Gaps in Guidelines for the Management of Diabetes in Low- and Middle-Income Versus High-Income Countries—A Systematic Review

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Mayowa O. Owolabi,¹ Joseph O. Yaria,² Meena Daivadanam,^{3,4} Akintomiwa I. Makanjuola,² Gary Parker,⁵ Brian Oldenburg,⁶ Rajesh Vedanthan,⁷ Shane Norris,⁸ Ayodele R. Oguntoye,² Morenike A. Osundina,² Omarys Herasme,⁷ Sulaiman Lakoh,² Lugman O. Ogunjimi,² Sarah E. Abraham,² Paul Olowoyo,⁹ Carolyn Jenkins,¹⁰ Wuwei Feng,¹⁰ Hernán Bayona,¹¹ Sailesh Mohan,¹² Rohina Joshi,¹³ Ruth Webster,¹³ Andre P. Kengne,¹⁴ Antigona Trofor,¹⁵ Lucia Maria Lotrean,¹⁶ Devarsetty Praveen,¹⁷ Jessica H. Zafra-Tanaka,¹⁸ Maria Lazo-Porras,¹⁸ Kirsten Bobrow,¹⁹ Michaela A. Riddell,²⁰ Konstantinos Makrilakis,²¹ Yannis Manios,²² and Bruce Ovbiagele,¹⁰ for the COUNCIL Initiative*

OBJECTIVE

The extent to which diabetes (DM) practice guidelines, often based on evidence from high-income countries (HIC), can be implemented to improve outcomes in low- and middle-income countries (LMIC) is a critical challenge. We carried out a systematic review to compare type 2 DM guidelines in individual LMIC versus HIC over the past decade to identify aspects that could be improved to facilitate implementation.

RESEARCH DESIGN AND METHODS

Eligible guidelines were sought from online databases and websites of diabetes associations and ministries of health. Type 2 DM guidelines published between 2006 and 2016 with accessible full publications were included. Each of the 54 eligible guidelines was assessed for compliance with the Institute of Medicine (IOM) standards, coverage of the cardiovascular quadrangle (epidemiologic surveillance, prevention, acute care, and rehabilitation), translatability, and its target audiences.

RESULTS

Most LMIC guidelines were inadequate in terms of applicability, clarity, and dissemination plan as well as socioeconomic and ethical-legal contextualization. LMIC guidelines targeted mainly health care providers, with only a few including patients (7%), payers (11%), and policy makers (18%) as their target audiences. Compared with HIC guidelines, the spectrum of DM clinical care addressed by LMIC guidelines was narrow. Most guidelines from the LMIC complied with less than half of the IOM standards, with 12% of the LMIC guidelines satisfying at least four IOM criteria as opposed to 60% of the HIC guidelines (P < 0.001).

CONCLUSIONS

A new approach to the contextualization, content development, and delivery of LMIC guidelines is needed to improve outcomes.

Diabetes (DM), a metabolic disease with detrimental effects on various organs in the body, is a leading cause of morbidity and mortality in low- and middle-income countries (LMIC) (1,2). The World Health Organization (WHO) 2016 *Global Report on Diabetes* stated that as of 2012, the lower socioeconomic class of the middle-income countries (MIC) had the highest mortality attributed to high glucose across all age-groups (1,3). Furthermore, at ages above 50 years, DM-associated mortalities from LMIC were

¹University of Ibadan, Ibadan, Nigeria ²University College Hospital, Ibadan, Nigeria ³Department of Food, Nutrition and Dietetics, Uppsala University, Uppsala, Sweden

⁴Department of Public Health Sciences, Karolinska Institutet, Solna, Sweden

⁵University College London, London, U.K.⁶The University of Melbourne, Melbourne,

Australia ⁷Icahn School of Medicine at Mount Sinai, New York. NY

⁸University of the Witwatersrand, Johannesburg, South Africa

⁹Federal Teaching Hospital, Ido-Ekiti, Nigeria ¹⁰Medical University of South Carolina, Charleston. SC

¹¹Fundación Santa Fe de Bogotá Hospital, University of the Andes, Bogota, Colombia

¹²Public Health Foundation of India, New Delhi, India

¹³The George Institute for Global Health, The University of New South Wales, Sydney, Australia ¹⁴South African Medical Research Council, Cape Town, South Africa

¹⁵Grigore T. Popa University of Medicine and Pharmacy, Iaşi, Romania

¹⁶Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania 222

markedly greater than those from highincome countries (HIC) (1). Specifically, the African, Eastern Mediterranean, and South-East Asia regions had age-standardized mortality rates above 100 per 100,000, while the European and Western Pacific regions and the Americas had rates of 55.7, 67, and 72.6 per 100,000, respectively (1). Therefore, there is an urgent need to ensure best treatment and prevention practices to curb the burden of this disease, especially in LMIC.

Factors that limit the application of standard interventions in LMIC include political instability, poor health literacy, limited health budgets, limited facilities, inadequate clinical expertise and personnel, poor drug supply, out-of-pocket health expenditures, barely existent health insurance systems, and behavioral factors (4-8). Paradoxically, only about 10% of the global research capacity and health care resources to investigate and apply novel context-specific sustainable solutions to overcome such challenges are located in LMIC, which bear most of the burden (7-9). Nevertheless, pragmatic steps need to be taken urgently to combat the burden of DM in LMIC.

Clinical practice guidelines containing pragmatic, appropriate, and standardized actions to be taken by various stakeholders and policy makers could help improve outcomes (10,11). However, the major challenge is the extent to which these guidelines can be implemented in LMIC. To be successful, interventions should be Affordable, Practicable, cost-Effective, Acceptable, Safe, and Equitable according to the APEASE criteria (12). Therefore, the one-guideline-fits-all approach may no longer be applicable in LMIC. Adapting international guidelines to the socioeconomic context of LMIC with a focus on suitable strategies and a wider target audience might be a better option for the control of DM. It is not clear whether existing guidelines for DM in LMIC addressed these considerations in order to enhance their impact (13).

OBJECTIVE

We therefore carried out a systematic review to compare clinical guidelines for type 2 DM in individual LMIC versus HIC over the past decade. We aimed to determine specific gaps in content, quality of evidence, trustworthiness, considerations for implementation, dissemination to empower all relevant stakeholders, and suitability of the proposed solutions.

RESEARCH DESIGN AND METHODS

This systematic review was designed and presented using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (14).

Selection Criteria

All country-specific recommendations published from 2006 to 2016 for management of type 2 DM listed in the searched databases were included. For duplicate guidelines, the most current was considered. Guidelines published exclusively for type 1 DM and guidelines with inaccessible full publications were excluded. In guidelines with recently published updates, information was extracted from both the updated and the original publications.

Information Sources

Identified guidelines regarding type 2 DM management were sourced mainly from electronic medical databases—PubMed, African Journals Online, Directory of Open Access Journals, Google Scholar, and Excerpta Medica Database. National DM guidelines by ministries of health were sought using Google. Websites of diabetes associations and every individual country's ministry of health were also searched for guidelines. Members of the Global Alliance for Chronic Diseases (GACD) Research Network involved in DM prevention and control research across the globe (15) were also approached to provide relevant guidelines when they could not be accessed directly. Some of these were obtained from the national diabetes associations.

Search Strategy

Based on the PICO strategy (Supplementary Data Appendix I) (16), the following search terms were employed: topic = "country name" AND topic = "guideline" OR "consensus" OR "protocols" OR "standards" OR "recommendations" AND topic = "diabetes". Secondary search items included the name of continents, implementation, prevention, translation, and society while tertiary search items included the name of the association, society, group, and organization. We specifically searched all data sources for guidelines for every country. The classification of countries by income was based on the 2016 World Bank classification (17).

Study Selection

Six individuals were independently tasked with the search of guidelines using the above-mentioned search strategies and information sources. Details—titles, year of publication, and author—of each guideline found were entered into individual Excel spreadsheets. This information was collated by J.O.Y., with duplicates and irrelevant records removed. Based on abstracts, potentially relevant publications were identified with full-text articles outsourced for acquisition, with M.D. and O.H. also providing full-text articles. Eligibility was assessed by J.O.Y. and A.I.M.

Data Extraction and Quality Assessment

Necessary information from each selected guideline was extracted into a predesigned structured evaluation form independently by the assessors (J.O.Y., A.R.O., M.O.O., and S.E.A.). The proforma was created to assess the target audience; spectrum of clinical conditions covered; attention to ease of implementation (translatability) and ethical, legal, and socioeconomic issues; and trustworthiness using grading scales and Institute of Medicine (IOM) guidelines (18). The data extracted was confirmed by S.L., L.O.O., A.R.O., and M.O.O. prior to analysis.

- ¹⁷The George Institute for Global Health, New Delhi, India
- ¹⁸Universidad Peruana Cayetano Heredia, Lima, Peru ¹⁹University of Cape Town, Cape Town, South Africa
- ²⁰Monash University, Melbourne, Australia ²¹National and Kapodistrian University of
- Athens, Athens, Greece
- ²²Harokopio University, Athens, Greece

Corresponding author: Mayowa O. Owolabi, mayowaowolabi@yahoo.com.

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M.O.O. and J.O.Y. contributed equally to this work.

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Non-English guidelines were reviewed independently by two individuals from each respective language. In the few events of difference in assessments between reviewers, joint review was conducted by all members of the panel to arrive at a consensus rating.

Data Items

Each guideline was assessed for compliance with the IOM standards for developing clinical practice guidelines (Supplementary Data Appendix II) (18), coverage of the cardiovascular quadrangle (surveillance, prevention, acute care, and rehabilitation) (13), translatability (13), revision date, and its target audiences as stated in the guidelines text. In the event that the intended audience was not stated by the guideline, none was assumed. Target audiences were divided into providers, patients, populace, policy makers, implementation partners (e.g., professional bodies, advocates, relevant nongovernmental organizations, etc.), and payers (entities other than patient that finance or reimburse the cost of health services) (13). A guideline was deemed to have complied with each IOM standard when all the stated IOM requirements were met (18). A guideline was judged to have ethical, legal, social, and psychological considerations when information concerning ethical dilemmas, DM-related legal issues, the impact of DM on daily routines and relationships, and psychological issues were explicitly stated. A guideline was deemed translatable when solutions were categorized according to the ease of successful implementation (13).

Data Synthesis and Analysis

Information from the proforma was transferred into Microsoft Excel for data cleaning. Tables summarizing guideline characteristics were designed for review purposes. Univariate analysis was carried out to assess income class differences in selected variables. A *P* value <0.05 was deemed significant. Stata Data Analysis and Statistical Software version 12 (StataCorp, College Station, TX) was used for statistical analysis.

RESULTS

A total of 2,695 titles were identified after an electronic title search was carried out, and 27 additional guidelines were received from members of the GACD Research Network. Out of these, 2,510 titles were discarded because they were either duplicates or titles not reflecting DM guidelines. Of the 186 manuscripts finally screened, 108 were eligible, and 56 manuscripts from 55 countries were included for analysis after applying the inclusion and exclusion criteria (Supplementary Fig. 1).

According to the WHO report, 126 countries reported having a national guideline for DM management (1). However, after a thorough online search of medical databases and individual health ministry websites, guidelines for over half of these countries were not found. In contrast, DM guidelines were seen for a few countries that were not captured by the WHO report. Of the 56 guidelines, 7 (12%) were from low-income countries (LIC), 10 (18%) from lower-MIC, 19 (34%) from upper-MIC, and 20 (36%) from HIC. None of the LIC had guidelines that addressed DM alone. Rather, they had guidelines for a myriad of conditions, called standard treatment guidelines, of which DM was one of the conditions.

National guidelines identified for individual countries, based on the 2016 World Bank classification (17), were the following.

- LIC: Afghanistan, Ethiopia, Liberia, Malawi, Tanzania, Uganda, Zimbabwe
- Lower-MIC: Ghana, India, Kenya, Kiribati, Nigeria, the Philippines, Solomon Islands, Sri Lanka, Swaziland, Zambia
- Upper-MIC: Belize, Botswana, Brazil, China, Colombia, Ecuador, Fiji, Jamaica, Libya, Malaysia, Mauritius, Mexico, Panama, Peru, Romania, South Africa, Saint Lucia, Turkey, Tuvalu
- HIC: Argentina, Australia, Bahrain, Bermuda, Canada, Chile, England, Greece, Hong Kong, Ireland, Italy, Korea Republic, New Zealand, Scotland, Singapore, Spain, Sweden, U.S., Wales

The guidelines according to the country of origin, year of publication, title, and author are shown in Supplementary Tables 1–4. Almost all guidelines from LMIC were developed by the individual countries' ministries of health. However, over half of the guidelines from HIC were developed by diabetes associations and adopted by the country. DM guidelines from LMIC targeted mainly health care providers, with only few of the 28 guidelines that indicated their target audience stating it to be patients (2 [7%]), payers (3 [11%]), and policy makers (5 [18%]). This is in contrast to HIC guidelines that specified a target audience, which targeted more patients (8 [57%]), payers (5 [36%]), and policy makers (7 [50%]). However, DM guidelines in general were rarely developed to target the healthy population or health care partners (Fig. 1 and Supplementary Table 5).

Compared with HIC guidelines, the spectrum of DM clinical care addressed by LMIC guidelines was narrow. Surveillance and specific management of complications in DM were not addressed in any LIC guideline. Patient education and DM prevention were addressed in just one LIC guideline, and DM prevention was dealt with in less than half of the MIC guidelines. In contrast, apart from the DM guideline from Greece, all HIC guidelines discussed surveillance, and only 6 (30%) did not address DM prevention. Other spectra of care were handled by over half of the HIC guidelines (Fig. 2 and Supplementary Tables 6-8). LMIC guidelines, however, were more likely to discuss management of DM emergencies. The recent International Diabetes Federation (IDF) guideline, which cuts across LMIC and HIC regions, included recommendations for primary care with a wider spectrum than most LMIC guidelines. However, although surveillance and patient education were discussed, care in special situations, e.g., pregnancy and surgeries, was notably absent.

Few guidelines graded recommendations according to ease of translation into practice by all stakeholders (Supplementary Tables 9–11), with just 6 (17%) LMIC guidelines and 5 (25%) HIC guidelines (P = 0.452) doing so. Comparing guidelines from LMIC and HIC, DM-related social issues were considered in 4 (11%) LMIC guidelines (P = 0.031). Economic and psychological issues were considered in 6 (17%) and 4 (11%) LMIC guidelines, respectively, as opposed to 6 (30%) and 10 (50%) HIC guidelines, respectively; P = 0.244 and 0.001.

Most guidelines from LMIC complied with less than half of the criteria for trust-worthiness using the IOM standards (18) (Fig. 4 and Supplementary Tables 12–14). Four (11%) LMIC guidelines satisfied at least four IOM criteria as opposed to 12 (60%) HIC guidelines (P < 0.001). Most of the guidelines were

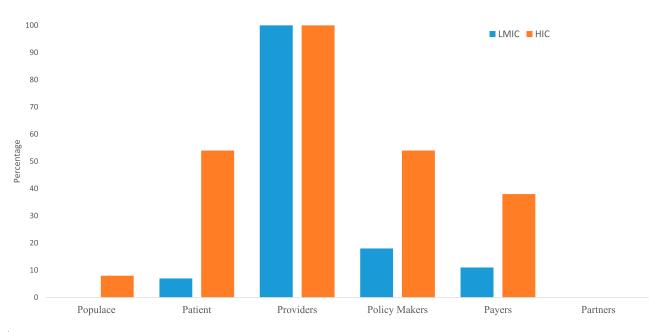


Figure 1—Distribution of target audience stated in LMIC and HIC DM guidelines. Each guideline was assessed for target audiences as stated in the guidelines text, with none assumed if the intended audience was not stated by the guideline.

more than 5 years old, and only 3 (9%) LMIC guidelines specified planned updates in contrast to 9 (45%) HIC guidelines (P = 0.002). There were also significant differences between LMIC and HIC guidelines in transparency (42% vs. 75%, P = 0.017), multidisciplinary approach (53% vs. 85%, P = 0.016), strength of recommendation (14% vs. 70%, *P* < 0.001), and articulation (44% vs. 90%, *P* = 0.001).

Detailed analysis of the guidelines are presented in Supplementary Tables 1–14, namely:

- Titles and authors of the guidelines used (Supplementary Tables 1–4)
- Stakeholder populations (6Ps patients, providers, payers, policy makers, populace, and partners) targeted by the guidelines (Supplementary Table 5)
- Spectrum of DM care addressed by the guidelines (Supplementary Tables 6–8)

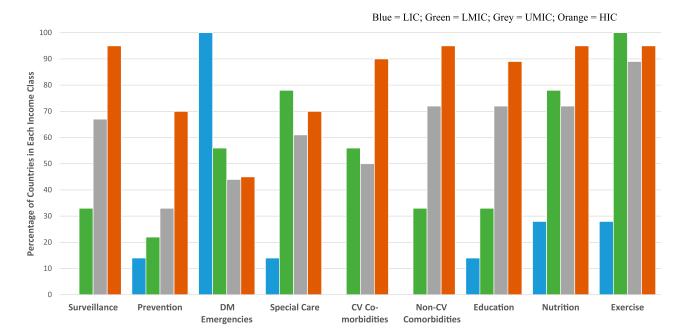


Figure 2—Spectrum of DM care addressed by DM guidelines. Each guideline was assessed with respect to surveillance, prevention, diabetes emergencies (diabetic ketoacidosis, hyperosmolar hyperglycemic state, and hypoglycemia), special care (glucose control during acute hospital admission for nonglucose issues, e.g., intensive care unit, surgeries, pregnancy, and Ramadan), cardiovascular (CV) comorbidities (hypertension, dyslipidemia, and obesity), and noncardiovascular comorbidities (e.g., diabetic foot, retinopathy, etc.).

- Translatability and ethical, legal, and socioeconomic considerations (Fig. 3 and Supplementary Tables 9–11)
- Trustworthiness of guidelines using the IOM standards (Supplementary Tables 12–14).

DISCUSSION

The quality and quantity of DM guidelines in LMIC did not measure up to those of the HIC. The lack of guidelines in numerous LMIC portend personal and public health implications. Without targeted contextualized (13) and appropriately communicated guidelines, care providers, patients, policy makers, payers, and communities are not guided adequately on the best practices to yield better outcomes (13). Considerations for contextualization should include factors related to each of the stakeholders, including external contextual factors (policies, incentivization structures, dominant paradigms, stakeholders' buy-in, infrastructure, and advances in technology), organizationrelated factors (culture, available resources, integration with existing processes, relationships, skill mix, and staff involvement), and individual professional factors (professional role, underlying philosophy of care, and competencies) (13). Contextualization involves designing and fitting the recommendations to the implementation environment and vice versa. It includes targeted packaging of solutions and their dissemination through novel interactive channels to mobilize every stakeholder so as to foster ownership by all (13). For example, the timely delivery of thrombolytic therapy to an eligible stroke patient involves coordinated action of all stakeholders and not just the health care providers. Contextualization will also ensure intervention sustainability as community ownership and mobilization crucial for sustainability are accounted for (5). Lack of contextualization may partly account for the poor outcomes (higher mortality) (1,3) of DM in LMIC compared with HIC.

Furthermore, not only are DM guidelines from LMIC narrow in spectrum of care addressed, especially those from LIC, they are also characterized by a dearth of trustworthiness as defined by IOM and a narrow target audience. A higher proportion of HIC guidelines underwent frequent review and fulfilled more IOM recommendations. In addition, the strength of recommendations and the levels of evidence were rarely specified in LMIC guidelines compared with HIC (Supplementary Tables 12–14). Most LMIC guidelines were either vague about or did not identify the source of their recommendations or the issue of ownership. However, recommendations from notable diabetes associations, WHO, and influential local practices were identified in the few LMIC guidelines that reported this. In contrast, most HIC guidelines are from diabetes professional associations, which may partly account for their better quality.

Furthermore, many LMIC guidelines did not adequately address management in special situations such as prolonged fasting (a common practice especially in some cultural settings [19]), surgeries, and hospitalization for acute illness. LMIC guidelines should be explicit about recommended action to be taken with respect to a particular circumstance, medication issues (how often, what dose, and what other options are available), which health care provider is best suited to take action, and indicators that guide the provider in deciding when to take action and when to stop. This is particularly necessary for guidelines for LMIC where access to health care is limited and provision of health services is more likely to be carried out mainly by community health workers and other nonprofessionals, e.g., peer

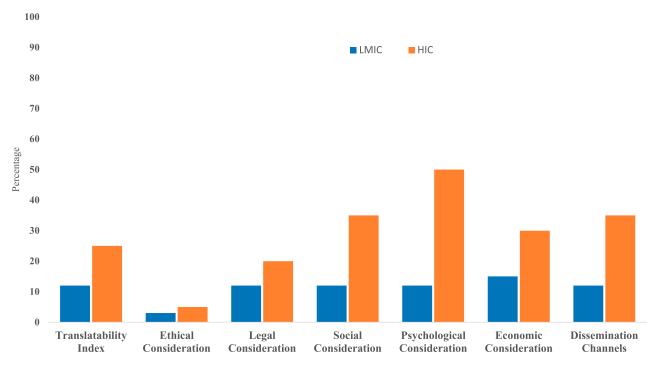


Figure 3—Translatability, ethical, legal, and socioeconomic considerations. A guideline was judged to have ethical, legal, social, and psychological considerations when information concerning ethical dilemmas, DM-related legal issues, the impact of diabetes on daily routines and relationships, and psychological issues were explicitly stated. A guideline was deemed translatable when solutions were categorized according to the ease of successful implementation.

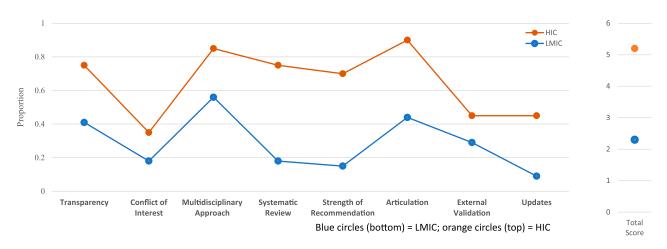


Figure 4—Profiles of IOM component and total scores for LMIC and HIC guidelines. Each guideline was assessed for compliance with the IOM standards for developing clinical practice guidelines. A point was awarded for each standard satisfied, and the total score for each guideline was computed. Univariate analysis was carried out to assess income class differences. Individual IOM components are indicated on the horizontal axis. Proportion of IOM standard and mean total score are reported.

supporters (20). Such recommendations may facilitate the reduction of disease burden, complications, and risk factors.

Furthermore, including justification for recommendations, e.g., results of landmark clinical trials or locally derived evidence, as a way of increasing compliance is also worth considering (10). However, this may increase the bulkiness of the guidelines, and too much information can dissuade the reader. We recommend the insertion of links to external sources to avoid this.

LMIC guidelines discussed secondary prevention but were less likely to attend to primary prevention. In addition to providing care for those who already have DM, the effort may also be invested in preventing further increase in the burden through prevention of new acquisition of the disease. The lack of expertise, infrastructure, and a financing system to manage complications and comorbidities associated with DM can be viewed as a justification for considering this approach. Although the evidence for effective primary prevention of DM is very recent (21,22) and strategies for implementing them in LMIC need to be developed, solutions that cut across population strata with minimal or no cost could be encouraged.

Patient education was rarely addressed in LMIC guidelines despite evidence of its longstanding importance as a component in the management of DM (23,24). Coupling recommendations with education and training interventions improves uptake (10). This is because health care providers, patients, and other stakeholders are unlikely to adjust their current practices without the adequate knowledge and skill set to effect necessary action (10). This led the American Diabetes Association to design national standards for selfmanagement education in DM (23). While other HIC did not have guidelines on DM education as detailed as those from the American Diabetes Association, there was at least a component within the guideline that enlightened its target audience on patient education. It is notable, however, that the IDF included patient education and the need for a structured program in its recommendation for primary care (25).

Educating the patient goes beyond ensuring the patient adheres to the recommended treatment; it helps the health provider to understand the patient's priorities, lifestyle, and state of mind (23). This enables management priorities to be readjusted. Incorporating cultural and religious beliefs into the education module, using native language, and providing family-tailored intervention have been shown to improve knowledge, self-management behaviors of patients with DM, and ultimately clinical outcomes (26-28). Frequent communication, which is key to improving long-term outcomes, can also be carried out by trained community health workers and peer supporters, with a long-term view to institutionalizing these health systems (20,29,30). Concise practice points containing key action items can be developed and disseminated through mass media and user-friendly interactive modern communication channels, including mobile phone applications, which can be quickly and easily accessed by health care providers in clinical environments (13).

For the implementation of these guidelines, there is a need for an expansion of the target audience by both LMIC and HIC with specific tasks that get all stakeholders involved (31,32). A healthy lifestyle is an essential component of DM management, and this measure is also important for the entire population. Therefore, targeting the seemingly healthy populace in DM guideline development seems justified. There is a higher chance of achieving implementation when there is a real implementation plan in place.

Introducing a section on setting up a DM care delivery system targeting policy makers, patients, providers, payers, the populace, partners, and other relevant stakeholders should be encouraged. The role of each stakeholder should be defined within various settings and programs based on resources readily available in such settings. A good example is the evidence-based simple protocol for nurseled diabetes care (33) in sub-Saharan Africa, where health care access is suboptimal (34). This plan would require inclusion of policy makers (to provide infrastructure), health financiers (payers), and other partners.

Most reviewed guidelines did not address the roles of payers, with an almost universal lack of coverage regarding the role of partners in DM management in both LMIC and HIC guidelines. For example, the IDF focused its latest publication on clinicians even with the clinical practice recommendations designed for managing type 2 DM at the primary care level (25). These often excluded stakeholders nonetheless constitute "the bridge" over which "the car" (DM guidelines) must pass to reach its destination desired outcomes (13). Careful case studies into successful diabetes care delivery (20,33,35) illustrating unique roles of these stakeholders offer examples that can be adapted for redesigning health systems in local settings (34).

Indeed, with a faster rate of increasing DM prevalence in LMIC when compared with HIC (36,37), innovative and properly contextualized guidelines are direly needed. The uniqueness of various countries with respect to socioeconomy, lifestyle, service delivery, health care policies, and probably pharmacogenomics informs the need for adaptation of DM guidelines to suite the country's needs in the pursuit of precision medicine (38,39). Wide disparities in standards of living within a given country inform the need for all countries—LMIC and HIC—to design guidelines that provide options for rural and urban areas. However, a limited number of guidelines—LMIC and HIC inclusive—took into consideration ease of implementation apropos of social, economic, ethical, and legal barriers.

Grading recommendations in accordance with the nature and relative complexities of barriers that need to be navigated for successful implementationtranslatability scale (13)—is therefore advised. A good example is the IDF's global guideline (40), which was emulated by the Sri Lankan and Indian guidelines (41,42) where recommendations were divided into minimal, standard, and comprehensive care. The Belize guideline (43) also separated investigations into two categories: the required minimum and those to be carried out only if clinically indicated. These approaches can be improved upon with ethical, legal, sociocultural, and economic factors considered prior to ranking of recommendations. Proposing a reduction of alcohol consumption, though cheap, may turn out to be more difficult than expected due to unique sociocultural characteristics of a region or country. However, if these factors are considered and accounted for while designing guidelines, then they can influence the grading of recommendations according to ease of implementation. These

factors can also be modified to improve ease of implementation. It is presumed that the integration of sociodemographic, cultural, and economic considerations into the design and grading of recommendations should aid in reducing intracountry urban-rural disparity in guideline implementation as various health delivery levels are more likely to find such guidelines useful despite differences in the implementation environments.

Currently, guidelines from LMIC are largely adapted from existing HIC guidelines without due considerations about implementation. Relevant locally derived evidences are commonly not used in the development of these guidelines. This is probably due to the paucity of local evidences, poorly designed clinical studies, and low weight of evidence. Taking into consideration the socioeconomic barrier in LMIC, studies could be conducted to review the use of screening options that involve the use of risk assessment tools, e.g., the AUSDRISK in Australia (44) and the FINDRISC in Brazil (45). Some recommendations can be adjusted to suit patients in rural areas or those with limited access to an endocrinologist. The Wales guideline's "eatwell plate" (46) is a tool that LMIC can adapt to assist in communicating the message of portion control in the context of locally available foods. LMIC can also adopt the clarity of a number of HIC guidelines that extend to detailed dietary recommendations for comorbidities like dyslipidemia, hypertension, and the like.

Limitations and Future Directions

Guidelines published online were more likely to be included in the review. It is likely that guidelines that were not published on any of the databases searched were also not identified for the review because not every national association or official body could be individually contacted. However, members of the GACD network additionally contacted many of their national diabetes associations and official bodies to identify additional guidelines that were not available online. Exclusion of regional and international guidelines, done to enable categorization based on economic status, may introduce selection bias. Most guidelines for lower-MIC and LIC were either mainly designed for primary care with recommendations for referral to other centers or they were not dedicated DM guidelines but rather

standard treatment guidelines for noncommunicable diseases (which include DM). We compared these guidelines with HIC guidelines because there were no other documented practice guidelines in these regions. Indeed, LMIC suffer more from lack of personnel in primary care settings in rural areas (47), as the adequately trained medical doctors favor the urban regions and untrained health care personnel run the rural health care (47,48). Therefore, upgrading the guidelines for use in these settings could help improve services through training.

CONCLUSIONS

DM guidelines are a guide to health care providers and other stakeholders with a view to reducing the population burden of DM and improving clinical outcomes. However, most LMIC guidelines fall short of the basic criteria including clinical applicability, clarity, and rigorous dissemination plan as well as socioeconomic and ethicallegal contextualization. It should be noted that the availability of national guidelines does not necessarily translate to awareness or implementation of such guidelines by health care providers and other stakeholders. Engagement and effective communication with all stakeholders including patients, health care providers, policy makers, payers, and other implementation partners are required for success.

A new approach to the contextualization, content, and delivery of LMIC guidelines is therefore recommended. Guideline(s) should be broad based with respect to the spectrum of DM care and intended target audience. They should recommend clear up-to-date clinical interventions carefully contextualized with respect to specific sociocultural and economic barriers and facilitators. This should go a long way in reducing the burden of DM generally and in LMIC particularly.

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