

STATE-OF-THE-ART REVIEW

Synthesis: Deriving a Core Set of Recommendations to Optimize Diabetes Care on a Global Scale



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Abstract

BACKGROUND Diabetes afflicts 382 million people worldwide, with increasing prevalence rates and adverse effects on health, well-being, and society in general. There are many drivers for the complex presentation of diabetes, including environmental and genetic/epigenetic factors.

OBJECTIVE The aim was to synthesize a core set of recommendations from information from 14 countries that can be used to optimize diabetes care on a global scale.

METHODS Information from 14 papers in this special issue of *Annals of Global Health* was reviewed, analyzed, and sorted to synthesize recommendations. PubMed was searched for relevant studies on diabetes and global health.

FINDINGS Key findings are as follows: (1) Population-based transitions distinguish region-specific diabetes care; (2) biological drivers for diabetes differ among various populations and need to be clarified scientifically; (3) principal resource availability determines quality-of-care metrics; and (4) governmental involvement, independent of economic barriers, improves the contextualization of diabetes care. Core recommendations are as follows: (1) Each nation should assess region-specific epidemiology, the scientific evidence base, and population-based transitions to establish risk-stratified guidelines for diagnosis and therapeutic interventions; (2) each nation should establish a public health imperative to provide tools and funding to successfully implement these guidelines; and (3) each nation should commit to education and research to optimize recommendations for a durable effect.

CONCLUSIONS Systematic acquisition of information about diabetes care can be analyzed, extrapolated, and then used to provide a core set of actionable recommendations that may be further studied and implemented to improve diabetes care on a global scale.

KEY WORDS diabetes, recommendations, global, diabetes care, type 2 diabetes, type 1 diabetes, public policy

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INTRODUCTION

The 2014 International Diabetes Federation (IDF) Global Diabetes Scoreboard¹ serves as the central resource for current epidemiology, societal drivers,

and teleological strategy to combat diabetes as a serious chronic disease among the regions and nations of the world. The growing interest in diabetes, extending beyond local dimensions and onto a global scale, is reflected by a geometric surge in PubMed citations

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on the topic (Table 1). In 2014, Dr. Michael Bergman edited a compilation of papers on diabetes care from 13 different global regions from a preventive care and public health perspective, further advancing our understanding of this field.² When considering one of the prime drivers—economics—there is an organic nature to the rise in diabetes prevalence, particularly in low-income and lower middle income countries, with insufficient funding impairing diabetes care and an unhealthy population impairing economic growth. But it is the complex interplay of all the drivers (Table 2), exerting effects with varying degrees from one region to another, that creates an entangled state of diabetes that needs to be dissected, interrogated, and reimaged. This level of complexity transcends the identification of 70 loci associated with type 2 diabetes (T2D), identified by genome-wide association studies and reviewed by Hara et al,³ by including transgenerational effects on the neonate (including epigenetic changes on beta-cell function),^{4–6} specific nutrient-gene interactions,⁷ differential associations of polymorphisms (eg, KCNJ11) with South Indian versus East Asian populations,⁸ adaptive mitochondrial DNA mutations/polymorphisms,⁹ stress-hormonal-metabolic interactions, effects of social context and culture on disease expression, and obesity and simple dietary issues, to name just a few. In addition, population ancestry-related differences in disease expression, giving rise to intermediate phenotypes, are due to a distribution spectrum of risk alleles and further represent the complex interactions of the environment

and genome.¹⁰ Thus, contrary to contemporary linear approaches that use generalized decision algorithms, behavioral economics, and governmental policy making, the goal here is to discern emergent properties that can generate a few key recommendations, perhaps as part of a future network of innovative solutions that optimizes patient care across diverse settings.

Although it is important to provide context for region-specific diabetes care, this context extends beyond simple comparisons to the American health care system. In the United States, overt shortcomings in diabetes care are in a population-based domain (eg, disparities accessing health care, poor distribution and implementation of evidence-based guidelines, and a fragmented health care system with inadequate community engagement) and an individual patient-based domain (eg, health care professional [HCP]–patient communication issues, an individual’s insurance coverage, and inertia implementing precision or personalized preventive care, consisting of structured lifestyle recommendations, optimal pharmacotherapy, and complication management). However, a global context involves a greater number of variables and combinatorial interactions, many of which still need to be learned. In other words, it is as important for one region to provide context for another region with shared cultures as it is for many different individual regions to cumulatively inform the world as a whole.

METHODS

The purpose of this paper is to create a core set of actionable recommendations that can improve patient outcomes on a global scale. Leading researchers in diabetes care from around the world, with a focus on developing nations, were invited to contribute articles for this special issue of *Annals of Global Health* and include summary statements of key findings. Each author was asked to focus on specific drivers contributing to the unique expression of diabetes and current care plans in their respective nations. Authors were also encouraged to incorporate information not only from PubMed and the English language literature but also from other databases, the gray literature, and local academic sources in their native languages. This information was then compiled, classified, analyzed, and subjected to a synthetic cognitive process to arrive at relevant conclusions and recommendations believed to have positive impact, if successfully implemented, on diabetes—a complex, chronic disease. This process is presented in a logical and tractable format.

Table 1. Surge in PubMed Citations Using Search Terms “Diabetes” and “Global”

Year range	No. total citations	No. review articles	No. clinical trials	No. Guidelines
2011-2015 (%)	4785	1086 (22.7)	221 (4.6)	6 (0.1)
2006-2010 (%)	2067	626 (30.3)	116 (5.6)	14 (0.7)
2001-2005 (%)	982	346 (35.2)	79 (8.0)	5 (0.5)
1996-2000 (%)	341	86 (25.2)	32 (9.4)	3 (0.9)
1991-1995 (%)	141	29 (20.6)	18 (12.8)	0
1986-1990 (%)	57	8 (14.0)	4 (7.0)	0
1981-1985 (%)	40	2 (5.0)	0	0
1976-1980 (%)	7	1 (14.3)	0	0
1971-1975 (%)	1	0	0	0
Before 1971 (%)	0	0	0	0

* Percentages use total citations as the denominator. PubMed search conducted on January 1, 2016. The interval growth in total citations has been consistently 2- to 3-fold every 5 years for last 2 decades. The growth in citation type is geometric with only 1 exception (a spike in guidelines from 2006 to 2010). There is a relative expansion of review articles compared with clinical trials and guidelines from 1-fold in 1986-1990 to about 5-fold in 2011-2015, suggesting a rising interest in analyses and opinions.

Table 2. Drivers of Diabetes Care*

Type	Driver
Biological	<p>Role of specific genetic mutations and polymorphisms on beta-cell function, insulin sensitivity, intermediary metabolism, and target organ predisposition for diabetes-related complications</p> <p>Epigenetic effects of specific nutrients, dietary patterns, physical inactivity, infectious agents, and environmental toxins/disruptors</p> <p>Anthropometrics (BMI, WC, sarcopenia, obesity, sarcopenic obesity, etc.)</p> <p>Susceptibilities to infection, CKD, CVD, and CVA</p>
Cultural/lifestyle	<p>Culturally sensitive recommendations</p> <p>Hunger/starvation</p> <p>Healthy eating</p> <p>Reduce physical activity</p> <p>Improve sleep hygiene</p> <p>Tobacco use</p> <p>Alcohol use</p> <p>Crime, danger, war, and stress</p> <p>Increase awareness of disease, complications, and effects on quality of life</p> <p>Attitudes toward health care</p> <p>Use of alternative care</p> <p>Religious dictates</p> <p>Geography, climate, and terrain (limiting access to health care)</p> <p>Built environment (urban vs rural) and advertising</p> <p>Ethnic diversity</p>
Socioeconomic	<p>Gross domestic product</p> <p>Personal income levels</p> <p>Funding for health care coverage, especially the disenfranchised</p> <p>Diabetes-related health care expenditures (diagnostics, medications, supplies, etc.)</p> <p>Funding for prevention programs, comprehensive services, distribution, and other relevant policies</p> <p>Public-private partnerships</p> <p>Funding for high-technology diabetes care (CSII, CGM, etc.)</p>

(Continued)

Table 2. continued

Type	Driver
Political and legislative	<p>Governmental actions on human rights</p> <p>Discrimination against/protection for people with diabetes</p> <p>Gender discrimination</p> <p>Corruption</p> <p>Engagement: policy reform for population-based care</p> <p>Adoption of Global Monitoring Framework for NCD</p> <p>Targeting childhood obesity, diabetes prevention, and marketing to children</p> <p>Improved gestational diabetes detection and care of pregnant women with and without diabetes</p> <p>Primordial prevention programs in pregnancy and in those patients with family history of diabetes</p> <p>Limit salt, saturated fat, trans fat, added sugar</p> <p>Promote physical activity</p> <p>Diabetes Awareness Month</p> <p>World Diabetes Day</p> <p>Fragmented health care system</p> <p>Collaboration with stakeholders, such as the pharmaceutical industry</p>
Education	<p>Patient-centered care</p> <p>Individual/group counseling</p> <p>Self-management education</p> <p>HCP-centered (formal and continuing medical education) literacy</p> <p>Identify local champions</p>
Research	<p>Monitoring and surveillance systems</p> <p>Create and use registries</p> <p>Conduct well-designed and relevant clinical trials</p>

BMI, body mass index; CKD, chronic kidney disease; CSII, continuous subcutaneous insulin infusion; CGM, continuous glucose monitoring; CVA, cerebrovascular accident (stroke); CVD, cardiovascular disease; HCP, health care professional; NCD, noncommunicable disease; WC, waist circumference.
* Primary sources are the International Diabetes Federation¹ and Bergman.² See text for other references. Drivers can be specific, nonspecific, positive, negative, or unclear.

One advantage of these methods is the use of gray literature from around the world. Gray literature pertains to information not controlled by commercial publishers but spans academia, government,

policy, industry, and business. With an explosion and prioritization of information in global endeavors, gray literature is found in print and electronic formats, typically technical in nature, and not available through conventional literature searching. However, rather than being relegated to inferior or supportive documentation, gray literature findings can plug knowledge gaps that are critical to the intended synthetic process for this paper. This is still a relatively limited effort reflected by the relative paucity of nations sampled, but it may stimulate an expanded effort in the future.

RESULTS

Each paper in this special issue provides a different perspective on diabetes care, but in aggregate they reveal interesting commonalities and distinguishing features.

Commonalities include:

- Very high economic burden, in terms of both direct and indirect costs, of diabetes;
- Insufficient funding to optimize diabetes care, especially in low- to middle-income nations;
- Nascent or early efforts to establish, populate, and analyze surveys and registries to base advances on real-world data;
- Need for more governmental policy making and intervention to provide funding for research, education, reimbursements, and infrastructure (eg, diagnostics, medications, and self-monitoring), structured lifestyle change, improved awareness and adherence, and coordination and distribution of resources; and
- Need to create local or transculturalized foreign evidence-based guidelines and then implement on a national scale.

As part of a strategy to discover emergent properties, key distinguishing features are sorted as descriptors and provided in [Table 3](#). Of these, many require additional comment.

In Latin America, Brazil has undergone a period of tremendous and unprecedented economic transition accompanied by hyperinflation—14.2 quadrillion percent from 1961 to 2006.¹¹ As a result of an expanding middle and upper class, more money is available for food and consequently a cultural transition has occurred, with increased Westernized (unhealthy) dietary patterns. In a recent study, McEvoy et al¹² used a random-effects meta-analysis limited to only a posteriori (factor [principal component] and cluster) analyses and found a 15% lower risk for T2D in the highest category of a healthy/prudent dietary pattern (high intake of fruit,

vegetables, and complex carbohydrates; low intake of refined carbohydrates, processed meat, and fried food). Colombia is experiencing high rates of demographic and epidemiologic transition with drops in fertility, mortality, and population growth rates coupled with the highest source of refugees in Latin America and high rates of forced displacement and disappearance. In addition, there are marked differences in nuptiality, family formation, and family planning between urban and rural areas. Ultimately, these factors have led to the dual nutritional burden of under- and overweight.¹³ These factors greatly impede any progress optimizing the diabetes care model in Colombia. In Venezuela, the very high violent crime rate, in which staged planned and expressed kidnappings represent 2 of the most prevalent crimes, murder, shortages, and food insecurity (see later) dominate the psychological and emotional disposition of the population. The resultant allostatic load model of stress leads to unhealthy lifestyle behaviors and immune-neuroendocrine mechanisms that can adversely affect diabetes care.¹⁴ Moreover, it is thought that an adverse lifestyle contributes to the low-grade inflammation observed in patients with T2D.¹⁵ It is therefore not surprising that in a survey of Latinos with T2D, Concha et al¹⁶ found positive patient attitudes about having conversations with an HCP about emotions. Egede and Ellis¹⁷ performed a qualitative aggregation analysis of studies and found that depression was associated with decreased adherence, poor metabolic control, higher complication rates, decreased quality of life, increased health care use and cost, increased disability and lost productivity, and increased mortality risk. In a later paper confirming these results with an international array of authors, Fisher et al¹⁸ emphasized the association of depression and diabetes and argued for a therapeutic approach involving an integrated model of chronic physical and mental disorders that incorporates self-management and problem solving. The associations of psychiatric disease and diabetes have also been highlighted in a study by Okasha and Radwan¹⁹ in Egyptians.

In Europe, in the Republic of Macedonia, insulin and related supplies are free of charge to patients with diabetes, but as expected, this has created a T2D care plan overwhelmed by insulin use with relatively little oral pharmacotherapy and lifestyle management.²⁰ This exemplar demonstrates the need for evidence-based guidelines and algorithms, as well as revamping of population-based nutritional recommendations.

Table 3. Primary Results from this Special Issue on Diabetes Care by Nation*

Region	Nation	Key distinguishing features	Relevance
Latin America	Brazil	High inflation rate	Economic driver for unhealthy, Westernized dietary patterns
	Colombia	High demographic transition	Urbanization with increased risks and unhealthy lifestyles
	Panama	Surveys and registries	Proactive role in adapting care model to improve outcomes
	Peru	Need for governmental policies	Coordination of care with governmental oversight
	Venezuela	High crime rate	Allostatic stress model of chronic disease
Europe	Macedonia	Overuse of insulin	Health care policy for plant-based eating patterns
	Italy	Constitutionally guaranteed right to health	Implementation of national patient-centered diabetes care plan
Africa	Egypt	Environmental drivers: pesticides, pollution, and hepatitis C virus	Incentive for governments to fund research on chronic disease
	Nigeria	Poverty and food insecurity	Dominant role of economics and health care infrastructure
Asia	India	Sarcopenic obesity, dietary patterns, and poverty	Role of research on biologic and lifestyle drivers
	Iran	Governmental engagement	To address a fragmented health care system, especially in rural/remote areas
	Malaysia	Chronic care model Transculturalizing guidelines	Coordination of all elements of care for chronic disease
	Philippines	Poor adherence and awareness	Create public policy to address behaviors
	Vietnam	Cultural transitions and lifestyle	Structured lifestyle change

* A set of key findings for each nation is provided in summary tables at the end of each paper in this issue. The most distinguishing key features for each nation are presented in this table.

In Africa, Egyptian researchers recognize the role of infectious agents (eg, hepatitis C virus—though still controversial), pesticides, pollutants, and other endocrine-disrupting compounds in diabetes pathophysiology, as supported by epidemiological associations and some pathophysiological evidence; however, this requires further study to improve the built environment (the human-made physical world we live in).^{21–23} Using a random-effects meta-analysis of 10 studies, Balti et al²⁴ found an association of major air pollutants with an increased risk for T2D. Food insecurity afflicts nearly 795 million people in the world²⁵ and is of particular concern in Nigeria, where people lack regular and predictable access to sufficient food and compensate by overconsuming nutrient-dense, generally high glycemic index meals. An association between T2D and food insecurity was demonstrated by cross-sectional analysis of results from the 1999–2002 National Health Examination and Nutrition Examination Survey.²⁶

In Asia, there are many different cultures and expressions of diabetes. The Asian Indian diabetes phenotype of decreased muscle mass, inflammation, and increased insulin resistance with elevated waist circumference (WC) despite a normal body mass index (BMI), in the context of changing dietary patterns and ongoing poverty, raises many challenges to diabetes care.²⁷ Physical activity and exercise, particularly progressive resistance training, have been

associated with beneficial effects on T2D²⁸ and should be encouraged for Asian Indians. India is a nation of contrasts and ethnic diversity, highlighting the need for an emphasis on personalized lifestyle change as well as a better understanding of biological drivers. In Malaysia, a detailed chronic care model is being developed to address the fragmented health care system and improve diabetes management.²⁹ In fact, Chan et al³⁰ describe the Joint Asia Diabetes Evaluation program, which integrates informatics, logistics, primary and specialized HCP, evidence-based medicine, and holistic approaches into a more accessible, affordable, and sustainable “high-tech / soft-touch” model. Transculturalization protocols have been described for Brazil,³¹ Venezuela,³² India,³³ and Malaysia³⁴ to adapt Western evidence-based recommendations on diabetes and nutrition.³⁵ Creating culturally sensitive recommendations for local use enhances the precision of care and likelihood of successful implementation and improved outcome metrics. Awareness of diabetes as a chronic disease and adherence with a diabetes care plan are problems shared by all the nations in this special issue, though underscored in the Philippines paper. Attempts at designing behavioral medicine interventions have not been overly successful, and in fact, the lack of a standardized approach precludes valid meta-analyses of approaches for patients with T2D.³⁶

ANALYSIS

Drivers for diabetes development and expression are sorted into 3 a posteriori types of descriptors: those that pertain to health care system infrastructure, those that pertain to culture, and those that pertain to biology. Three a priori classifiers for ways to optimize diabetes are knowledge, public health, and durability, which are intended to generate a core set of recommendations. Many areas around the world have decreased access to medical knowledge and decreased funding levels for local (relevant) research, basic, translational, and clinical. The public health model of chronic disease is a necessary component for successful population-based diabetes care. Any set of recommendations will become antiquated over time unless there are protocols in place to ensure some element of durability as health care changes, drivers evolve, and generations of patients and HCP turn over.

Nine cells are created as descriptors and classifiers are cross-tabulated (Table 4) in a simplistic effort to detect emergent properties that can be used to formulate a core set of actionable recommendations. Important explanations for each cell are provided here.

In cell 1, knowledge about the health care infrastructure requires formal cost-effectiveness assessments, including utilization,³⁷ cost-utility,³⁸ and pharmacoeconomic studies³⁹ for a specific local population. This will need to incorporate structured lifestyle change, efforts to address a fragmented health care system, and modalities to facilitate acquisition and dissemination of information, such as web-based learning.⁴⁰ In cell 2, knowledge should be acquired about the effects of cultural variables on diabetes care. The transcultural Diabetes Nutrition algorithm project, conceived in 2010 and culminating in various papers^{31–35} and a content validation study,⁴¹ focuses on culturally sensitive lifestyle recommendations in diabetes and provides a protocol for adapting guidelines. In addition, behavioral medicine and adherence research need to be advanced for more standardized approaches. In cell 3, the knowledge base for biological drivers needs to be expanded with funded research on basic cellular and molecular mechanisms of disease, including epigenetics to account for how different environmental exposures affect gene expression, translational and clinical trial data, and well-designed surveys, epidemiological studies, and drug development protocols.⁴² It is important that local data are generated to facilitate development of local guidelines, rather than exclusively depending on transculturalization protocols to adapt foreign evidence and opinions. This is

particularly applicable for anthropometrics, such as BMI, WC, or other indices.⁴³

In cell 4, public health initiatives to improve the health care infrastructure and built environment will need to be centered on developing an effective (integrated) chronic care model for diabetes. Busetto et al⁴⁴ propose that successful models will need comparative outcome measures, establishing a chain of evidence with intermediate outcome measures, and contextualizing the model within the respective complex social system. The use of registries to monitor patients, mine data, and adapt models is also becoming more available and integrated into diabetes care models.⁴⁵ Perhaps one of the more complicated issues here involves appropriate pharmacotherapy in nations where options are very limited. More specifically, current US diabetes algorithms do not favor sulfonylureas as part of monotherapy, dual therapy, or even triple therapy because of risks of hypoglycemia and other morbidities.⁴⁶ However, in many nations represented in this special issue, sulfonylureas figure much more prominently because of increased affordability and availability. This is exactly the type of decision making that needs to be evaluated in a chronic disease care model, particularly with the constraints found in developing nations. In cell 5, various public policies will need to be considered that can change an unhealthy culture of living. This includes behavioral economics, oriented toward attitudes about risk,⁴⁷ or legislative acts that encourage healthy eating and avoiding unhealthy foods (eg, foods high in sodium, saturated fat, and trans fat) and behaviors (tobacco or excessive alcohol use) and promote physical activity (eg, using running trails, swimming pools, and other athletic facilities). In many cases, religious dictates provide rigid constraints that affect diabetes care and unfortunately impair caregivers' abilities.^{48,49} Therefore, HCPs must learn about these religious factors to optimize diabetes care.⁵⁰ In some cases, prejudice and discrimination based on religious and ethnic differences affect diabetes care by violating human and social rights. According to the Diabetes Attitudes Wishes and Needs 2 (DAWN2) study, based on data from 17 nations, 11%–28% of people with diabetes feel discriminated against.⁵¹ Benedetti⁵² reviews this topic and finds that discrimination affects relationships, quality of life, finances, leisure activities, and psychosocial well-being, all having potential roles in diabetes management. These issues will also need to be addressed on a large scale with public health policy. In cell 6, effective policy making in a public health model requires up-to-date scientific information and may benefit from better collaboration among

Table 4. Analysis: Cross-tabulation Matrix of Classifiers and Descriptors to Detect Emergent Properties for Diabetes Care*

Descriptors			
Classifier	Infrastructure	Culture	Biology
Knowledge	(1) Pharmacoeconomics Effects of lifestyle change Optimal coordination of health care systems Web-based learning	(2) Surveys on attitudes/awareness Effects of lifestyle components Behavioral medicine research Effects of folk (alternative) medicine Culturally sensitive variables	(3) Basic research Diabetes-related genes Epigenetic mechanisms Complication mechanisms Effects of body composition Effects of pathogens/EDC Effects of DSN Relevant clinical trials Epidemiology
Public Health	(4) Build chronic care models Develop partnerships Community engagement Determine funding levels Marketing campaigns Policy consistent with CPG Prevention programs Improve literacy Address human rights Informatics/registries	(5) Nutritional recommendations Physical activity programs Stress reduction programs Address multiethnic issues Policy making on unhealthy foods, tobacco, and alcohol Behavioral economics Religious dictates	(6) Integrate scientific evidence with policy making Collaborate with pharmaceutical industry to ensure adequate pharmacotherapy available
Durability	(7) Patient education Self-management HCP training HCP-patient communication skills Identify local champions Technology (eg, crowdsourcing, telemedicine)	(8) Transculturalize CPG	(9) Research funding

CPG, clinical practice guidelines; DSN, dietary supplements and nutraceuticals; EDC, endocrine-disrupting compounds; HCP, health care professional.
* Cell numbers (1-9) are given in parentheses. See text for explanations.

government, academia, and industry.⁵³ Of course, adequate funding will be required for all of these public health initiatives.

In cells 7-9, durability for any systems-based recommendations will require educational and research programs that can span generations of patients and HCPs. For instance, Tekola-Ayele et al⁵⁴ point out that after many years preoccupied with infectious disease threats, African nations are behind in using high-

throughput genotyping and unraveling the genetic epidemiology of noncommunicable diseases, such as diabetes. Patient education for self-management also confers durability; this includes self-administration of injectables, such as insulin, and self-monitoring of blood glucose. In 2005, Bergenstal et al⁵⁵ reported the results of a global consensus conference on self-monitoring of blood glucose that can serve as a starting point for individual nations. Many innovations in

Table 5. Synthesis of Core Recommendations to Improve Diabetes Care on a Global Scale

Classifier	Recommendation
Knowledge base	Each nation assesses the region-specific epidemiology, scientific evidence base, especially regarding biological drivers, and population-based transitions to identify higher risk people and establish risk-stratified guidelines for diagnosis and therapeutic interventions
Public health	Each nation establishes a public health imperative to acquire the necessary tools (diagnostics, drugs, supplies, etc.) and funding to successfully implement culturally sensitive guidelines, as well as developing metrics to evaluate and improve these guidelines
Durability	Each nation commits to education and research, with particular focus on pathophysiology and continued interaction on a multinational scale, to advance and optimize the previously listed recommendations for a durable effect

diabetes care will need to be leveraged through the use of high technology, such as handheld devices, crowdsourcing, crowdfunding, telemedicine, and artificial intelligence decision support software to attract and retain patient interest and motivation.⁵⁶ As with many of the initiatives discussed earlier, the major constraint on educational and research advances will be adequate funding, requiring thoughtful prioritization of objectives and deliverables.

SYNTHESIS

Various recommendations can be formulated based on emergent concepts from the analysis of evidence on diabetes care in different nations around the world. There are 3 recommendations in the domains of knowledge, public health, and durability (Table 5). These are all potentially actionable, as the necessary resources for implementation exist, albeit nominally in some regions. The first recommendation relates to expanding the knowledge base but with a strategy directed toward risk stratification. Various risk-stratification scoring systems exist at all levels of preventive care, but many require recalibration⁵⁷ and incorporation of more personalized information, such as transcultural factors, to improve performance. This would allow more pervasive application of public health initiatives in the second recommendation to improve diabetes care

across socioeconomic and disease severity strata. Risk stratification becomes even more relevant when considering the antidiabetes drugs under development and how they can be optimally and cost-effectively used (peroxisome proliferator-activated receptor agonists/modulators, glucokinase activators, glucagon receptor antagonists, anti-inflammatory agents, G-protein coupled receptor agonists, gastrointestinal peptide agonists [other than glucagon-like peptide 1], apical sodium-dependent bile acid transporter inhibitors, sodium/glucose cotransporter 1 and dual 1/2 inhibitors, and 11-beta-hydroxysteroid dehydrogenase 1 inhibitors).⁵⁸ If the current status is inadequate use of diabetes pharmacotherapy, then how can new drugs be introduced and then used to improve this condition, especially with limited funds? The answer may reside in appropriate use of integrated chronic care models with high-performance risk stratifiers. Durability of these recommendations in a changing health care landscape is mandatory and can be facilitated by funding educational programs for patients and HCPs, as well as relevant research projects. These 3 recommendations serve as a starting point to address the complex nature of global diabetes care—to treat populations and individuals, to recognize similarities and differences, and to move more quickly than ever, as the diabetes epidemic has thus far been deaf to our calls for action.

REFERENCES

1. International Diabetes Federation. Global diabetes scorecard. Brussels, Belgium: IDF. Available at: <http://www.idf.org/global-diabetes-scorecard/assets/downloads/Scorecard-29-07-14.pdf>; 2014. Accessed January 1, 2016.
2. Bergman M. Global Health Perspectives in Prediabetes and Diabetes Prevention. Hackensack, NJ: World Scientific Publishing; 2014.
3. Hara K, Shojima N, Hosoe J, Kadowaki T. Genetic architecture of type 2 diabetes. *Biochem Biophys Res Commun* 2014;452:213–20.
4. Mitanhez D, Burguet A, Simeoni U. Infants born to mothers with gestational diabetes mellitus: mild neonatal effects, a long-term threat to global health. *J Pediatr* 2014;164:445–50.
5. Nielsen JH, Haase TN, Jaksch C, et al. Impact of fetal and neonatal environment on beta cell function and development of diabetes. *Acta Obstet Gynecol* 2014;93:1109–22.
6. Ashwal E, Hadar E, Hod M. Diabetes in low-resourced countries. *Best Pract Res Clin Obstet Gynaecol* 2015;29:91–101.
7. Berna G, Oliveras-Lopez MJ, Jurado-Ruiz E, et al. Nutrigenetics and nutrigenomics insights into diabetes etiopathogenesis. *Nutrients* 2014;6:5338–69.
8. Phani NM, Guddattu V, Bellampalli R, et al. Population specific impact of genetic variants in KCNJ11 gene to type 2 diabetes: a case-control and meta-analysis study. *PLoS One* 2014;9:e107021.
9. Wallace DC. A mitochondrial paradigm of metabolic and degenerative diseases, aging, and cancer: a dawn for evolutionary medicine. *Annu Rev Genet* 2005;39:359–410.
10. Freedman BI, Divers J, Palmer ND. Population ancestry and genetic risk for diabetes and kidney, cardiovascular, and bone disease: modifiable environmental factors may produce the cures. *Am J Kidney Dis* 2013;62:1–20.
11. Davidson JD. Brazil Is the New America. Hoboken, NJ: John Wiley & Sons; 2012.
12. McEvoy CT, Cardwell CR, Woodside JV, Young IS, Hunter SJ, McKinley MC. *A posteriori* dietary patterns are related to risk of type 2 diabetes: findings from a systematic review and meta-analysis. *J Acad Nutr Diet* 2014;114:1759–75.
13. Sarmiento OL, Parra DC, Gonzalez SA, González-Casanova I,

- Forero AY, Garcia J. The dual burden of malnutrition in Colombia. *Am J Clin Nutr* 2014;100:1628S–35S.
14. Steptoe A, Hackett RA, Lazzarino AI, et al. Disruption of multisystem responses to stress in type 2 diabetes: investigating the dynamics of allostatic load. *Proc Natl Acad Sci U S A* 2014;111:15693–8.
 15. Kolb H, Mandrup-Poulsen T. The global diabetes epidemic as a consequence of lifestyle-induced low-grade inflammation. *Diabetologia* 2010;53:10–20.
 16. Concha JB, Mezuk B, Duran B. Culture-centered approaches: the relevance of assessing emotional health for Latinos with type 2 diabetes. *BMJ Open Diabetes Res Care* 2015;3:e000064.
 17. Egede LE, Ellis C. Diabetes and depression: global perspectives. *Diabetes Res Clin Pract* 2010;87:302–12.
 18. Fisher EB, Chan JCN, Nan H, Sartorius N, Oldenburg B. Co-occurrence of diabetes and depression: conceptual considerations for an emerging global health challenge. *J Affect Disord* 2012;142(Suppl):S56–66.
 19. Okasha T, Radwan AS. The bidirectional relation between psychiatric disorders with selected cardiovascular and endocrinal diseases: an Egyptian perspective. *Curr Psychiatry Rep* 2015;17:528–36.
 20. Smokovski I. The challenge of diabetes treatment in Macedonia. *EPMA J* 2014;5(Suppl 1):A68.
 21. Cuadros DF, Miller FD, Nagelkerke N, Abu-Raddad LJ. Association between HCV infection and diabetes type 2 in Egypt: is it time to split up? *Ann Epidemiol* 2015;25:918–23.
 22. Raafat N, Abass MA, Salem HM. Malathion exposure and insulin resistance among a group of farmers in Al-Sharkia governate. *Clin Biochem* 2012;45:1591–5.
 23. Jaacks LM, Staimez LR. Association of persistent organic pollutants and non-persistent pesticides with diabetes and diabetes-related health outcomes in Asia: a systematic review. *Environ Int* 2015;76:57–70.
 24. Balti EV, Echouffo-Tcheugui JB, Yako YY, Kengne AP. Air pollution and risk of type 2 diabetes mellitus: a systematic review and meta-analysis. *Diabetes Res Clin Pract* 2014;106:161–72.
 25. McGuire S; Food and Agriculture Organization of the United Nations, International Fund for Agricultural Development, World Food Program. The state of food insecurity in the world 2015: Meeting of the 2015 international hunger targets: taking stock of uneven progress. Rome: FAO, 2015. *Adv Nutr* 2015;6:623–4.
 26. Seligman HK, Bindman AB, Vittinghoff E, Kanaya AM, Kushel MB. Food insecurity is associated with diabetes mellitus: results from the National Health Examination and Nutrition Examination Survey (NHANES) 1999–2002. *J Gen Intern Med* 2007;22:1018–23.
 27. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian Scenario. *Indian J Med Res* 2007;125:217–30.
 28. Thent ZC, Das S, Henry LJ. Rose of exercise in the management of diabetes mellitus: the global scenario. *PLoS One* 2013;8:e80436.
 29. Ramli AS, Taher SW. Managing chronic diseases in the Malaysian primary health care—a need for change. *Malays Fam Physician* 2008;3:7–13.
 30. Chan JCN, Ozaki R, Luk A, et al. Delivery of integrated diabetes care using logistics and information technology—the Joint Asia Diabetes Evaluation (JADE) program. *Diabetes Res Clin Pract* 2014;106(Suppl 2):S292–304.
 31. Moura F, Salles J, Hamdy O, et al. Transcultural diabetes nutrition algorithm: Brazilian application. *Nutrients* 2015;7:7358–80.
 32. Nieto-Martinez R, Hamdy O, Marante D, et al. Transcultural diabetes nutrition algorithm (tDNA): Venezuelan application. *Nutrients* 2014;6:1333–63.
 33. Joshi SR, Mohan V, Joshi SS, Mechanick JI, Marchetti A. Transcultural diabetes nutrition therapy algorithm: the Asian Indian application. *Curr Diab Rep* 2012;12:204–12.
 34. Hussein Z, Hamdy O, Chia YC, et al. Transcultural diabetes nutrition algorithm: a Malaysian application. *Int J Endocrinol* 2013;2013:679396.
 35. Mechanick JI, Marchetti AE, Apovian C, et al. Diabetes-specific nutrition algorithm: a transcultural program to optimize diabetes and pre-diabetes care. *Curr Diab Rep* 2012;12:180–94.
 36. Sapkota S, Brien J, Greenfield J, Aslani P. A systematic review of interventions addressing adherence to anti-diabetic medications in patients with type 2 diabetes—impact on adherence. *PLoS One* 2015;10:e0118296.
 37. Polinski JM, Kim SC, Jiang D, et al. Geographic patterns in patient demographics and insulin use in 18 countries, a global perspective from the multinational observational study assessing insulin use: understanding the challenges associated with progression of therapy (MOSAIC). *BMC Endocr Disord* 2015;15:46.
 38. Zhong Y, Lin PJ, Cohen JT, Winn AN, Neumann PJ. Cost-utility analyses in diabetes: a systematic review and implications from real-world evidence. *Value Health* 2015;18:308–14.
 39. Seuring T, Archangelidi O, Suhrcke M. The economic costs of type 2 diabetes: a global systematic review. *Pharmacoeconomics* 2015;33:811–31.
 40. Chai JP, Chung LC, Wong RY, et al. An evaluation of a web-based diabetes education program designed to enhance self-management among patients living with diabetes. *Comput Inform Nurs* 2012;30:672–9.
 41. Hamdy O, Marchetti A, Hegazi R, Mechanick JI. The transcultural diabetes nutrition algorithm toolkit: survey and content validation in the United States, Mexico, and Taiwan. *Diabetes Technol Ther* 2014;16:378–84.
 42. Tiwari P. Recent trends in therapeutic approaches for diabetes management: a comprehensive update. *J Diabetes Res* 2015;2015:340838.
 43. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev* 2010;23:247–69.
 44. Busetto L, Luijkx KG, Elissen AM, Vrijhoef HJ. Intervention types and outcomes of integrated care for diabetes mellitus type 2: a systematic review. *J Eval Clin Pract* [e-pub ahead of print], <http://dx.doi.org/10.1111/jep.12478>; 2015.
 45. Gabbay RA, Khan L, Peterson KL. Critical features for a successful implementation of a diabetes registry. *Diabetes Technol Ther* 2005;7:958–67.
 46. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm 2015. *Endocr Pract* 2015;21:438–47.
 47. Emoto N, Okajima F, Sugihara H, Goto R. Behavioral economics survey of patients with type 1 and type 2 diabetes. *Patient Prefer Adherence* 2015;9:649–58.
 48. Hassanein M. Ramadan focused diabetes education; a much needed approach. *J Pak Med Assoc* 2015;65(Suppl 1):S76–8.
 49. Grajower MM, Zangen D. Expert opinion and clinical experience regarding patients with type 1 diabetes mellitus fasting on Yom Kippur. *Pediatric Diabetes* 2011;12:473–7.
 50. Green V. Understanding different religions when caring for diabetes patients. *Br J Nurs* 2004;13:658–62.
 51. Peyrot M, Kovacs Burns K, Davies M, et al. Diabetes Attitudes Wishes and Needs 2 (DAWN2): a multinational, multi-stakeholder study of psychosocial issues in diabetes and person-centred

- diabetes care. *Diabetes Res Clin Pract* 2013;99:174–84.
52. Benedetti MM. Discrimination and diabetes. *Diabetes Res Clin Pract* 2014;103:338–40.
53. Lee PY, Lee YK, Ng CJ. How can insulin initiation delivery in a dual-sector health system be optimized? A qualitative study on healthcare professionals' views. *BMC Public Health* 2012;12:313.
54. Tekola-Ayele F, Adeyemo AA, Rotimi CN. Genetic epidemiology of type 2 diabetes and cardiovascular diseases in Africa. *Prog Cardiovasc Dis* 2013;56:1–17.
55. Bergenstal RM, Gavin JR. Global Consensus Conference on Global Monitoring Panel. The role of self-monitoring of blood glucose in the care of people with diabetes: report of a global consensus conference. *Am J Med* 2005;118:1S–6S.
56. Rigla M. Smart telemedicine support for continuous glucose monitoring: the embryo of a future global agent for diabetes care. *J Diab Sci Technol* 2011;5:63–7.
57. van der Leeuw J, van Dieren S, Beulens JW, et al. The validation of cardiovascular risk scores for patients with type 2 diabetes mellitus. *Heart* 2015;101:222–9.
58. Mittermayer F, Caveney E, De Oliveira C, et al. Addressing unmet medical needs in type 2 diabetes: a narrative review of drugs under development. *Curr Diab Rev* 2015;11:17–31.