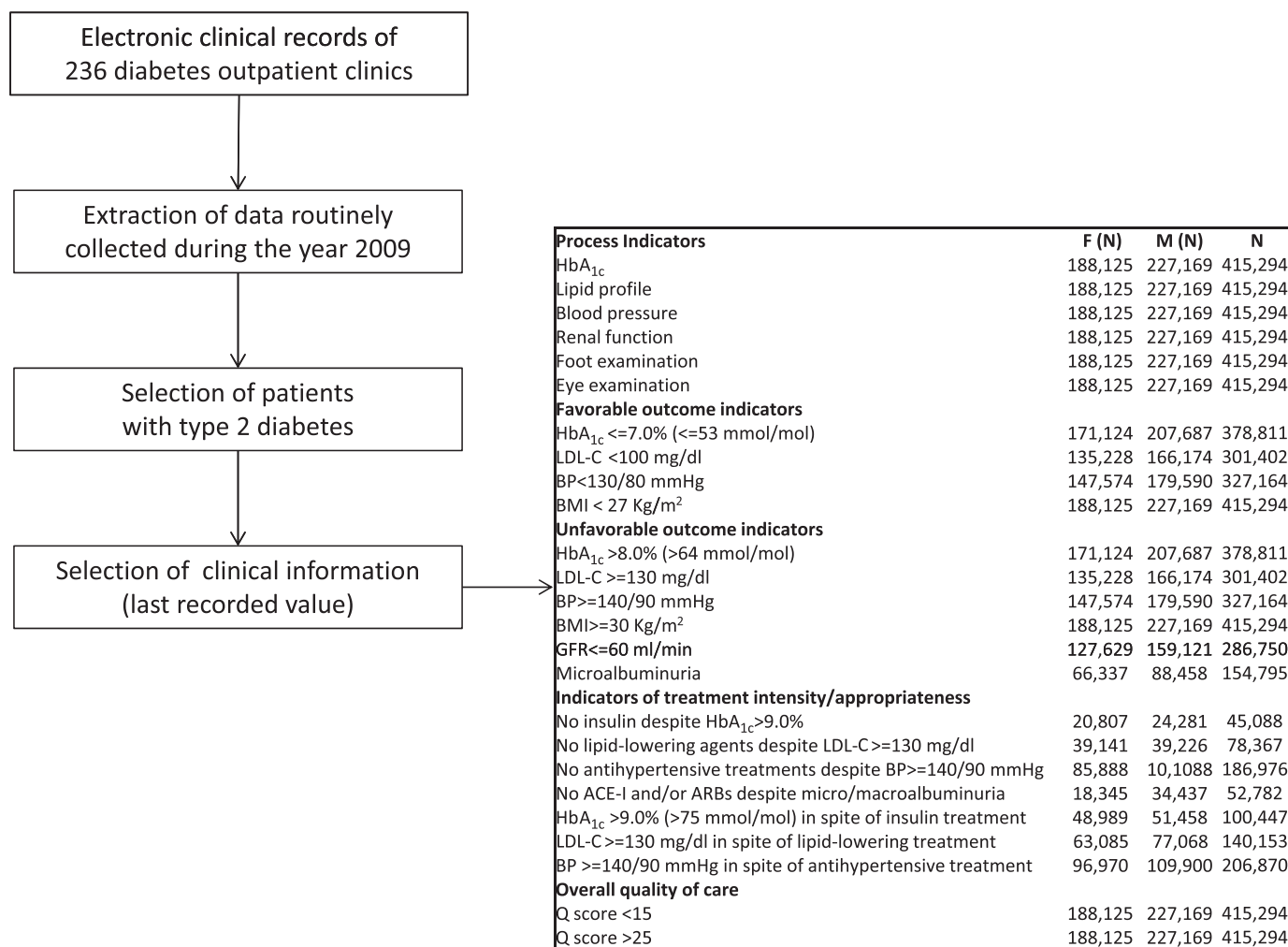
Patient characteristics and quality indicators according to sex were described as mean and SD or frequencies. Between-group statistical tests were not applied; in fact, due to the large sample size, even trivial differences reached statistical significance.

To take into consideration unbalanced characteristics of the two sexes, the likelihood of women as compared with men (reference class) to be monitored for specific clinical parameters, to reach specific clinical outcomes, and to be treated with specific classes of drugs has been investigated through multilevel logistic regression analyses, adjusted for age, diabetes duration, BMI, and, in a separate model, clustering effect; the participating diabetes outpatient clinics accounted for the clusters. Results are expressed as odds ratio (OR) and 95% CI. Analyses were performed on the whole sample as well as in two different age-groups, i.e.,  $< 75$  vs.  $\geq 75$  years of age.

For each indicator, we estimated the intraclass correlation coefficient (ICC) to evaluate the extent to which the indicator varied between centers as compared with within-center variation, taking patient case mix into account (17). The higher the ICC, the greater the influence of the center level on the quality-of-care indicator.

The intercenter variability in the difference between men and women achieving the targets of HbA<sub>1c</sub>, LDL-C, and BP was also investigated using multilevel models adjusted for age, diabetes duration, BMI, and clustering effect.

**RESULTS**—Overall, 415,294 patients with type 2 diabetes referred to 236 diabetes outpatient centers during the year 2009 were evaluated; of them, 188,125 (45.3%) were women and 227,169 (54.7%) were men. Patient characteristics according to sex are summarized in Table 1. The data show some substantial differences in the between-sex clinical characteristics. Women had an older age (30.5% of women vs. 20.8% of men were  $> 75$  years of age), had a slightly higher diabetes duration ( $11.1 \pm 9.8$  vs.  $10.0 \pm 9.1$  years), and were more obese (average BMI  $29.2 \pm 4.6$  kg/m<sup>2</sup> in men vs.  $30.2 \pm 5.9$  kg/m<sup>2</sup> in women). Smoking was more prevalent



**Figure 1**—Flowchart of data selection and sample size for each indicator (n).

among men. Similar proportions of women and men were treated with insulin, lipid-lowering agents, and antihypertensive drugs (Table 1); when evaluating the different classes of drugs and their combinations, no difference was found (Supplementary Table 1), except for a wider use of diuretics in women than in men (35.9 vs. 27.6%, respectively). The analyses by age class showed similar patterns in individuals below and over 75 years of age (Table 1).

All process indicators were slightly but systematically more favorable in men than in women. Adjustment for patient case mix and clustering attenuated sex differences; despite that, women still showed a lower likelihood to be monitored for diabetes complications, particularly foot and eye complications.

As for intermediate outcomes, the proportion of individuals reaching satisfactory HbA<sub>1c</sub>, LDL-C, BP, and BMI values was systematically lower for women

than for men. Adjustment for patient case mix and clustering effect confirms that women were 14% less likely than men to reach the HbA<sub>1c</sub> target, 27% less likely to reach the LDL-C target, and 20% less likely to reach the BMI target. On the other hand, the likelihood of reaching the BP target was slightly higher in women than in men. These findings are mirrored by those relative to unfavorable outcomes. Fully adjusted models show that women were 11% more likely than men to have HbA<sub>1c</sub> levels >8.0% (>64 mmol/mol), 41% more likely to have LDL-C levels ≥130 mg/dL, 50% more likely to have a BMI ≥30 kg/m<sup>2</sup>, and 32% more likely to have a GFR ≤60 mL/min. On the other hand, women were 48% less likely than men to have micro/macroalbuminuria. No major differences were detected for BP.

Data on the use of drugs show mixed results. The likelihood of not being treated with insulin in the presence of elevated

HbA<sub>1c</sub> values or with antihypertensive agents in the presence of elevated BP values was lower in women than in men, whereas no sex difference emerged in the use of lipid-lowering drugs in the presence of elevated LDL-C levels. Women had a 10% higher probability than men of not being treated with ACE-I or ARBs in the presence of micro/macroalbuminuria. Women also showed a 14% higher likelihood of having HbA<sub>1c</sub> levels >9.0% (>75 mmol/mol) despite insulin treatment and a 42% higher likelihood of having LDL-C levels ≥130 mg/dL despite lipid-lowering treatment (Table 2).

The analysis of overall quality of care, as summarized by the Q score, shows that women had a 17% greater likelihood of having a score <15 and an 11% lower likelihood of having a score >25 as compared with men. The contribution of between-center variability was substantial for process measures and moderate for intermediate outcomes, as

Table 1—Patient characteristics according to sex

Patient characteristics	Mean (SD) or %					
	Overall		Age <75 years		Age ≥75 years	
	M	F	M	F	M	F
n	227,169	188,125	179,807	130,518	47,210	57,230
%	54.7	45.3	57.9	42.1	45.2	54.8
Age (years)	65.7 ± 11.1	68.4 ± 11.4	61.9 ± 9.2	63.1 ± 9.2	79.8 ± 3.7	80.6 ± 4.1
Smokers (%)	21.5	11.8	24.1	14.6	10.2	4.6
Diabetes duration (years)	10.0 ± 9.1	11.1 ± 9.8	9.0 ± 8.3	9.7 ± 8.8	13.9 ± 10.9	14.3 ± 11.0
Diabetes duration classes (%)						
≤2	16.8	15.1	18.4	17.0	10.8	10.7
2–5	17.3	16.1	18.8	18.0	11.7	11.6
5–10	24.3	22.7	25.5	24.5	19.9	18.6
>10	41.5	46.1	37.3	40.4	57.6	59.1
HbA <sub>1c</sub> (%)	7.4 ± 1.5	7.5 ± 1.5	7.5 ± 1.6	7.5 ± 1.5	7.3 ± 1.3	7.5 ± 1.4
HbA <sub>1c</sub> (mmol/mol)	57 ± 16.4	58 ± 16.4	58 ± 17.5	58 ± 16.4	56 ± 14.2	58 ± 15.3
BMI (kg/m <sup>2</sup> )	29.2 ± 4.6	30.2 ± 5.9	29.4 ± 4.7	30.8 ± 6.0	27.9 ± 4.0	28.6 ± 5.0
Total cholesterol (mg/dL)	182.3 ± 40.8	194.4 ± 40.9	183.8 ± 41.3	195.5 ± 41.2	176.2 ± 38.0	191.9 ± 40.0
HDL-C (mg/dL)	46.3 ± 12.6	53.3 ± 14.0	46.0 ± 12.4	53.1 ± 13.9	47.7 ± 13.1	53.7 ± 14.5
LDL-C (mg/dL)	106.6 ± 34.0	112.5 ± 34.8	107.5 ± 34.3	113.3 ± 35.1	103.0 ± 32.2	110.5 ± 33.9
Triglycerides (mg/dL)	151.7 ± 121.6	143.4 ± 88.3	157.2 ± 130.1	145.7 ± 94.0	129.3 ± 72.9	137.7 ± 72.1
Systolic BP (mmHg)	138.6 ± 18.7	139.9 ± 19.4	138.0 ± 18.5	138.7 ± 19.1	140.9 ± 19.2	142.9 ± 19.6
Diastolic BP (mmHg)	79.3 ± 9.8	78.9 ± 9.7	79.9 ± 9.8	79.4 ± 9.7	77.0 ± 9.6	77.7 ± 9.7
Diabetes treatment (%)						
Diet and lifestyle	7.8	6.4	8.0	6.8	7.2	5.5
Oral agents	63.4	60.4	65.0	63.0	57.4	54.6
Oral agents + insulin	13.3	16.7	13.5	17.0	12.6	16.1
Insulin	15.5	16.4	13.6	13.1	22.8	23.8
Lipid-lowering agents	41.2	41.2	42.2	43.0	37.3	37.5
Antihypertensive treatment	56.6	61.0	54.6	58.3	64.3	67.3
≥2 antihypertensive agents	33.0	36.1	36.4	41.1	46.7	53.1
Aspirin	29.2	26.0	28.1	23.8	33.4	31.2

documented by intraclass correlations (Table 2).

Finally, we examined the between-center variability in the proportion of men and women reaching the desired therapeutic targets (Fig. 2). In almost all the centers, the percentage of men reaching the LDL-C target was higher than in women, with differences exceeding 5% in most of the centers. Similarly, the proportion of patients reaching the HbA<sub>1c</sub> target was in favor of men in the vast majority of the centers. As for the BP target, no clear trend in favor of men or women emerged.

Supplementary Table 2 reports the results of the analyses performed separately in individuals below and over 75 years of age. These analyses show that sex disparities are more pronounced in older people, particularly with reference to the attainment of HbA<sub>1c</sub> and BP targets. In fact, elderly women were 27% less likely than men to reach an HbA<sub>1c</sub> level ≤7.0% (OR 0.73 [95% CI 0.71–0.75]) and 17%

less likely to reach a BP target <130/80 mmHg (0.83 [0.79–0.87]).

**CONCLUSIONS**—Data from AMD Annals show that in Italy, despite equity of access to specialist care and universal coverage of health care costs, sex disparities are still present. Between-sex differences in the prevalence and treatment of cardiovascular risk factors are less pronounced in Italy than in other countries, not only those where cultural barriers or deprivation can be responsible for lower levels of care provided to women (18,19) but also in other European countries (20,21) or in the U.S. (22–24). In Spain, data from electronic databases of primary care showed a slightly better metabolic control in women than in men, in contrast with AMD Annals, although BP and lipid control were in favor of men (10). In the context of a pay-for-performance initiative in the U.K., women were 13% less likely to be monitored for HbA<sub>1c</sub>, BP, lipid profile, and smoking and 25% less likely

to reach the recommended therapeutic target than men, although no major differences in metabolic control were detected (11). In the vast majority of studies, women were less likely to reach the recommended targets as well as receive treatment and monitoring. Constantly, the wider gap was related to the lipid target; women had higher LDL-C levels than men and were less likely to be receiving lipid-lowering therapy (25,26).

Our findings call for a revision of clinical practice. In fact, it is alarming that the likelihood to reach specific clinical outcomes is systematically unfavorable for women as compared with men. The likelihood of receiving poorer quality of care is partly reduced but remains consistently higher for women, even after taking into consideration the baseline differences in patient characteristics (especially the higher proportion of elderly patients, a longer diabetes duration, and the higher BMI in women) and the effect of clustering. To this respect, our study

Table 2—Quality indicators of diabetes care according to sex

	Quality indicators (%)		Crude OR (95% CI)	OR adjusted for case mix (age, diabetes duration, BMI) (95% CI)	OR adjusted for case mix and cluster (95% CI)	ICC
	M	F				
Process indicators						
HbA <sub>1c</sub>	92.6	92.2	0.95 (0.93–0.97)	0.97 (0.94–1.00)	1.01 (0.98–1.05)	0.35
Lipid profile	74.1	72.4	0.91 (0.90–0.93)	0.95 (0.93–0.96)	0.97 (0.95–0.99)	0.33
BP	79.1	78.4	0.96 (0.95–0.98)	1.02 (1.00–1.05)	1.01 (0.98–1.04)	0.61
Renal function	42.4	40.1	0.91 (0.90–0.93)	0.93 (0.92–0.94)	0.96 (0.94–0.97)	0.77
Foot examination	14.0	12.1	0.84 (0.83–0.86)	0.88 (0.86–0.89)	0.90 (0.88–0.92)	0.62
Eye examination	34.3	30.7	0.85 (0.84–0.86)	0.89 (0.87–0.90)	0.91 (0.90–0.92)	0.34
Favorable outcome indicators						
HbA <sub>1c</sub> ≤7.0% (≤53 mmol/mol)	45.5	41.7	0.85 (0.84–0.87)	0.88 (0.87–0.89)	0.86 (0.85–0.87)	0.10
LDL-C <100 mg/dL	44.6	38.4	0.78 (0.76–0.79)	0.74 (0.73–0.75)	0.73 (0.72–0.75)	0.03
BP <130/80 mmHg	15.4	14.9	0.96 (0.94–0.98)	1.06 (1.04–1.08)	1.05 (1.03–1.07)	0.12
BMI <27 kg/m <sup>2</sup>	34.8	31.5	0.85 (0.83–0.86)	0.81 (0.80–0.83)	0.80 (0.81–0.83)	0.06
Unfavorable outcome indicators						
HbA <sub>1c</sub> >8.0% (>64 mmol/mol)	26.9	29.1	1.12 (1.10–1.14)	1.09 (1.07–1.11)	1.11 (1.09–1.12)	0.07
LDL-C ≥130 mg/dL	23.6	28.9	1.31 (1.28–1.33)	1.40 (1.37–1.43)	1.41 (1.38–1.43)	0.03
BP ≥140/90 mmHg	56.2	58.1	1.09 (1.07–1.10)	0.97 (0.95–0.98)	0.98 (0.96–0.99)	0.09
BMI ≥30 kg/m <sup>2</sup>	37.1	46.8	1.47 (1.45–1.49)	1.50 (1.48–1.52)	1.50 (1.50–1.54)	0.06
GFR ≤60 mL/min	17.7	26.4	1.65 (1.61–1.68)	1.32 (1.29–1.35)	1.32 (1.30–1.35)	0.04
Microalbuminuria	38.9	27.7	0.60 (0.58–0.61)	0.53 (0.51–0.54)	0.52 (0.50–0.53)	0.02
Indicators of treatment intensity/appropriateness						
No insulin despite HbA <sub>1c</sub> >9.0% (>75 mmol/mol)	47.3	37.6	0.69 (0.64–0.74)	0.77 (0.74–0.81)	0.76 (0.73–0.80)	0.07
No lipid-lowering agents despite LDL-C ≥130 mg/dL	58.5	58.3	1.21 (0.95–1.54)	0.99 (0.96–1.03)	0.98 (0.95–1.02)	0.27
No antihypertensive treatments despite BP ≥140/90 mmHg	34.2	29.8	0.75 (0.63–0.90)	0.93 (0.91–0.95)	0.90 (0.88–0.92)	0.39
No ACE-I and/or ARBs despite micro/macroalbuminuria	34.3	34.6	0.89 (0.79–1.00)	1.10 (1.06–1.15)	1.10 (1.05–1.15)	0.31
HbA <sub>1c</sub> >9.0% (>75 mmol/mol) despite insulin treatment	24.8	26.5	1.09 (1.06–1.12)	1.13 (1.10–1.17)	1.14 (1.10–1.17)	0.06
LDL-C ≥130 mg/dL despite lipid-lowering treatment	21.1	25.9	1.28 (1.21–1.34)	1.42 (1.38–1.46)	1.42 (1.38–1.46)	0.03
BP ≥140/90 mmHg despite antihypertensive treatment	60.5	62.2	1.21 (1.16–1.27)	1.01 (0.99–1.03)	1.02 (1.00–1.04)	0.09
Overall quality of care						
Q score <15	7.2	8.5	1.34 (1.25–1.45)	1.15 (1.12–1.18)	1.17 (1.14–1.20)	0.11
Q score >25	38.0	34.2	0.73 (0.70–0.77)	0.89 (0.87–0.90)	0.89 (0.87–0.90)	0.14

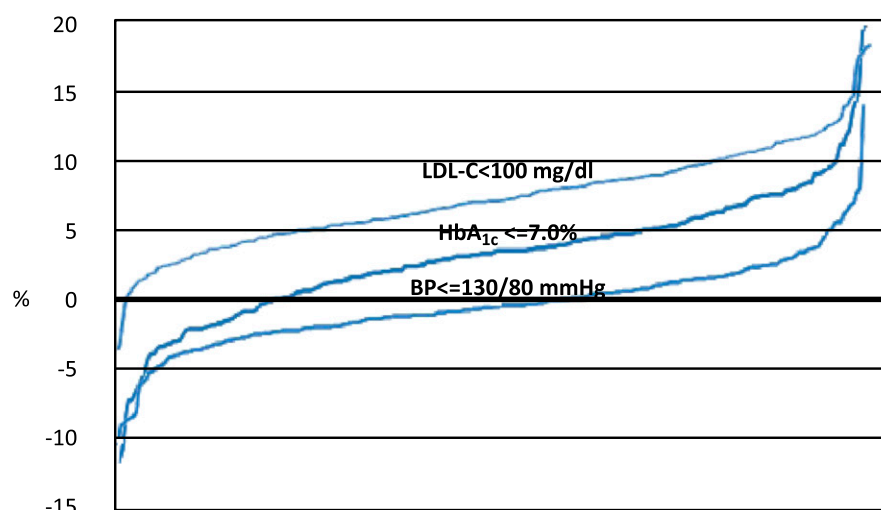
The first two columns show crude percentages by sex. The subsequent columns show the likelihood (OR and 95% CI) of women as compared with men (reference class) to be monitored for specific clinical parameters, to reach specific clinical outcomes, and to be treated with specific classes of drugs. ORs are crude, adjusted for patient case mix only (age, diabetes duration, and BMI), and adjusted for case mix and clustering effect.

confirms that not taking patient case mix and clustering effect into consideration may lead to biased results (27,28). On the other hand, when the analyses were performed separately in individuals below and over 75 years of age, sex disparities were still documented in younger people and were further increased in elderly patients.

Our findings do not seem to be explained by a lower propensity of physicians to treat women. In fact, the proportion of women treated with insulin,

statins, or antihypertensive agents was equal or even greater than that of men. Also, women were more likely than men to be treated with insulin and antihypertensive agents and equally likely to be treated with lipid-lowering drugs in the presence of elevated values. The greater difficulty in reaching the targets can be related to the use of a lower aggressive approach (i.e., prescription of lower doses), poorer compliance of women, or between-sex physiopathological differences. For

example, data on sex differences in carbohydrate metabolism showed that during submaximal endurance exercise, women oxidize more lipid and less carbohydrate as metabolic substrates than men (29). In addition, prior research demonstrated the existence of sex differences in drug responses, due to differences in pharmacodynamics and pharmacokinetics (30). On this issue, a study documented that statin therapy after an acute myocardial infarction is associated with reduced rates of all-cause and



**Figure 2**—Intercenter variability in the percentage difference of men and women achieving the main clinical therapeutic targets.

cardiac mortality, but the degree of risk reduction is lower for women than for men (31). Furthermore, women experience a higher incidence of adverse drug reactions than men. Sex-specific differences in the pharmacokinetics and pharmacodynamics of drugs are still unclear (32). Another element calling for possible intrinsic physiopathological sex differences is the impairment in the renal function that follows different pathways with a higher prevalence of microalbuminuria in men and more frequently reduced GFR in women (33), as also documented in our study.

Apart from biomedical differences, the documented differences could also be explained in terms of behavioral factors. Information on psychosocial characteristics and adherence to treatments is lacking in AMD Annals. Nevertheless, in the AMD BENCHMARKING Network for Clinical and Humanistic Outcomes in Diabetes (BENCH-D) study (34), women showed a higher prevalence of depression, as documented by a two times higher likelihood than men of being in the lowest quartile of the WHO-5 well-being index score; the study also showed that lower levels of psychological well-being were associated with lower levels of satisfaction with treatment, diabetes empowerment, and self-care attitudes and with a worse perception of barriers to medication. All these factors can negatively affect compliance with medical recommendations.

Recently, a new conceptual model has been developed to explain sex differences in health: neither exclusively biomedical explanations nor exclusively social explanations. The model intends to bridge

and integrate these dichotomous perspectives as the key to establishing new policies to increase opportunities and provide incentives for pursuing health (35). The existence of mixed mechanisms is also suggested in our study by the analysis of between-center variability. For LDL-C, in almost all the centers (233 out of 236), the proportion of men reaching the target was higher than that of women. Such a systematic difference can hardly be explained by the attitudes of the physicians or the patients, and the existence of pathophysiological differences between sexes may play an important role. On the other hand, for the attainment of the HbA<sub>1c</sub>, men were more likely than women to reach the target of  $\leq 7.0\%$  in 80% of the centers (190 out of 236 centers), thus suggesting the existence of a mixed effect of physiological mechanisms and attitudes. As for BP targets, the direction and magnitude of the between-center difference was variable, thus suggesting that different physician- and patient-related factors, rather than physiopathology, may play a crucial role.

Our study has strengths and limitations. The main strengths are the sample size and the data source, which are largely representative of the quality of diabetes care provided to both sexes in Italy. A limitation is that we missed information on drug doses, sociodemographic and socioeconomic characteristics, and micro- and macrovascular diabetes complications, which could aid in understanding the reasons for the results obtained. Also, our findings refer to patients attending

specialist centers and cannot be generalized to patients cared for by general practitioners.

In conclusion, our data strongly suggest that the greater difficulty in reaching LDL-C targets in women is mainly related to pathophysiological factors, whereas patient and physician attitudes can play an important role in other process measures and outcomes. These findings underline the need for diversifying the care and specializing the support provided to men and women based on sociodemographic, clinical, and psychological characteristics.

Further research is required to improve the knowledge about mechanisms underlying these differences. The regular evaluation of quality-of-care indicators with initiatives such as the AMD Annals is the first fundamental step to identify the main areas of interventions and monitor the desirable increase in equity during the time.

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