BMC Endocrine Disorders

RESEARCH **Open Access**

Identify unmet needs in diabetes care in Shandong, China: a secondary analysis of a cross-sectional study using cascade of care framework

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Abstract

Background The continuum management of diabetes remains under-evaluated in China. This study aimed to estimate the proportions of diabetes adults at each stage of the cascade of care framework in Shandong, China.

Methods We conducted a secondary analysis using the 2018 China Adult Chronic Disease and Nutrition Surveillance (CACDNS) data in Shandong. This nationwide cross-sectional survey was conducted between September and November 2018, investigating the major chronic diseases among Chinese adults through interviews, physical examinations, and laboratory tests. We employed the cascade model to examine the proportion of diabetes adults, including both type 1 and type 2, from diabetes screening, diagnosis, pharmaceutical and non-pharmaceutical treatments, to single and comprehensive management targets, and quantified the attrition between each stage. Diabetes screening was defined as participants reported to have ever received a blood glucose test. Diabetes diagnosis was defined as: 1) fasting plasma glucose (FPG) ≥ 126 mg/dL, or 2) 2-h oral glucose tolerance test (2 h-OGTT) ≥ 200 mg/dL, or 3) hemoglobin A1c (HbA1c) ≥ 6.5%, or 4) self-reported diabetes. Diabetes management targets included: 1) single glycemic target of personalized HbA1c level, 2) comprehensive ABC targets of personalized HbA1c level, blood pressure (BP) < 140/80 mm Hg, and low-density lipoprotein cholesterol (LDL-c) level < 2.6 mmol/L, 3) lifestyle target of not currently smoking. The estimated proportion was calculated through self-reported diabetes status and FPG, 2h-OGTT and HbA1c. The number of diabetes cases in Shandong was extrapolated using the 2018 provincial census data for adults aged 18 years and above (N = 80.6 million). The cascade of diabetes care was further examined by age, sex, and Basic Public Health Service (BPHS) enrollment.

Results This secondary analysis included 8,462 individuals (47.8% males, median age: 49.0), among whom 12.4% had diabetes (self-reported: 4.2%, newly diagnosed: 8.2%) and 41.1% had prediabetes. In 2018, an estimated 9.2 million adults in Shandong had diabetes, with 6.4 million (69.6%) receiving diabetes screening but 6.2 million (67.7%) remaining unaware of their conditions. Among self-reported diabetes adults, 2.7 million (86.4%) and 2.8 million (89.6%)

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received pharmaceutical and non-pharmaceutical treatment, respectively. Of those with treatments, 1.2 million (58.2%) met personalized glycemic target. A rapid decline, however, was observed in BP (31.1%) and LDL-c (39.3%) control among diabetes patients with multimorbidity (≥ 2 diseases). Ultimately, 0.1 million self-reported diabetes adults (3.8%) achieved the ABC targets. BPHS Enrollment slightly improved comprehensive management with ABC targets.

Conclusions A significant unmet need exists for diabetes adults from screening to management, particularly the comprehensive management of glycemia, BP and LDL-c levels among those with multimorbidity. Tailored strategies and appropriate allocation of healthcare resource is needed to addressing gaps in care continuum and reduce long-term disease burden.

Keywords Diabetes mellitus, Cascade of care, China, Glycemic control, Disease management

Background

Diabetes is a major global public health problem, with an estimated 529 million cases in 2021 and projected to reach 1.31 billion by 2050, resulting in nearly one trillion dollars in annual expenditure [1]. China shares a remarkably large number of diabetes and related mortality [2]. Since 1990, a more than twofold increase has been observed in mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs) [3]. It is common for diabetes patients to have the coexistence of hypertension, dyslipidemia, and obesity [4]. The high prevalence of multimorbidity was associated with increased catastrophic health expenditure [5] and excess risk of disability and mortality [6, 7]. Therefore, a comprehensive control of glycemia, blood pressure (BP) [8], and lipid levels [9], accompanied with lifestyle change of stopping smoking and managing weight [10], is proposed to maximally reduce the diabetes morbidity and enhance the overall health benefits [4, 11–13].

To depict disease journey from screening to management, the concept of "cascade of care" is introduced. The cascade model provides a visual form of care continuum in terms of disease screening, diagnosis, treatment, and management, and allows healthcare professionals to identify any insufficiency during care delivery. Despite being previously initiated in the HIV epidemic [14], mapping the cascade of care is currently widely accepted and employed in chronic disease research [15–19], for example, to identify the fragility [15–17, 20] and to explore the opportunity for improved diabetes outcomes [21].

In China, previous studies have too often focused on single glycemic control or segmented care delivery assessments [22–24]. Limited evidence of diabetes care as entire spectrum is available. Moreover, the one-fit-all HbA1c cut-off without consideration of age or multimorbidity status may underestimate the overall disease burden and fail to illustrate the actual benefits of early intervention to asymptomatic hyperglycemia patients.

Shandong ranked as the second most populous province in China, with over 100 million residents. The estimated diabetes prevalence and mortality were above the national average [23, 24], and the related costs were 14 billion dollars in 2019 and projected to double by 2030 [25]. Given the substantial disease burden, our study leveraged the 2018 China Adult Chronic Disease and Nutrition Surveillance (CACDNS) data in Shandong, employing a cascade approach to delineate gaps in diabetes care delivery, including both type 1 and type 2.

Methods

Study design

We performed a secondary analysis from the cross-sectional survey data in Shandong as part of the CACDNS, and this study was reported in accordance with the STROBE guidelines[26]. As part of the China Chronic Disease and Risk Factor Surveillance (CCDRFS), CACDNS employed a stratified multistage cluster sampling scheme to collect nationally representative data from noninstitutionalized adults aged 18 or older from September to November 2018. In total, 302 survey sites were selected as primary sampling units, three townships and two administrative villages were randomly selected by population size as the first and second sampling stages. Every 60 households were randomly selected as one group from each village and at least 45 households within the group were selected to participate in the study. The nonagricultural population rate, urbanization rate, and total population were considered to ensure that the data were also representative at the provincial level. Data were collected through household and individual interviews, standardized physical examinations, and laboratory tests of fasting blood and urinary samples. The study design and detailed sampling strategy were described elsewhere [27].

Participants

Within each selected household, all non-pregnant adults aged 18 and above were invited to the study. A total of 8,264 adults responded and completed the interview. After excluding respondents with missing demographic characteristics (age and sex), 8,262 were included in the analysis.

Data collection and measurements

The data was collected through structured questionnaires by in-person interviews, physical examinations, and laboratory tests. The face-to-face interviews were administrated by trained survey interviewers. The questionnaires mainly included general demographic information, lifestyle habits, disease history and medication use (diabetes, hypertension, cardiovascular diseases), and healthcare utilization[28, 29]. The physical examination measured the height, weight, waist circumference, and BP of the participants. The laboratory tests included routine blood test, urine analysis, blood biochemistry, lipid profile, and comprehensive blood sugar index.

As primary biochemical indicators of diabetes, FPG and 2 h-OGTT were measured using the hexokinase enzymatic method, and HbA1c was measured using a HemoCue Hb 201 + Analyzer. Lipids were measured as 1) total cholesterol: CHOD-PAP; 2) triglyceride (TG): GPO-PAP; and 3) low-density lipoprotein (LDL-c) and high-density lipoprotein (HDL-c): enzymatic colorimetric. Serum creatinine was tested through sarcosine oxidase. Fasting morning urine was collected, and microalbumin was measured using immunoturbidimetry. All laboratory tests followed national standard brochures. Participants with self-reported diabetes did not receive the 2 h-OGTT test. Two or three brachial artery BP measurements (OMRON HBP-1300 BP Monitor) were performed by physicians after 5 min of resting in a seated position participants in a separate and quiet room. Two repeated measurements of waist circumference were performed on the exhale of participants in a standing-up position. The average value of the measurements was used. Participants who had at least one physical examination or diabetes screening during the last 12 months were deemed to attend health checkups. The eligibility of BPHS involvement was confined to adults aged 35 years or greater. Participants reported to receive BPHS service were regarded to join the BPHS program. Current smoking was defined as participants reporting smoking at the time of the study. The sex of the participants was self-identity.

Definitions of clinical outcome

The screening for diabetes was defined as participants reporting ever received blood glucose tests, either at home or in medical institutions. The definition of diabetes employed a dual classification: 1) a positive response of participants to the question 'Other than during pregnancy, have you ever been told by a doctor or health professional from the community health center or above that you have diabetes; 2) participants who met any of the three diagnostic criteria that FPG was 7.0 mmol/L (126 mg/dL) or higher, HbA1c was greater than or equal to 6.5%, or 2 h-OGTT was 11.1 mmol/L (200 mg/dL) or higher. Prediabetes was defined as participants with FPG between 5.6 mmol/L (100 mg/dL) and 7.0 mmol/L (126 mg/dL), HbA1c greater or equal to 5.7% and less than 6.5%, or 2 h-OGTT between 7.8 mmol/L (140 mg/dL) and 11.1 mmol/L (200 mg/dL) [30]. Participants with average systolic BP $\geq$ 140 mmHg or diastolic BP $\geq$ 90 mmHg, or took any antihypertensive treatment were considered having hypertension [31]. Metabolic conditions were defined as follows: 1) central obesity with waist circumference $\geq$ 90 cm for men and $\geq$ 85 cm for women; 2) FPG of 6.1 mmol/L or greater, 2 h-OGTT of 7.8 mmol/L or greater, or receiving any antidiabetic treatment; 3) elevated systolic BP $\geq$ 130 mmHg or diastolic BP $\geq$ 85 mmHg or receiving any antihypertensive treatment; 4) elevated TG > 1.7 mmol/L; and 5) HDL-c < 1.04 mmol/L [11].

Diabetes management contains two stages, a single glycemic HbA1c control as the primary target, and a synthesis control with additional BP and lipids (abbreviated as "ABC targets") [22, 32]. The personalized single glycemic targets were proposed to combine HbA1c with age and concurrent cardiovascular diseases (CVD) [18, 33, 34]. Our analysis used the following criteria: 1) participants younger than 45 years and had no CVD-related complications (< 6.5%), or complications (< 7.0%); 2) participants between 45 and 64 years and had no CVD-related complications (< 7.0%), or complications (< 8.0%); and 3) participants older than 65 years and had no CVD-related complications (< 7.5%), or complications (< 8.0%). The goal of the BP target varied across recommendations. The American Diabetes Association (ADA) proposed controlling BP under 140/80 mmHg, while the Chinese Diabetes Society (CDS) suggested a more aggressive target of lowering BP than 130/80 mmHg, a less intensive BP control was advocated by the Eight Joint National Committee (JNC 8) to target 140/90 mmHg or lower [35]. We examined the proportion of diabetes-hypertension adults (either self-reported or BP $\geq$ 140/90 mmHg) with BP control applying all three criteria (ADA, CDS, JNC 8).

Based on the American College of Cardiology (ACC) and American Heart Association (AHA) [36], the primary prevention of CVD was defined as patients between 45 and 75 years with diabetes, or less than 75 years and LDL-c $\geq$ 4.9 mol/L to lower LDL-c less than 2.6 mmol/L; secondary prevention was defined as diabetes patients less than 75 years with any concurrent CVD to lower LDL-c less than 1.8 mmol/L. In the context of ABC targets, lipid control was aimed to achieve LDL-c less than 2.6 mmol/L. Subgroup analysis of diabetes-hyperlipidemia, and LDL-c followed the criteria for the given group.

Definition of cascade of care

The cascade of care was mainly categorized into screening for diabetes, disease diagnosis, treatment, and single or comprehensive management targets (Fig. 1).

Screening for diabetes acted as the first stage of the cascade model. In our study, participants reported receiving blood glucose tests at home or in medical institutions were deemed to have diabetes screened.

Diabetes diagnosis was the second stage. We employed a dual classification if people self-reported to be diagnosed with diabetes by healthcare professionals, or those who met the diagnostic criteria through biochemical tests. For self-reported diabetes adults, they were deemed to be aware of their disease condition. For non-self-reported diabetes adults, the disease condition remained unknown until the study was conducted.

Treatment of diabetes was the third stage. This stage was further divided into three categories: pharmaceutical treatment, non-pharmaceutical treatment, and combined treatments, all of the information was self-reported and meticulously documented via in-person interviews. Pharmaceutical treatment mainly included oral antidiabetic (OAD) drugs and insulin use. Non-pharmaceutical treatment included dietary control, more frequent physical activity, and glucose monitoring. Adults who took both approaches to treat their diabetes were deemed to receive combined treatments.

The last stage was diabetes management, including single glycemia control and comprehensive management of glycemia, BP, and lipid levels in multimorbidity. From the perspective of lifestyle change, stopping smoking was further added as one of the management targets (abbreviated as "ABCS targets").

The denominator of each stage was the number of participants met the diabetes diagnostic criteria at the time of study conduction. The unmet need in diabetes care was therefore the attrition between given stages.

Statistical analysis

The analysis was conducted using SAS, version 9.4 (SAS Institute Inc.) to adjust for complex survey design. We examined the normality of continuous variables using Shapiro–Wilk test. Data were reported using percentages for categorical variables, mean, standard deviation, median and interquartile range (IQR) for continuous measures. To examine the differences across diabetes (self-reported and newly diagnosed), prediabetes and normoglycemia groups, we conducted Kruskal–Wallis test for continuous variables and chi-square (χ^2) test for categorical variables. Variables with missing data were analyzed by excluding the specific missing data. The sample weights were accounted for selection probabilities and non-response during the estimation. The estimated prevalence was based on self-reported, FPG, HbA1c, or

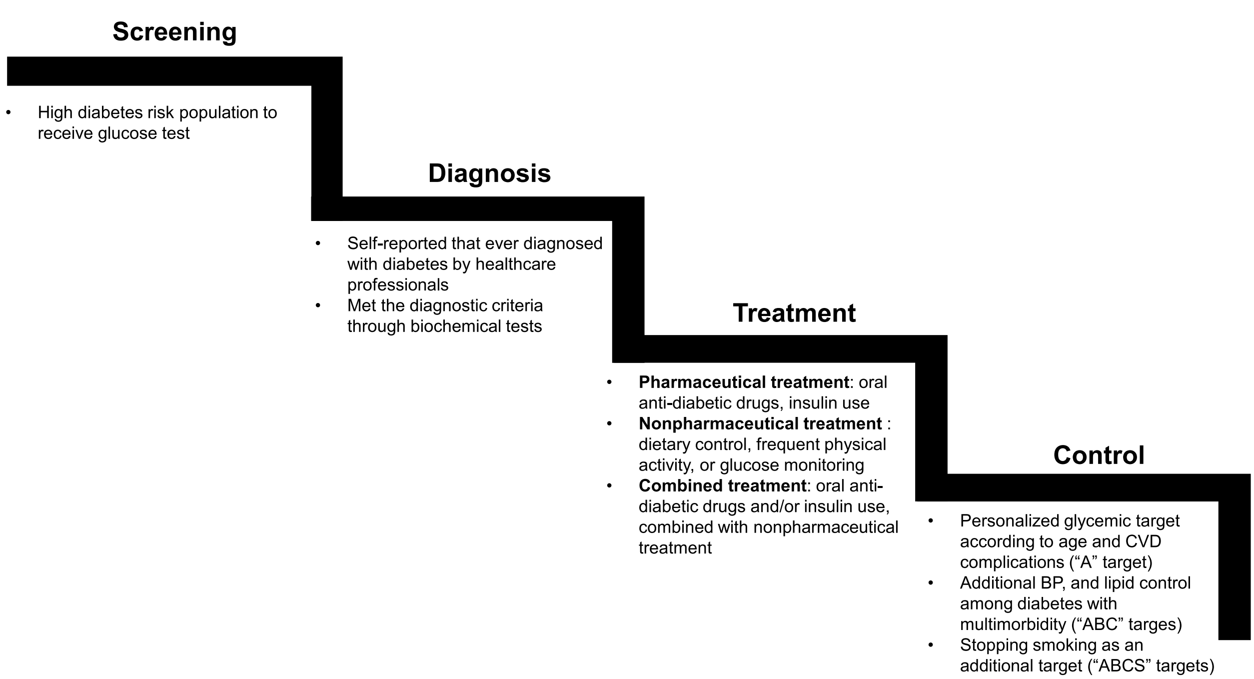

Fig. 1 Cascade of care model used for diabetes. This flowchart illustrated cascade of diabetes care continuum from screen to control

2 h-OGTT of 8,462 study participants. We multiplied the age-adjusted prevalence to extrapolate the estimated number of diabetes cases in Shandong using the 2018 provincial resident population aged greater than or equal to 18 years ($N = 80.6$ million, Additional file 1: Table S1) [37]. For participants with diabetes, the mean HbA1c and FPG (PROC SURVEYMEANS), the proportion of antidiabetic treatment, and the magnitude of single and comprehensive targets (PROC SURVEYFREQ) were calculated. In terms of achieving the single or synthesis targets of diabetes, we assigned 100 to positive response and 0 to negative response and used PROC SURVEYREG to estimate the age-adjusted prevalence. To incorporate the multistage sample design, we used the Taylor series linearization to estimate the standard errors based on primary sampling unit. A stratified analysis of age groups, sex, and participation in BPHS was explored.

Results

Sample characteristics

The study included 8,462 participants with the median age of 49 years old. Among those, 4,045 (47.8%) were male and 4,417 (52.2%) were female. In total, 1,053 participants had diabetes, of which 360 were self-reported and 693 were newly diagnosed during the study. A total of 3,480 (41.1%) adults were experiencing the prediabetes stage (Additional file 1: Fig. S1). Older age, living in rural areas, fewer years of education, central obesity, and insufficient vegetable intake were related to diabetes (p value: < 0.001) (Table 1, Additional file 1: Table S2). Diabetes adults had more metabolic conditions (83.6% among self-reported diabetes, 82.8% among newly diagnosed diabetes), concurrent CVD (12.5% among self-reported diabetes, 5.5% among newly diagnosed diabetes), and impaired renal function (Table 1).

Cascade of diabetes care in Shandong, China

After applying a complex survey design with a provincial population age structure, an estimated 9.2 million (11.4%) adults in Shandong had diabetes, of whom 6.4 million reported to ever screening their blood glucose level at home or in medical institutions. 3.0 million diabetic adults self-reported to aware of their disease condition, while 6.2 million remained unknown (Fig. 2). In terms of diabetes treatment, an estimated 2.4 million self-reported adults took OAD, 0.7 million adults ever used insulin, and 0.4 million received both medications to lower their glycemic level. For non-pharmaceutical treatment, 2.4 million diabetes adults were taking dietary control, 1.6 million were exercising more frequently, and 2.2 million were continually monitoring their glucose level (Fig. 3). A total of 2.8 million diabetes adults reported at least one lifestyle change to manage their glycemic level. Regarding combined treatments, 2.6 million diabetes adults were estimated to employ at least one pharmaceutical treatment, accompanied by one lifestyle behavior (Fig. 2). In terms of primary glycemic control, an estimated 1.2 million self-reported diabetes adults met personalized single HbA1c targets.

Diabetes adults with concurrent hypertension or elevated risk of CVD were examined in detail. An estimated 1.83 million (61.7%) of self-reported diabetes adults had hypertension (self-reported or BP ≥ 140/90 mmHg), of whom 1.14 million (38.5%) took antihypertensive medication to lower the blood pressure. The estimated number of adults with well-controlled BP was 0.36 million (JNC 8 BP), 0.15 million (ADA BP), and 0.02 million (CDS BP), respectively (Fig. 4a). Similarly, 2.16 million (72.9%) of self-reported diabetes adults were eligible to receive statins as the primary prevention of CVD. Of those, 0.48 million (16.3%) reported taking statins and 0.13 million (4.4%) met the control target (LDL-c < 2.6 mmol/L). An estimated 0.34 million (11.3%) of self-reported diabetes adults were eligible for statins as secondary prevention, 0.07 million (2.2%) were being treated, and 0.01 million (0.2%) were successfully controlled (LDL-c < 1.8 mmol/L) (Fig. 4b). Combing each composite target of HbA1c, BP and LDL-c, only 0.1 million of the self-reported diabetes adults ultimately met the synthesis ABC or ABCS targets (Fig. 2).

Cascade of diabetes care by age, sex, BPHS enrollment

A stratified analysis was conducted to examine the disparities across age and sex. Females tended to be aware of their diabetes condition, and males were more likely to remain unaware of the elevated glycemia. Compared to the young and elder adults, people aged 45–64 years were not in favor of attending health checkups or joining the BPHS, preferred to take OAD drugs to lower glycemia levels, and were less likely to achieve the composite ABC or ABCS targets. Young adults aged 18–44 years had worse glycemic control but a relatively higher proportion of CDS BP and lipid control. Males had an overall weakened link to healthcare or pharmaceutical treatments, their combined ABC or ABCS targets were unsatisfactory compared to females, although they performed better in LDL-c and CDS BP control (Table 2).

The study further examined the performance of BPHS in diabetes management. Every 8.8 in 10 self-reported diabetes adults enrolled in the BPHS were taking OAD medications, 20% higher than those not joined in the program. The use of insulin, however, appeared in the opposite direction. Adults who did not join the BPHS were more likely to take insulin (24.6% vs. 28.3%) and to meet glycemic targets (56.3% vs. 61.8%). Diabetes adults reported receiving diet and physical activity counseling

Table 1 Comparison of the Characteristics of Shandong adults in 2018 (sample population)[*]

Characteristic	Self-reported Diabetes ($N = 360$)	Newly diagnosed Diabetes ($N = 693$)	PreDiabetes ($N = 3,480$)	Normoglycemia ($N = 3,929$)	P value[a]
Age, years					
18–44	31 (8.6%)	137 (19.8%)	1,012 (29.1%)	2,159 (55.0%)	< 0.001[b]
45–64	210 (58.3%)	392 (56.6%)	1,789 (51.4%)	1,392 (35.4%)	
65–90	119 (33.1%)	164 (23.7%)	679 (19.5%)	378 (9.6%)	
Age, median (IQR), years	60 (52–67)	55 (48–64)	52 (42–63)	43 (31–53)	< 0.001[b]
Male	159 (44.2%)	390 (56.3%)	1,747 (50.2%)	1,749 (44.5%)	< 0.001[b]
Rural	222 (61.7%)	412 (59.5%)	2,063 (59.3%)	2,141 (54.5%)	< 0.001[b]
Educational level					
≤ Primary School	181 (50.3%)	288 (41.6%)	1,412 (40.6%)	1,008 (25.7%)	< 0.001[b]
Junior Secondary School	101 (28.1%)	255 (36.8%)	1,235 (35.5%)	1,583 (40.3%)	
Senior Secondary School	62 (17.2%)	116 (16.7%)	535 (15.4%)	708 (18.0%)	
≥ Junior College	16 (4.4%)	34 (4.9%)	298 (8.6%)	630 (16.0%)	
Annual household income (Yuan)					
0–35,000	165 (45.8%)	310 (44.7%)	1,535 (44.1%)	1,486 (37.8%)	< 0.001[b]
35,000–69,999	90 (25.0%)	186 (26.8%)	975 (28.0%)	1,273 (32.4%)	
70,000–104,999	42 (11.7%)	78 (11.3%)	402 (11.6%)	493 (12.5%)	
105,000–1,200,000	29 (8.1%)	45 (6.5%)	235 (6.8%)	261 (6.6%)	
Refused	10 (2.8%)	18 (2.6%)	86 (2.5%)	119 (3.0%)	
No health insurance	10 (2.8%)	16 (2.3%)	109 (3.1%)	126 (3.2%)	< 0.001[b]
Ever screening for diabetes[c]	358 (99.4%)	452 (65.2%)	1742 (50.1%)	1784 (45.4%)	< 0.001[b]
BPHS involvement	248 (68.9%)	N.A	N.A	N.A	N.A
Currently Smoking	56 (15.6%)	164 (23.7%)	807 (23.2%)	767 (19.5%)	< 0.001[b]
0–400 g/d of fruits or vegetables	139 (38.7%)	220 (31.8%)	1,113 (32.1%)	1,138 (29.0%)	< 0.001[b]
Central Obesity[d]	208 (57.8%)	419 (60.5%)	1,629 (46.8%)	1,265 (32.2%)	< 0.001[b]
BMI,kg/m^2 [d]					
lowest (13.5) < 24.0	84 (23.3%)	152 (21.9%)	1,121 (32.2%)	1,736 (44.2%)	
24.0–27.9	157 (43.6%)	274 (39.5%)	1,411 (40.5%)	1,466 (37.3%)	
28.0-highest (55.0)	118 (32.8%)	267 (38.5%)	947 (27.2%)	721 (18.4%)	
History of CVD	45 (12.5%)	38 (5.5%)	131 (3.8%)	71 (1.8%)	< 0.001[b]
MetS	301 (83.6%)	574 (82.8%)	1,839 (52.8%)	1,010 (25.7%)	< 0.001[b]
HbA1c, mean (SD), %[e]	7.3 (1.6)	6.5 (1.4)	5.4 (0.4)	5.1 (0.3)	< 0.001[b]
FPG, mean (SD), mmol/L[f]	8.9 (2.9)	8.1 (2.7)	5.9 (0.4)	5.1 (0.3)	< 0.001[b]
2 h-OGTT, median (IQR), mmol/L[g]	N.A	12.2 (9.3–15.2)	6.5 (5.4–7.9)	5.3 (4.6–6.1)	< 0.001[b]
BP, mean (SD), mmHg[h]					
Systolic	143.0 (19.3)	142.0 (18.4)	135.0 (18.0)	128.0 (16.5)	< 0.001[b]
Diastolic	82.4 (10.2)	83.4 (10.6)	80.7 (10.8)	77.8 (10.3)	< 0.001[b]
Cholesterol, median (IQR), [f]					
Total, mmol/L	5.2 (4.5–5.9)	5.3 (4.7–6.0)	5.1 (4.5–5.8)	4.7 (4.1–5.3)	< 0.001[b]
HDL, mmol/L	1.3 (1.1–1.5)	1.3 (1.1–1.6)	1.4 (1.1–1.7)	1.4 (1.2–1.7)	< 0.001[b]
LDL, mmol/L	3.1 (2.5–3.8)	3.3 (2.6–3.8)	3.1 (2.6–3.7)	2.8 (2.3–3.4)	< 0.001[b]
Triglycerides, mmol/L	1.7 (1.1–2.5)	1.6 (1.1–2.4)	1.7 (0.9–1.9)	1.1 (0.8–1.6)	< 0.001[b]
Serum Creatinine, median (IQR), µmol/L	64.0 (55.0–76.0)	68.0 (57.0–79.0)	68.0 (59.0–79.0)	67.0 (58.0–78.0)	< 0.001[b]
Albuminuria, mg/g [i]					< 0.001[b]
Normalbuminuria	282 (78.3%)	601 (86.7%)	3,226 (92.7%)	3,674 (93.5%)	
Microalbuminuria	66 (18.3%)	73 (10.5%)	177 (5.1%)	144 (3.7%)	
Macroalbuminuria	11 (3.1%)	12 (1.7%)	21 (0.6%)	15 (0.4%)	
eGFR, mL/min/1.73m^2 [j]					< 0.001[b]
Normal	249 (69.2%)	500 (72.2%)	2,516 (72.3%)	3,263 (83.0%)	
Mild	98 (27.2%)	187 (27.0%)	929 (26.7%)	637 (16.2%)	

Table 1 (continued)

Characteristic	Self-reported Diabetes ($N=360$)	Newly diagnosed Diabetes ($N=693$)	PreDiabetes ($N=3,480$)	Normoglycemia ($N=3,929$)	P value[a]
Moderate to terminal	13 (3.6%)	6 (0.9%)	35 (1.0%)	26 (0.7%)	

Abbreviations: *BPHS* Basic Public Health Services, *CVD* Cardiovascular disease, *MetS* Metabolic syndrome, *HbA1c* Hemoglobin A1c, *FPG* Fasting plasma glucose, *2 h-OGTT* Two-hour oral glucose tolerance test, *BP* blood pressure, *HDL* High-density lipoprotein, *LDL* low-density lipoprotein, *eGFR* estimated glomerular filtration rate

[*] The results presented in the table were calculated based on survey participants. Continuous variables are described by the mean (SD), while categorical variables are described by n (%)

[a] Values were calculated using the Kruskal–Wallis test for continuous variables and the chi-squared test for categorical variables

[b] Statistically significant ($P<0.05$, two-sided test)

[c] Ever screening for diabetes included receiving blood glucose test at home or in medical institutions

[d] Participants with missing data on BMI or waist circumference were excluded from the analysis ($n=8$, one in prevalent diabetes, one in prediabetes, and six in normoglycemia)

[e] Participants with missing data on HbA1c were excluded from analysis ($n=11$, four in prediabetes, and seven in normoglycemia)

[f] Participants with missing data on FPG, total cholesterol, HDL-c, LDL-c, triglycerides, and serum creatinine were excluded from analysis ($n=3$, all in normoglycemia)

[g] Participants with missing data on 2 h-OGTT were excluded from analysis ($n=599$, 360 in prevalent diabetes, 88 in newly diagnosed diabetes, 84 in prediabetes, and 67 in normoglycemia)

[h] Participants with missing data on SBP and DBP were excluded from analysis ($n=10$, one in prevalent diabetes, two in prediabetes, and seven in normoglycemia)

[i] Normalbuminuria, microalbuminuria, and macroalbuminuria were defined as having a urinary albumin–creatinine ratio of less than 30, 30 to 300, and greater than 300 mg/g, respectively

[j] Normal, mild, and moderate to terminal were defined as having an eGFR of more than 90, 60 to 90, and less than 60 mL/min/1.73m^2, respectively

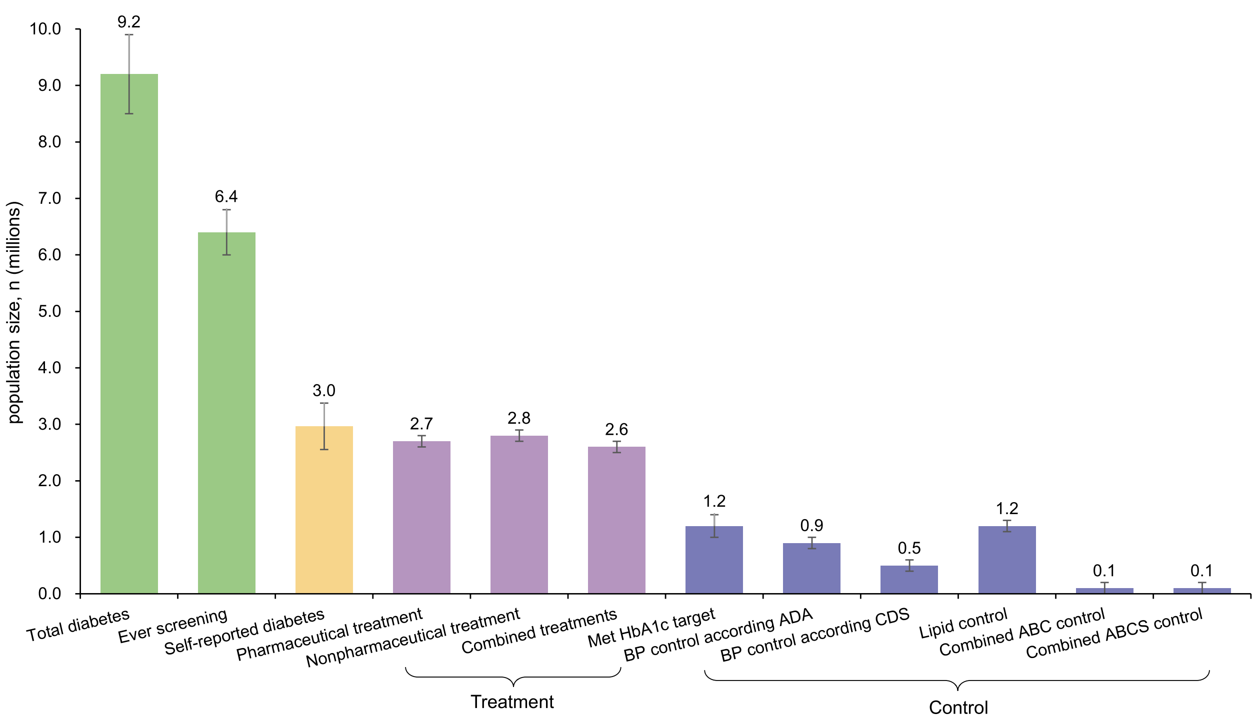

Fig. 2 Cascade of care for diabetes adults aged 18 years or older in Shandong, 2018. There estimated 9.2 million diabetes in Shandong, of whom 6.4 million had ever received blood glucose test at home or in medical institutions, and 3.0 million self-reported to be diagnosed with diabetes. Of those self-reported cases, 2.8 million received any of dietary control, frequent physical activity, or glucose monitoring, 2.7 million diabetes received either OAD or insulin treatment, and 2.6 million received antidiabetic treatment plus any of dietary control, frequent physical activity, or glucose monitoring. The rest bar showed single target of HbA1c, BP, or LDL-c, as well as comprehensive control with composite indicators, only 0.1 million had ultimate composite ABC control

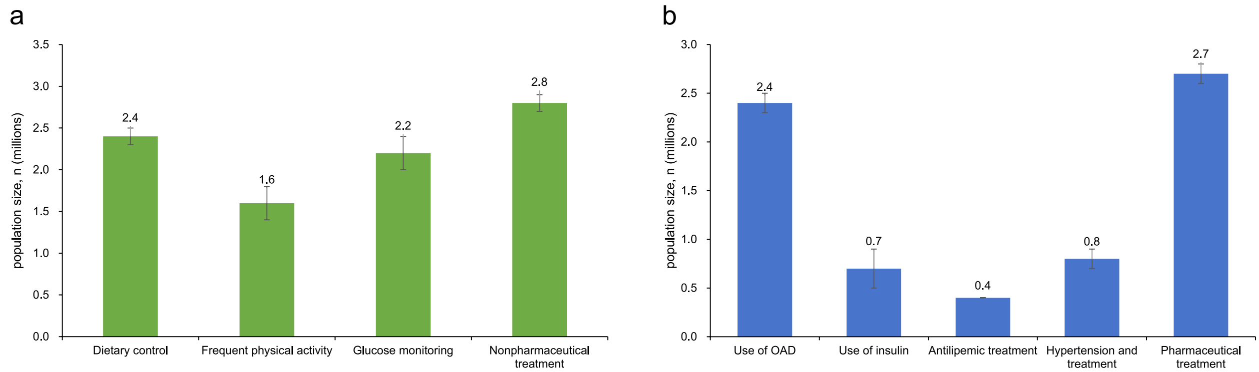

Fig. 3 Treatment for self-reported diabetes adults aged 18 years or older in Shandong, 2018. Figure 3a illustrated non-pharmaceutical treatment regarding dietary control, frequent physical activity, glucose monitoring, or any of those treatments in Shandong adults with self-reported diabetes. Figure 3b showed pharmaceutical treatment, including use of OAD, insulin, antihypertensive or antilipemic drugs among diabetic multimorbidity adults, and any medication use for anti-diabetic purpose

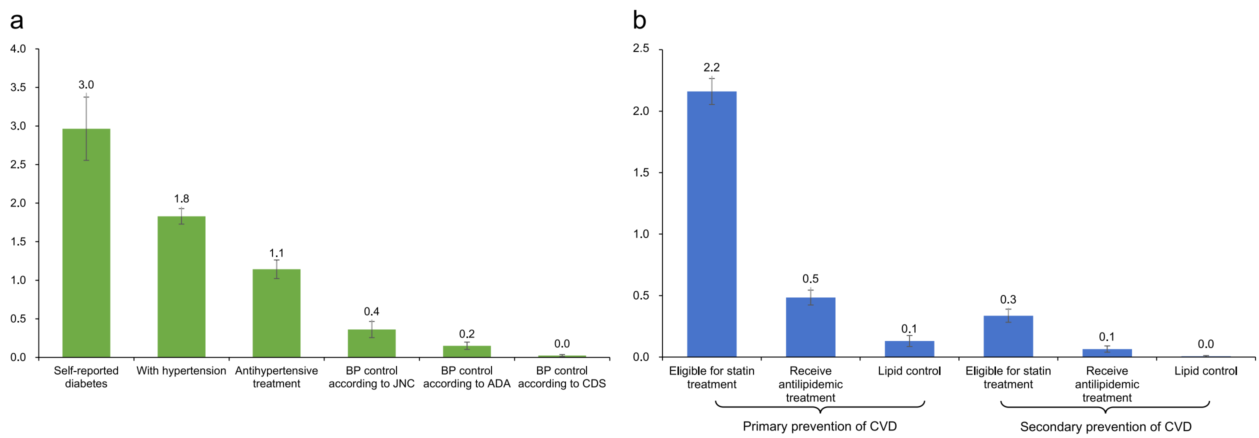

Fig. 4 Cascade for self-reported diabetes adults who were eligible, treated, and had controlled BP and lipid. Figure 4a showed 61.7% of self-reported diabetes had multimorbidity with hypertension, 38.5% received anti-hypertensive treatment, and 12.2%, 5.1%, and 0.8% had BP controlled according to JNC, ADA, and CDS, respectively. Figure 4b illustrated the eligible for statins, treatment of antilipidmic drugs, and lipid control as primary or secondary prevention of CVD, respectively, only 4.4% and 0.2% had ultimate lipid controlled as primary and secondary prevention of CVD among self-reported diabetes

through the BPHS were 91.2% and 83.7%, respectively. BPHS in general conferred a slightly better comprehensive control of diabetes, with 4.9% vs. 3.1% in ABC targets and 4.6% vs. 2.4% in ABCS targets, respectively (Fig. 5).

Discussion

The cascade model revealed a prominent insufficiency of diabetes care in Shandong, China. Approximately 70% of diabetes adults claimed to ever received blood glucose test, however, over half of them remained unaware of their glycemic status until detected by our study. The overall disease unawareness among diabetes adults was about 60%, 10% higher than the national average [23]. Similar to the results of a prior study [22], our investigation noted that about 40% of self-reported diabetes adults met the single glycemic HbA1c target but less than 1 in 25 of them met the composite glycemic, BP, LDL-c (ABC targets) or with additional nonsmoking (ABCS targets). The shrunk number along each cascade stage revealed an overall less satisfactory diabetes control in Shandong.

Among the participants with diabetes in our study, approximately 23% were unscreened and undiagnosed, and 43% were screened but undiagnosed. The findings are consistent with previous studies [38, 39], implying that the low and stagnated rate of awareness and diagnosis impedes diabetic patients to be captured by the healthcare system. Since 2009, China launched BPHS and employed high-risk screening strategy for diabetes [40], that is, offering diabetes tests to individuals who were overweight, with family history of diabetes, physical

Table 2 Cascade of Care for diabetes adults aged 18 years or older, by age and sex

Variable	Age Group			Sex	
	18–44 y	45–64 y	65–90 y	Male	Female
Total with diabetes (95% CI), n (millions)	**1.9 (1.7–2.1)**	**4.7 (4.0–5.3)**	**2.7 (2.2–3.1)**	**5.0 (4.5–5.6)**	**4.2 (3.6–4.8)**
Ever screening for diabetes (SE), %	99.1 ± 0.9	92.3 ± 2.2	95.1 ± 2.4	90.7 ± 2.4	96.5 ± 2.2
Self-reported diabetes (95% CI), n (millions)	**0.2 (0.2–0.3)**	**1.7 (1.4–2.0)**	**1.1 (0.9–1.3)**	**1.3 (1.1–1.5)**	**1.6 (1.4–1.9)**
Use of OAD (SE), %	79.3 ± 7.5	81.7 ± 2.6	77.8 ± 4.3	74.6 ± 3.0	84.6 ± 3.5
Use of Insulin (SE), %	23.3 ± 9.7	30.1 ± 9.7	19.6 ± 3.0	25.9 ± 2.8	25.7 ± 9.7
Dietary control (SE), %	84.0 ± 6.9	84.1 ± 4.7	70.1 ± 5.1	77.5 ± 6.0	80.4 ± 4.5
Frequent physical activity (SE), %	60.3 ± 8.6	50.5 ± 4.2	41.9 ± 5.3	57.9 ± 7.0	40.3 ± 6.9
Glucose monitoring (SE), %	79.8 ± 9.9	71.8 ± 5.5	70.4 ± 4.1	70.0 ± 5.1	73.5 ± 5.4
Meet personalized HbA1c target (SE), %	22.3 ± 9.7	51.2 ± 7.3	77.2 ± 4.0	55.9 ± 4.5	60.0 ± 8.8
BP < 140/80 mmHg (SE), %	30.1 ± 7.7	33.2 ± 6.1	29.3 ± 3.2	29.9 ± 3.8	32.9 ± 7.8
BP < 130/80 mmHg (SE), %	26.8 ± 8.6	11.2 ± 4.3	4.6 ± 0.9	14.7 ± 4.1	6.3 ± 1.6
LDL-c level < 2.6 mmol/L (< 100 mg/dL) (SE), %	54.2 ± 9.9	27.9 ± 3.2	20.6 ± 5.2	35.5 ± 3.9	20.9 ± 3.0
Nonsmoker (SE), %	85.2 ± 7.6	86.4 ± 4.0	83.8 ± 3.4	68.4 ± 5.8	99.3 ± 0.5
Meet ABC targets (SE), %	3.3 ± 3.3	3.1 ± 1.5	6.5 ± 3.2	3.3 ± 2.0	5.1 ± 2.5
Meet ABCS targets (SE), %	3.3 ± 3.3	2.3 ± 1.5	6.5 ± 3.2	2.4 ± 2.0	5.1 ± 2.5

Abbreviations: *BPHS* Basic Public Health Services, *OAD* oral antidiabetic drug, *BP* blood pressure, *LDL* low-density lipoprotein, *ABC* combined control of hemoglobin A_{1c} level, BP, and LDL-c level, *ABCS* combined control of ABC plus no currently smoking

inactivity, hypertension, dyslipidemia, or having a history of CVDs[41]. In the implementation, however, it relies on individuals to take the initiative to visit specialists for a particular reason, and they are offered the test while they are there. Such opportunistic screening might be attributed to a lack of risk perception of high-risk individuals and limited capacities in community healthcare centers [42]. As shown in our study, 50% of prediabetes adults did not receive diabetes screening, perhaps indicating people at high risk did not recognize their risk until any manifestation onset. On the other hand, providing education and standard training to general practitioners (GPs) in community healthcare centers has been proven to significantly increase the screening rate of high-risk individuals [40].

As observed in our study, there was an enormous loss from screening to diagnosis. Unlike the United States where unsatisfying diabetes diagnosis was mainly due to unaffordable health insurance [33], more than 90% of study participants held health insurance (Table 1). However, the widespread coverage did not guarantee a timely diagnosis. In our study, males aged 45–64, living in rural areas were subject to the delayed diagnosis. The finding is in line with a 2013 national diabetes prevalence survey[43], indicating a persistent pattern in the diagnosis stage. The delayed diagnosis is associated with an individual's motivation, the shortage of GPs, and the medical tests provided by medical institutions. Individuals with asymptomatic diabetes may not be aware of long-term disease morbidity and are less motivated to seek medical attention until complications risen. Meanwhile, the average waiting time and insurance co-pay across different grades of hospitals [44] could also influence the motivation. From the perspective of human resources, the ratio of healthcare providers to annual clinical visits in Shandong is 1 to 1,100 [37]. The shortage of health providers further exaggerates the loss in the diagnosis stage. Moreover, majority of the community healthcare centers do

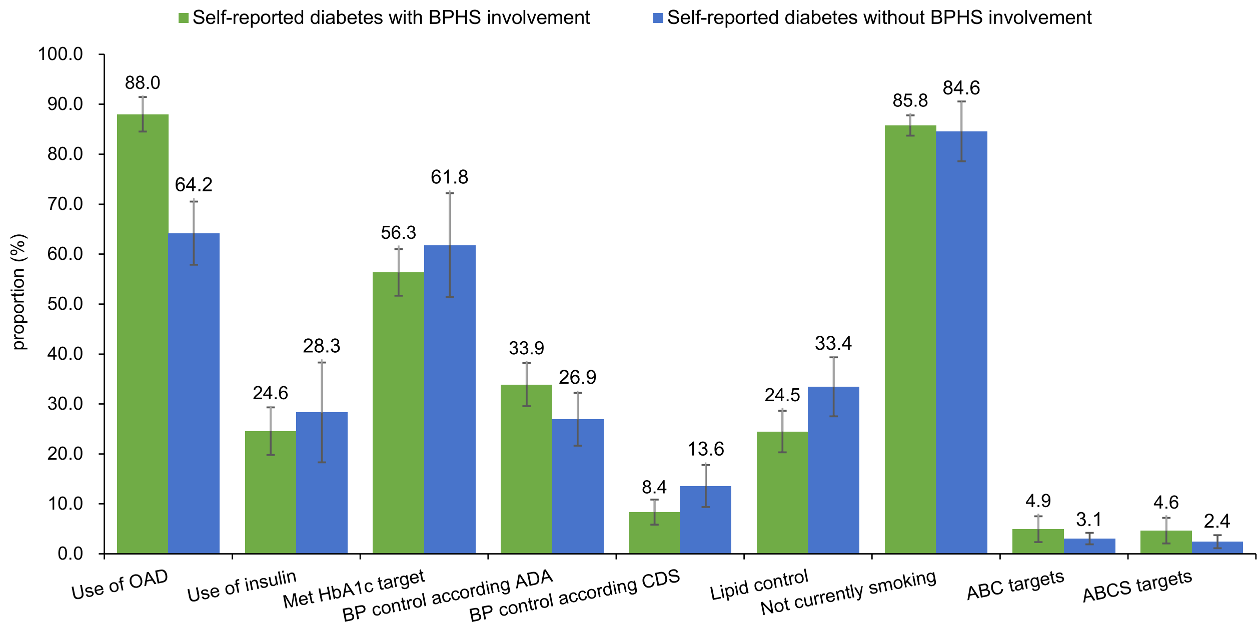

Fig. 5 Cascade of care for self-reported diabetes adults regarding BPHS involvement, including treatment, single and comprehensive control

not provide 2 h-OGTT test, diabetes patients with normal FPG and HbA1c but high 2 h-OGTT could subsequently be missed in such case [39].

Our study indicated relative high proportion of treatment but substantially disappointing management among diabetes adults in Shandong. As reported above, over 90% of diagnosed diabetes adults reported to receive pharmaceutical or non-pharmaceutical treatment, however, 41.8% met the single HbA1c target, and less than 4% achieved comprehensive ABC targets. The insufficient control of the three ABC targets in China is not an isolated phenomenon but also observed in other developing countries [15, 16, 45–48]. Except Iran reported 42% ABC targets achievement [49], the comprehensive management in South Africa [46], Brazil [47], and Kuwait [48], was 8.5%, 12.5%, 7.4%, respectively. As highlighted by Naidoo, et al., diabetes patients had inadequate glycemic and lipid level control, even within a managed healthcare organization [46]. The insufficient management of the three ABC targets, particularly in developing countries, may be attributed to healthcare policy, medication regimen, and patients' education. The findings of our study and previous studies highlight this unsatisfactory and indicate that atherosclerotic risk is not minimized among the majority of diabetes patients.

The suboptimal achievement of diabetes management was found in all subgroups in our study. In line with previous studies, young diabetes adults were less likely to achieve glycemic, ABC, and ABCS control [50, 51]. Females had a relatively better control in the composite target but poorer lipid control than males [22, 50, 52]. Diabetes adults not enrolled in BPHS had a poorer achievement in composite target, a shortfall that may be partially attributed to inadequate adherence to medication regimens. A prior meta-analysis emphasized pharmacotherapy adherence in mitigating the risk of all-cause mortality and hospitalization in diabetes patients [53]. It is suggested that healthcare providers implement an integrated disease management with a multimorbid-centric strategy, to assess risks and adjust glucose, BP, and lipid medications dynamically for diabetes patients [54].

Our study adopted the definitions of 'control target' from various recommendations and guidelines. Rather than applying a single target of glycemia level, we used a personalized target with additional consideration of age and CVD risk. Moreover, we defined BP control according to JNC 8, ADA, and CDS, and the percentages of well-controlled BP were 12.2%, 5.1%, and 0.8%, respectively, among the diagnosed adults. The rigorous CDS BP targets further profound the gap and pose an unprecedented challenge to diabetes care.

Although preventing kidney failure is not one of the control targets, chronic kidney disease (CKD) is common among diabetes individuals, and life-long hemodialysis in the terminal stage deteriorates the quality of life, medical expenses, and mental health[55, 56]. In our data, more than 30% of adults with diabetes had impaired renal function, above the national average of 21.8% [57]. Meanwhile, the high proportion of prediabetes with the urgency of early intervention could not be ignored.

Strengths and limitations

This study has several strengths. First, the high response rate with complete information on representative and high-quality data was available. We described the cascade of care for diabetes adults with a full panel of diagnostic indicators, which provide an accurate estimation of each cascade stage. Moreover, we further described the age, sex, and BPHS disparities in this cascade to explore the deficits in subgroups, which could help achieve diabetes precision management. In addition, we provided the results of the cascade with the multimorbidity of hypertension and lipid control as prevention of CVD.

Our findings are subject to some limitations. First, our analyses were based on regional representative data, and the findings cannot be generalized to other regions. This cross-sectional study was conducted in 2018, and we could not observe the trend of diabetes care over time. Second, we did not assess the diabetes screening and retention in BPHS since no related questions were available in the survey. Future questionnaires with screening and time or age of participation in BPHS will allow for a complete assessment on the role of BPHS in the cascade model. Third, diabetes and hypertension were measured at a single visit, while the actual diagnosis relies on two or three separate measurements at different visits. Finally, the information on diabetes treatment was collected via self-reports. Although this method has been extensively used in the large-scale population study with high validity, information bias may still occur, particularly among elderly individuals [58].

Conclusions

In conclusion, we used a cascade of care framework to describe diabetes screening, diagnosis, treatment, and management in Shandong, China. Our study found that six in ten adults with diabetes were not aware of their glycemia status, and the composite control was consistently low among both diagnosed and newly diagnosed adults indicating a large unmet need, especially for those with multimorbidity. Tailored strategies and appropriate health resource allocation should be considered to address the gaps in care continuum, affecting an estimated of 9.2 million adults in Shandong.

Abbreviations

2 h-OGTT	2-hour oral glucose tolerance test
ABC	Synthesis control of glycemic HbA1c, BP and lipid
ABCS	Synthesis control of glycemic HbA1c, BP and lipid plus nonsmoking
ADA	American Diabetes Association
AHA	American Heart Association
BP	Blood pressure
BPHS	The National Basic Public Health Services
CACDNS	China Adult Chronic Disease and Nutrition Surveillance
CDS	Chinese Diabetes Society
CVD	Cardiovascular diseases
DALYs	Disability adjusted life years
eGFR	Estimated glomerular filtration rate
FPG	Fasting plasma glucose
GPs	General practitioners
HbA1c	Glycated hemoglobin A1c
HDL-c	High-density lipoprotein
JNC 8	Eight Joint National Committee
LDL-c	Low-density lipoprotein
MetS	Metabolic syndrome
OAD	Oral anti-diabetic
YLDs	Years lived with disability

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01796-x.

Supplementary Material 1.

Acknowledgements

The authors thank Dr. Enying Gong for helpful discussions during the development of the study and all participants in this study.

Clinical trial number

Not applicable.

Authors' contributions

Ruitai Shao and Yueqing Wang conceived the idea for this study. Yueqing Wang and Jie Ren led the data analysis and verification. Yueqing Wang, Xin Chai, and Yachen Wang wrote the first draft of the manuscript with substantial revisions from Ruitai Shao, Juan Zhang and Zilong Lu. Jing Dong, Xiaolei Guo, and Junli Tang collected and verified data, Jixiang Ma and Xuejun Yin commented the manuscript and participated the discussion. All authors provided crucial input on multiple iterations of the manuscript. All authors had full access to the data and had final responsibility for submission for publication.

Funding

This study was supported by grants from the nonprofit Central Research Institute Fund of the Chinese Academy of Medical Sciences (Grant No. 2021-RC330-004).

Data availability

The data that support the findings of this study are available from Shandong Centers for Disease Control and Prevention, but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of Shandong Centers for Disease Control and Prevention.

Declarations

Ethics approval and consent to participate

The ethical committee of the Chinese Center of Disease Control and Prevention approved the study at April 27th, 2018 (No. 201819). All study participants were informed about the purpose of the study and additional information was given as they need. Written informed consent was obtained from all participants. We had complied with the Declaration of Helsinki Ethical Principles for medical research involving human subjects.

Consent for publication

This manuscript does not report any private data such as individual details, images or videos; therefore, consent for publication is not applicable.

Competing interests

The authors declare no competing interests.

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Received: 30 December 2023 Accepted: 2 December 2024
Published online: 18 December 2024

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