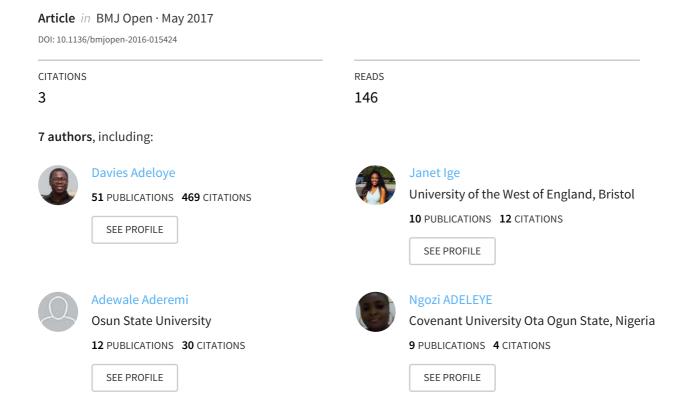
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# Estimating the prevalence, hospitalisation and mortality from type 2 diabetes mellitus in Nigeria: A systematic rev....



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## BMJ Open Estimating the prevalence, hospitalisation and mortality from type 2 diabetes mellitus in Nigeria: a systematic review and meta-analysis

Davies Adeloye,<sup>1,2</sup> Janet O Ige,<sup>3</sup> Adewale V Aderemi,<sup>4</sup> Ngozi Adeleye,<sup>5</sup> Emmanuel O Amoo,<sup>1</sup> Asa Auta,<sup>6</sup> Gbolahan Oni<sup>1</sup>

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<sup>1</sup>Demography and Social Statistics, Covenant University, Ota, Nigeria <sup>2</sup>Centre for Global Health Research, Usher Institute, University of Edinburgh, Edinburgh, UK <sup>3</sup>Faculty of Health and Applied Sciences, University of the West of England, Bristol, UK <sup>4</sup>Department of Biochemistry, College of Health Sciences. Osun State University, Osogbo, Nigeria <sup>5</sup>Economics and Development Studies, Covenant University, Ota, Nigeria

#### Correspondence to

Dr Davies Adeloye; bummyadeloy@gmail.com

<sup>6</sup>School of Pharmacy and

Biomedical Sciences, University of Central Lancashire, Preston,

#### **ABSTRACT**

Background There is not yet a comprehensive evidencebased epidemiological report on type 2 diabetes mellitus (T2DM) in Nigeria. We aimed to estimate country-wide and zonal prevalence, hospitalisation and mortality rates of T2DM in Nigeria.

Methods We searched MEDLINE, EMBASE, Global Health, Africa Journals Online (AJOL) and Google Scholar for population and hospital-based studies on T2DM in Nigeria. We conducted a random-effects meta-analysis on extracted crude estimates, and applied a meta-regression epidemiological model, using the United Nations demographics for Nigeria in 1990 and 2015 to determine estimates of diabetes in Nigeria for the two years. Results 42 studies, with a total population of 91 320, met

our selection criteria. Most of the studies selected were of medium quality (90.5%). The age-adjusted prevalence rates of T2DM in Nigeria among persons aged 20-79 years increased from 2.0% (95% CI 1.9% to 2.1%) in 1990 to 5.7% (95% CI 5.5% to 5.8%) in 2015, accounting for over 874 000 and 4.7 million cases, respectively. The pooled prevalence rate of impaired glucose tolerance was 10.0% (95% CI 4.5% to 15.6%), while impaired fasting glucose was 5.8% (95% CI 3.8% to 7.8%). Hospital admission rate for T2DM was 222.6 (95% CI 133.1 to 312.1) per 100 000 population with hyperglycaemic emergencies, diabetic foot and cardiovascular diseases being most common complications. The overall mortality rate was 30.2 (95% CI 14.6 to 45.8) per 100 000 population, with a case fatality rate of 22.0% (95% CI 8.0% to 36.0%).

Conclusion Our findings suggest an increasing burden of T2DM in Nigeria with many persons currently undiagnosed, and few known cases on treatment.

#### INTRODUCTION

Many studies have reported increasing prevalence of type 2 diabetes mellitus (T2DM) globally. 1-3 According to International Diabetes Federation (IDF), there were over 151 million people with diabetes in 2000, 194 million in 2003,<sup>2</sup> 246 million in 2006,<sup>5</sup> 285 million in 2010<sup>45</sup> and 415 million in 2015.<sup>6</sup> The WHO reported that people living with diabetes globally increased from 108 million

#### Strengths and limitations of this study

- ► This study provides a comprehensive report on the epidemiology of type 2 diabetes mellitus (T2DM) in Nigeria since the last nationwide survey of noncommunicable diseases in 1997.
- Estimates provided are based on original population and hospital-based studies on type 2 diabetes conducted across the six geopolitical zones of Nigeria.
- The study is limited by lack of data on T2DM in northern parts of Nigeria, suggesting the need for more research in the region.

in 1980 to 422 million in 2014, with overweight and obesity being major risk factors. This increase was also observed in Africa, with diabetes cases increasing from 4 million to 25 million between 1980 and 2014. Research findings have shown that prevalence rates of diabetes in urban Africa are in fact similar with, or even higher than, what is obtained in some developed countries.<sup>89</sup> This has been linked to rapidly changing demographic trends, increased rate of urbanisation, unhealthy diets and gradual adoption of Western lifestyles in many African settings. 10

In Nigeria, the most populous country in Africa, the prevalence of T2DM has been high and still increasing, with the country widely reported as having Africa's highest burden of diabetes. 10 11 However, there are no known country-wide surveys or any reported attempt within Nigeria in recent times to specifically estimate the burden of diabetes in the country. The last national survey of non-communicable diseases (NCDs) was conducted in 1997 with a prevalence of 2.2% reported for diabetes, <sup>12</sup> and the 2003 national NCDs survey was mainly in the South-West region and results were inconclusive. 13 In the 2013 IDF global study, a prevalence of 5% was

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estimated for Nigeria, accounting for 3.9 million cases among persons aged 20–79 years. The researchers specifically noted that Nigeria was among countries without up-to-date data on diabetes; hence, the Nigerian estimate was modelled from pooled estimates in Cameroon, due to relatively similar geographic, ethnic and socioeconomic patterns with Nigeria.

Due to the relatively limited epidemiological evidence on the burden of T2DM in Nigeria,  $^{11\,14}$  the few reported estimates may have been based on advanced modelling and extrapolation of very scarce data, and may not necessarily represent the true burden of the disease in the country.8 15 The WHO reports that there is still need for more research on the burden of diabetes, including country-specific response to diabetes treatment and management, and anthropological and cultural perspectives of diabetes in Africa.<sup>7</sup> 16 With many research, treatment and management gaps remaining unaddressed, a study focusing on estimating the burden for appropriate public health and policy response has been widely advocated.<sup>14</sup> We aimed to systematically review the literature on T2DM in Nigeria towards providing national and regional estimates of the prevalence (including undiagnosed cases, persons on treatment and mean fasting plasma glucose (FPG) concentration), hospitalisation and mortality from T2DM in Nigeria.

#### **METHODS**

This study was conducted in accordance with the supplementary MOOSE guidelines of systematic reviews of observational studies.<sup>17</sup>

#### Search terms and strategy

Further to an initial scoping exercise with a librarian, Medical Subject Headings (MeSH), search terms and text words that fit into relevant health databases, including MEDLINE, EMBASE, Global Health and Africa Journals Online (AJOL), were identified (table 1).

The databases' search was conducted on 10 February 2017, and limited to studies published between 1 January 1985 and 31 December 2016, to ensure a relatively consistent diabetes diagnostic criteria not earlier than the WHO 1985 guidelines, which reflects to some degree the current WHO and American Diabetes Association (ADA) case definitions. <sup>16</sup> 18-20 Unpublished documents were sourced from Google Scholar and online sites. The abstracts of all studies were reviewed and full texts of relevant studies were accessed. The references of initially accessed studies were further hand-searched for additional studies and data sources. The authors of relevant papers were contacted for missing information.

#### Eligibility criteria

Studies were included in the review if they met the following criteria: (1) population based conducted among adults aged 20 years or more, residing in Nigeria, and reporting the prevalence, undiagnosed cases and treatment rates of type 2 diabetes and/or prediabetes, or enough data to compute these estimates; or (2) hospital based and providing information on hospitalisations, complications, death rates or case fatality rates of T2DM in a Nigerian population.

We excluded studies that were (1) primarily on type 1 diabetes; (2) conducted on paediatric population (0–14 years), or among populations of Nigerian origin residing outside Nigeria; (3) hospital based without any report on

Table 1	Search terms
#	Searches
1	africa/ or africa, western/ or nigeria/
2	exp vital statistics/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp 'cost of illness'/
6	case fatality rate.tw
7	hospital admissions.tw
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp glucose metabolism disorders/ or exp diabetes mellitus/ or exp diabetes mellitus/ or exp diabetes mellitus, type 2/ or exp diabetic ketoacidosis/ or exp prediabetic state/ or exp glycosuria/ or exp hyperglycemia/ or exp glucose intolerance/
13	1 and 11 and 12
14	Limit 13 to '1985-current'

hospitalisations, or deaths due to diabetes complications; (4) solely based on self-reported diagnosis of T2DM; (5) on diabetes, but conducted among persons with co-morbidities; or (6) case series, reviews, commentaries, letters or editorials.

#### **Data extraction**

Literature search and assessment of eligible studies were conducted by two parallel reviewers, with an eligibility guideline to ensure that the selection criteria were consistently applied. Data on location, study period, study design, study setting (urban or rural), sample size, diagnostic criteria and mean age of the population were extracted. These were matched with corresponding data on mean FPG, prevalence, undiagnosed cases, persons on treatment, hospital admission rates, indications for admission, deaths and case fatality rates of T2DM (and for impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) when available). For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were included in the selected paper. Extracted data were sorted by geopolitical zones in Nigeria, and stored in Microsoft Excel file format.

#### **Quality assessment**

For each full text selected, we further screened for explicit description of methodology, case definitions, blood glucose measurements and generalisability of reported estimates to a larger population within the geopolitical zone. For case definitions, we included studies with diagnosis of (1) diabetes-defined as chronic metabolic condition characterised by raised blood glucose resulting from impairment in secretion of insulin, its action or both, based on FPG levels of ≥126 mg/dL (7.0 mmoL/L), or 2-hour postprandial glucose (2 hr-pG) reading of ≥200 mg/dL (11.1 mmoL/L) after a glucose load of 75 g, or random blood glucose (RBG) readings of  $\geq 200 \,\text{mg/dL}$  (11.1 mmoL/L);  $^{16.18-20}$  (2) impaired glucose tolerance—defined as elevated non-diabetic levels of blood glucose, based on blood glucose levels of ≥140 mg/dL (7.8 mmoL/L) 2 hours after consuming 75 g of glucose 16 18-20; and (3) impaired fasting glucose defined as elevated non-diabetic fasting blood glucose, based on blood glucose levels of  $110-125\,\mathrm{mg/dL}$  (6.1–6.9 mmoL/L). To allow for fairly consistent pooled estimates, we assessed the appropriateness of statistical analyses employed in the estimation of T2DM prevalence or mortality, and further assessed studies for heterogeneities within and outside various population groups. For the quality grading, we adapted a previously used quality assessment criteria for studies examining the prevalence of chronic diseases (see online supplementary file, for details of the grading criteria). 21-24 All studies graded as high or moderate quality were included, while the low-quality studies were excluded from the review.

#### **Outcome measures and analysis**

A random-effects meta-analysis, using DerSimonian and Laird Method,25 was employed on the individual study estimates to arrive at crude national and regional summary estimates of prevalence, hospital admission and mortality of T2DM in Nigeria. Standard errors were determined from the reported crude estimates and population denominators, assuming a binominal (or Poisson) distribution. Heterogeneity between studies was assessed using I-squared  $(I^2)$  statistics,  $^{26}$  and subgroup analysis was conducted to identify potential sources of heterogeneity. Population-based data (reporting on T2DM prevalence) and hospital-based data (reporting on hospitalisations, complications and deaths) were analysed separately. Due to limited data, a meta-regression epidemiological model was only applied to T2DM prevalence rates. The model was based on aggregated age from each study (as these had more data points), and adjusted for study period and sample size. Due to demographic and epidemiological transitions, it is understandable that the prevalence rates of diabetes and most chronic diseases may increase with age; 10 however, the relationship may not be linear. Hence, in our preliminary analyses, we experimented with various models (linear, exponential, polynomial, logarithmic, etc) to determine which was most predictive, that is, the model with the greatest proportion of variance  $(R^2)$  of diabetes prevalence as explained by age. This was applied to the final model, and the best fit was used to determine the number of T2DM cases at midpoints of the United Nation (UN) population 5-year age groups for Nigeria for the years 1990 and 2015. Our data analysis has been described in detail in previous studies.<sup>27 28</sup> All statistical analyses were conducted on STATA (Stata V.13).

#### **Ethical review**

This study is a review of publicly available literature and data on T2DM in Nigeria. Ethical review was therefore not required for this study. The study was however conducted in strict compliance to the MOOSE guidelines.

#### **RESULTS**

#### Search results

Our databases' search returned 1664 studies (MEDLINE 505, EMBASE 975, Global Health 132 and AJOL 52). Additional seven studies were identified through Google Scholar and search of reference list of relevant studies. There were 1232 studies assessed after duplicates were removed. On applying the inclusion and exclusion criteria, 1164 studies were excluded, and of the remaining 68 studies, 26 were excluded on applying the quality criteria (table 2, see online supplementary file). A total of 42 studies 29-70 were finally selected for the review (figure 1).

#### Study characteristics

Of the 42 retained studies, 36 were population-based cross-sectional studies reporting on prevalence of T2DM



Table 2 Chara	Characteristics of retained T2DM studies in Nigeria	ned T2DM stu	dies in Nigeria							
Zones	Location	Period	Design	Setting	Sample size	Diagnostic criteria	Age (years)	Mean FPG (mmol/I)	T2DM Prevalence (%)	Quality Grading
North-Central	llorin, Kwara State <sup>29</sup>	1988	Population-based cross-sectional study	Mixed	2800	2 hr-pG or RBG>11.1 mmoL/L	<b>20</b> 9	4.6	1,4	Moderate
	llorin, Kwara State <sup>30</sup>	2008	Population-based cross-sectional study	Urban	281	FPG>7 mmoL/L, RBG>11.1 mmoL/L	50.5	ı	1.5	Moderate
	Gindiri, Plateau State <sup>31</sup>	2014	Population-based cross-sectional study	Rural	295	FPG>7 mmoL/L	47.5	5.9	5.1	Moderate
North-East	Maiduguri, Bornu State <sup>32</sup>	2009	Population-based cross-sectional study	Urban	242	WHO 1999	44.4	1	7.0	Moderate
	Maiduguri, Borno State <sup>33</sup>	1999	Population-based cross-sectional study	Rural	200	FPG>7 mmoL/L	45.5	5.2	2.6	Moderate
North-West	Dakace Village, Zaria, Kaduna State <sup>34</sup>	2007	Population-based cross-sectional study	Rural	299	WHO 1998	59.4	ı	2.0	Moderate
	Sokoto, Sokoto State <sup>35</sup>	2011	Population-based cross-sectional study	Urban	389	WHO 1999	39.3	5,4	4.6	Moderate
	Sokoto, Sokoto State <sup>36</sup>	2013	Population-based cross-sectional study	Rural	393	WHO 1999	38.5	5.0	0.8	Moderate
	Katsina, Katsina 2006 State <sup>37</sup>	2006	Population-based cross-sectional study	Urban	300	FPG>7 mmoL/L, self- report, known diabetic on treatment	37.6	4.6	5.3	Moderate
South-East	Umuahia, Abia State <sup>38</sup>	2000–2004	Hospital-based retrospective record review	Urban	1124˚	FPG>7 mmoL/L, past diabetes history, admission diagnosis	$55^{\dagger}$	l	14 <b>.</b> 0 <sup>‡</sup>	Moderate
	Umudike, Abia State <sup>39</sup>	2014	Population-based cross-sectional study	Urban	365	WHO-IDF 2006	46	4.8	3.0	Moderate
	Imezi-Owa, Enugu State <sup>40</sup>	2011	Population-based cross-sectional study	Rural	858	WHO 1998	29 <b>.</b> 8	4.6	4.4	Moderate
	Aba, Abia State⁴¹	2009–2011	Hospital-based retrospective record review	Urban	853*	FPG>7 mmoL/L, past diabetes history, admission diagnosis	5 <b>6.</b> 4 <sup>†</sup>	ı	ı	Moderate
	Nkanu East LGA, Enugu State <sup>42</sup>	2013	Population-based cross-sectional study	Rural	824	WHO-IDF 2006	51.1	5.3	4.8	Moderate
	Abia State <sup>43</sup>	2013	Population-based cross-sectional study	Mixed	2983	FPG>7 mmoL/L, RBG>11.1 mmoL/L, self report	41.7	1	വ	Moderate

Table 2 Continued	nued									
Zones	Location	Period	Design	Setting	Sample size	Diagnostic criteria	Age (years)	Mean FPG (mmol/I)	T2DM Prevalence (%)	Quality Grading
	Abia State <sup>44</sup>	2011–2012	Population-based cross-sectional study	Mixed	2183	FPG>7 mmoL/L	43.7	I	3.6	Moderate
	Naze, Owerri, Imo State <sup>45</sup>	2009	Population-based cross-sectional study	Urban	253	FPG>7 mmoL/L	53.4	5.8	6.7	Moderate
South-South	Port Harcourt, Rivers State <sup>47</sup>	2010	Population-based cross-sectional study	Rural	200	WHO-IDF 2006	41.3	4	2.2	Moderate
	Uyo, Akwa Ibom 2008–2010 State <sup>46</sup>	2008–2010	Population-based cross-sectional study	Urban	3500	FPG>7 mmoL/L, 2 hr-pG or RBG>11.1 mmoL/L	49.8	1	10.5	Moderate
	Calabar, Cross Rivers State <sup>48</sup>	2014	Population-based cross-sectional study	Urban	1134	WHO 1999	38.9	1	6.5	High
	Esan South, Edo State <sup>49</sup>	2013	Population-based cross-sectional study	Rural	845	WHO-IDF 2006	56.4		4.6	Moderate
	Port Harcourt, Rivers State <sup>50</sup>	2001	Population-based cross-sectional study	Urban	403	2hr-pG or RBG>11.1mmoL/L	61.5	7,45	26.3	Moderate
	Port Harcourt, Rivers State <sup>51</sup>	2000	Population-based cross-sectional study	Urban	502	2 hr-pG or RBG>11.1 mmoL/L, WHO 1999	48	<b>4.8</b>	8.9	High
	Ndokwa West LGA, Delta State <sup>52</sup>	2014	Population-based cross-sectional study	Mixed	422	ADA 2003, WHO 1999	40.6	5.1	5.4	Moderate
	Calabar, Cross River State <sup>53</sup>	2006–2010	Hospital-based retrospective record review	Urban	360	FPG>7 mmoL/L, past diabetes history, admission diagnosis	48.5 <sup>†</sup>	1	±8.0	Moderate
South-West	Ido-Ekiti, Ekiti State <sup>55</sup>	2003–2007	Hospital-based retrospective record review	Urban	118	FPG>7 mmoL/L, past diabetes history, admission diagnosis	57†	I	3.0⁴	Moderate
	Ikeja, Lagos State <sup>54</sup>	1990–2000	Hospital-based retrospective record review	Urban	242	FPG>7 mmoL/L, past diabetes history, admission diagnosis	ı	1	2.3.0 <sup>‡</sup>	Moderate
	Ikeja, Lagos State <sup>56</sup>	2006	Hospital-based prospective observational study	Urban	206∞	WHO 1999, past diabetes history	1	I	73.0 <sup>‡</sup>	Moderate
	Ogbomoso, Oyo 2013 State <sup>57</sup>	2013	Population-based cross-sectional study	Urban	206	2hr-pG or RBG>11.1mmoL/L	45.3	1	1.5	Moderate

Table 2 Cor	Continued									
Zones	Location	Period	Design	Setting	Sample size	Diagnostic criteria	Age (years)	Mean FPG (mmol/I)	T2DM Prevalence (%)	Quality Grading
	ljora, Ajegunle and Makoko, Lagos State <sup>58</sup>	2010–2012	Population-based cross-sectional study	Urban	2434	2hr-pG or RBG>11.1mmoL/L	51	I	3.4	Moderate
	Ogun State <sup>59</sup>	2013	Population-based cross-sectionals study	Mixed	58657	FPG>7 mmoL/L, RBG>11.1 mmoL/L	40.7	5.5	5.1	Moderate
	Osogbo, Osun State <sup>60</sup>	2009	Population-based cross-sectional study	Urban	586	FPG>7 mmoL/L, RBG>11.1 mmoL/L, known diabetic on treatment	42.4	5.0	3.8	Moderate
	Ibadan and Igbo-Ora, Oyo State <sup>61</sup>	1994	Population-based cross-sectional study	Mixed	500	FPG>7 mmoL/L, 2hr- pG>11.1 mmoL/L	8.09	4.3	1.6	Moderate
	Aaye Ekiti, Ekiti State <sup>62</sup>	2013	Population-based cross-sectional study	Rural	208	ADA 2003	8.99	4.6	4.8	Moderate
	Lagos, Lagos State <sup>63</sup>	1988	Population-based cross-sectional study	Urban	1617	2 hr-pG or RBG>11.1 mmoL/L	44.2	4.4	1.8	Moderate
	Ibadan, Oyo State <sup>64</sup>	2010–2011	Population-based cross-sectional study	Urban	301	WHO-IDF 2006	49	1	4.7	Moderate
	Egbeda, Oyo State <sup>65</sup>	2002–2005	Population-based cross-sectional study	Rural	2000	WHO-IDF 2006	42.1	6.4	2.5	Moderate
	Ibadan, Oyo State <sup>66</sup>	1995	Population-based cross-sectional study	Urban	245	WHO 1985	62	4.8	2.8	Moderate
	Ido-Ekiti, Ekiti State <sup>67</sup>	2015	Population-based cross-sectional study	Rural	750	ADA 2012, WHO-IDF 2006	61.7	1	6.8	Moderate
	Ibadan, Oyo State <sup>68</sup>	1995	Population-based cross-sectional study	Urban	849	WHO 1985	40.8	4.4	0.8	High
Multizonal	Interstate <sup>69</sup>	1999	Population based	Mixed	928	WHO 1998	49.5	ı	1.0	Moderate
	Interstate <sup>70</sup>	2012	Population-based cross-sectional study	Mixed	1595	RBG>11.1 mmoL/L, self-report	55.9	1	3.3	High

'Represents T2DM hospital admissions; ADA 2003, <sup>18</sup> WHO 1985, <sup>19</sup> WHO 1998, <sup>20</sup> WHO-IDF 2006. <sup>16</sup>

†Represents mean age at death. ‡Represents case fatality rates (expressed as proportion of deaths from T2DM hospital admissions). ADA, American Diabetes Association; FPG, fasting plasma glucose; IDF, International Diabetes Federation; RBG, random blood glucose; T2DM, type 2 diabetes mellitus; 2hr-PG, 2-hour postprandial glucose.

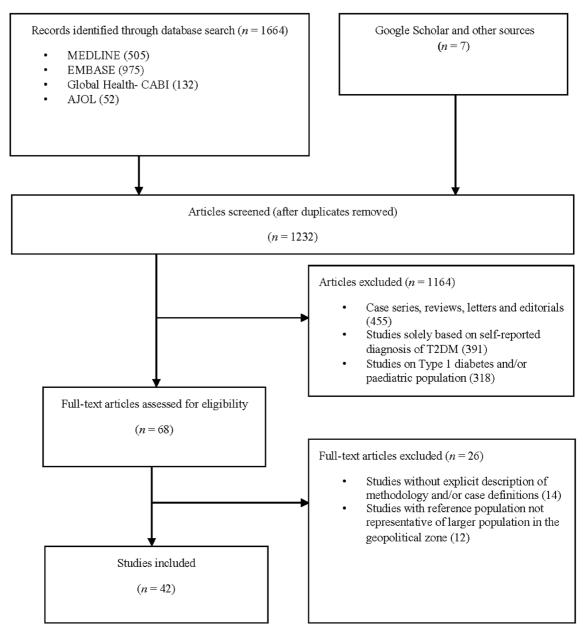


Figure 1 Flow chart of selection of T2DM studies in Nigeria. AJOL, Africa Journals Online; T2DM, type 2 diabetes mellitus.

and 6 were hospital based reporting on hospitalisations, complications and deaths from T2DM (table 2). Most studies (15) were conducted in the South-West region of Nigeria, followed by the South-East and South-South with 8 studies each. The North-West had four studies, North-Central three and North-East two. Two studies were conducted across multiple regions in the country. Study period ranged from 1988 to 2015, with 20 studies (47.6%) conducted after 2010. There were 23 studies (54.7%) conducted in urban settings. Excluding hospital-based studies, the total population included in the review was 91 320, with a mean age of 48.9 years (table 2). Of the 42 included studies, 4 (9.5%) met the criteria for high level of quality while 38 (90.5%) met the criteria for moderate level of quality. The risk of bias observed across studies included selection bias due to sampling (33.3%, 14/42) and non-reporting of response rate (35.7%, 15/42). Measurement bias was minimal as all the included studies used standard diagnostic criteria to ascertain the prevalence of diabetes. However, the funnel plot was asymmetrical, with this suggestive of publication bias across selected studies (figure 2).

### **Outcome measures**

#### Prevalence rates

The lowest prevalence of T2DM was 0.8% recorded in Ibadan, South–West Nigeria in 1995,<sup>68</sup> and Sokoto, North–West Nigeria in 2013,<sup>36</sup> both with mean ages 38.3 and 40.8 years, respectively. The highest prevalence rates of T2DM were reported among oil company workers in Port Harcourt in 2001 (26.3%, mean age 61.5 years)<sup>50</sup> and Uyo in 2010 (10.5%, mean age 49.8 years),<sup>46</sup> in

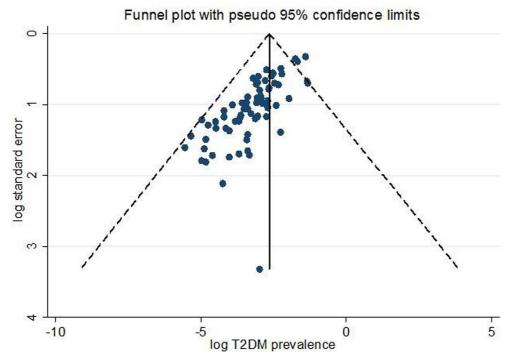


Figure 2 Funnel plot showing distribution of selected studies. T2DM, type 2 diabetes mellitus.

Author	Study year	Geopolitical zone		T2DM Prevalence % (95% CI)	% Weig
Jrban			l i		
Akintunde et al	2014	SW	- I	1.50 (-0.16, 3.16)	2.87
Akinwale Pet al	2011	SW		3.40 (2.68, 4.12)	3.20
Ayodele et al	2009	SW		3.80 (2.25, 5.35)	2.92
Eiike et al	2014	SE	-	3.00 (1.25, 4.75)	2.83
Ekpeyong et al	2009	SS		10.50 (9.48, 11.52)	3.12
Enang et al	2014	SS	i	6.50 (5.07, 7.93)	2.97
Gezawa et al	2009	NE	1 50	7.00 (3.79, 10.21)	2 14
Vwafor & Owhoii	2001	SS	1 -	26.30 (22.00, 30.60)	1.67
Vvenwe et al	2000	SS	100	6.80 (4.60, 9.00)	2.62
Oghagbon et al	2008	NC	-	1.50 (0.08, 2.92)	2.97
Ohwovoriole et al	1988	sw		1.80 (1.15, 2.45)	3.22
Diewale & Adeiumo	2011	SW		4.70 (2.31, 7.09)	2.53
Diatunbosun et al	1995	SW		0.80 (0.20, 1.40)	3.23
	1995	SW			2.69
Owoaje et al Sabiret al	2011	NW		2.80 (0.74, 4.86)	2.68
	2006			4.60 (2.52, 6.68)	
Sani et al		NW .		5.30 (2.76, 7.84)	2.48
Subtotal (1-squared = 1	90.0%, p	0.000)	~	5.28 (3.54, 7.02)	44.13
Rural			i i		
Alikor & Emem-Chioma	2010	SS	<b></b> !	2.20 (0.91, 3.49)	3.03
Dahiru et al	2007	NW		2.00 (0.05, 3.95)	274
Ejim et al	2011	SE	<b>★</b>	4.40 (3.03, 5.77)	2.99
sara & Okundia	2013	SS	<u>₩</u>	4.60 (3.19, 6.01)	2.98
Vwatu et al	2013	SE	<b>→</b>	4.80 (3.34, 6.26)	2.96
Ogunmola et al	2013	SW		4.80 (0.69, 8.91)	1.75
Okesina et al	1999	NE		2.60 (1.21, 3.99)	2.98
Oladapo et al	2004	SW	<b>◆</b> ¹	2.50 (1.82, 3.18)	3.21
Oluyombo et al	2015	SW	-	6.80 (5.00, 8.60)	2.81
Sabir et al	2013	NW		0.80 (-0.08, 1.68)	3.16
Fagurum et al	2014	NG	T	5.10 (2.01, 8.19)	2.20
Subtotal (1-squared = )			<b>\$</b>	3.51 (2.45, 4.57)	30.80
Mixed			1 1		
viixeo Erasmus et al	1988	NC	<b>□</b>	1.43 (0.99, 1.87)	3.25
Erasmus et al Ezenwaka et al	1988	SW	X .	1.43 (0.99, 1.87)	3.09
Kyari et al	2012	Nat SE		3.30 (2.42, 4.18)	3.16
Ogah et al				3.60 (2.93, 4.27)	3.21
Oguoma et al	2014	SS	-	5.40 (3.24, 7.58)	2.65
Okpechi et al	2012	SE		3.60 (2.93, 4.27)	3.21
Rotimi et al	1999	Nat		1.00 (0.33, 1.67)	3.21
Alebiosu et al	2013	SW		5.10 (4.92, 5.28)	3.28
Subtotal (I-squared = 1	98.1%, p	0.000)	19	3.08 (1.63, 4.53)	25.07
Overall (I-squared = 9	6.4%, p =	0.000)	፟፟፟፟፟	4.09 (3.29, 4.88)	100.0
NOTE: Weights are fro	m randor	effects analysis	1 !		

Figure 3 Pooled prevalence rate of T2DM in Nigeria.T2DM, type 2 diabetes mellitus.

Table 3 Pooled prevalence rates of T2DM, IGT, IFG and mean FPG in Nigeria ΑII Men Women **Pooled estimate Pooled estimate Pooled estimate** I<sup>2</sup>, p value l<sup>2</sup>, p value l<sup>2</sup>, p value **Extracted data** (95 % CI) (95 % CI) (95 % CI) T2DM (%) 4.1 (3.3 to 4.9) 96,4%. 4.4 (3.3 to 5.9) 92.9%, p=0.000 4.1 (3.1 to 5.1) 90.4%, p=0.000 p=0.000Undiagnosed 39.4 (26.0 to 52.7) 92.5%, T2DM (%) p=0.000T2DM on 32.7 (23.5 to 41.8) 44.2%, treatment (%) p=0.111IGT (%) 10.0 (4.5 to 15.6) 98.0%, 10.3 (0.7 to 19.9) 97.8%, p=0.000 11.9 (2.5 to 21.2) 97.4%, p=0.000 p=0.000IFG (%) 5.8 (3.8 to 7.8) 93.4%. 4.9 (2.6 to 7.2) 89.7%, p=0.000 4.8 (3.0 to 6.6) 85.1%, p=0.000 p=0.000Mean FPG 5.1 (4.9 to 5.4) 5.0%, p=0.395 4.6 (4.0 to 5.2) 4.7 (4.0 to 5.3) 10.0%, p=1.000 10.0%, p=0.999 (mmol/L)

South–South Nigeria, which is possibly due to the higher socioeconomic statuses in these settings (table 2).

From all studies, the pooled crude prevalence of T2DM was 4.1% (95% CI 3.3% to 4.9%), with 4.4% (95% CI 3.3% to 5.9%) among men and 4.1% (95% CI 3.1% to 5.1%) among women. In the subgroup analysis, the prevalence was higher among urban dwellers at 5.3% (95% CI 3.5% to 7.0%), compared with 3.5% (95% CI 2.5% to 4.6%) among rural dwellers (figure 3, table 3).

The South-South region of Nigeria had the highest pooled prevalence of T2DM at 8.5% (95% CI 5.1% to 11.9%), followed by the North-East and South-East regions, at 4.6% (95% CI 0.3% to 8.8%) and 3.7% (95% CI 3.3% to 4.2%), respectively. The North-Central had the lowest pooled prevalence at 2.0% (95% CI 0.7% to 3.3%). Over the study period, the highest prevalence of T2DM was observed in the period 2000-2009 and 2010-2015 at 6.9% (95% CI 3.9% to 10.1%) and 4.0% (95% CI 3.3% to 4.7%), respectively. The pooled prevalence rates in the period 1985-1989 and 1990-1999 were 1.6% (95% CI 1.2% to 1.9%) and 1.4% (95% CI 0.8% to 2.1%), respectively. In the age group analysis, the highest prevalence was observed in the older age intervals of 60-69, 70-79 and 80+ years at 6.8% (95% CI 4.1% to 9.5%), 6.4% (95% CI 1.7% to 11.1%) and 9.9% (95% CI 2.7% to 17.2%), respectively (table 4).

Undiagnosed cases of T2DM, expressed as a percentage of all T2DM cases in each study, ranged from 7.8% in Uyo (South–South) $^{46}$  to 75% in Dakace village in Zaria (North–West), $^{34}$  with a pooled rate of 39.4% (95% CI 26.0% to 52.7%). T2DM cases on treatment, also expressed as a percentage of all T2DM cases in each study, ranged from 19.6% in Ido-Ekiti (South–West) $^{67}$  to 50% in Sokoto (North–West), $^{37}$  with a pooled rate of 32.7% (95% CI 23.5% to 41.8%) (table 3).

From all studies, prevalence of IGT ranged from 2.2% in Ibadan (South–West) $^{68}$  to 19.6% in Calabar (South–South), $^{48}$  and IFG from 1.1% in Umudike (South–East) $^{39}$  to 16.9% in Sokoto (North–West). $^{35}$  The pooled prevalence of IGT was 10.0% (95% CI 4.5% to 15.6%), with 10.3% (95% CI 0.7% to 19.9%) among men and 11.9% (95% CI 2.5% to 21.2%) among women. The pooled prevalence of IFG was 5.8% (95% CI 3.8% to 7.8%), with 4.9% (95% CI 2.6% to 7.2%) among men and 4.8% (95% CI 3.0% to 6.6%) among women (figures 4 and 5, and table 3).

The mean FPG concentration was not too different across studies ranging from 4.0 mmoL/L in Port Harcourt (South–South)<sup>47</sup> to 5.9 mmoL/L in Gindiri-Plateau (North-Central),<sup>31</sup> with a pooled rate of 5.1 mmoL/L (95% CI 4.9 to 5.4) (figure 6). The pooled mean FPG rates among men and women were also almost the same at 4.6 mmoL/L (95% CI 4.0 to 5.2) and 4.7 (95% CI 4.0 to 5.3), respectively (table 3).

#### Hospitalisation, mortality and case fatality rates

Hospital data on T2DM were based on catchment population of the hospital. Crude hospital admission rate ranged from 23.9 to 763.8 per 100 000 population, with a pooled rate of 222.6 (95% CI 133.1 to 312.1) per 100 000 population. Hyperglycaemic emergencies (mainly diabetic ketoacidosis and hyperosmolar non-ketotic coma), diabetic foot, uncontrolled hypertension and stroke were the most common complications or indications of admission, with pooled rates at 36.1% (95% CI 13.9% to 58.4%), 19.6% (95% CI 12.3% to 26.9%), 16.7% (95% CI 13.4% to 20.1%) and 8.7% (95% CI 7.4% to 10.0%), respectively (table 5).

The crude mortality rate for T2DM ranged from 0.97 to 105.3 per 100000 population. The overall mortality

<sup>\*</sup>Represents percentage of overall T2DM cases; there were no data to pool estimates separately for men and women.

I<sup>2</sup> represents the variation in pooled estimate attributable to heterogeneity.

p Value represents level of significance.

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus.

Table 4 Overview of	subgroup meta-analysis	s of type 2 diabetes mel <b>l</b> itus (T2DM) in Ni	geria
Subgroup		T2DM prevalence % (95% CI)	l², p value
Setting	Urban	5.3 (3.5 to 7.0)	96.6%, p=0.000
	Rural	3.5 (2.5 to 4.6)	84.0%, p=0.000
	Mixed <sup>*</sup>	3.1 (1.6 to 4.5)	98.1%, p=0.000
Geopolitical zone	North-Central	2.0 (0.7 to 3.3)	62.4%, p=0.070
	North-East	4.6 (0.3 to 8.8)	83.5%, p=0.014
	North-West	3.0 (0.8 to 5.2)	84.4%, p=0.000
	South-East	3.7 (3.3 to 4.2)	0.0%, p=0.414
	South-South	8.5 (5.1 to 11.9)	96.8%, p=0.000
	South-West	3.2 (1.9 to 4.5)	96.8%, p=0.000
Year	1985–1989	1.6 (1.2 to 1.9)	0.0%, p=0.354
	1990–1999	1.4 (0.8 to 2.1)	54.3%, p=0.068
	2000–2009	6.9 (3.9 to 10.1)	97.3%, p=0.000
	2010–2015	4.0 (3.3 to 4.7)	90.1%, p=0.000
Age (years)	20 <b>–</b> 29	1.1 (0.3 to 1.9)	80.3%, p=0.000
	30–39	4.7 (2.9 to 6.6)	91.9%, p=0.000
	40–49	4.1 (3.1 to 5.1)	96.5%, p=0.000
	50–59	5.1 (3.5 to 6.7)	92.4%, p=0.000
	60–69	6.8 (4.1 to 9.5)	95.0%, p=0.000
	70 <b>–</b> 79	6.4 (1.7 to 11.1)	74.2%, p=0.021
	80+	9.9 (2.7 to 17.2)	16.1, p=0.275

<sup>\*</sup>Study conducted in rural and urban settings with an overall estimate reported.

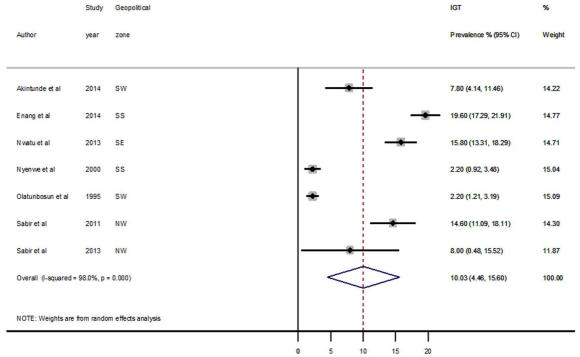


Figure 4 Pooled prevalence rate of IGT in Nigeria. IGT, impaired glucose tolerance.

I<sup>2</sup> represents the variation in pooled estimate attributable to heterogeneity.

p Value represents level of significance.

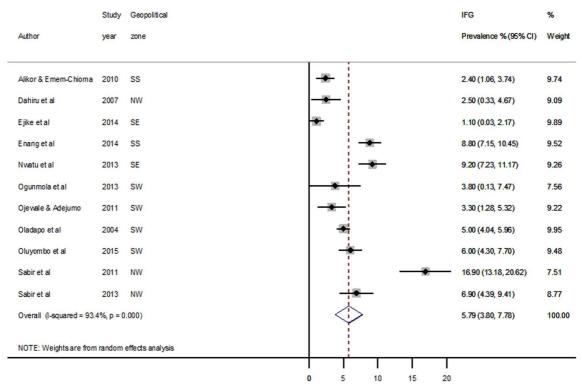


Figure 5 Pooled prevalence rate of IFG in Nigeria. IFG, impaired fasting glucose.

rate from all studies was 30.2~(95%~CI~14.6~to~45.8) per  $100\,000~\text{population}$ , with a case fatality rate of 22.0%~(95%~CI~8.0%~to~36.0%) (table 5). Assuming sociodemographic and epidemiological changes in Nigeria were fully

considered, this would amount to 54297 (26249–82344) deaths in Nigeria in 2015 based on the UN population projections for Nigeria.

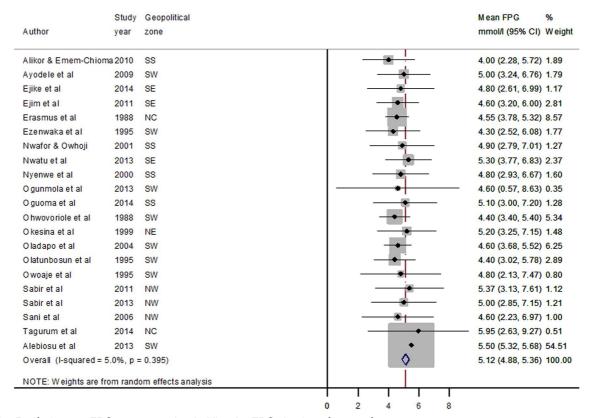


Figure 6 Pooled mean FPG concentration in Nigeria. FPG, fasting plasma glucose.

Table 5 Hospitalisation, mor	tality and case fatality rate of typ	oe 2 diabetes me <b>ll</b> itus (T2DM) in	Nigeria
Data		Pooled estimate (95% CI)	l², p value
Hospital admission rate (per	100 000)	222.6 (133.1 to 312.1)	99.8%, p=0.000
Indication for hospital admissions <sup>†</sup> (%)	Hyperglycaemic emergencies	36.1 (13.9 to 58.4)	99.4%, p=0.000
	Diabetic foot	19.6 (12.3 to 26.9)	95.7%, p=0.000
	Uncontrolled hypertension	16.7 (13.4 to 20.1)	43.6%, p=0.170
	Stroke	8.7 (7.4 to 10.0)	0.0%, p=0.574
	Neuropathy	7.7 (2.3 to 13.2)	95.1%, p=0.000
	Sepsis	7.7 (5.3 to 10.1)	0.0%, p=0.732
	Hypoglycaemia	5.1 (0.9 to 9.3)	94.8%, p=0.000
	Nephropathy	4.2 (3.2 to 5.3)	27.0%, p=0.250
Mortality rate* (per 100 000)		30.2 (14.6 to 45.8)	99.2%, p=0.000
Case fatality rate <sup>‡</sup> (%)		22.0 (8.0 to 36)	99.5%, p=0.000

<sup>\*</sup>Estimate based on reference population of the hospital catchment area.

#### Meta-regression model

The meta-regression modelling, adjusted for study period and sample size, was applied to mean ages and crude prevalence rates from all studies, as these generated more data point. The modelling revealed an increasing prevalence with age (p<0.05) (table 6, figure 7).

Using the UN demographic projections for Nigeria, the age-adjusted prevalence rates of T2DM in Nigeria were 2.0% (95% CI 1.9% to 2.1%) and 5.7% (95% CI 5.5% to 5.8%) in 1990 and 2015, accounting for over 874000 and 4.7 million T2DM cases, respectively, among persons aged 20–79 years. This represents over 440% increase in overall T2DM cases among persons aged 20–79 years between the two years (table 7).

#### **DISCUSSION**

With over 50% of studies conducted after 2010, our report suggests that research outputs on T2DM in Nigeria may be gradually increasing, although these may not be evenly distributed across the country as most studies (79%) originated form the Southern parts of the country. The evidence pool of diabetes, as reported by many experts, still remain limited across Nigeria and many parts of Africa.  $^{16}$ 

Our 1990 estimate is in keeping with the 1997 nationwide diabetes prevalence (2.2%) reported by Akinkugbe. 12 Although Abubakari and Bhopal reported a relatively higher diabetes prevalence (6.8%) in 2000,<sup>71</sup> this may be expected as the seven studies included in their report were conducted among persons aged 40 years or older, and mainly in Southern parts of Nigeria, where we also reported higher prevalence rates in contrast to the Northern regions. However, our 2015 prevalence may further indicate an increasing trend in the prevalence of diabetes in Nigeria with over 440% increase in T2DM cases over the 1990 estimate. This is an important finding in this study, which is in congruence with the estimates reported by Guariguata and colleagues in the IDF global study, with a diabetes prevalence rates of 5% reported for Nigeria in 2013.8 The increasing rate of T2DM has also been documented across several African settings. 1 3-5 7 72 Mbanya and colleagues specifically noted that diabetes prevalence is increasing in sub-Saharan Africa, with a regional prevalence of 2%-3% in mid-1990s increasing to about 4.6% in 2010.10 However, the 2015 Nigerian T2DM prevalence reported in this study is higher than the prevalence of adult diabetes reported in Cote d'Ivoire (2.3%), Ghana (1.9%) and Senegal (1.8%), according to

Table 6 Resu	Its of the meta-regre	ession modelling				
Prevalence	Coef.	Std. Err.	t	P>t	Upper 95% CI	Lower 95% CI
Age	0.0898737	0.0411097	2.19	0.032	0.0078621	0.1718853
Year	0.1253705	0.0630606	1.99	0.051	-0.000432	0.251173
_cons	-251 <b>.</b> 0127	126.3341	<b>-1.</b> 99	0.051	-503.0424	1.017032

Note:REML estimate of between-study variance (tau2)=16.33.

<sup>†</sup>Percentage of all T2DM hospital admissions.

<sup>‡</sup>Represents proportion of deaths from T2DM hospital admissions.

<sup>%</sup> residual variation due to heterogeneity (I-squared\_res)=92.55%.

Proportion of between-study variance explained (Adj R-squared)=11.44%.

Joint test for all covariates in Model (F)=4.90.

With Knapp-Hartung modification Prob > F=0.0102.

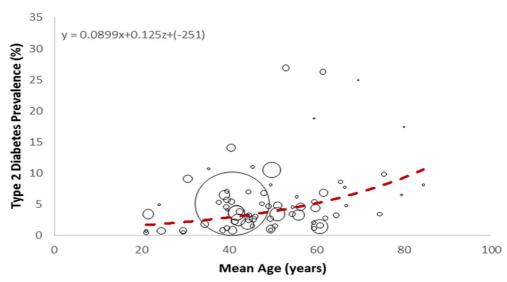


Figure 7 Meta-regression epidemiological modelling showing relationship between prevalence of T2DM and mean age of the population T2DM, type 2 diabetes mellitus.Note: T2DM prevalence (y), age (x), year (z) and size of the bubble correspond to study sample size. Coefficients of 'x' and 'z' are '0.0899' and '0.125' for the meta-regressed line, with an intercept of '-251'.

the 2015 IDF atlas, <sup>6</sup> suggesting a relatively higher burden in Nigeria compared with other West African countries.

Meanwhile, the mean country-wide FPG estimated in this study, to the best of our knowledge, is the first reported in Nigeria. At a mean FPG concentration of 5.1 mmoL/L, many people across Nigeria may apparently be approaching the prediabetic states. This therefore may be suggestive of the high IGT and IFG prevalence rates reported in this study. The implication,

based on experts' reports, is that regions with relatively low diabetes prevalence but with fairly high prevalence of IGT and IFG may be at an early phase of a diabetes epidemic.<sup>73</sup> The sex distribution of our estimate is also consistent with many reports, with IGT affecting more women than men, and IFG vice versa.<sup>16</sup> There is still no sufficient explanation for this sex difference, but increasing prevalence of diabetes observed among African women may be due to the relatively higher

Table 7 Age-ad	djusted prevalence ra	tes and cases of ty	ype 2 diabetes r	nellitus (T2DM) in Ni	geria in 1990 and 2	2015
	1990			2015		
Age group	Nigeria population (000s)	Prevalence* (%)	T2DM cases (000s)	Nigeria population (000s)	Prevalence* (%)	T2DM cases (000s)
20–24	8160.431	0.52	42.744	15981.820	3.66	584.743
25–29	6920.907	0.97	67.361	14051.040	4.11	577 <b>.</b> 259
30–34	5833.290	1.42	82.996	12102.270	4.56	551.597
35–39	4876.116	1.87	91.295	9982.646	5.01	499.861
40–44	4140.621	2.32	96.137	7767.685	5.46	423.867
45–49	3579.784	2.77	99.207	6008.701	5.91	458.783
50–54	2949.801	3.22	95.007	4993.836	6.36	381.901
55–59	2373.829	3.67	87.127	4146.148	6.81	339.846
60–64	1861.811	4.12	76.703	3325.733	7.25	300.795
65–69	1373.048	4.57	62.739	2554.200	7.70	256.224
70–74	905.270	5.02	45.434	1821.521	8.15	208,264
75–79	499.574	5.47	27.318	1077.611	8.60	156.711
Total (age adjusted) 20–79 years	43474.480	2.01	874.068	83813.210	5.66	4739.851
Lower Cl	-	1.88	817.321	-	5.50	4609.726
Upper CI	-	2.14	930.354	-	5.81	4869.547

<sup>\*</sup>Estimate based on meta-regression epidemiological modelling adjusted for year and sample size from each study.

prevalence of overweight and obesity among women across many African settings,<sup>71 74</sup> who have wrongly associated this with healthy living, and possibly been contented with the better social status it offered them.

Rapid urbanisation, as an important driver of the increasing burden of T2DM in Africa, <sup>10</sup> was also confirmed in our report, with prevalence among urban dwellers well above the rural dwellers. Africa, and Nigeria in particular, is experiencing fastest rate of urbanisation globally, with over a third of the population currently residing in urban areas, and this is expected to increase to about 45% by 2025.<sup>75</sup> This may also explain the higher T2DM prevalence in Southern Nigeria, a relatively urbanised region compared with the Northern parts, which is in fact further characterised by nomadic lifestyles. Age was another factor noted in our report, with higher prevalence rates observed in the older age groups. Experts have revealed a rising prevalence of diabetes with increasing age, particularly due to continued exposure to several other risks occasioned by prolonged life. 10 7

Our estimated mortality rate from T2DM in Nigeria is relatively lower compared with the overall rate (111.1 per 100 000 population) reported for the African region in the WHO global report. This may be due to the few data points on diabetes deaths in our study, and the fact that individual mortality rates were based on 'large' reference population of the hospital where the study was conducted. In the 2016 WHO diabetes profile, about 28000 diabetes deaths were estimated in Nigeria, stating however that the estimates have high degree of uncertainty as there were no available national mortality data to compute these estimates. 15 However, our estimates show hospital admissions (from complications) and case fatality rates were comparatively higher in Nigeria, with hyperglycaemic emergencies, diabetic foot and cardiovascular diseases being the most common indications. In Nigeria, there have been reports that many diabetes cases present to health facilities at advanced stages of the disease.<sup>14</sup> Acute complications of diabetes, mainly diabetic ketoacidosis, hyperosmolar non-ketotic coma and hypoglycaemia, are frequent indications of hospital emergencies in Nigeria, with high mortalities recorded.<sup>56</sup> High numbers of undiagnosed cases and low treatment rates, as estimated in our study, may also be major factors responsible for the prevalent complications and high mortality rates. Recent reports within Nigeria show that undiagnosed cases of diabetes accounted for about 40% of the diabetes burden in the country. 11 According to IDF, about two million undiagnosed diabetes cases were estimated in Nigeria in 2013, with this responsible for over 40000 deaths resulting from diabetes and its complications in the country.<sup>8</sup> Personal health cost from diabetes, mostly out of pocket, may have also affected hospital visits and use of medications. The lack of a fully functional and equitable national health insurance scheme<sup>14</sup> means many people with diabetes would prefer to stay at home, visit substandard facilities or patronise traditional herbal healers, due to high cost of treatment and medications,

only to present at an advanced stage of the disease to standard health facilities with widespread complications. Kirigia and colleagues estimated that the 7.1 million cases of diabetes reported in Africa in 2000 accounted for a regional economic loss of about 25.5 billion US\$, equivalent to about \$3633 per diabetic case. The need for insulin and other medications was responsible for the bulk of the direct cost, accounting for about \$8.1 billion (\$1154/diabetic case).

While we attempted to provide population representative estimates of the burden of T2DM in Nigeria, we however could have been limited by a number of factors. First, retained studies were not evenly spread across various parts of Nigeria. Most studies selected were conducted in the Southern geopolitical zones of Nigeria, with the Northern zones having nine studies (21.4%). Data from many studies were also incomplete, as results of some studies, with explicit sampling strategy and study designs, were not always detailed. Besides, data points on age and sex-specific prevalence, including corresponding prevalence for urban and rural settings, were not always provided across studies. There were also sources of heterogeneity from study designs, measurement protocols and individual and population differences across selected studies. However, our selection and quality criteria may have excluded low-quality studies, and we conducted subgroup meta-analyses on selected studies to identify other sources of heterogeneity that may further aid the interpretation of results. There were few data points from hospital-based studies and representative population denominators were not provided. As hospital admissions and mortality rates were based on relatively larger catchment population of the hospital, an underestimation may not be ruled out. Finally, although we controlled for study period and sample population in our modelling, we are aware there could be uncertainties in our reported estimates of T2DM in Nigeria for 1990 and 2015, as varying population contexts, blood glucose measurements, case definitions and social determinants of health, beyond mean age of the population, are important factors that could have affected real-time trends. However, with 42 studies selected across all six geopolitical zones of Nigeria, and a total population of 91 320 included, our estimates may still point to a near-precise burden of T2DM in Nigeria.

#### Conclusion

Our findings suggest an increasing burden of T2DM in Nigeria with many persons currently undiagnosed, and few known cases on treatment. The rising burden of diabetes has presented huge cost to individuals, society and the Nigerian government. There is still need for more research on T2DM, including specific response to diabetes treatment and management, particularly in Northern Nigeria, where few researches have been conducted to date. We hope our findings may help towards improved research, control, treatment and policy response to diabetes in Nigeria.

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Contributors DA conceptualised the study. DA, JOI and AA conducted the literature searches. JOI, AA and AVA extracted all data with oversight from DA. DA, NA and EOA performed all statistical analyses. DA and JOI drafted the paper. DA, AVA, AA, EOA and GO contributed to writing of the final version of the paper and checked the paper for important intellectual content.

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