UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
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PROGRAMA DE PÓS-GRADUAÇÃO EM EPIDEMIOLOGIA

TESE DE DOUTORADO

Panorama global da mortalidade evitável em jovens com diabetes e carga de diabetes e hiperglicemia em adultos nas Américas.

Global view of the amenable mortality from diabetes in the young and burden of diabetes and hyperglycemia in adults in the Americas

Aluno de doutorado: Ewerton Luiz Porto Cousin Sobrinho
Orientador: Prof. Dr. Bruce B. Duncan
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Porto Alegre, janeiro de 2020

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A apresentação deste projeto de tese é exigência do Programa de Pós-graduação em Epidemiologia, Universidade Federal do Rio Grande do Sul, como requisito para obtenção do título de Doutor.

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SUMÁRIO

ABREVIATURAS

AL	América Latina
CID	Classificação Internacional de Doenças
COMO	*Comorbidity Correction*
DALYs	Anos de vida ajustados para incapacidade - *Disability Adjust Life Years*
DCNT	Doenças Crônicas Não Transmissíveis
GBD	Estudo da Carga Global de Doenças - *Global Burden of Disease Study*
IHME	*Institute for Health Metrics and Evaluation*
IMC	Índice de Massa Corporal
MS	Ministério da Saúde
NICE	*National Institute for Health and Care Excellence*
OMS	Organização Mundial da Saúde
SDI	Índice sócio demográfico - *Socio-demographic Index*
SEV	Síntese de exposição de risco - *Summary Exposure Value*
TMREL	Risco mínimo teórico de exposição ao risco - *Theoretical Miminum Risk Exposure Level*
UFMG	Universidade Federal de Minas Gerais
YLDs	Anos vividos com incapacidade - *Years Lived with Disability*
YLLs	Anos de vidas perdidos por mortalidade prematura - *Years of Life Lost*

RESUMO

Contexto: As doenças crônicas não transmissíveis (DCNT) são responsáveis por mais de 60% da carga global de doenças avaliada em 2017. O custo das DCNTs são escalantes e poderão prejudicar o desenvolvimento econômico das nações. A Organização Mundial da Saúde lidera um esforço internacional para o controle e prevenção dessas doenças atualmente referido como Agenda 5x5 para DCNTs. Entre as principais 4 DCNTs, o diabetes é a única doença que apresentou aumento nas taxas padronizadas por idade nas últimas décadas, motivo de preocupação global. Digno de nota também, a mortalidade por diabetes em jovens é próxima de zero em países de alta renda com bons programas de atendimento, mas o panorama global não é conhecido. Dessa forma, um indicador da mortalidade por diabetes nesta faixa etária poderia demonstrar os graus de sucesso da implementação de cuidados básicos de saúde para diabetes e também monitorar os níveis de mudanças. A carga de diabetes em muitos países das Américas é muito alta quando comparada à carga global, embora até agora pouco tenha sido explorado para estampar as diferenças entre regiões e países. O objetivo desta tese é apresentar uma métrica para mortalidade por diabetes nos jovens no mundo; e descrever a carga de diabetes nas Américas em adultos.

Métodos: Foram utilizadas estimativas do Global Burden of Disease 2017. Para este estudo, mortes por diabetes foram consideradas quando o código CID10 reportado foi entre E10 e E14 e P70.2. Para as medidas não fatais, diabetes foi definido a partir de exame laboratorial de glicemia de jejum >7 mmol/L (126 mg/dL), ou uso de medicamento para diabetes. Hiperglicemia foi definida como resultado de glicemia de jejum maior que 4,8-5,4 mmol/L (86-97 mg/dL). Foram considerados indivíduos jovens aqueles menores de 25 anos de idade, e adultos aqueles com 25 anos ou mais. Foram apresentadas estimativas para mortalidade, prevalência, incidência, anos de vida perdidos (YLLs – years of life lost), anos de vida vividos com incapacidade (YLDs – years lived with disabilitty), e a soma dos dois últimos, anos de vida perdidos ajustados por incapacidade (DALYs – disability adjusted life years). Além disso, analisamos a correlação entre as taxas por idade padronizada e o Índice Sócio Demográfico (SDI – socio-demographic index)

Resultados: A taxa de mortalidade por idade padronizada devido ao diabetes em indivíduos menores de 25 anos diminuiu 20% entre 1990 e 2017, sendo 0,36 (Intervalo de Incerteza [II] I95%:0,33 – 0,38) mortes /100.000 em 2017. Os países de médio-baixo e baixo SDI apresentaram as maiores taxas, 0,48 (II95%:0,44 – 0,53) /100.000 e 0,44(II95%: 0,41 – 0,49)

/100.000. Essas taxas contrastam com as encontradas nos países de alto SDI, 0,11 (II95%:0,11 – 0,12) /100.000. Há notável variação mesmo entre países de SDI semelhante. As Américas apresentaram uma maior carga de diabetes do que a média mundial. Em 2017 a taxa de DALYs padronizada por idade nas Américas foi de 51,0 (II95%: 49,1 – 53,0)/100.000, um aumento de 17% em relação a 1990. As taxas de DALYs por idade padronizadas na América Latina Central (98,4 /100.000; 94,2 – 102,7) e no Caribe (74,9 /100.000; 70,3 – 79,8) foram notadamente maiores que nas demais regiões. Essas regiões também apresentaram altas prevalências de diabetes e altas frações atribuíveis na população para obesidade e alimentação inadequada. **Conclusão:** As estimativas da mortalidade por diabetes abaixo de 25 anos, supostamente decorrentes de complicações agudas do diabetes, foram cerca de quatro vezes mais altas em países de baixo/médio SDI comparativamente aos de alto SDI, sugerindo que essa métrica seja um bom indicador para monitorar os cuidados básicos para o diabetes. A carga de diabetes nas Américas é maior que a carga global, especialmente na América Latina Central e no Caribe.

ABSTRACT

Background: The noncommunicable diseases (NCDs), accounted for more than 60% of the global disease burden in 2017. The costs of NCDs are high, and could spoil the economic development of nations. The World Health Organization leads an international effort to control and prevent these diseases currently referred as the 5x5 Agenda for NCDs. Of the 4 major NCDs, diabetes is the only one that shows increasing in the age-standardized deaths and DALYs rates in recent decades, cause of global concern. Noteworthy also, diabetes mortality in young people is close to zero in high-income countries with good health care programs, but the global picture is unknow. Thus, an indicator of diabetes mortality in this age group can demonstrate the degree of success of implementing basic health care for diabetes and also monitor levels of change. The burden of diabetes in many countries of the Americas are very high compared to the global average, however, to date, little effort has been done for highlight the differences between regions and countries. The purpose of this dissertation is to present a metric of diabetes mortality in young people worldwide; and describes the burden of diabetes in the Americas in adults.

Methods: Was used estimates from the Global Burden of Disease (GBD) 2017. For this study, diabetes deaths were defined when the ICD10 code reported was between E10 and E14 and P70.2. For nonfatal measures, diabetes was defined as fasting blood glucose≥ 7 mmol / L (126 mg / dL), or use of diabetes medication. Hyperglycemia, referred as High Fasting Plasma Glucose, was defined as a result of fasting glucose greater than 4.8-5.4 mmol / L (86-97 mg / dL). We considered young people those under 25 years old, and adults those aged 25 years or older. We presented estimates for deaths, prevalence, incidence, years of life lost (YLLs), years lived with disabilities (YLDs), and the sum of the last two, disability adjusted life years (DALYs). In addition, we analyzed a correlation between age-standardized rates and the Socio-Demographic Index (SDI).

Results: The age-standardized mortality rate due to diabetes in young decreased by 20% between 1990 and 2017, being 0.36 (Uncertainty Interval [UI] I95%: 0.33 - 0.38) deaths / 100,000 in 2017. The low-middle and low SDI countries had the highest age-standardized mortality rates, 0.48 (UI95%: 0.44 - 0.53) / 100,000 and 0.44 (UI95%: 0.41 - 0.49) / 100,000 respectively. These rates contrast with those found in the high SDI countries, 0.11 (UI95%: 0.11 - 0.12) / 100,000. Was found a notably variation between countries with similar SDI.

The Americas had a greater burden of diabetes than the world average. In 2017, the age-standardized DALYs rate in the Americas was 51.0 (UI95%: 49.1 - 53.0) / 100,000, an increase of 17% from 1990. The age-standardized DALYs rates in Central Latin America (98.4 / 100,000; 94.2 - 102.7) and the Caribbean (74.9 / 100,000; 70.3 - 79.8) were notably higher than in other regions. These regions also showed high diabetes prevalence, and high population attributable fractions for obesity and poor diet.

Conclusion: The diabetes mortality in young, mostly due to acute diabetes complications, were about 4 times higher in the low and low-middle SDI countries, compared to the high SDI countries, suggesting that this metric is a good indicator for monitoring the basic care of diabetes. The burden of diabetes in the Americas is greater than globally, especially in Central Latin America and the Caribbean.

APRESENTAÇÃO

Este trabalho consiste na tese de doutorado intitulada “Panorama global da mortalidade evitável em jovens com diabetes e carga de diabetes e hiperglicemia em adultos nas Américas”, apresentada ao Programa de Pós-Graduação em Epidemiologia da Universidade Federal do Rio Grande do Sul, em 23 de janeiro de 2020. O trabalho é apresentado em três partes, na ordem que segue:

1. Introdução, Revisão da Literatura, Objetivos
2. Artigos
3. Considerações Finais.

Documentos de apoio estão apresentados nos anexos.

INTRODUÇÃO

Em 2015, as DCNT foram as principais causas de mortes globalmente, sendo responsáveis por 70% (40 milhões) do total de mortes no mundo.(1) A Organização Mundial da Saúde (OMS) tem enfatizado a importância das Doenças Crônicas Não Transmissíveis (DCNT) e propondo estratégias para sua prevenção, (2) baseadas em quatro doenças e quatro fatores de risco.(3)

Estimativas econômicas sugerem que os custos com a epidemia de DCNT ameaçam o desenvolvimento econômico dos países de baixa e média renda.(4,5) Entretanto, as nações em geral não assumiram o desafio de confrontar as DCNT.(6) O diabetes foi identificado como uma das principais DCNTs nos seus Planos de Ações Globais.(2,7). E entre elas, o diabetes é a única doença que apresenta crescimento nas taxas padronizadas por idade para mortalidade e anos de vida ajustados por incapacidade (DALYs – *disability-adjusted life years*) entre 1990 e 2017, 11,6% e 16,9%, respectivamente.(8) Além disso, as previsões sugerem que em 2040 ocorrerão mais de 3 milhões de óbitos devido ao diabetes.(9)

Muitos países nas Américas têm alta prevalência de diabetes e estima-se que a região tenha observado um total aproximado de 350 mil óbitos em 2016.(10–12) No entanto, poucos estudos avaliam o panorama do diabetes e níveis intermediários de glicemia, conhecidos por pré-diabetes(13) ou hiperglicemia intermediária(14). Esses estudos poderiam evidenciar que regiões nas Américas apresentam as maiores cargas de diabetes, explorando que fatores poderiam contribuir para essas diferenças.

Óbitos devido ao diabetes em menores de 25 anos de idade são ocasionados majoritariamente por complicações agudas do diabetes, nomeadas cetoacidose diabética, estado hiperglicêmico hiperosmolar e hipoglicemia. Mortes devidas a essas complicações agudas alcançaram níveis próximos de zero em países de alta renda, onde existe boa cobertura para cuidados de saúde integrados.(15) Sendo assim, é razoável assumir que a mortalidade por complicações agudas do diabetes deveria ser perto de zero, globalmente, se cuidados de saúde semelhantes fossem fornecidos, incluindo disponibilidade e acesso a insulina.(16,17) Embora esses cuidados ainda não sejam a realidade ao redor do mundo, alguns países de baixa e média renda tiveram rápidos avanços no cuidado do diabetes. Não há um indicador simples de mortalidade que permita monitorar a qualidade dos cuidados de saúde para minimizar óbitos evitáveis por essas complicações em pessoas com diabetes, principalmente naquelas com diabetes tipo 1.

Os dados do estudo da Carga Global de Doenças (*Global Burden of Disease*, GBD), permitem explorar a possibilidade de um indicador de óbitos evitáveis em pessoas com diabetes. O indicador poderia ser desenvolvido para pessoas com idade abaixo de 25 anos, quando a principal causa de óbito são as complicações agudas do diabetes tipo 1, supostamente evitáveis com boa cobertura de atendimento básico.

O GBD, com seus métodos padronizados, realizados através de uma coleta dados de maneira sistemática, gera estimativas, globais e para regiões e países. Essas estimativas são obtidas por uma ferramenta atualizada e publicamente disponível, permitindo monitoramento simples dos níveis de mortalidade e de carga de doenças nos países e regiões, assim como suas tendências.

Assim, essa tese tem por objetivo descrever a carga e tendência de diabetes nas Américas e suas regiões entre 1990 e 2017, assim como apresentar uma métrica para mortalidade por diabetes nos jovens no mundo entre 1990 e 2017.

JUSTIFICATIVA

Segundo dados do GBD, as DCNT foram responsáveis por 73% das causas de morte no mundo em 2017, valor 27% maior do que em 1990 (61%).(8) Em termos de proporção de DALYs, o aumento é ainda maior, 44%, passando de 43% do total dos DALYs em 1990 para 62% em 2017.(8) O número de DALYs devido ao diabetes aumentou 117% em 2017 em relação a 1990, sendo o aumento e o envelhecimento da população os principais responsáveis.(8) Alguns países das Américas apresentam altas prevalências, tendo passado por rápida transição epidemiológica, com aumento e envelhecimento populacional, e rápida transição nutricional, sem estarem preparados para lidar com esta carga adicional de doença, que se soma a problemas de natureza infecciosa, nutricional ou materno-infantil ainda não controlados.

O diabetes além de ser uma das principais DCNTs, é também um fator de risco para outras DCNT através da hiperglicemia. Dentre as DCNTs, o diabetes e hiperglicemia são as condições consideradas mais fora de controle.(18,19) Por essa razão, pode-se afirmar que o diabetes e seus fatores de risco recebem menos atenção nas políticas públicas do que deveriam. Uma das possíveis causas para isso seria a falta de dados para documentar sua importância.(20) Os resultados dessa proposta pretendem contribuir com a descrição das cargas e tendências do diabetes nas Américas, contribuindo para sua "*advocacy*" para governos e sociedade.

Para tanto, serão realizadas análises sobre o estado atual e as tendências recentes do diabetes e seus fatores de risco nas Américas. O projeto GBD, o qual a base é o *Institute for Health Metrics and Evaluation* (IHME) da Universidade de Washington, Seattle, estabeleceu-se como líder na produção de dados dessa natureza, gerando estimativas da carga de doenças para aproximadamente 195 países e territórios, e contendo informações de mortalidade e incapacidade para 359 doenças e lesões, além de sequelas e fatores de risco, por idade e sexo.(10,21–24)

Outro aspecto importante a ser tratado, ainda se observa um grande número de mortes por complicações agudas do diabetes em países de baixa e média renda, que poderiam ser evitados com cuidados de saúde adequados e acesso e disponibilidade de insulina. Um estudo realizado no Brasil, demonstra que com a implementação do Sistema Único de Saúde, com acesso a cuidados de saúde, incluindo insulina; foi observada uma rápida diminuição de mortes por complicações agudas do diabetes.(25) Um indicador para monitorar anualmente os cuidados de saúde dos diabéticos e dos avanços alcançados, destacando aonde medidas preventivas poderiam ser tomadas, poderia contribuir para diminuir esses óbitos. O GBD permite explorar métricas simples para detectar essas mortes, potencialmente evitáveis, gerando um panorama global para identificar contrastes e sinalizar países que requerem maior intervenção.

REVISÃO DE LITERATURA

1 Diabetes

Diabetes mellitus é uma doença crônica caracterizada pelo aumento do nível de glicose na corrente sanguínea devido a não produção ou produção insuficiente do hormônio insulina.(26) A insulina é produzida pelas células beta no pâncreas, e tem por função o transporte da glicose da corrente circulatória até o interior das células, onde é convertida em energia. A falta de produção, ou produção insuficiente, frequentemente frente a níveis elevados de resistência à insulina, faz com que os níveis de glicose na corrente sanguínea fiquem elevados, o que é chamado de hiperglicemia, e que é a marca do diabetes.

O quadro de hiperglicemia durante um largo período de tempo pode causar danos a vários órgãos, levando ao desenvolvimento de complicações de saúde que podem causar a morte.

1.1 Classificação

Os dois principais tipos de diabetes são o diabetes tipo 1 e o diabetes tipo 2, mas há também outros tipos específicos de diabetes e uma hiperglicemia detectada na gravidez, chamada de diabetes gestacional.(27)

O diabetes tipo 1 é caracterizado por processo autoimune de destruição das células betas do pâncreas, o que resulta em dependência de insulina externa para sobrevida. A não reposição eleva a glicemia e evolui para cetoacidose, coma e morte.(27) Esse tipo de diabetes é mais comum em crianças e adolescentes.

O diabetes tipo 2 é a forma mais frequente da doença, correspondendo a 90% de todos os casos de diabetes globalmente. É caracterizado por disfunções na sensibilidade e na secreção da insulina, e por aumento da produção de glicose pelo fígado.(27,28)

O diabetes é diagnosticado laboratorialmente através de uma glicemia plasmática de jejum maior ou igual que 126 mg/dL (7,0 mmol/L), ou glicemia plasmática pós 2h sobrecarga maior ou igual a 200mg/dL (11,1 mmol/L), ou hemoglobina glicada maior ou igual a 6,5.(29) Além disto, existem níveis de glicose que não são tão altos para serem definidos como diabetes, mas também não podem ser classificados como normais, chamados níveis intermediários de hiperglicemia, referidos como pré-diabetes ou hiperglicemia intermediária.(13,29)

1.2 Fatores de risco para diabetes

Revisão sistemática guarda-chuva ampla sobre os fatores de risco para o diabetes tipo 2 mostra fatores com convincente ou forte evidência, sendo os principais os fatores alimentares, a obesidade, a inatividade física, e outras condições médicas (como a síndrome metabólica).(30)

A história familiar de diabetes é um fator de risco bem conhecido e marcadores genéticos específicos estão sendo investigados podendo futuramente auxiliar na predição do diabetes. O sexo feminino foi considerado fator de risco pela sua maior prevalência em estudos de auto-relato, mas na maior parte do estudos que utilizam medidas laboratoriais a prevalência é discretamente mais elevada em homens.(31,32) Minorias, provavelmente em função das condições desfavoráveis de vida enfrentadas, frequentemente apresentam maior prevalência.(32)

A alimentação inadequada é um dos principais fatores de risco para diabetes, e também é um fator de risco para a obesidade, considerada o principal fator de risco para o diabetes tipo 2. Revisão sistemática publicada em 2019 avalia a evidência que apoia vários fatores alimentares no desenvolvimento do diabetes tipo 2, mostrando que existe uma forte evidência do aumento da incidência de diabetes associada a um alto consumo de bebidas açucaradas, carnes vermelhas, carnes processadas, e bacon.(33) Por outro lado, fatores alimentares protetores para a incidência de diabetes foram o consumo de grão integrais e cereais, e também o consumo moderado de álcool.(33) As análises realizadas pelo GBD encontraram resultados semelhantes, sendo os principais fatores de risco para diabetes o consumo deficiente de grãos integrais, castanhas, sementes, e frutas frescas, e alto do consumo de bebidas açucaradas, carnes processadas e a carne vermelha.(23) O consumo de alimentos ultra processados tem aumentado durante as últimas décadas(34) e mostrou-se associado ao ganho de peso (35,36) e ao diabetes(37).

Outros fatores de risco para diabetes são inatividade física, estresse e tabagismo.(28) A poluição do ar vem sendo apontada como importante fator de risco como sumarizado em revisão sistemática. (38)

Os principais fatores de risco cardiometabólicos são: resistência à insulina, hiperglicemia intermediária (pré-diabetes), hipertensão e diabetes gestacional.

A região das Américas apresenta um baixo consumo de alimento dos alimentos considerados protetores para diabetes, além de apresentar um maior consumo de bebidas açucaradas, quando comparados com os valores globais.(39)

1.2.1 Obesidade

O índice de massa corpórea (IMC) elevado foi responsável por 46% da carga de diabetes no mundo em 2017, um aumento de 55% em relação a 1990, sendo o principal fator de risco para diabetes.(8) A obesidade é uma doença caracterizada pelo excesso da gordura corporal não saudável.(28) Estima-se que no mundo 107 milhões de crianças são obesas, e 603 milhões de adultos.(19)

Para definir esse aumento é utilizada a medida do IMC, que é o peso dividido pela altura ao quadrado. Em adultos, indivíduos com IMC entre 25 e 29,9 kg/m² são considerados com sobrepesos, já indivíduos com IMC maior ou igual a 30 kg/m² são considerados obesos.(40) A obesidade pode ser definida em 3 classes, sendo a classe 1 de 30 a 34,9kg/m², classe 2 de 35 a 39,9kg/m² e a classe 3 acima de 40,0kg/m².(40)

Para crianças e adolescentes a definição de obesidade a partir do IMC é feita através de curvas do crescimento utilizando escore z e desvios padrão de acordo com a idade.

Entre 1990 e 2015 a prevalência de indivíduos obesos tem aumentado globalmente, tanto para crianças e adolescentes, como nos adultos, com prevalências de 5% e 12% respectivamente.(19) O pico de prevalência observado foi nas idades de 60 a 64 anos nas mulheres e 50 a 54 anos nos homens(19) (Figura 1)

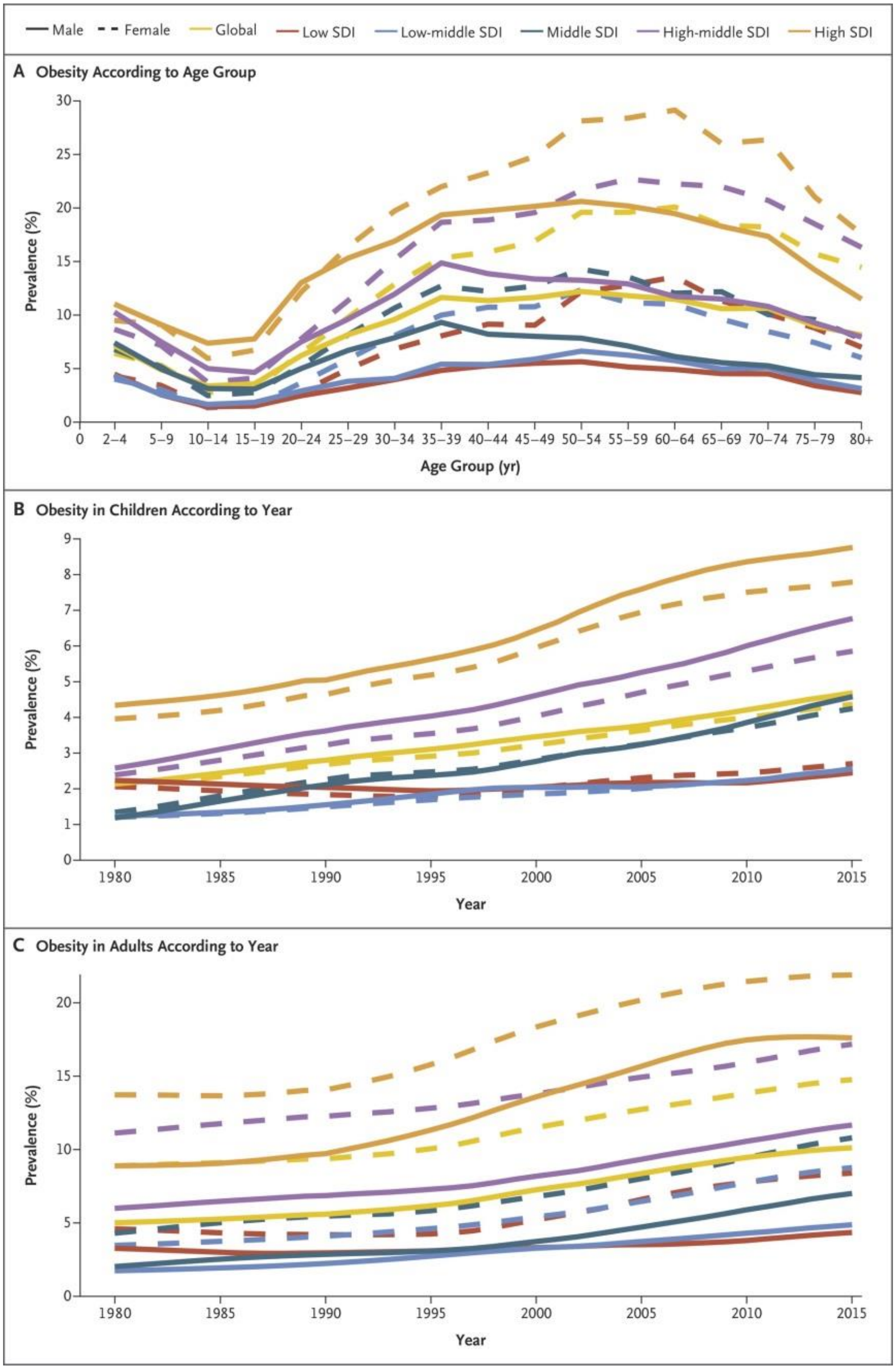

Figura 1 – Prevalência de obesidade a nível global, e de acordo com o índice-sócio demográfico. Fonte: GBD 2015 Obesity Collaborators. "Health effects of overweight and obesity in 195 countries over 25 years." New England Journal of Medicine 377.1 (2017): 13-27.(19)

A obesidade é causada por uma ingestão excessiva de calorias em relação ao gasto energético por um longo período de tempo.(28) Fatores genéticos, ambientais, comportamentais e metabólicos através de suas complexas interações são os principais responsáveis pelo aumento do peso. Fatores genéticos, através de mutações genéticas, são responsáveis primários de obesidade apenas para um pequeno percentual dos indivíduos obesos. Diferentes fatores comportamentais modificáveis estão associados a esse aumento do peso, entre eles destacam-se a dieta não saudável, baixa atividade física, sedentarismo e poucas horas de sono.(41) Dentre os fatores dietéticos, atualmente tem se destacado o consumo de alimentos ultraprocessados, com o maior consumo deste tipo de alimentos estando associado a um maior risco de desenvolverem sobrepeso e obesidade(35,36).

Uma vez instalada, obesidade é extremamente difícil de ser revertida, salientando a importância de sua prevenção(41) A obesidade é um fator de risco para diversas doenças, e obesidade abdominal está associada à resistência à insulina.(28,41) Além disto, o risco para desenvolver diabetes tipo 2 aumenta linearmente conforme aumenta o IMC.(28) O IMC elevado é também um fator de risco para síndrome metabólica, hipertensão, doença cardíaca coronariana, doenças cerebrovasculares e tromboembólicas, dislipidemia, doenças respiratórias, câncer, assim como doenças musculo-esqueléticas.(28)

As ações para a prevenção da obesidade estão relacionadas ao controle de seus fatores de risco. Estas práticas começam desde o início da vida, com aleitamento materno, e cuidados na infância e adolescência com alimentação saudável e atividade física, que devem ser mantidos na vida adulta.(41) O National Institute for Health and Care Excellence (NICE) tem recomendações para prevenir o excesso de ganho de peso.(42) Essas recomendações baseiam-se principalmente em estimular a realização de atividade física, a ter hábitos dietéticos que reduzem o risco de excesso de ingestão calórica, limitar o consumo de álcool e o auto monitoramento regular do peso. Além disto, comunicar os benefícios da manutenção do peso saudável, e da melhora gradual da atividade física e hábitos dietéticos. (41,42)

1.3 Prevenção do diabetes e suas complicações

A prevenção do diabetes pode ser realizada primeiramente pelo controle na população dos principais fatores de risco para a doença. Além disto, pode ser feita pela identificação dos indivíduos com maior risco de desenvolver diabetes, como naqueles que apresentam tolerância a glicose diminuída. A detecção através do teste de tolerância à glicose é muito complexa para ser feita largamente na população, podendo então ser realizada através de estratégias escalonadas iniciando com escores de risco simples para, após isso, realizar o teste de tolerância a glicose. Intervenções de mudanças no estilo de vida podem prevenir ou retardar o aparecimento da doença em aproximadamente 50% dos casos com tolerância à glicose alterada. Em casos onde a mudança no estilo de vida não consiga ser efetiva, pode ser realizado o tratamento farmacológico, com antidiabéticos orais.(41)

Indivíduos com diabetes têm maior probabilidade de mortalidade prematura, existindo uma relação entre níveis acima de 100mg/dl de glicose de jejum e o risco de morte.(43) Essas mortes não necessariamente são causadas pelo diabetes, mas o diabetes pode levar a aumento de mortes associados a doenças cardiovasculares, câncer, doenças renais, doenças infecciosas, causas externas, e doenças degenerativas.(43)

Além disto, a diabetes tem um importante papel econômico, contribuindo para custos tanto diretos com o tratamento e manejo da doença, como também com custos.(44) Estes custos têm grande impacto em países de média e baixa renda, com grande variabilidade entre os países.(44)

O tratamento do diabetes difere em relação ao tipo de diabetes. Nos casos de diabetes tipo 1, onde ocorre deficiência na produção de insulina, o tratamento é baseado no monitoramento da glicose com administração de insulina por injeção ou bomba externa. Nestes casos a dosagem sendo ajustada de acordo com os resultados do auto monitoramento da glicose, a ingestão de alimentos e realização de atividade física.(28)

Nos casos de diabetes tipo 2, onde existe um deficiência relativa na produção de insulina, juntamente com resistência da insulina e aumento da produção de glicose pelo fígado, o tratamento é iniciado com mudanças comportamentais de estilo de vida, principalmente de dieta e atividade física, objetivando também a redução do peso; e também tratamento farmacológico, através de medicamentos de primeira linha.(41) Quando o quadro de hiperglicemia ainda não estiver sobre controle, pode ser introduzido conjuntamente medicamentos de segunda e terceira linha. Em casos específicos de indivíduos com dificuldade de controle metabólico, juntamente com obesidade grau 2 ou mais (IMC $\geq$35kg/m²), pode ser recomendada cirurgia bariátrica.(41)

As complicações causadas pelo diabetes podem ser agudas, nomeadas cetoacidose diabética, estado hiperglicêmico hiperosmolar e hipoglicemia; ou crônicas, micro e macro-vasculares. As complicações agudas do diabetes podem gerar um risco a vida imediato, e necessitam de um cuidado adequado para a recuperação do indivíduo. As complicações crônicas microvasculares são comuns e causam incapacidade nos indivíduos diabéticos, como a retinopatia diabética, a neuropatia diabética; já a nefropatia diabética, pode levar a falência renal.

1.4 Níveis e tendências

Globalmente, estima-se que existam aproximadamente 500 milhões de pessoas com diabetes em 2017, sendo 23 milhões de casos novos neste ano.(24) O número de casos prevalentes aumentou 29,8% entre 2007 e 2017, nesse mesmo período, a taxa de prevalência aumentou 14,7% , chegando a 6,2 por casos prevalentes por 100,000.(24)

Nas Américas, a prevalência de diabetes em adultos foi estimada entre 7,3% e 8,3%, e com um aumento de 22,5% entre 2007 e 2017, valores maiores do que os estimados globalmente.(8,12) Alguns países das Américas estão entre os com índices mais altos de prevalência de diabetes, como Trinidad e Tobago e Porto Rico.(8)

Em 2015, estima-se que no Brasil 12 milhões de pessoas tinham diabetes(20) Entre 2010 e 2015, foi estimado que ocorreram 450 mil novos casos por ano, com um aumento na taxa de incidência nesse período de 75%, apresentando a taxa de incidência em 2015 de 0,63%. A prevalência de diabetes aumentou 69% nesse período passando de 3,6% em 1990 para 6,1% em 2015. Um dos fatores associados ao aumento da prevalência de diabetes é o envelhecimento da população, uma vez que o aumento da prevalência de diabetes entre 1990 e 2015 padronizado por idade foi de 17%.(20)

1.5 Mortalidade

O número de mortes causadas pelo diabetes no mundo aumentou 34,7% [32,2 – 37,3] entre 2007 e 2017, chegando a aproximadamente 1,4 milhões em 2017.(21) Já a taxa de mortes por idade padronizada teve um aumento de 1,2% [-0,7 a 3,1] entre 2007 e 2017, correspondendo a 17,5 por 100.000 em 2017.(21)

De acordo com a Organização Pan Americana de Saúde, houve um total de aproximadamente 350 mil mortes devido a diabetes em 2016 nas Américas. com uma taxa de 33.1 por 100.000 habitantes, sendo maior na região do Caribe não latina.(12) Já, pelas estimativas do GBD, o total número de mortes foi de 263 mil em 2017, e a taxa de 25,6.(8) O diabetes estava entre as três principais causas de morte na maioria dos países das Américas.

1.6 Carga de doença

Quando analisados os anos de vidas perdidos por mortalidade prematura (YLLs – *Years of Life Lost*), em termos de números absolutos houve um aumento de 29,9%[27,2 – 32,4] entre 2007 e 2017, por outro lado, as taxas de YLLs padronizadas por idade apresentaram aumento de 0,7% (-1,4 a 2,6) no mesmo período.(21) A diabetes não é apenas uma causa de morte, mas também uma doença que gera incapacidade, em 2017 ocupou o quarto lugar entre as causas de anos vividos com incapacidade (YLDs - *Years Lived with Disability*), correspondendo a mais de 38 milhões de YLDs, um aumento de 30% desde 2007 em termos de números absolutos.(24) Quando analisados taxas de YLDs por idade padronizada, houve um aumento de 3,9% entre 2007 e 2017.(24)

Em termos de DALYs, o aumento global absoluto devido a diabetes entre 2007 e 2017 foi de 30%, e entre 1990 e 2016 foi de 117%, totalizando mais de 67 milhões de DALYs em 2017.(10) Grande parte desde aumento se deve ao aumento da população e ao envelhecimento da população, com as taxas padronizadas por idade mostrando um aumento de apenas 16,9% entre 1990 e 2017, e de 2,5% entre 2007 e 2017. Para 19 dos 37 países da super região GBD America Latina e Caribe, a diabetes apresenta o valor de DALYs observado maior do que seria o esperado de acordo com o SDI de cada país.(45) Além disso, o diabetes é a principal causa de DALYs em alguns países das Américas, como México, Trinidad e Tobago e Jamaica.(8)

O Brasil apresenta taxas da DALYs mais altas do que as mundiais, tanto para todas as idades, como quando padronizadas por idade.(20) Entre 1990 e 2016 houve um aumento de 118,6% em números de DALYs atribuíveis a diabetes, sendo 42% devido ao aumento da população, 72% devido ao envelhecimento da população e 4,6% devido ao aumento da taxa.(20)

2 Plano de enfrentamento / Metais globais OMS e Plano enfrentamento DCNT Brasil

Em virtude do aumento das DCNT, em 2012 na Assembleia Mundial de Saúde, aprovou a meta de redução de 25% da mortalidade prematura por DCNT globalmente, entre os anos de 2013 e 2020. Para atingir este objetivo, foram definidas metas para serem alcançadas, na redução dos quatro principais fatores de risco para DCNT, que são: consumo de tabaco, consumo nocivo de álcool, alimentação não saudável, e inatividade física.(2,46)

Em consulta com os Estados membros foi definido um quadro de monitoramento com indicadores, compreendendo mortalidade e morbidade, fatores de risco, e resposta dos sistemas nacionais.(47)

No Brasil, o Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas Não Transmissíveis 2011-2022, do Ministério da Saúde (MS), teve como objetivo preparar o Brasil para deter e enfrentar as DCNT nesses 10 anos.(46) O Plano aborda os quatro principais grupos de doenças, que são circulatórias, câncer, respiratórias crônicas e diabetes. Desta maneira promovendo o desenvolvimento e a implementação de políticas públicas efetivas, integradas, sustentáveis; baseadas em evidências para prevenção e controle das DCNT e seus fatores de risco; adicionalmente, fortalecendo os serviços de saúde voltados às DCNT.(46)

Para combater a obesidade e diabetes, a OMS adotou o Plano de Ação Global para prevenção e controle de DCNT, com metas de parar o crescimento da prevalência de diabetes em indivíduos adultos (≥18 anos) e também a prevalência de sobrepeso e obesidade em crianças e adolescentes, e deter o crescimento do excesso de peso (IMC≥25k/m²) em indivíduos adultos, (≥ 18 anos).(2) No Brasil, o plano de enfrentamento teve objetivos semelhantes para deter a obesidade, tanto para crianças e adolescentes como para adultos.(46) Para o diabetes, embora não tenham sido definidas ações diretas para redução da prevalência no plano de enfrentamento no Brasil, o mesmo aborda a redução dos fatores de risco em comum aos quatro principais grupos de DCNT, incluído o diabetes.(2,19,46)

3 Global Burden of Disease

O estudo Carga Global de Doença (GBD – *Global Burden of Disease*) é descrito como um esforço científico sistemático para quantificar a magnitude das doenças, lesões e fatores de risco. O estudo consegue descrever as estimativas por sexo, para faixas de idade, e diferentes períodos de tempo.(48)

O objetivo do estudo é auxiliar os tomadores de decisão em políticas de saúde a identificarem os principais problemas sofridos para cada região, e assim serem mais efetivos em suas ações. Essas estratégias podem ser feitas a níveis locais, regionais, nacionais e globais, utilizando as melhores evidencias de dados atualizados.(48)

No ciclo GBD 2017 foram apresentados resultados para 195 países e territórios, e com dados subnacionais alguns países. Descrevendo estimativas para 359 doenças e lesões e 84 fatores de risco e combinações desses fatores, com informações entre 1990 e 2017.

As informações são obtidas através de dados vitais governamentais, censos e estudos de base populacional. O GBD disponibiliza seus dados de forma aberta, após as publicações principais "*capstone*". E disponibiliza todas as fontes de dados e programações utilizadas para ser o mais transparente possível.(10,21–24)

Para realizar as estimativas por localidade, sexo, idade, e ano, o GBD utiliza seus métodos padronizados de análise. Entre as ferramentas utilizadas estão o CODEm (*Cause of Death Ensemble model*), que é um conjunto de modelos utilizado para estimar a mortalidade; DisMod MR 2.1 que é uma meta-regressão Bayesiana, e ST-GPR (*Spatio Temporal Gaussian Process Regression*). O GBD está em constante evolução e a cada ciclo são realizados avanços em termos de inclusão de novos estudos, e aprimoramento dos métodos e criação de novas ferramentas.

3.1 Rede GBD Brazil

A rede GBD Brazil Network foi criada em 2015, sendo uma parceria entre o Ministério da Saúde, IHME, Universidade Federal de Minas Gerais (UFMG) e demais colaboradores do GBD, e tem por objetivo melhoras os dados fornecidos pelo Brasil para o estudo, estimar os dados por estados, buscando no futuro ter dados a níveis de regiões de saúde. Além disso, também busca realizar estudos sobre a carga de doença no Brasil, indicando os principais focos de novas políticas de saúde.

Outro objetivo do GBD Brazil *Network* é facilitar o uso de dados do GBD pelos tomadores de decisões políticas públicas. Recentemente foi publicado um volume do Saúde Brasil com análises das principais doenças por estados, realizadas pelas próprias secretarias estaduais de saúde para a identificação de prioridades em saúde.(49) Atualmente está sendo realizada a tradução do *GBD online course* para português, para realizar treinamentos para os gestores e tomadores de decisão de políticas em saúde, assim como também, equipes de saúde.

3.2 Principais Indicadores

3.2.1 Mortalidade

O GBD produz estimativas dos valores absolutos e taxas de mortalidade para os países e territórios. As estimativas são baseadas em dados de registros vitais e censos dos países, assim como estudos de autopsias verbais e pesquisas. Resumidamente, as estimavas de mortalidade são geradas a partir da padronização das fontes de dados, mapeando os códigos da Classificação Internacional de Doenças (CID) 9 e CID 10 para causas de morte, e gerando valores separados por sexo e idade, quando são obtidos apenas dados gerais. Após isso é feita a redistribuição dos chamados “garbage codes”, que são causas que não podem ser atribuídas a causas básicas de morte (como por exemplo, mortes por sepse, consideradas causas implausíveis para serem verdadeiras causas básicas de morte). A redistribuição dos “*garbage codes*” para causas plausíveis é realizada utilizando métodos de redistribuição através de regressões e proporções. Após isso, múltiplos modelos são aplicados, levando em conta subnotificação de óbitos quando necessário, para estimar as causas de morte através do conjunto de modelos do GBD (CODEm - *Cause of Death Ensemble model*). Após isto é realizada o procedimento de correção “CodCorrect” para garantir a consistência interna entre todas as causas de morte, para que a soma de todas as causas de morte não seja diferente do número total de mortes em determinado ano, sexo, idade, localidade.(21,22)

O GBD apresenta causas de morte divididas hierarquicamente, sendo mutuamente exclusivas e coletivamente exaustivas. Após isso são feitas correções para algumas doenças específicas que podem apresentar características diferentes, como subnotificadas ou muito notificadas em algum período, como o HIV e o Alzheimer.

3.2.2 YLLs

Os anos de vidas perdidos, YLLs, são uma medida de mortalidade prematura. O cálculo dos YLLs é feito baseado na expectativa de vida padrão para cada grupo de 5 anos de faixa etária, e assim decrescidos a idade em que a pessoa morreu. Por exemplo, se uma pessoa tinha 60 anos no momento de morte e a expectativa de vida padrão para indivíduos com 60 anos é de 28 anos (ou seja, até 88 anos), a morte desse indivíduo representa uma perda de 28 YLLs. A expectativa de vida padrão é baseada no menor risco de morte, entre países do mundo, para cada faixa etária de 5 anos. Para evitar problemas com baixos números, foram utilizados somente países com populações com mais de 5 milhões de indivíduos. Para o GBD 2017 a expectativa de vida padrão no nascimento foi de 86.6 anos.

3.2.3 YLDs

Os anos vividos com incapacidade, YLDs, são a medida de morbidade do estudo. Cada doença pode apresentar sequelas, e essas sequelas geram a incapacidade. Estudos realizados em cinco países (Bangladesh, Indonésia, Peru, Tanzânia e Estados Unidos) foram utilizados para padronizar o peso da incapacidade do estado de saúde gerado por uma determinada sequela. O cálculo para gerar o YLDs é baseado em prevalência da sequela da doença e multiplicado pelo peso da incapacidade atribuída o estado de saúde desta sequela. Este peso é expresso comparando-se o valor de uma vida com a incapacidade específica em comparação com o valor de uma vida em plena saúde. Por exemplo, um ano vivido com cegueira completa (peso da incapacidade do estado de saúde = 0,187) é avaliado como o equivalente a 0,813 (= 1-0,187) anos de vida em saúde plena. Nesse sentido, tecnicamente, YLDs são expressos em anos de vida perdidos devido à presença de incapacidade. Isso permite comparar a carga de mortalidade e a de morbidade baseando-se na mesma escala.

Para corrigir o efeito causado pelas comorbidades, é realizado o processo de micro-simulação chamado de COMO (*Comorbidity Correction*), isto é, utilizado para evitar a superestimação dos YLDs para indivíduos que apresentem mais de uma morbidade. O COMO estima a co-ocorrência de sequelas de doenças em 40,000 indivíduos simulados para cada combinação de localidade, idade, sexo e ano, baseados na independência na probabilidade de ter qualquer sequela das doenças incluídas, baseadas nas prevalências das doenças.(24) A fórmula para essa incapacidade conjunta é um menos a multiplicação da soma de um menos o peso da incapacidade de cada. E a partir do total dessa incapacidade cumulativa, é realizada a ponderação para cada causa separadamente. Sendo assim, na presença de comorbidades, o valor da incapacidade de uma causa será menor do que quando uma causa gerar incapacidade sem a presença de outra, conforme demonstrado na formula abaixo.(24)

$$Simulant\ DW_l = 1 - \prod_{k=i}^{j}(1 - DW_k)$$

Onde DW_k é o peso da incapacidade para a sequela da doença k^{th} que o simulado *I* adquiriu.

$$ADW_{lk} = \frac{DW_k}{\sum_{k=i}^{k=j} DW_k} * Simulant\ DW_l$$

Onde ADW_{Ik} é o peso da sequela atribuível para a sequela da doença *k* no simulado *I*, DWk é o peso da incapacidade para a sequela *k*, e DW_I é o peso da incapacidade para o simulado *I* a partir da combinação de todas as sequelas adquiridas.

$$YLD\ Rate_k = \frac{\sum_{l=1}^{n} ADW_{lk}}{n}$$

3.2.4 DALYs

Os anos de vida perdidos ajustados para incapacidade, DALYs, são a medida sumária que junta mortalidade prematura e incapacidade. Essa medida foi desenvolvida por Murray em 1991. E é formada pela soma dos YLLs e YLDs. Essa métrica permite comparar diferentes tipos de doenças, algumas que causam mais incapacidade (p.ex., dor lombar), com outras cuja carga é principalmente mortalidade (p.ex., infarto de miocárdio).(10)

3.2.5 PAF

O GBD identifica a fração atribuível populacional (PAF – *Populational Attributable Fraction*) para todos os fatores de risco. Este valor considera o quanto diminuiria a carga de doença se um determinado fator de risco estivesse no seu nível mínimo, chamada de TMREL (*theoretical minimum risk level*). Para realizar o cálculo da PAF para cada fator de risco são necessários as estimativas do nível de exposição ao fator, o contrafato do fator (o TMREL), e o risco relativo do desfecho dos níveis do fator, em relação ao TMREL.(23) A PAF é calculada de maneira independente para cada par de fator de risco e desfecho. Nesse processo, o GBD também leva em conta a mediação. Sendo assim, uma mesma morte por uma causa, pode ser atribuída a mais de um fator de risco. Por exemplo, um indivíduo pode ter atividade física insuficiente, que levou a ter IMC elevado, que levou a ter hiperglicemia, que causou diabetes, e esta foi sua causa de morte. Para este indivíduo; esses três fatores de risco pontuariam como fatores de risco para a morte por diabetes.(23)

A formula para o cálculo da fração atribuível populacional para fatores de risco contínuos é apresentada abaixo:(23)

$$PAF_{joasgt} = \frac{\int_{x=l}^{u} RR_{joasg}(x)P_{jasgt}(x)dx - RR_{joasg}(TMREL_{jas})}{\int_{x=l}^{u} RR_{joasg}(x)P_{jasgt}(x)dx}$$

Onde: PAF*joasgt* é a fração atribuível populacional para a causa *o* devido ao fator de risco *j* para o grupo etário *a*, sexo *s*, localidade *g*, e ano *t*. RR*joasg*(*x*) é o risco relativo como função do nível de exposição *x* para o fator de risco *j* para a causa *o*, grupo etário *a*, sexo *s*, localidade *g*, com o mínimo nível de exposição observado como *l* e o máximo como *u*. P*jasgt*(*x*) é a distribuição da exposição em *x* para o grupo etário *a*, sexo *s*, localidade *g*, e ano *t*. TMRELjas é o TMREL para o fator de risco *j*, grupo etário *a*, e sexo *s*.(23)

3.2.6 Intervalo de incerteza

Para reportar a incerteza das estimativas, o GBD utiliza o Intervalo de Incerteza de 95% para cada estimativa. Para criar esses intervalos são gerados 1000 "*draws*", representando a incerteza de cada passo dos processos de estimação – a distribuição de erros de amostragem das fontes de dados, as correções para erros de medidas, as estimativas de erros residuais de não amostragem, e as seleções dos modelos utilizados. Então os percentis 2,5 e 97,5 são utilizados como os limites do intervalo.(21)

3.2.7 Definição de diabetes

No GBD 2017, foram geradas estimativas para diabetes por tipo pela primeira vez. O GBD define que a morte é devido ao diabetes quando a causa básica de morte é os códigos E10-E14, exceto os códigos ".02" que são classificados como doença renal crônica devido ao diabetes. Para esta tese, a fim de avaliar a mortalidade e carga total devido ao diabetes, foram incluídos tanto os casos de diabetes como de doença renal crônica devido ao diabetes.(21)

Para a estimação da carga não fatal do diabetes, o diabetes foi definido como glicemia de jejum maior ou igual que 126 mg/dL (7mmol/L) ou estar em tratamento para diabetes. Em estudos com glicemia de pós carga ou hemoglobina glicada foram realizados "*crosswalks*" de correspondência com glicemia de jejum para permitir sua inclusão dentro de uma medida única. Para definir diabetes, o GBD utilizou apenas estudos de base populacional com testes laboratoriais.(24)

3.2.8 Definição de hiperglicemia como fator de risco

O GBD também considera a diabetes e níveis menores de hiperglicemia como um fator de risco para outras doenças através do fator de risco denominado Glicose plasmática de jejum elevada (*High Fasting Plasma Glucose* – HFPG). A HFPG é definida com um valor de glicemia de jejum maior que o "TMREL, nível teórico de risco mínimo de exposição. O TMREL para HFPG é um valor entre 86 e 97 mg/dL (4,8 – 5,4 mmol/L). Para estimar a distribuição de HFPG por localidade, idade, sexo e ano são utilizados dados contínuos de glicemia, e quando não são relatados de forma contínua, também a prevalência de diabetes. A carga do fator de risco HFPG é definida a partir do cálculo do PAF. No caso específico do par HFPG e diabetes, 100% da carga de diabetes é mediada via HFPG.(10) A Figura 2 demonstra o fluxograma das dimensões da carga de diabetes e HFPG, e seus fatores de risco.

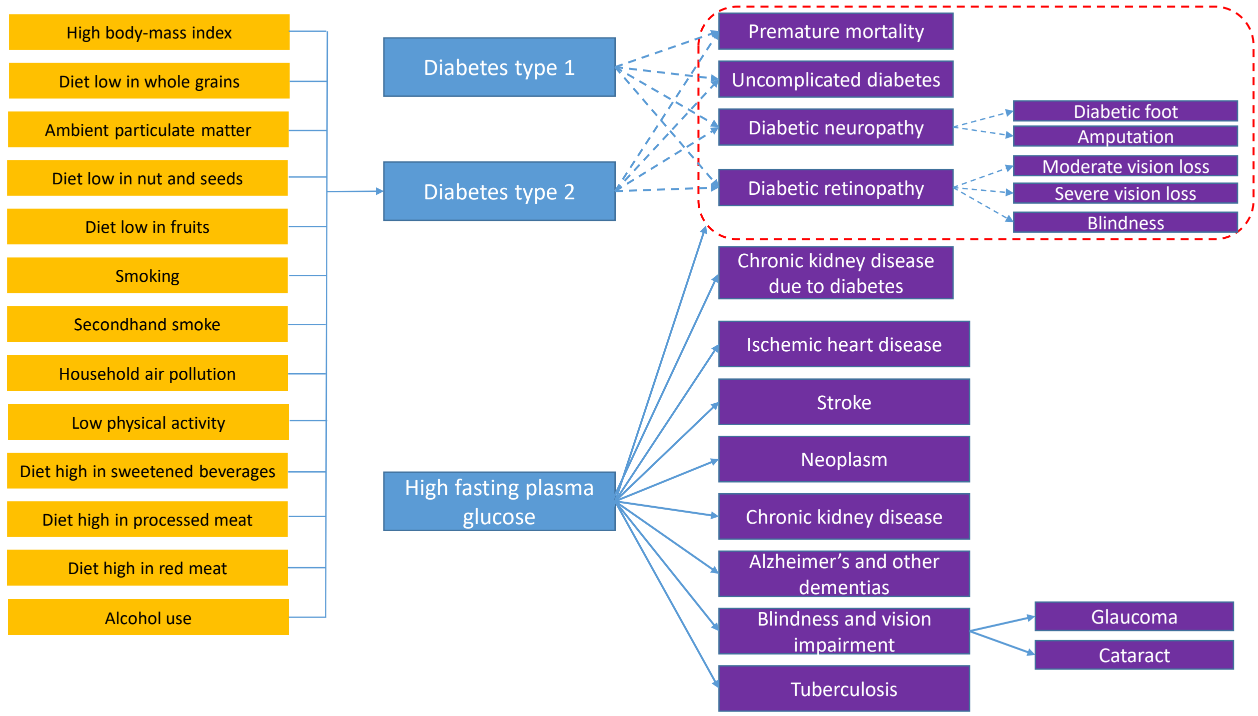

Figura 2. Dimensões da carga de diabetes e índice glicêmico plasmático elevado atribuíveis aos fatores de risco do GBD.

OBJETIVOS

Objetivo Geral

Desenvolver e descrever uma métrica para mortalidade por diabetes nos jovens (abaixo de 25 anos de idade) no mundo; e descrever a carga de diabetes nas Américas em adultos entre 1990 e 2017.

Objetivos Específicos

1. Desenvolver e descrever uma métrica para mortalidade por diabetes abaixo de 25 anos e caracterizar sua variabilidade em grupos com diferente desenvolvimento sociodemográfico.
2. Descrever a carga e as tendências de diabetes em adultos nas Américas e suas regiões, identificando fatores que podem explicar diferenças nessas cargas.

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ARTIGO 1

Burden of Diabetes Mellitus and Hyperglycemia in Adults in the Americas, 1990 -2017: GBD 2017 study

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Abstract

Background

Some countries in the Americas have a very high prevalence of diabetes, but the burden of diabetes in the hemisphere has been little investigated. Thus, our objective is to describe the burden of diabetes and hyperglycemia in the Americas in 2017 and evaluate trends in burden, incidence, prevalence and risk factors between 1990 and 2017.

Methods

We used estimates from the Global Burden of Disease (GBD), Injuries, and Risk Factors Study 2017. For this report, we evaluate the burden of diabetes in the Americas, and its regions and countries, using estimates for DALYs (disability-adjusted life years) lost, deaths, prevalence and incidence from 1990 to 2017. We analyzed individuals aged 25 or older. Diabetes was defined by ICD 10 codes E10-E14, as a fasting plasma glucose $\geq$7 mmol/L (126 mg/dL) or by being on treatment for diabetes. Additionally, we analyzed the burden of hyperglycemia as a risk factor.

Findings

We estimated 352,769 (95% UI 340,170-366,155) adults 25 or older died due to diabetes in the Americas in 2017. The age-standardized death rate was 51.0 per 100,000 (95% UI: 49.1-53.0) in this year, 23% higher than that globally, and was highest in Central Latin America and the Caribbean. In terms of DALYs lost, the age-standardized rate was 2,052 (95%UI: 1,742 to 2,421) per 100,000 in 2017, 18% higher than the equivalent estimate for 1990. The prevalence of diabetes in the Americas, substrate for the burden, increased by 40% over the period, reaching 11.7% (95%UI: 9.4% – 11.2%) in 2017. Central Latin America, the Caribbean, and North America presented the highest prevalence. The main risk factors for the burden were high BMI and dietary factors.

Interpretation

The prevalence and burden of diabetes in the Americas are greater than world averages. The regions of Central Latin America and the Caribbean have a disproportionately large burden. High BMI and dietary factors, which produce a high incidence and subsequently a high prevalence of diabetes, appear to be the main culprits. Public policies acting on these and other risk factors to decrease diabetes incidence, and actions to permit health systems to provide effective and cost-efficient care for those with diabetes are much needed.

Introduction

The World Health Organization has highlighted the importance of the non-communicable disease burden around the world, encouraging the creation of strategies for its prevention and control.[1] In so doing, it currently focuses on five disease groups – cardiovascular diseases, cancer, chronic obstructive lung disease, diabetes and mental health.[2]

While changes since 1990 in the crude rates of DALYs globally for the other four groups range from minimal increases (5.5% for mental diseases and 3.3% for cancer) to decreases, the rate for diabetes has increased 53%[3]. Recent estimates suggest that this increase will continue, with deaths due to diabetes more than doubling by the year 2040.[4] Diabetes is not only a major cause of death, but also a major driver of disability, being the 3rd leading cause of years lived with disability for males and the 5th for females in 2017. Its crude rate of disability increased 15.5% in males and 14.9% in females over the decade 2007-2017.[5]

As previously documented, many countries in the Americas have high diabetes prevalences and major diabetes-related disease burdens.[6,7] Yet, to date, little focus has been placed on diabetes, and on the lesser but still abnormal states of hyperglycemia – termed intermediate hyperglycemia[8] or pre-diabetes[9] – in the Americas. Such a focus can highlight American regions and countries where the burden is notably greater, and showcase the contribution of the varying prevalence of diabetes and its major risk factors to the size and distribution of the burden. The Global Burden of Disease (GBD) Injuries, and Risk Factors Study, given its standardized methodological approach applied across countries, is an important resource for exploring this burden and for clarifying if current tendencies are approximating America´s burden to that of other parts of the world or exacerbating the difference.

Thus, the objective of this study is to describe the burden of DM and hyperglycemia and evaluate trends and causes of this burden in the Americas between 1990 and 2017.

Methods

We applied standard GBD methods. The GBD Study aims to produce consistent and comparable estimates for diseases and risk factors in mortality and morbidity for all locations in the world. Its methodological approaches have been described extensively elsewhere[5,6,10–12]. Briefly, the GBD generates estimates of prevalence, incidence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) lost for 359 diseases and injuries, and of the prevalence and impact of 84 risk factors for 195 countries and territories.

For this study we analyzed estimates for adults (aged 25 years or older) across the region the Americas, including 37 countries. and territories. We also detailed results for 6 regions – North America, the Caribbean, Central Latin America, Andean Latin America, Tropical Latin America, and Southern Latin America. The complete list of the countries and territories included in each region is detailed in Supplementary Table 1. For all our analyses, we merged data on type 1 and type 2 disease.

For mortality estimation, the GBD gathers data from vital registration, sample registration, and censuses and surveys to determine the all-cause number of deaths for each age, sex, location, and year. Within the GBD process, cause of death is based on the underlying cause as originally determined in the data sources, and classified according to the International Classification of Diseases (ICD), versions 9 and 10. In ICD-10, codes E10-E14 and P70.2 were used to classified deaths occurring due to diabetes or to CKD due to diabetes, and in ICD-9, code 250. These ICD codes are then organized into GBD causes and, when data were not furnished in detail, split into age-sex groupings. Garbage codes – ICD codes that are not plausible underlying causes of deaths – are redistributed to plausible ones using regression or proportional redistribution methods.[10] To deal with underreporting and other causes of uncertainty in the data, the GBD Cause of Death Ensemble model (CODEm) is then used to produce the estimates of total deaths due specifically to diabetes and to chronic kidney disease due to diabetes.[10] Finally, the cause of death correction procedure (CodCorrect) combines data from models for all the distinct causes of deaths in order to establish estimates for each cause that, as a whole, are consistent with all-cause mortality estimates for each specific sex, age, year, and location. For all burden analyses, we aggregated the GBD categories of diabetes and of chronic kidney disease (CKD) due to diabetes. Thus, whenever diabetes burden is presented, it always includes the burden which the GBD defines as resulting from CKD due to diabetes.

For estimation of the non-fatal diabetes burden, we defined diabetes as the presence of hyperglycemia above internationally accepted cut-off points. To produce a single indicator of hyperglycemia, GBD transforms (“cross-walks”) survey data of post-challenge glucose and glycated hemoglobin into fasting plasma glucose equivalents, defining diabetes as a fasting plasma glucose ≥7 mmol/L (126 mg/dL) or being on treatment for diabetes. Information from population-based surveys with laboratory measurement was synthesized to produce estimates of the overall diabetes prevalence and incidence, using DisMod-MR 2.1, a Bayesian meta-regression tool.[5]

For CKD due to DM, GBD first defines CKD as a permanent abnormality of kidney function, indicated by a low estimated glomerular filtration rate (eGFR) and/or an elevated urinary albumin-to-creatinine ratio (ACR). It then applies the Bayesian meta-regression tool DisMod-MR 2.1, which takes data collected from different sources, corrects for inconsistencies, and fills in gaps when data are incomplete, to estimate the proportion of CKD due to diabetes or to other specific etiologies. More detailed methodological information on this process can be found elsewhere.[5]

To estimate measures of burden beyond that of deaths, we used the measures of premature deaths (YLLs), disability (YLDs), and their sum, overall disease burden – DALYs. In the GBD, YLLs for each death due to diabetes (or to any other specific cause), are calculated as the difference between the age in which a death occurred and the standard life expectancy for that given age. YLDs are based on the presence of less than optimum health states resulting from disease sequelae. The prevalence of diabetes sequelae, within a given age/sex/time/location strata, are estimated as the prevalence of the diabetes times the likelihood of it producing the sequelae. Sequelae, in turn, result in reduced states of health. Disability weights express the relative devaluation of the health state resulting from given sequelae in comparison to a state of full health. For instance, a year lived with complete blindness (health state disability weight=0.187) is valued as the equivalent to 0.813 (=1-0.187) years in complete health.[13] YLDs from complications of diabetes for a given year and location are calculated by multiplying the prevalence of each diabetes sequela in a strata by its health state disability weight[13] and then summing across sequelae within and across the age/sex strata.[5] YLDs can be interpreted as the equivalent years of life lost due to living with disability. A comorbidity correction (COMO) is then applied to adjust downward the final estimate of YLDs due to diabetes to account for the fact that more than one cause may produce a given sequela. Once YLLs and YLDs have been calculated, DALYs are produced as their sum.

Risk factor estimation

The GBD also defines the burden of diabetes indirectly. This indirect burden is expressed within the GBD by evaluating hyperglycemia – including both diabetes and intermediate hyperglycemia – as a risk factor, denominated high fasting plasma glucose (HFPG). For this purpose the distribution of fasting plasma glucose is summarized from surveys with laboratory measurement of hyperglycemia.

HFPG, a continuous variable, is defined for a given population as the distribution of fasting glucose values greater the theoretical minimum-risk exposure level (TMREL) of 4.8-5.4 mmol/L (86-97 mg/dL). The GBD applies its Spatial-Temporal Gaussian Process Regression (ST-GPR) to estimate HFPG from the data of the multiple underlying surveys, many of which frequently provide only mean glucose levels or overall diabetes prevalence. This approach provides an estimated continuous distribution of glycemia for each specific location, age, sex, and year strata of populations. Estimates are interpolated for years without data, and extrapolated from external sources (e.g., a country´s region and its neighboring countries) for countries lacking their own data. Levels of covariates – the prevalence of obesity and lag-distributed income – associated with glycemic level are used in this modelling to adjust the extrapolated values upward or downward.[12] These HFPG distributions are then contrasted against the TMREL, using estimates of the relative risk of outcomes at different levels of HFPG obtained from reviews of the literature to produce the population attributable fraction (PAF) of disease burden due to HFPG for 15 outcomes for which diabetes and/or hyperglycemia have been shown to confer risk. The PAF for HFPG is defined as the proportion of the disease burden which would be eliminated if the hyperglycemia was reduced to its counterfactual level of minimum risk. The PAF for a given risk factor-outcome pair, as explained in greater detail elsewhere,[12] is estimated independently of mediation of its effects on the outcome through other risk factors and incorporates all burden for the outcome that is attributable to the risk, directly and indirectly. In later steps aggregating the PAF across risk factors, a mediation adjustment is applied to avoid double counting of risk.

We report the 95% uncertainty intervals (UI) for each estimate. These are obtained by running 1000 draws of each step of the estimation processes described above, propagating the values through the overall analysis, and taking the final 2.5th and 97.5th percentile values as UI limits.

Finally, the GBD expresses the level of development of a country or other geographic area by its socio-demographic index (SDI). The SDI is an indicator derived from the joint measures of lag-distributed income per capita, average educational attainment of those older than 15 years old, and total fertility under age 25. The SDI value ranges between 0.0 to 1.0, with a value of 0.0

interpreted as the joint lowest income per capita, lowest education attainment, and the highest fertility rate. The SDI values for each country in the Americas has been previously reported.[14]

Results

Burden of DM

An estimated total of 352,769 (95% UI 340,170-366,155) adults living in the Americas in 2017 died due to diabetes, representing 5.4% of all deaths in the region.

The crude diabetes mortality rate was 57.1 (95%UI: 55.1-59.3) per 100,000 and the age-standardized death rate was 51.0 per 100,000 (95% UI: 49.1-53.0), 42% and 17% higher, respectively, than the equivalent rates in 1990. When compared to the world´s global age-standardized rates, rates in the Americas were 23% higher and also suffered a 40% larger increase from 1990. However, although rates are higher overall, they vary greatly across the regions investigated. Central Latin America (from Mexico to Columbia and Venezuela; 98.4/100,000; 95%UI: 94.2-102.7) and the Caribbean (74.9/100,000; 95%UI: 70.3-79.8) had the highest age-standardised mortality rates in 2017. In contrast, the high SDI regions North America and Southern Latin America (Argentina, Chile and Uruguay) had rates approximately half to one-third of these – 31.3/100,000 (95%UI: 29.8-32.7) and 38.7/100,000 (95%UI: 35.5-42.1) respectively. Trends in these age-standardized rates, while similar in the Americas to the overall global rate, also showed considerable variation by region. The Andean Latin America (Bolivia, Ecuador and Peru) showed an increase in the percentage change in age-standardised deaths rate of 25.5% and Central Latin America an increase of 12.2%. All other regions showed a decrease in age-standardized rates between 1990 to 2017, with North America having the largest decrease, 28%. (Table 1).

Levels and trends in crude and age-standardized DALY rates due to diabetes in adults between 1900 and 2017 also show higher burden in the Americas than globally. The age-standardized diabetes DALY rate in the Americas was 2,052 (95%UI: 1,742 to 2,421) per 100,000 in 2017, 18% higher than the equivalent estimate for 1990, and 19% higher than the world´s 2017 global average. These rates of DALYs and their trends also showed major regional differences. Central Latin America (3,419; 95%UI: 2,986 to 3,951 /100,000) and the Caribbean (2,765; 95%UI: 2,387 to 3,230 /100,000) had the highest age-standardised diabetes DALY rates, these estimates being 116% and 74% higher than the region of lowest burden in the Americas, North America (1,586; 95%UI: 1,295 to 1,927 DALYs/100,000). The crude DALY rate for the

Americas was 2,218 (95%UI: 1,887 to 2,614)/100,000 population, up 36% from 1990. Over this period, the crude DALY rate increased in every region of the Americas, the highest increase being in North America, up 47%. In 2017, Central Latin America (3,236.7; 95%UI: 2,815.7-3,748.4 per 100,000) and the Caribbean (2,827.8; 95%UI: 2,443.0-3,302.4 per 100,000) presented the highest crude DALY rates, both with rates approximately twice that of the lowest region. (Figure 1)

In 1990, the majority of America´s regions had 50% or less of burden accruing from premature mortality. However, over the period, YLDs have increased as a fraction of total burden such that, in 2017, most regions displayed 50% or more of burden as resulting from disability. The high-SDI regions, North America and Southern Latin America, presented the highest fraction arising from disability. (Supplementary Figure 2)

The age-standardised DALY rates for the Americas were 22% higher in males than females in 2017, increasing 26% since 1990 for males and 10% for females. In 2017 a higher burden in males than females was observed in all regions except the Caribbean and Andean Latin America, where the burdens were similar for both sexes. North America had the highest increase in males (36%) in the period, and the Andean Latin America the highest increase in females (15%). (Supplementary Figure 1) DALYs due diabetes accrued principally between the ages of 65 and 89, with similar age pattern of burden seen in all regions. (Supplementary Figure 3)

Figure 2 shows maps of age-standardised diabetes DALY rates, percentage change in these rates between 1990 and 2017, and the fraction of total all-cause DALYs attributable to diabetes. In Panel A, the countries in red color located in Central Latin America and the Caribbean showed the highest rates. The country with the highest rate – Trinidad and Tobago – had a rate (5,714; 95%UI 4,823 to 6,793 per 100,000) more than 5 times that of the country with the lowest rate – Canada (1,092; 95%UI 782 to 1,250 /100,000). As seen in Panel B, the change in the age-standardised DALY rate between 1990 and 2017, also varied widely. Considering extreme examples, in Guatemala the rate increased 131% and in El Salvador 96%; while in Colombia the rate decreased 26% and in Cuba 22%. (Supplementary Table 2) As seen in Panel C, the fraction of total 2017 DALYs due to diabetes varied more than three-fold, representing, for example, 15.3% of total DALYs in Trinidad and Tobago, while only 4.4%% in Canada. More than 10% of total adult disease burden was attributable to diabetes in Mexico, Jamaica, Puerto

Rico, and several of the smaller countries of the Caribbean. The mean for the Americas was 6.1%, while it was 4.5% for the world, overall.

Burden of HFPG

Figure 3 shows the age-standardized rate of DALYs attributable to HFPG in 1990 and 2017, with color-coding indicating groups of causes. Interestingly, overall burden, when defined by HFPG, was roughly similar in the Americas (3,733.9/100,000) and globally (3,828.6/100,00). This equality resulted from the higher burden globally of cardiovascular disease attributable to HFPG offsetting the higher burden due directly to diabetes (and CKD due to diabetes) in the Americas. Of note, in 2017 only slightly more than half of the overall age-standardized burden of hyperglycemia in the Americas (3,733.9 per 100,000) was directly due to diabetes (2,051.9 per 100,000), while the other approximate half was due to indirect causes measured exclusively through HFPG. Indirectly, 1,060.9 DALYs/100,000 were accrued from cardiovascular diseases and 326.6 DALYs/100,000 from CKD not primarily due to diabetes (green parts of the columns). From 1990 to 2017, the age-standardized DALY rate attributable to HFPG was stable in the Americas overall, while it increased in Central Latin America and North America, mainly due to increases in burden directly due to diabetes and to CKD not due to diabetes. All the other regions had a decrease in age-standardized HFPG rates. A major decrease in the fraction of burden due to CVD is notable in all regions over the period. The same is seen, though in a much smaller scale, for tuberculosis. Major increases occurred in the burden directly due to diabetes and arising from CKD due to other causes

Incidence and Prevalence

To explore the causes of this high and variable burden, we next describe the prevalence and incidence of diabetes. As seen in Table 1, this prevalence is 14% higher than the global prevalence. In the regions of greatest DALY rates – Central Latin America and the Caribbean – and in North America, prevalence was highest, being 13.5% (95%UI: 12.4 – 14.8), 12.6% (95%UI 11.5 – 13.8) and 13.4% (95%UI: 12.5 – 14.4), respectively. Tropical Latin America had the lowest prevalence – 7.0% (6.4 – 7,8). The crude prevalence of diabetes in adults in the Americas increased

40% between 1990-2017, reaching 11.7% (95%UI: 9.4% – 11.2%) in 2017. The age-standardized increases in prevalence were large and similar in the Americas and globally. Within the Americas, increases were greatest in North America (38.6%) and in Andean Latin America (24.2%). With the aging of the populations, all regions experienced important increases in crude prevalence, the largest being for North America, 64.3%.

The overall crude yearly diabetes incidence rate in the Americas in 2017, 5.23 (95%UI: 4.83 – 5.70) new cases per 1000, was also 18% higher than the global estimate. Incidence varied considerably across regions of the Americas. Similar to what was found with respect to the other disease metrics, Central Latin America and North America, with 6.05 (95%UI: 5.50 – 6.67) and 5.97 (95%UI: 5.49 – 6.46) new cases annually per 1,000 respectively, presented the highest rates. Tropical Latin America presented the lowest incidence rate – 3.27 (95%UI: 2.95 – 3.64) new cases per 1,000.

Figure 4 demonstrates the varying temporal trends in age-standardized prevalence and incidence over the almost 3 decades of surveillance. However, the constant result, with the exception of Tropical Latin America, was an increase in incidence and prevalence from 1990 to 2017. We observed less deterioration in terms of mortality than in terms of prevalence in most regions – large increases in the age-standardized prevalence rate occurred in all regions and decreases in the age-standardized mortality rate in some. (Supplementary Figure 4)

Risk Factors for Diabetes

As presented in Table 2, the main risk factor for the diabetes burden in the Americas in 2017 was high body mass index (high BMI), with 58.6% (95%UI: 46.3 to 69.3) of diabetes DALYs being attributable (PAF) to it in 2017, up from 45.2% in 1990. This PAF was 34% greater, in relative terms, in the Americas than globally in 2017. The PAFs of DALYs caused by diabetes in the Americas due to dietary risks and air pollution were 34.5% and 16.4%, respectively, in 2017. The PAF for dietary factors was 6% higher and for air pollution 17% lower than those globally. The main dietary risk factors were low intakes of whole grains, nuts and seeds, and fruit; except of Mexico, where high intake of sweetened beverages was the major dietary risk factor for diabetes [data not shown]. The PAF due to tobacco, which was also slightly lower than the world average, decreased over the period, from 16.5% in 1990 to 11.4% in 2017.

Discussion

The burden of diabetes is somewhat larger in the Americas compared to the world. Yet, rather than presenting a uniformly greater burden, the Americas house a major multi-regional hotspot for diabetes prevalence and burden, centered in Central Latin America, the Caribbean and the United States. Greater progress in controlling diabetes mortality than prevalence was observed over time. Trends found in diabetes incidence and prevalence suggest that this diabetes burden, along with the additional indirect burden of metabolic derangement, expressed by the GBD as HFPG, will increase in the Americas over the foreseeable future. High BMI and inadequate nutrition are the main risk factors.

The magnitude of the current burden in the Americas is huge – 6.1% of the overall adult disease burden, being >10% in many countries of Central Latin America and the Caribbean, and 15.3% in the most affected country – Trinidad and Tobago. This is particularly true considering that these percentages don´t consider the other approximately half of the hyperglycemia burden caused indirectly through other diseases, principally cardiovascular ones, and accounted for in the GBD through the risk factor HFPG.

The somewhat greater progress in controlling age-standardized diabetes mortality than its incidence and prevalence suggests that policies affecting diabetes have been focused more on avoiding death from diabetes complications than on prevention of diabetes. The resultant prolonged longevity, together with a rising incidence, increased the morbidity burden in recent years. This is particularly true for North America, which is currently presenting a very high diabetes prevalence, relatively low mortality, and a large fraction of diabetes DALYs due to YLDs.

Our findings are consistent with a worldwide population-based pooled analysis showing that the prevalence of diabetes has been rising in countries of the Americas as well as globally over the last decades.[7,15] They are also consistent with recent estimates for Andean countries showing the large impact of overweight and obesity on diabetes risk.[16] Worldwide, the estimates show that the number of deaths due to the NCDs are increasing yearly, reaching 40 million, 75% of all deaths, in 2017.[10] One of the United Nation´s sustained development goals for 2030 is to reduce premature mortality due to the NCDs by one-third.[17] However, countries are not taking up the challenge to confront the NCDs.[18] In part due to this, mortality due to diabetes in the Americas, as we show, has been moving in the opposite direction. The epidemiological transition, which produces population aging, is in high gear in low and middle-income countries, a grouping which includes the majority of America´s nations. This aging, applied to the age-standardized trends we have described, is driving the huge increase in diabetes burden shown here and in a less-focused fashion elsewere.[10,19,20] Recent projections estimate that in 2050 more than 80 million people will be living with diabetes just in three countries of the Americas – the United States, Mexico and Brazil.[21] Additionally, in an increasingly elderly population, the concomitance of other diseases with diabetes creates so-called multimorbidity, further amplifying the challenge to health systems to provide the adequate care.[22]

Projections suggest that the countries which will experience the largest increase in NCD burden will be those least prepared to incorporate this change, mostly because of their difficulty to increase spending in health and the existence of health systems which are ill-prepared to manage chronic diseases such as diabetes and its complications.[20] The resultant costs of this NCD epidemic are estimated to be of sufficient size to significantly impact overall economic development.[23,24]

Actions to prevent this burden should focus on the main risk factors for diabetes – excess of weight and inadequate diet. [12,25,26] The prevalence of obesity, the main contributor for the diabetes burden, has been increasing in all the regions of the Americas in the past decades, especially in North America.[15,25] In terms of poor nutrition, second in importance among risk factors for diabetes and first as a cause of obesity, the Americas present low consumption of many foods shown to be protective against diabetes and a much higher consumption of sweetened beverages than globally.[26] Ultra-processed foods, consumption of which as a percent of total caloric intake has increased considerably in the Americas during the decades of the obesity epidemic,[27] by leading populations to migrate from what were basically healthy traditional diets to current unhealthy ones, may be a major vector providing greater exposure to a wide variety of dietary risks.[28,29]

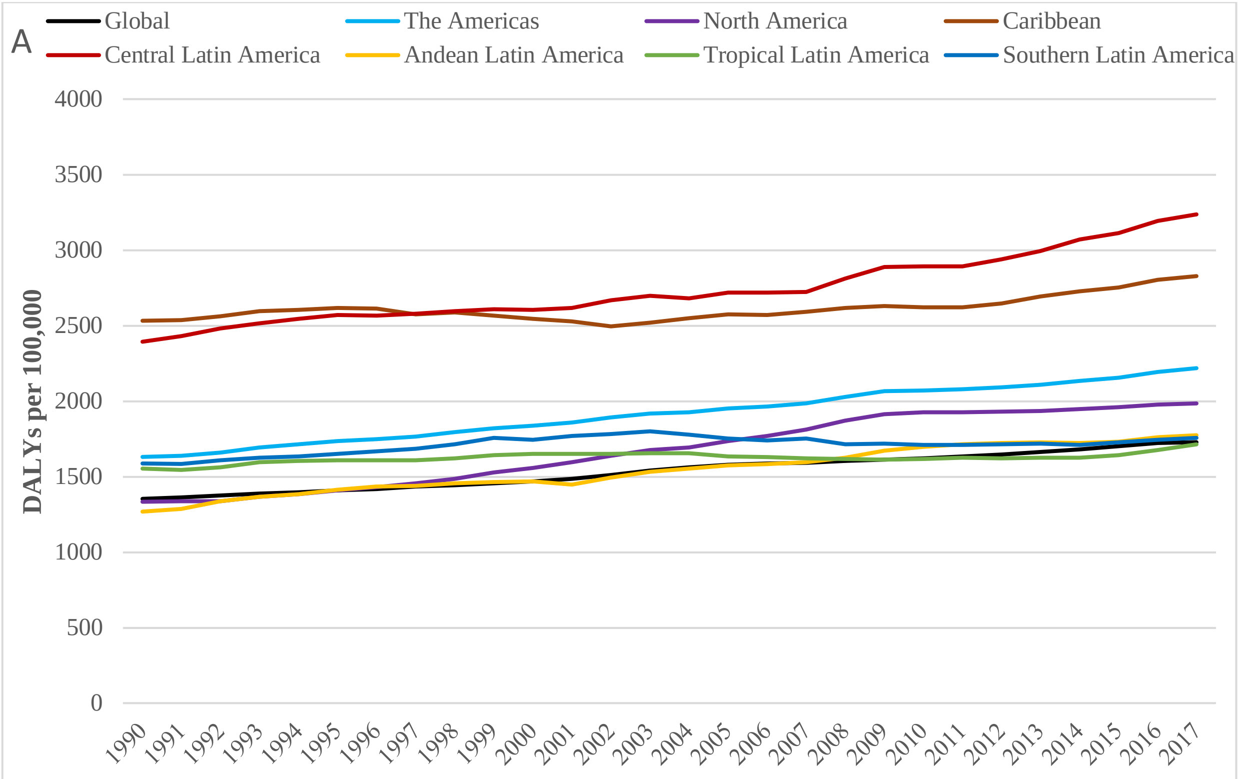
Our study has limitations, many of which are inherent to the GBD approach.[5,10,12] The goal of expressing incidence, prevalence and the multiple metrics of burden yearly for hundreds of locations is far from a trivial one. Many locations and years lack good quality data, leading to the necessity of extrapolation of the results of others through modelling, resulting in imprecise results. Additionally, we have presented data only for adults 25 and over, given that GBD estimates HFPG only for those 25 and above. However, the complex methods used by the GBD and the support from hundreds of international collaborators who work to identify and correct weaknesses found, minimize this imprecision. In this regard, specifically, the estimates of prevalence and incidence in Brazil, which represents >95% of the Tropical Latin America population, are based to date on relatively few very small studies, and are lower than those found in many nationally representative surveys applying alternative methodologies. [7,30,31] These estimates merit revision, especially now that a nationally representative, laboratory-based study of diabetes prevalence is available.[32] As incidence and prevalence are inputs used to calculate many of the aspects of burden, the real size of the diabetes burden in the Tropical Latin America region may well be larger than shown.

Yet, this detailed description of the diabetes burden and its trend in the Americas highlights the magnitude of the problem, identifies countries and regions within the hemisphere where the diabetes burden is notably greater and thus requires special attention from policymakers, and showcases major risk factors related to this burden. The standard methodological approach developed by GBD facilitates this type of study, with estimates for each country or regional grouping, by sex, age, and year.

Conclusion

The burden of diabetes in the Americas is very high when compared to the global one. The region houses a major multi-regional diabetes hotspot, impacting, in terms of burden, Central Latin America and the Caribbean. Throughout the Americas and within the most affected regions, high BMI and dietary factors appear to be the main culprits for the current situation, acting through increasing diabetes incidence. Stronger public health policies and actions are needed to decrease diabetes incidence. Health systems throughout the region will need to adapt to this reality so as to provide effective and cost-efficient care for the many who will be affected in the coming years.

Figure 1 – Trends in all-ages (A) and age-standardised (B) DALY rates by region, 1990-2017.



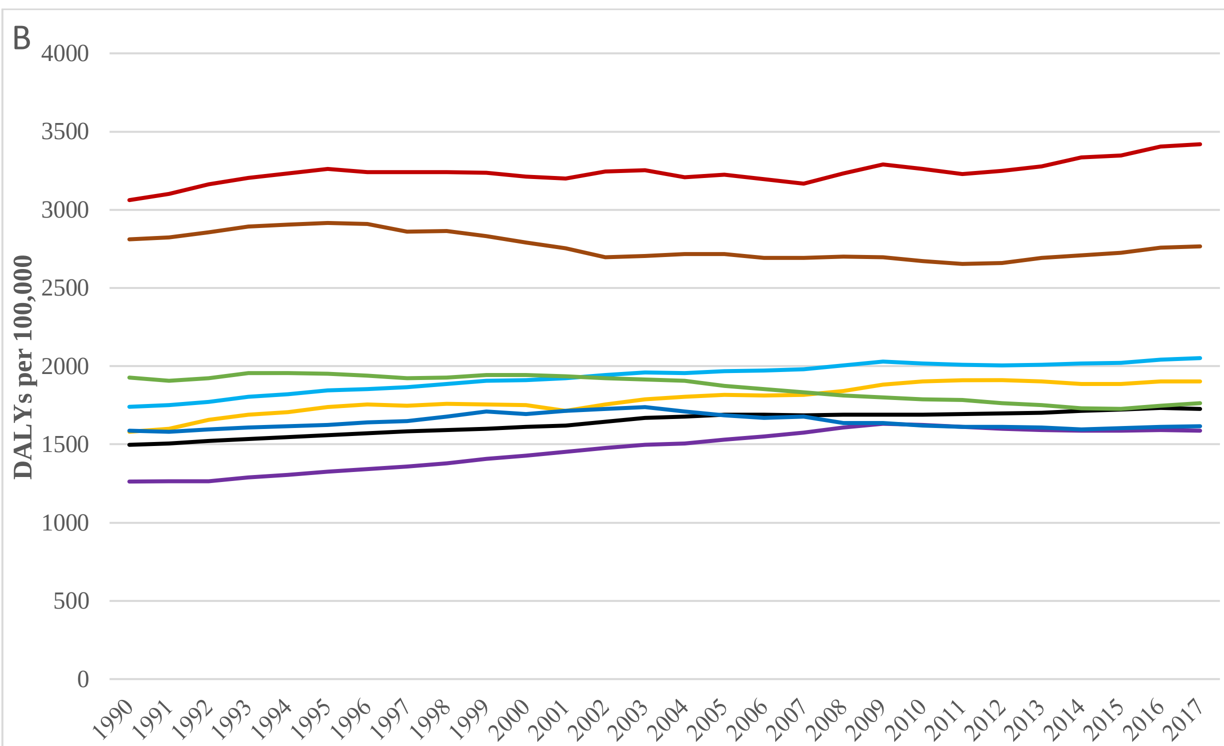


Figure 2 – (A) Age-standardised diabetes DALY rate per 100,000 in 2017, (B) Percentage change in age-standardised DALY rate between 1990-2017, (C) percent of total DALYs due to diabetes in 2017.

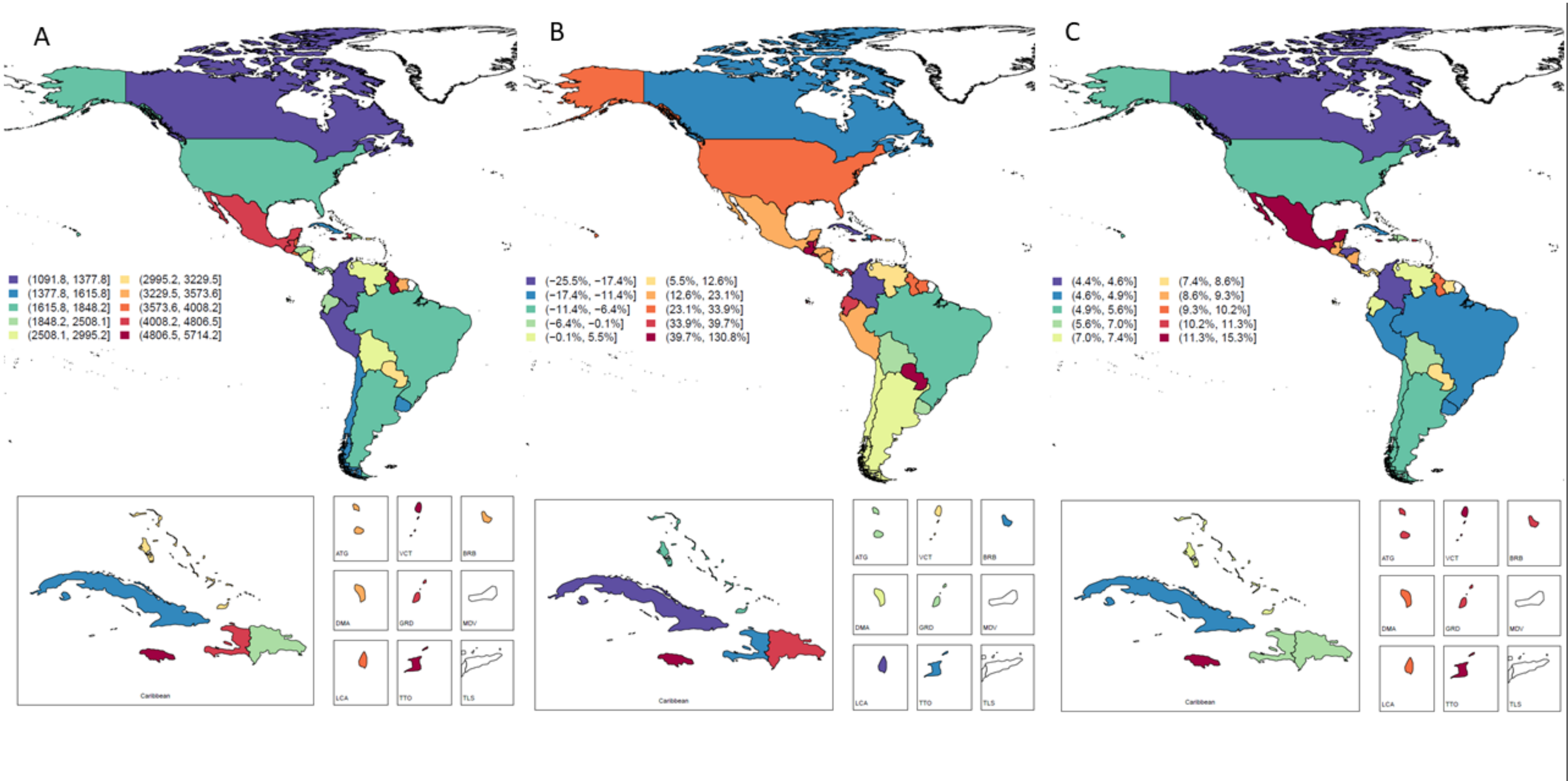
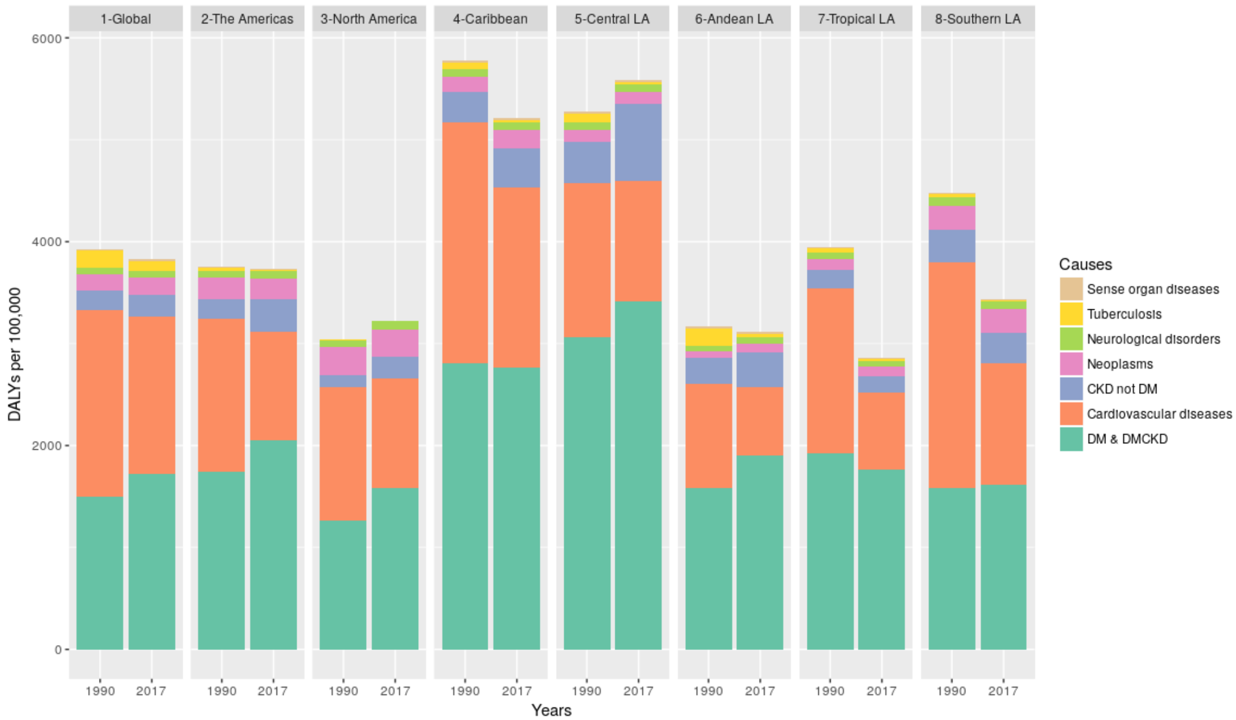


Figure 3 – High fasting plasma glucose age standardized DALY rate in adults (aged 25 plus) in the Americas by cause in 1990 and 2017.



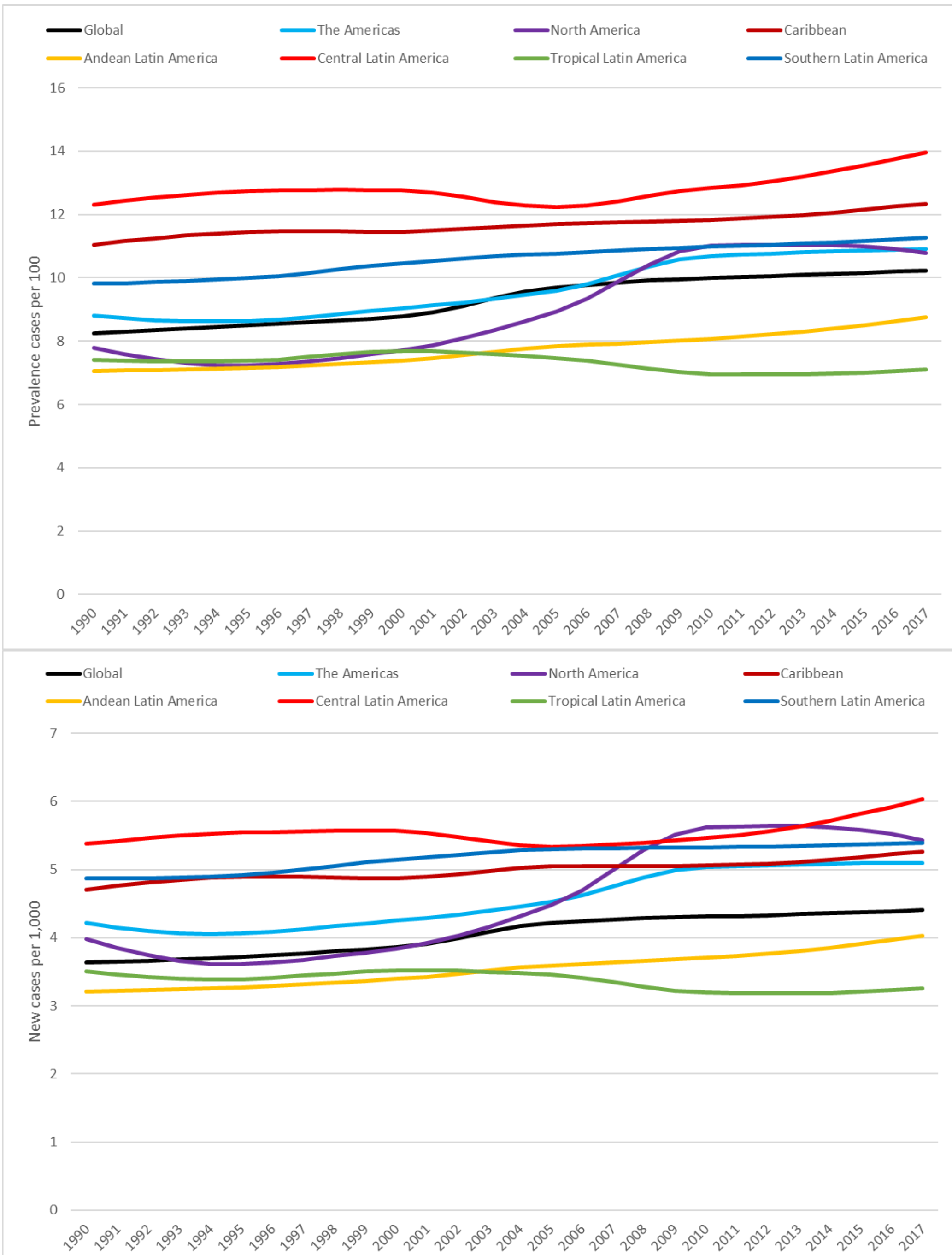


Figure 4 – Trends in age-standardised prevalence and incidence rates in the Americas regions and globally, 1990 – 2017.

Table 1 - All ages and age-standardised deaths, prevalence and incidence rates in adults* in the Americas, 2017.

	Deaths rates				Incidence rates			Prevalence rates		
Location	**All ages 2017**	**Percent change 1990-2017**	**Age-standardised 2017**	**Percent change 1990-2017**	**All ages 2017**	**Percent change 1990-2017**		**All ages 2017**	**Percent change 1990-2017**	
	/100,000		**/100,000**		**/1,000**	**All ages**	**Age-std**	**/100**	**All ages**	**Age-std**
Global	**40.2 (38.9 to 41.6)**	**33.7**	**41.6 (40.2 to 43.1)**	**12.4**	**4.44 (4.00-4.91)**	**26.1**	**21.1**	**10.2 (9.4-11.2)**	**34.8**	**23.9**
The Americas	**57.1 (55.1 to 59.3)**	**42.2**	**51.0 (49.1 to 53.0)**	**17.4**	**5.24 (4.83 to 5.70)**	**30.4**	**20.8**	**11.7 (10.8 to 12.6)**	**40.0**	**23.7**
North America	43.92 (41.8 to 46.1)	38.6	31.3 (29.8 to 32.7)	-28	5.97 (5.49 to 6.46)	55.6	36.6	13.4 (12.5 to 14.4)	64.3	38.6
Central LA	88.0 (84.2 to 91.8)	48.2	98.4 (94.2 to 102.7)	12.2	6.05 (5.50 to 6.67)	19.1	12.1	13.5 (12.4 to 14.8)	30.2	13.5
Caribbean	76.7 (72.0 to 81.7)	11.9	74.9 (70.3 to 79.8)	-7	5.32 (4.81 to 5.87)	17.4	12.0	12.6 (11.5 to 13.8)	22.9	11.8
Andean LA	48.2 (44.3 to 52.4)	60.4	53.5 (49.1 to 58.2)	25.5	3.95 (3.58 to 4.36)	33.0	25.6	8.3 (7.6 to 9.2)	38.8	24.2
Tropical LA	51.5 (49.9 to 53.3)	30	56.0 (54.2 to 57.9	-4	3.27 (2.95 to 3.64)	0.1	-7.0	7.0 (6.4 to 7.8)	11.1	-4.2
Southern LA	44.2 (40.6 to 48.1)	12.9	38.7 (35.5 to 42.1)	-4.4	5.54 (4.99 to 6.09)	13.6	10.9	12.1 (11.0 to 13.3)	23.3	14.8

* $\geq$25 years

LA=Latin America

Table 2 -Population attributable fraction for each risk factors for diabetes in 1990 and 2017

	The Americas		Global	
Risk factor	**PAF DALYs 1990**	**PAF DALYs 2017**	**PAF DALYs 1990**	**PAF DALYs 2017**
High body-mass index	45.2% (33.1 to 56.9)	58.6% (46.3 to 69.3)	28.1% (18.0 to 39.6)	43.6% (32.7 to 54.3)
Dietary risk factors	33.2% (26.2 to 40.5)	34.5% (27.7 to 41.6)	31.3% (23.9 to 38.9)	32.5% (24.8 to 40.6)
Air pollution	17.2% (11.1 to 22.3)	16.4% (9.8 to 23.0)	18.3% (12.7 to 21.7)	19.8% (13.5 to 23.6)
Tobacco	16.5% (12.6 to 20.1)	11.4% (8.2 to 14.2)	14.9% (11.0 to 18.4)	13.4% (9.5 to 16.8)
Low physical activity	2.6% (0.6 to 4.8)	2.7% (0.6 to 5.1)	2.2% (0.5 to 4.2)	2.4% (0.5 to 4.7)

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Supplemental Material ("ANEXO 1")

Supplement to "**Burden of Diabetes Mellitus and Hyperglycemia in Adults in the Americas, 1990 -2017: GBD 2017 study",** Ewerton Cousin, Maria Inês Schmidt, Rafael Lozano, Ashkan Afshin, Liane Ong, other authors, Mohsen Naghavi, Bruce B. Duncan.

Contents

Monitoring levels and trends in diabetes mortality under age 25 years around the globe

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Background

Mortality due to diabetes under age 25, nearly all of which is due to acute complications, should be near zero with provision of basic diabetes health care and access to insulin. An indicator estimating diabetes deaths in this age group could highlight the degree of success in implementing basic care of diabetes and in monitoring changes in the level of this care. Our objective was thus to create the metric of amenable diabetes mortality among those under 25 years to gauge the current status and past trends in the implementation of these basic actions in the care of diabetes in countries across the world.

Methods

We used estimates of the Global Burden of Disease (GBD), Injuries, and Risk Factors Study 2017. For this study, deaths due to diabetes were those reported as E10-E14 and P70.2 for years using ICD10 codes. We calculated the age-standardised death rates due to diabetes per 100,000 population under 25 in 1990 and 2017 and trends during the period. We analyzed the correlation of these age-standardised rates with the Socio-Demographic Index (SDI) and described their variability within SDI groups.

Findings

The age-standardised death rate of diabetes under 25 decreased by 20% from 1990 to 2017, being 0.36 (95%UI: 0.33 to 0.38) /100,000 globally in 2017. A total of 11,643 deaths occurred. Highest age-standardised mortality rates were seen in low-middle – 0.48 (95%UI: 0.44 to 0.53)/100.000 – and low – 0.44 (95%UI: 0.41 to 0.49)/100,000 – SDI countries. These rates contrast with. 0.11 (95%UI: 0.11 to 0.12)/100.000 in high SDI countries. Low- and low-middle SDI countries also had the lowest decreases in mortality from 1990 to 2017, -23% and -17% respectively. Large residual variability exists within the SDI groups. In terms of countries, Afghanistan had the highest mortality rate in 2017 – 1.39 (95%UI: 0.91 to 1.96)/100,000, and Mauritius showed the greatest increase between 1990 – 2017 – 97.4%.

Interpretation

Mortality rates due to diabetes under 25, mostly due to acute complications, present an unacceptably high burden in low and middle-income countries, indicating variable and frequently inadequate management of diabetes. This information can serve as a readily available and frequently updated indicator for the surveillance and monitoring of the adequacy of diabetes care globally.

Funding: Bill & Melinda Gates Foundation

Introduction

Diabetes mellitus has been identified by the United Nations and the World Health Organization as one of the five major non-communicable diseases (NCDs) in their Action Plan to confront the NCDs challenge.[1,2] Prevention and management of the chronic complications among those with type 1 diabetes are complex, long-lasting and costly endeavors.[3] In contrast, acute complications, namely diabetic ketoacidosis, diabetic coma and hypoglycemic coma, are amenable to a minimal core of actions which depend strongly on the availability and affordability of insulin and on the access to an integrated care including some glucose monitoring and promptly available services for acute decompensation. Provision of care has proven effective in reducing mortality due to acute complications to near zero in high income countries.[4] Thus, it is reasonable to assume that mortality due to the acute complications of diabetes would be close to zero globally if similar care were provided, including availability of affordable insulin. [5,6]

While such quality of care is not yet a reality around the world, many low- and middle-income countries (LMICs) have made rapid advances to improve diabetes care. In Brazil, a rapid decrease in deaths due to acute complications was observed from 1991 to 2010 following the implementation of the National Health System, which increased access to care, including to insulin, for those with diabetes.[7]

Mortality data, the most readily available of health statistics worldwide, could be used to track levels and trends in mortality due to diabetes in youth, which is amenable to basic diabetes care. Restricting analyses to deaths under 25 years limits the scope of the indicator so as to represent mortality almost exclusively due to acute complications.[8] The indicator, while mainly reflecting the quality of care administered to those with type 1 diabetes, also allows evaluation of trends in type 2-related mortality in youth, a matter of recent concern in high income countries.[9]

The Global Burden of Disease study, which systematically collects mortality data, currently offers estimates of mortality rates by age group and disease for 195 countries and territories. It thus potentially permits development of a simple, readily available and up-to-date indicator of amenable diabetes mortality, that is to say, mortality under 25, mostly due to acute complications of type 1 diabetes and almost completely avoidable given a minimal level of diabetes care.[10] Our objective was thus to create and describe this metric of diabetes mortality under 25 years in countries across the world.

Methods

We used estimates of the Global Burden of Disease (GBD), Injuries, and Risk Factors Study 2017. The GBD applies a standard methodological approach to generate estimates for mortality and cause of death for diseases for 195 countries and territories. The general methods used to generate these estimates have been described elsewhere.[10–13]

Basically, the data sources for causes of deaths were obtained from vital registration systems, verbal autopsies, and other surveillance systems from 1980 to 2017. A star rating system identifies country performance in the percentage of well-certified deaths. This definition uses completeness of reporting of cause of death, the fraction of causes attributable to garbage codes, and the fraction of deaths attributed to detailed GBD causes. Values of the classification for each country can be found elsewhere.[14] Data inputs used to generate the estimates are available at http://ghdx.healthdata.org/gbd-2017/data-input-sources.

Briefly, mortality estimates were generated through standarisation of input data, International Disease Classification (ICD) code mapping for diabetes and other GBD causes, and age-sex splitting of data from sources providing only overall summaries. After this, garbage codes (i.e., ICD codes, such as sepsis, considered to be implausible as the true underlying causes of death) were redistributed to plausible causes using regression or proportion redistribution methods. Several models, which take underreporting of deaths into consideration when necessary, were then applied to estimate causes of deaths, with the GBD Ensemble model (CODEm) being used to summarize their results. For the estimation of diabetes, the GBD applies two distinct models, one for ages under 15 (calculating deaths assumed to be due only to type 1 diabetes), and the other for ages 15 and above, representing deaths not distinguished by the type of diabetes which caused them. In this latter case, additional calculations then separate deaths by type of diabetes for each age strata.[10]

For all models generated, GBD then applies a cause of death correction procedure (CoDCorrect) to establish estimates which, as a whole, are consistent with all-cause mortality levels for each sex-year location, guaranteeing that the estimates by cause are mutually exclusive and collectively exhaustive. Further details on these procedures can be found elsewhere.[10,13]

For this study, deaths from diabetes were those coded as E10-E14 and P70.2 for years using ICD10 codes, englobing the GBD classifications of both deaths due to diabetes and deaths due to chronic kidney disease due to diabetes. We restricted our country analysis to those with population greater than 1 million people in 2017, given that countries with small populations could present high variability in rates.

We used the GBD Socio-Demographic Index (SDI) groups to explore the difference in mortality rates between countries with different levels of development. The SDI is a summary indicator of development based on indices of the total fertility rate under the age of 25, mean education for those ages 15 and older, and lag-distributed income per capita. The SDI values range between 0.0 to 1.0, a value of 0.0 being interpreted as characterizing the least developed location, one with the highest fertility rate, lowest education attainment, and the lowest income per capita. Detailed information about SDI calculation, and the SDI values for each country has been described elsewhere.[10]

We report the 95% uncertainty interval (UI) for each estimate. To calculate this interval, we ran 1000 draws, representing the uncertainty in steps of the estimation process, distribution of sampling error in input data, corrections for measurement error, estimates of residual non-sampling error, and model selection; and then took the 2.5th and 97.5th percentiles as the endpoints of the interval.

Role of the Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Globally there were 11,643 (95%UI: 10,900 to 12,438) diabetes deaths under age 25 in 2017, this number representing a decrease of 6% in relation to 1990 (12,435; 95%UI: 11,293 to 13,639) In 2017, deaths in low and middle-income countries corresponded to 96.5% of all deaths in this age range worldwide, although only 90% of those under 25 live in these countries. The global age-standardised diabetes death rate under age 25 was 0.36 (95%UI: 0.33 to 0.38) in 2017, as opposed to 0.44 (95%UI: 0.40 to 0.49) per 100,000 in 1990, a decrease of 20% over the period.

All SDI groups showed a decrease in age-standardised rates of deaths from diabetes from 1990 to 2017, but low-middle and low SDI groups remained with very high rates in 2017, respectively 0.48 (95%UI 0.44 to 0.53 per 100,000) and 0.44 (95%UI: 0.41 to 0.49) per 100,000. In contrast, the rate in high SDI countries was 0.11 (95%UI: 0.11 to 0.12), and only 385 (95%UI:

370 to 400) individuals died from diabetes in this group of countries in 2017. The highest decrease in the rate was observed for the high-middle SDI group, approximately 50% over the period, reaching 0.19 (95%UI: 0.18 to 0.20) deaths per 100,000 in 2017. The lowest relative decrease in age-standardised mortality rate was seen in low-middle SDI group, being only 17%. (Figure 1A)

Rates of mortality from diabetes were low before age 14 for all SDI groups, increasing considerably thereafter, and reaching the highest rates at ages 20-24, particularly for low to middle SDI groups. The low SDI group had the highest death rate for under 5 (0.40/100,000; 95%UI: 0.32 – 0.47), being 4.7 times higher than the high SDI group (0.07/100,000; 95%UI: 0.06 – 0.08). For the age group 20-24, the estimates were 2.5 times higher in low-middle SDI than high SDI group. (Figure1B)

Countries with the highest age-standardised diabetes deaths rate in 2017 were Afghanistan, Haiti, and Zimbabwe, with rates of 1.39 (95%UI: 0.91 to 1.96), 1.19 (95%UI: 0.93 to 1.58), and 1.00 (95%UI: 0.81 to 1.23)/100,000 respectively. Countries with lowest age-standardised diabetes deaths rates in 2017 were Switzerland (0.03, 95%UI: 0.02 to 0.03), Cyprus (0.03; 95%UI: 0.03 to 0.03), and Slovenia (0.03; 95%UI: 0.03 to 0.04)/100,000. The estimate for Afghanistan was 53 times that of Switzerland. (Figure 2A) In general, the regions of Oceania, Caribbean, and Central Asia had high age-standardised deaths rates. In contrast, the regions High Income Asia-Pacific and Western Europe had the lowest age-standardised mortality rates. (Supplementary Table 1) The percent of total deaths under 25 from diabetes varied from 0.1% in South Sudan to 1.1% in Mauritius in 2017. (Figure 2B)

The age-standardised diabetes death rates from 1990 to 2017 increased 97.4% in Mauritius, 95.1% in Philippines, and 90.8% in Guatemala. In contrast, large decreases were seen for Belarus (75.5%), Singapore (74.1%) and Turkey (72.4%). In general, countries of Central Asia and Sub-Saharan Africa and North America had high increases, and countries from East Asia, and High Income Pacific-Asia had the large decreases. (Figure 3).

Figure 4 shows in inverse correlation of the age-standardised mortality rates in countries with the SDI value in 2017 (r^2=-0.51). However, considerable variation can be seen in age-standardised diabetes deaths rates within each SDI group. Countries with extreme rates in each SDI group are presented in Table 1. In the high SDI group, the estimated deaths rate varied in 2017 from 0.03/100,000 in Switzerland to 0.25/100,000 in Latvia. In the low SDI group, they varied from 0.29/100,000 in Nepal to 1.39/100,000 in Afghanistan. In general, the absolute difference between the highest and the lowest rate in each group decreased from 1990 to 2017, the opposite occurring with respect to the relative difference (Data not shown).

In our analyses, 88% of deaths globally, and 92% of those in the high SDI countries, were ascribed to type 1 diabetes in 2017. As a sensitivity analysis, we reproduced all figures, excluding deaths due to type 2 disease. Mortality rates, though slightly smaller, maintained virtually identical patterns as those shown in the original figures (data not shown).

Discussion

Despite the general progress in mortality from diabetes under 25 observed in recent decades, large disparities across countries persist in 2017, mortality being nearly 5 times greater in low- and low-middle SDI than in high SDI countries. That high SDI countries had nearly zero deaths in 2017 highlights the preventability of these premature deaths. That SDI explained only part of these differences suggests that variability in access to care resulting from policy decisions also plays a role.

The findings of nearly zero deaths in high SDI countries are consistent with those of previous reports focused on type 1 diabetes mortality. [16,17] GBD estimates of mortality according to type of diabetes, which were presented for the first time in GBD 2017, ascribe 88% of deaths globally, and 92% in high SDI countries, as being due to type 1 diabetes. To avoid uncertainty in the classification of this amenable cause of death in countries with more limited quality of death certificates, we opted to analyze here all diabetes-related mortality under age 25.

To interpret the nearly five times greater risk of dying due to diabetes in low-middle income countries, presumably almost all due to type 1 diabetes, we must consider acute complications of diabetes as the main cause of death, which is consistent with previous reports.[8,17] For a person with type 1 diabetes to be able to survive, he/she needs, at minimum, a certain level of health care enabling the use of insulin daily and the provision of support for the management of acute conditions threatening diabetes control. Protocols have been developed in high income countries over the years to excel at this,[18] but less developed countries have faced obstacles, making the implementation of similar protocols less than adequate.

The rapid decrease in deaths due to acute complications in a LMIC [7] with increasingly adequate and accessible primary care and the provision of free or low-cost insulin highlights the preventability of such deaths even in settings having less resources.

More than 13 million people are living with type 1 diabetes and needing to use insulin daily.[12] The access and prices of the insulin vary across countries, being susceptible to increases by import taxes.[19] In countries with health systems requiring that diabetic individuals pay out-of-pocket, all or in part, for insulin as well as syringes, blood glucose meters, and the necessary health education, higher prices can make insulin inaccessible for some.[19–21] In fact, the recent increase in costs of insulin has raised the possibility that insulin underuse could increase mortality in those with type 1 diabetes even in some high-income countries.[22] For example, trends in hospitalization show an increase in the number of visits to emergency departments due to acute complications of diabetes in the US since 2010, with an increase of the deaths rate due to these conditions between 2010 and 2015.[23]

With this indicator of amenable deaths due to diabetes, we have mapped countries and regions that need greater action to prevent these deaths. Afghanistan and Haiti had the highest rates, followed by many countries in Sub-Saharan Africa, Central America, East Asia, and in countries neighboring Afghanistan. In Sub-Saharan Africa, for which the public health focus has been on high mortality due to communicable and childhood diseases,[10] death rates due diabetes are high and increasing. Though relatively few reports about type 1 diabetes in Sub-Saharan Africa are available, high death rates are likely being driven by inadequate diagnosis and treatment.[24]

Actions to prevent these deaths should be addressed, with prompt diagnosis and treatment of type 1 diabetes, and with the provision of basic care and education of patients and their family to mitigate these premature deaths.[24] The UN sustainable development goal 3 emphasizes the necessity of providing access to affordable essential medicines, and the WHO´s Global Target 9 for confronting NCDs focuses on the availability of essential medicines, including insulin.[1,2] To date, there has been no means of annual surveillance and monitoring of these goals for the world´s countries. The use of the age-standardised mortality rate from diabetes under 25 can help to track the achievement of these goals with respect to diabetes.

This study has some limitations that should be mentioned. One is the low rate of deaths from diabetes in this age range. Given this low rate, the large number of deaths in childhood in many LMICs could confound findings to some extent. Yet large variability in the rate of deaths from diabetes in countries with similarly large overall childhood mortality rates suggests that GBD modelling has largely avoided this problem. Another limitation is that deaths from diabetes when occurring under 5 years old are more likely to be due to monogenic diabetes, which may go undiagnosed in less sophisticated settings. However, the small fraction of deaths that occur under 5 years of age minimizes this problem. For the overall diabetes mortality estimation for ages 15 to 24, the covariates used were mainly related to type 2 diabetes. However, when we excluded deaths in this range due to type 2 diabetes, the differences found between countries were basically unchanged. There are additional limitations and biases common to the GBD methodological approach, which are described elsewhere in greater detail.[10] One important one is the low quality of data from some countries and years. In these cases, estimates based on regions and neighboring countries were extrapolated using the values of covariates to approximate the likely value for the country in question. The use a GBD´s complex methodology to address this problem and produce the most reliable and up to date estimates for each location, in this regard, is a strength of our approach.

Even with these limitations, this study was able to describe, for the first time, a cogent and comprehensive overview of the level and trends of deaths from diabetes under 25 across the world. It demonstrates that this metric could serve as an indicator of the current status and trends of amenable deaths due to diabetes.

Conclusion

Great variability in the rates of deaths from diabetes under 25, both between and within SDI groups, exist. While these rates are declining across the globe, the decrease is less pronounced in low- and low-middle SDI countries. The large variability in rates within each SDI group demonstrates that factors beyond developmental level, many presumedly related to the structure of and level of support given health care, are determinants of these rates. Diabetes mortality under 25 represents a readily available and frequently updated indicator which can be used in the surveillance and monitoring of the adequacy of diabetes care in low- and middle-income countries.

Figures

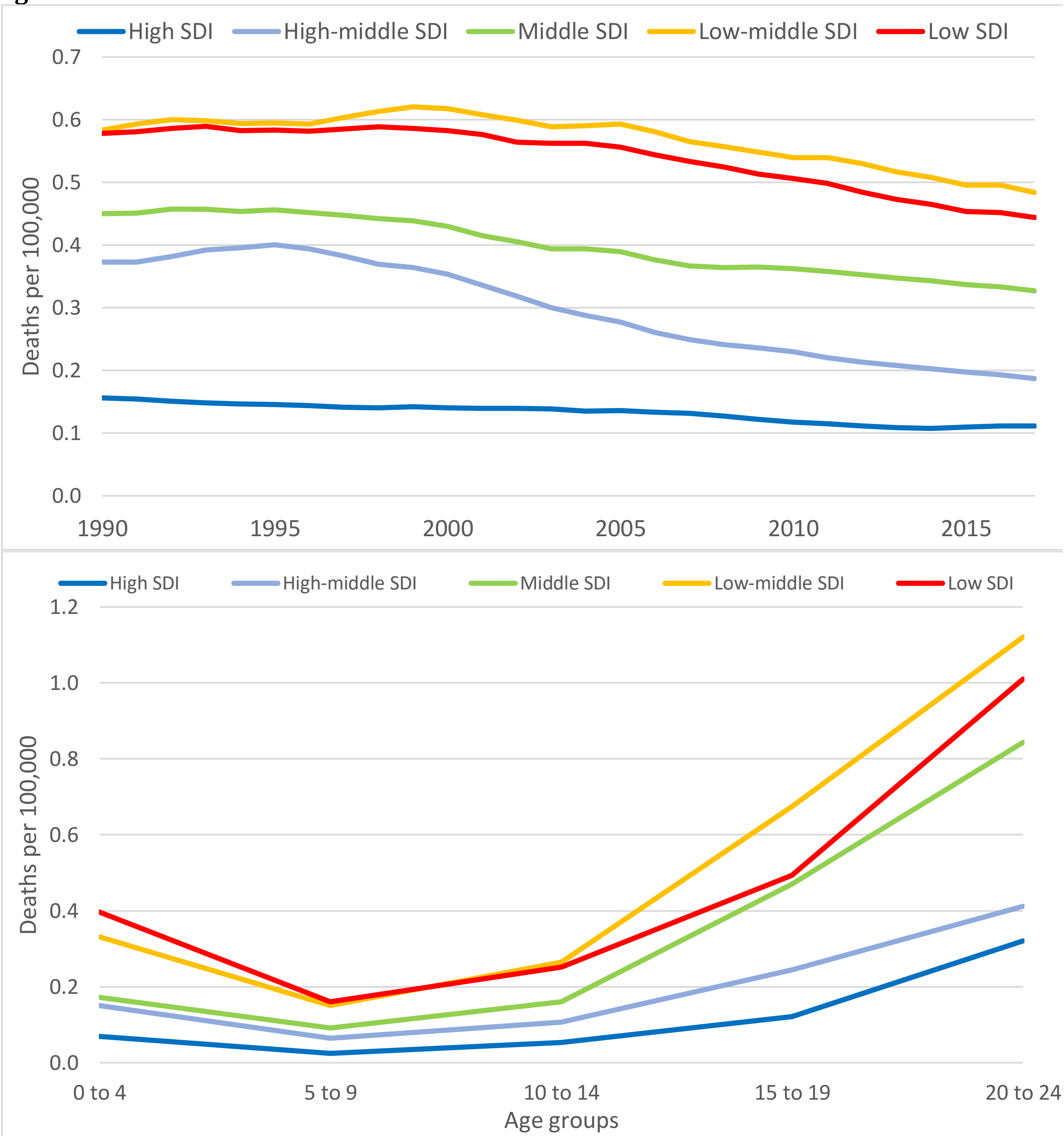
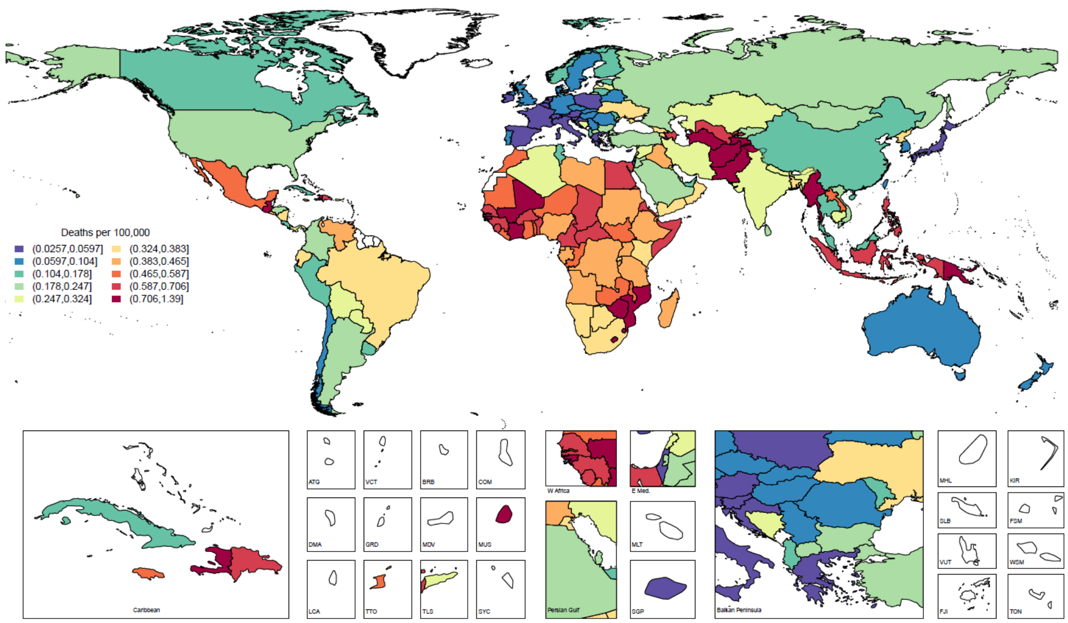


Figure 1 – Trends in age-standardised mortality diabetes rate in under 25 years old from 1990 to 2017 by socio-demographic index group (A), and Age pattern in 2017 (B).

Age−standardised Diabetes deaths per 100,000 in under 25 years old, 2017, both sexes



Diabetes, Percent of total deaths in under 25 years old, 2017, both sexes

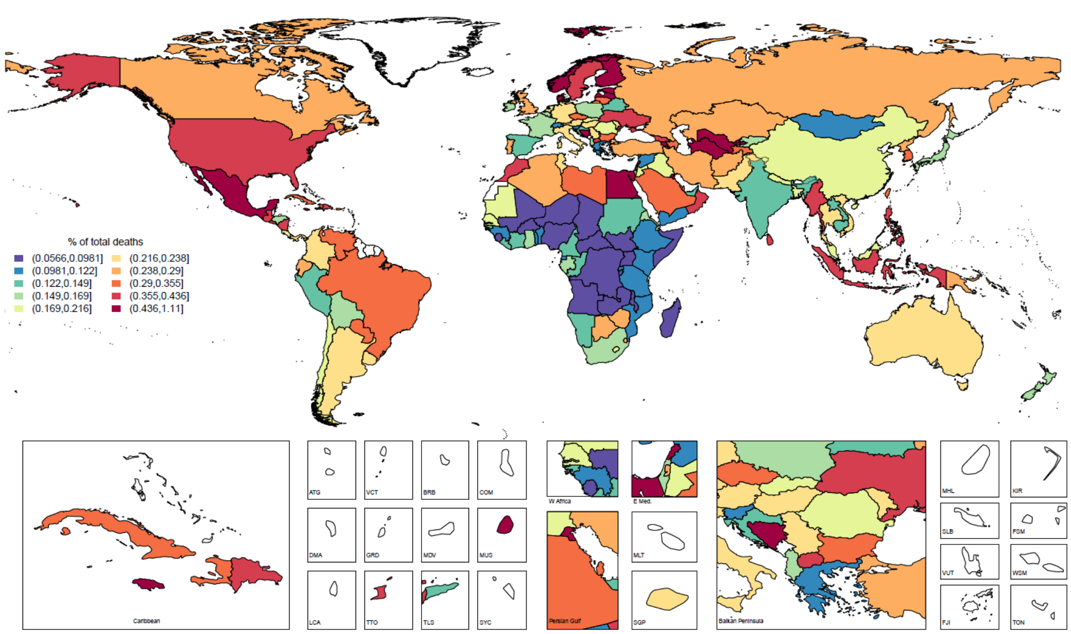


Figure 2 – Map of age-standardised deaths due to diabetes in under 25 years old (A), and percent of total deaths in 2017 (B).

Percentage change in age−standardised Diabetes deaths rate in under 25 years old, 1990−2017, both sexes

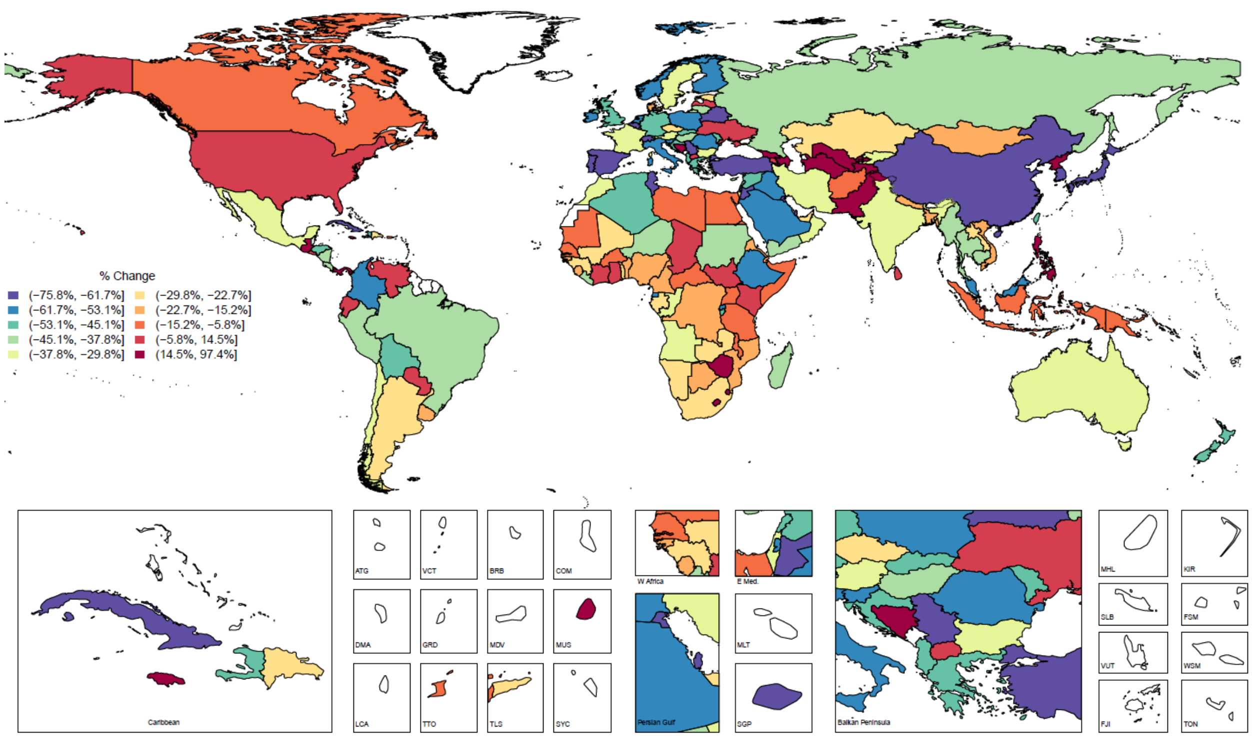


Figure 3 – Map of percentage change in age-standardised deaths due to diabetes in under 25 years old from 1990 to 2017.

Figure 4 – Scatter of age-standardised diabetes mortality rate in under 25 years old by Socio-demografic index in 2017, with SDI group cutoff points indicated by vertical lines.

Table 1 – The highest and the lowest age-standardised death rate due to diabetes in under 25 years old in 2017, and percentage change from 1990 to 2017, by SDI group.

	Age-standardised rate per 100,00 in 2017		Percentage change 1990-2017	
Location	Highest	Lowest	Most Unfavorable	Most Favorable
High SDI	Latvia (0.25)	Switzerland (0.03)	USA (-1.0%)	Singapore (-74.1%)
High-middle SDI	Mauritius (0.77)	Israel (0.05)	Mauritius (97.4%)	Belarus (-75.5%)
Middle SDI	Turkmenistan (0.81)	Costa Rica (0.11)	Philippines (95.1%)	Cuba (-67.8%)
Low-middle SDI	Zimbabwe (1.00)	Honduras (0.18)	Guatemala (90.8%)	Iraq (-61.0%)
Low SDI	Afghanistan (1.39)	Nepal (0.29)	Chad (6.3%)	Ethiopia (-54.1%)

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Supplementary Material (ANEXO 2)

Supplementary Table 1– Age-standardised deaths rate due to diabetes in under 25 years old in 1990 and 2017, percentage change 1990-2017, percent of total deaths, number of deaths, and population.

CONSIDERAÇÕES FINAIS

O diabetes está entre as cinco principais DCNT, e entre elas a única com um crescimento ainda não controlado. A carga de diabetes nas Américas, especialmente nas regiões da América Latina Central e o Caribe é muito alta quando comparada a global. O IMC elevado e alimentação inadequada são os principais fatores de risco para o diabetes, produzindo uma alta prevalência e também suas consequências, morbidade e mortalidade prematura. Politicas públicas precisam ser realizadas para parar o crescimento dos fatores de risco de diabetes, e assim consequentemente a sua incidência. Além disto, os sistemas de saúde precisam estar preparados para dar os cuidados necessários a estes indivíduos.

Já os casos de mortalidade por diabetes abaixo de 25 anos, que podemos assumir que são majoritariamente por complicações agudas do diabetes, apresentam uma grande variação ao redor do mundo. Essa variação existe ainda que seja controlado o índice sócio demográfico. A utilização das estimativas de mortalidade do GBD por diabetes abaixo de 25 anos pode ser utilizada como uma ferramenta para monitorar os avanços dos países, assim como o estado atual e as tendências. Medidas como melhora no cuidado a saúde do diabético, com acesso e disponibilidade a insulina demonstram uma melhora do resultado rapidamente, e podem ser aplicadas em países que ainda apresentam altas taxas de mortalidade.

ANEXO 1

Supplement to “**Burden of Diabetes Mellitus and Hyperglycemia in Adults in the Americas, 1990 -2017: GBD 2017 study”,** Ewerton Cousin, Maria Inês Schmidt, Rafael Lozano, Ashkan Afshin, Liane Ong, other authors, Mohsen Naghavi, Bruce B. Duncan.

Contents

Supplementary Table 1 – List of countries/territories, by region, that constitute the Americas.

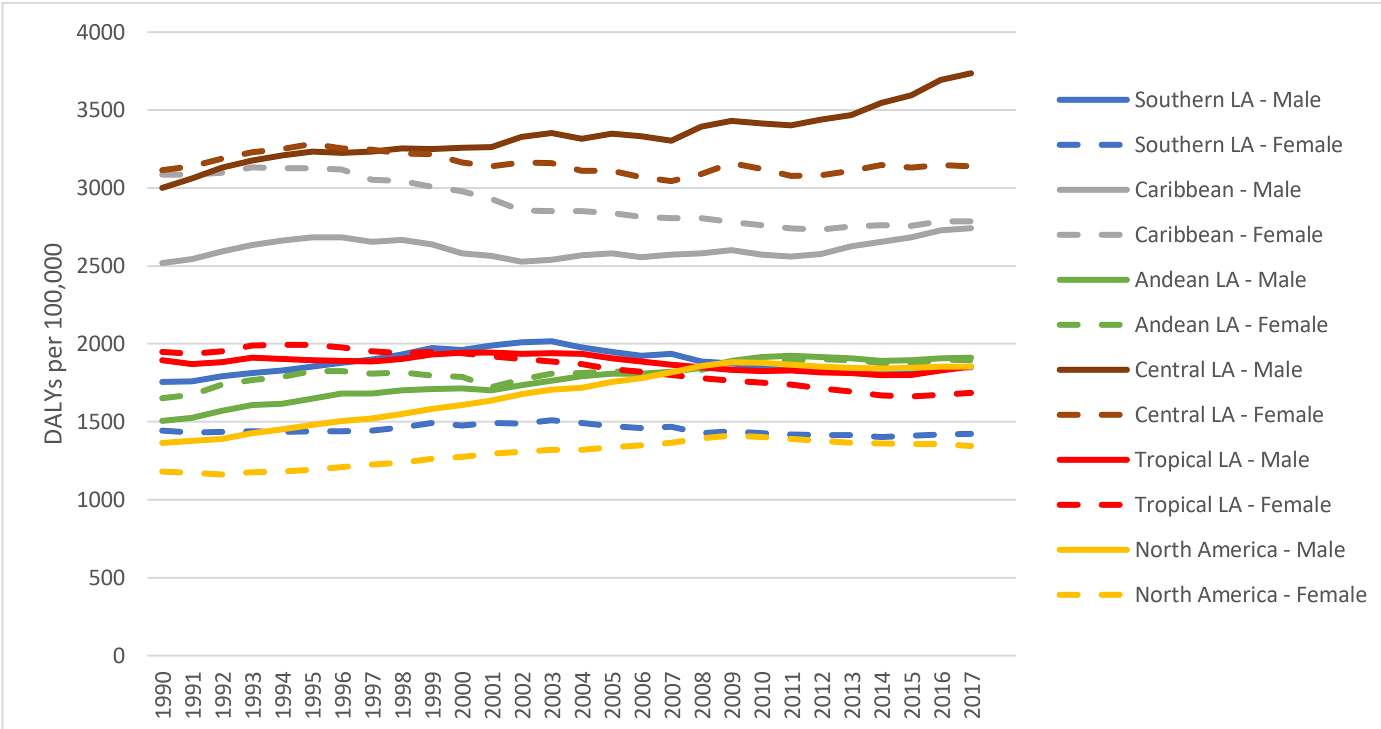
Region	Country/Territory
North America	Canada
	United States
Caribbean	Antigua and Barbuda
	Barbados
	Belize
	Bermuda
	Cuba
	Dominica
	Dominican Republic
	Grenada
	Guyana
	Haiti
	Jamaica
	Puerto Rico
	Saint Lucia
	Saint Vincent and Grenadines
	Suriname
	The Bahamas
	Trinidad and Tobago
	Virgin Islands, U.S.
Central Latin America	Colombia
	Costa Rica
	El Salvador
	Guatemala
	Honduras
	Mexico
	Nicaragua
	Panama
	Venezuela

Andean Latin America	Bolivia
	Ecuador
	Peru
Tropical Latin America	Brazil
	Paraguay
Southern Latin America	Argentina
	Chile
	Uruguay

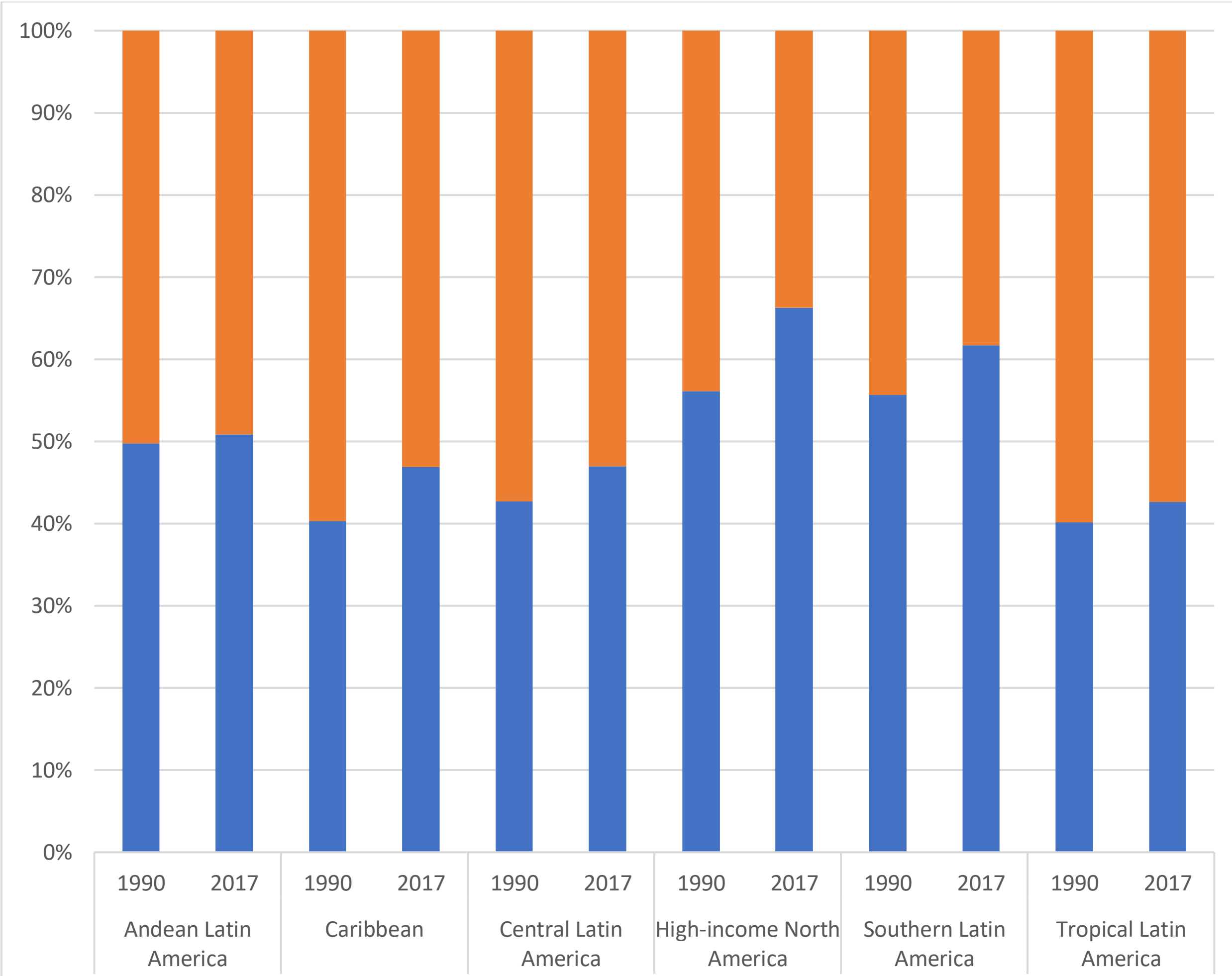
Supplementary Table 2 – Age standardized DALYs rate, percentage change, percent of total DALYs and ratio observed/expect by SDI, in the America's regions and countries for adults (25 years or older), 1990-2017.

Location	Age-standardised DALYs per 100,000	Age-standardised Percentage change 1990-2017	Percent of total DALYs	Ratio Observed/ expected
Global	**1726.41**	**15.3%**	**4.5%**	**0.82**
The Americas	**2051.89**	**17.9%**	**6.1%**	
North America	**1586.05**	**25.6%**	**5.0%**	
Canada	1091.78	-12.0%	4.4%	1.04
USA	1645.01	29.9%	5.1%	1.45
Caribbean	**2765.06**	**-1.6%**	**7.2%**	**1.32**
Antigua and Barbuda	3329.24	-6.2%	10.2%	1.82
The Bahamas	2995.20	-7.1%	7.3%	1.70
Barbados	3248.85	-11.8%	10.6%	2.26
Belize	3868.32	35.5%	8.9%	1.42
Bermuda	1608.44	-22.0%	6.5%	1.31
Cuba	1383.18	-22.1%	4.6%	0.84
Dominica	3566.14	1.7%	9.6%	2.06
Dominican Republic	2312.82	37.4%	5.7%	0.94
Grenada	4043.20	-0.2%	10.6%	2.18
Guyana	4953.81	23.5%	9.6%	2.06
Haiti	4311.70	-16.7%	6.9%	1.43
Jamaica	4832.27	39.8%	12.6%	2.40
Puerto Rico	3200.42	6.9%	11.1%	2.74
Saint Lucia	3655.03	-18.5%	10.2%	1.81
Saint Vincent and the Grenadines	4855.67	8.3%	11.7%	2.33
Suriname	3548.98	27.1%	8.5%	1.65
Trinidad and Tobago	5714.23	-16.1%	15.3%	3.27
Virgin Islands	3069.12	5.5%	8.3%	2.62
Central Latin America	**3418.93**	**11.7%**	9.9%	1.48
Colombia	1209.82	-25.5%	4.5%	0.57
Costa Rica	1307.51	-9.7%	4.5%	0.62
El Salvador	3603.60	95.5%	8.7%	1.54
Guatemala	4134.73	130.8%	9.3%	1.48
Honduras	1877.01	23.0%	4.5%	0.69
Mexico	4789.31	13.5%	13.1%	2.07
Nicaragua	2805.43	14.0%	8.7%	1.03
Panama	2114.88	34.9%	7.4%	1.06

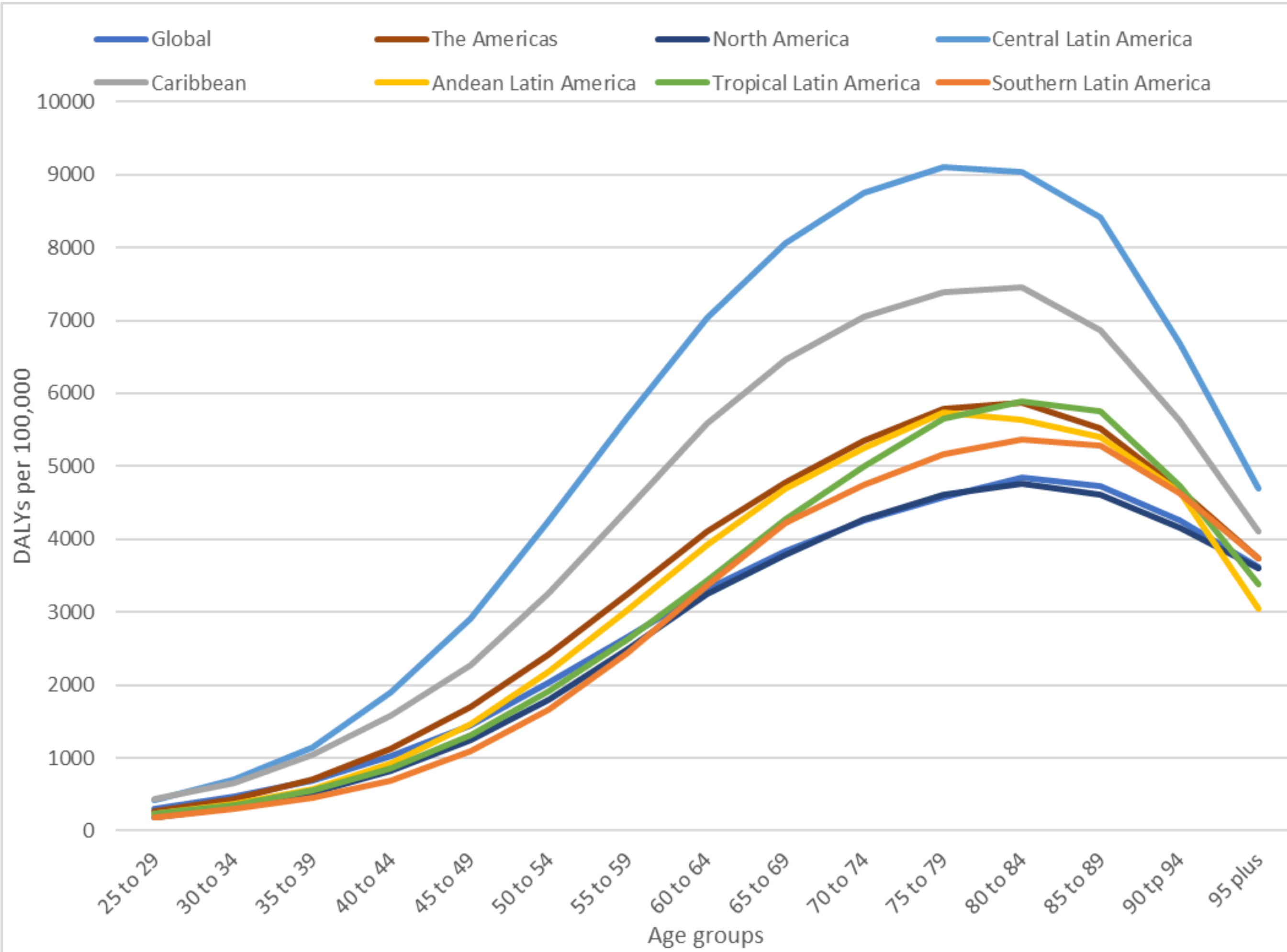
Venezuela	2592.23	11.4%	7.1%	1.14
Andean Latin America	**1903.51**	**20.4%**	**6.0%**	**0.82**
Bolivia	2828.64	-1.3%	7.0%	1.08
Ecuador	2451.97	39.7%	7.2%	1.06
Peru	1369.80	18.7%	4.9%	0.60
Tropical Latin America	**1763.56**	**-8.4%**	**4.8%**	**0.83**
Brazil	1732.80	-10.1%	4.7%	0.83
Paraguay	3075.78	62.5%	8.1%	1.20
Southern Latin America	**1615.49**	**1.8%**	**5.0%**	**0.97**
Argentina	1687.73	4.4%	5.0%	0.98
Chile	1467.43	0.0%	4.9%	0.93
Uruguay	1579.26	-6.1%	4.9%	1.04



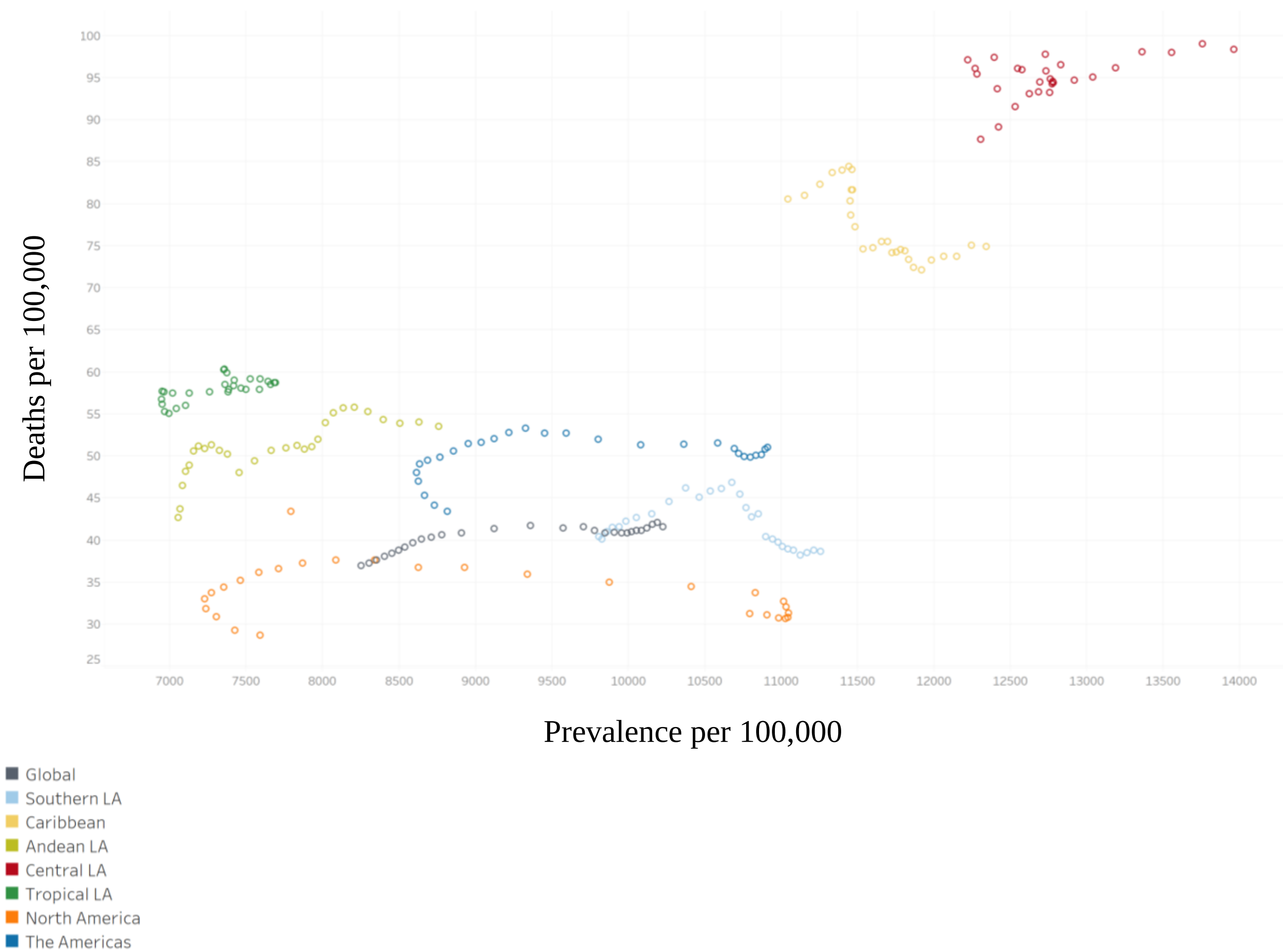
Supplementary Figure 1: Age-standardised DALY rates for regions of the Americas in 2017 for adult men (solid lines) and women (dashed lines).



Supplementary Figure 2 – Percent of total crude diabetes burden expressed as disability (Years lived with disability – YLDs; blue) and premature mortality (Years of life lost – YLLs; orange) among regions of the Americas, in 1990 and 2017.



Supplementary Figure 3 Distribution of DALYs due to diabetes across the lifespan for adults in 2017 in regions of the Americas.



Supplementary Figure 4 – Changes in the age-standardised death rate and age-standardised prevalence rate in regions of the Americas over time, from 1990 to 2017. Each point represents both rates for a given year for the regions shown.

ANEXO 2

Supplement to “**Monitoring levels and trends in diabetes mortality under age 25 years around the globe”** Ewerton Cousin, Maria Inês Schmidt, Bruce B. Duncan, Mohsen Naghavi

Supplementary Table 1 - Age-standardised deaths rate due to diabetes in under 25 years old in 1990 and 2017, percentage change 1990-2017, percent of total deaths, number of deaths, and population.

	Age-standardised deaths rate (per 100,000)									Percent of total deaths			Number of deaths due to DM		
	1990			2017			Percentage Change 1990-2017			2017			2017		
Location	**mean**	**lower**	**upper**	**mean**	**lower**	**upper**	**mean**	**lower**	**upper**	**mean**	**lower**	**upper**	**mean**	**lower**	**upper**
Global	**0.44**	**0.40**	**0.49**	**0.36**	**0.33**	**0.38**	**-19.7%**	**-25.8%**	**-12.9%**	**0.2%**	**0.1%**	**0.2%**	**11643**	**10900**	**12438**
Low SDI	**0.58**	**0.44**	**0.68**	**0.44**	**0.41**	**0.48**	**-23.2%**	**-33.6%**	**-0.4%**	**0.1%**	**0.1%**	**0.1%**	**3269**	**2983**	**3569**
Low-middle SDI	**0.58**	**0.52**	**0.65**	**0.48**	**0.44**	**0.53**	**-17.0%**	**-26.2%**	**-7.8%**	**0.2%**	**0.1%**	**0.2%**	**4292**	**3937**	**4703**
Middle SDI	**0.45**	**0.42**	**0.49**	**0.33**	**0.30**	**0.35**	**-27.4%**	**-32.0%**	**-23.3%**	**0.3%**	**0.3%**	**0.3%**	**2820**	**2618**	**3045**
High-middle SDI	**0.37**	**0.35**	**0.40**	**0.19**	**0.18**	**0.20**	**-49.9%**	**-53.5%**	**-46.7%**	**0.3%**	**0.2%**	**0.3%**	**854**	**802**	**910**
High SDI	**0.16**	**0.15**	**0.16**	**0.11**	**0.11**	**0.12**	**-28.8%**	**-31.9%**	**-26.0%**	**0.3%**	**0.3%**	**0.3%**	**385**	**370**	**400**
Central Europe, Eastern Europe, and Central Asia	**0.29**	**0.28**	**0.30**	**0.29**	**0.27**	**0.31**	**1.9%**	**-5.0%**	**7.8%**	**0.3%**	**0.3%**	**0.3%**	**387**	**360**	**413**
Central Asia	**0.40**	**0.38**	**0.43**	**0.58**	**0.52**	**0.63**	**42.8%**	**27.9%**	**56.7%**	**0.4%**	**0.3%**	**0.4%**	**236**	**214**	**259**
Armenia	0.35	0.31	0.40	0.36	0.31	0.41	2.2%	-14.7%	19.1%	0.61%	0.52%	0.69%	4	3	4
Azerbaijan	0.48	0.42	0.54	0.61	0.51	0.71	27.0%	3.8%	57.0%	0.33%	0.26%	0.42%	26	22	30
Georgia	0.25	0.22	0.28	0.33	0.29	0.37	32.7%	11.5%	54.3%	0.40%	0.33%	0.46%	4	3	4
Kazakhstan	0.40	0.37	0.44	0.28	0.24	0.33	-29.8%	-41.3%	-18.6%	0.25%	0.21%	0.29%	20	17	23
Kyrgyzstan	0.34	0.31	0.39	0.22	0.19	0.26	-35.7%	-44.8%	-25.7%	0.16%	0.13%	0.18%	7	6	8
Mongolia	0.30	0.25	0.38	0.25	0.20	0.29	-19.5%	-36.8%	2.2%	0.12%	0.10%	0.15%	3	3	4

Tajikistan	0.49	0.44	0.56	0.89	0.73	1.05	81.9%	49.8%	117.6%	0.31%	0.25%	0.38%	43	36	51
Turkmenistan	0.53	0.47	0.59	0.81	0.71	0.91	53.0%	30.5%	77.7%	0.45%	0.37%	0.56%	18	16	20
Uzbekistan	0.40	0.36	0.44	0.70	0.59	0.81	77.4%	48.9%	107.3%	0.50%	0.41%	0.60%	111	94	127
Central Europe	**0.18**	**0.17**	**0.19**	**0.09**	**0.08**	**0.09**	**-50.7%**	**-54.2%**	**-47.3%**	**0.2%**	**0.2%**	**0.2%**	**29**	**27**	**31**
Albania	0.21	0.18	0.25	0.12	0.09	0.14	-46.0%	-57.9%	-30.2%	0.15%	0.12%	0.19%	1	1	2
Bosnia and Herzegovina	0.17	0.14	0.21	0.28	0.23	0.34	66.8%	21.7%	118.2%	0.75%	0.62%	0.90%	3	3	4
Bulgaria	0.29	0.26	0.32	0.18	0.16	0.21	-36.1%	-45.4%	-24.0%	0.35%	0.30%	0.41%	3	3	4
Croatia	0.07	0.06	0.08	0.04	0.03	0.04	-45.6%	-53.0%	-36.3%	0.13%	0.12%	0.15%	0	0	1
Czech Republic	0.12	0.11	0.13	0.08	0.07	0.09	-28.9%	-39.3%	-16.0%	0.31%	0.27%	0.35%	2	2	3
Hungary	0.12	0.11	0.14	0.07	0.06	0.08	-44.0%	-51.4%	-34.5%	0.22%	0.19%	0.26%	2	2	2
Macedonia	0.22	0.18	0.25	0.21	0.18	0.25	-1.5%	-18.7%	20.4%	0.44%	0.36%	0.52%	2	1	2
Montenegro	0.27	0.23	0.31	0.18	0.15	0.21	-33.6%	-46.0%	-17.6%	0.53%	0.45%	0.63%	0	0	0
Poland	0.14	0.13	0.16	0.05	0.05	0.06	-61.2%	-66.9%	-54.1%	0.16%	0.14%	0.19%	6	5	7
Romania	0.25	0.23	0.28	0.10	0.09	0.11	-59.9%	-65.4%	-53.7%	0.18%	0.16%	0.21%	5	5	6
Serbia	0.22	0.18	0.26	0.07	0.06	0.08	-68.0%	-75.0%	-59.1%	0.24%	0.20%	0.28%	2	2	2
Slovakia	0.13	0.11	0.14	0.07	0.06	0.08	-45.4%	-55.5%	-34.5%	0.18%	0.15%	0.21%	1	1	1
Slovenia	0.07	0.06	0.08	0.03	0.03	0.04	-54.1%	-61.4%	-46.2%	0.12%	0.11%	0.14%	0	0	0
Eastern Europe	**0.30**	**0.29**	**0.31**	**0.21**	**0.19**	**0.22**	**-30.6%**	**-34.5%**	**-26.8%**	**0.3%**	**0.3%**	**0.3%**	**122**	**114**	**129**
Belarus	0.26	0.23	0.29	0.06	0.05	0.08	-75.5%	-79.8%	-69.7%	0.13%	0.10%	0.15%	2	1	2
Estonia	0.24	0.21	0.27	0.18	0.15	0.21	-26.5%	-40.7%	-9.7%	0.49%	0.41%	0.57%	1	1	1
Latvia	0.27	0.24	0.30	0.25	0.21	0.30	-5.3%	-23.2%	14.5%	0.57%	0.48%	0.68%	1	1	2
Lithuania	0.22	0.20	0.25	0.13	0.12	0.15	-39.0%	-48.7%	-27.7%	0.32%	0.28%	0.37%	1	1	1
Moldova	0.37	0.33	0.42	0.17	0.15	0.20	-53.1%	-60.5%	-44.7%	0.22%	0.18%	0.26%	2	2	2

Russian Federation	0.30	0.29	0.31	0.18	0.17	0.19	-41.0%	-43.4%	-38.8%	0.24%	0.23%	0.25%	73	68	75
Ukraine	0.30	0.28	0.33	0.34	0.29	0.38	11.8%	-3.9%	29.6%	0.38%	0.33%	0.44%	43	37	48
High-income	**0.16**	**0.15**	**0.17**	**0.12**	**0.11**	**0.12**	**-25.2%**	**-28.3%**	**-22.4%**	**0.3%**	**0.3%**	**0.3%**	**401**	**386**	**416**
Australasia	**0.12**	**0.11**	**0.13**	**0.07**	**0.07**	**0.08**	**-36.7%**	**-46.1%**	**-26.3%**	**0.2%**	**0.2%**	**0.2%**	**7**	**6**	**8**
Australia	0.12	0.11	0.13	0.08	0.07	0.09	-33.8%	-45.2%	-21.2%	0.23%	0.20%	0.26%	6	5	7
New Zealand	0.13	0.12	0.15	0.07	0.06	0.08	-48.7%	-55.2%	-42.2%	0.17%	0.15%	0.19%	1	1	1
High-income Asia-Pacific	**0.14**	**0.13**	**0.16**	**0.05**	**0.04**	**0.05**	**-66.9%**	**-69.8%**	**-64.1%**	**0.2%**	**0.2%**	**0.2%**	**24**	**22**	**25**
Brunei	0.87	0.69	1.07	0.61	0.52	0.72	-29.6%	-44.7%	-11.3%	0.90%	0.76%	1.06%	1	1	1
Japan	0.09	0.09	0.10	0.03	0.03	0.04	-64.5%	-67.0%	-60.3%	0.15%	0.14%	0.16%	10	9	11
South Korea	0.25	0.22	0.27	0.07	0.06	0.08	-71.2%	-75.6%	-66.5%	0.31%	0.27%	0.35%	12	10	13
Singapore	0.14	0.11	0.16	0.04	0.03	0.04	-74.1%	-78.9%	-65.6%	0.22%	0.18%	0.29%	1	1	1
High-income North America	**0.20**	**0.20**	**0.22**	**0.20**	**0.19**	**0.21**	**-1.7%**	**-7.6%**	**3.6%**	**0.4%**	**0.4%**	**0.4%**	**252**	**240**	**265**
Canada	0.12	0.11	0.14	0.11	0.09	0.12	-15.0%	-28.1%	0.2%	0.26%	0.23%	0.31%	12	10	14
Greenland	0.24	0.19	0.30	0.08	0.06	0.10	-66.1%	-77.0%	-54.4%	0.07%	0.06%	0.09%	0	0	0
USA	0.21	0.20	0.22	0.21	0.20	0.22	-1.0%	-6.8%	4.1%	0.38%	0.36%	0.40%	240	229	253
Southern Latin America	**0.21**	**0.20**	**0.23**	**0.16**	**0.14**	**0.18**	**-24.1%**	**-32.8%**	**-13.9%**	**0.2%**	**0.2%**	**0.2%**	**43**	**39**	**48**
Argentina	0.25	0.23	0.27	0.19	0.16	0.21	-24.6%	-35.0%	-12.2%	0.23%	0.20%	0.26%	35	30	40
Chile	0.13	0.11	0.14	0.09	0.07	0.10	-32.2%	-43.4%	-19.0%	0.17%	0.15%	0.20%	6	5	7
Uruguay	0.21	0.19	0.24	0.16	0.14	0.19	-22.1%	-35.3%	-6.0%	0.24%	0.20%	0.28%	2	2	3
Western Europe	**0.12**	**0.12**	**0.13**	**0.06**	**0.06**	**0.06**	**-51.2%**	**-54.2%**	**-48.4%**	**0.2%**	**0.2%**	**0.2%**	**75**	**71**	**79**

Andorra	0.13	0.10	0.17	0.07	0.06	0.09	-43.7%	-58.2%	-25.5%	0.34%	0.28%	0.40%	0	0	0
Austria	0.08	0.08	0.09	0.06	0.05	0.06	-32.7%	-42.9%	-21.0%	0.22%	0.19%	0.25%	1	1	2
Belgium	0.13	0.11	0.14	0.04	0.04	0.05	-64.9%	-70.8%	-58.0%	0.16%	0.13%	0.18%	1	1	2
Cyprus	0.05	0.05	0.06	0.03	0.03	0.03	-44.3%	-55.1%	-31.1%	0.11%	0.09%	0.13%	0	0	0
Denmark	0.12	0.11	0.14	0.10	0.09	0.12	-18.6%	-33.2%	-2.5%	0.44%	0.37%	0.51%	2	2	2
Finland	0.27	0.24	0.31	0.12	0.11	0.15	-54.5%	-63.0%	-44.9%	0.50%	0.42%	0.58%	2	2	3
France	0.07	0.07	0.09	0.05	0.04	0.05	-37.2%	-48.0%	-26.6%	0.16%	0.14%	0.18%	9	8	11
Germany	0.12	0.11	0.13	0.06	0.05	0.07	-48.0%	-56.1%	-39.1%	0.23%	0.20%	0.27%	14	12	16
Greece	0.07	0.06	0.09	0.04	0.03	0.04	-50.4%	-57.6%	-42.6%	0.11%	0.10%	0.13%	1	1	1
Iceland	0.05	0.05	0.06	0.03	0.02	0.03	-45.1%	-53.7%	-34.9%	0.12%	0.10%	0.13%	0	0	0
Ireland	0.10	0.09	0.12	0.04	0.04	0.05	-58.9%	-65.9%	-51.5%	0.15%	0.13%	0.17%	1	1	1
Israel	0.07	0.06	0.08	0.05	0.04	0.05	-33.3%	-45.3%	-21.9%	0.15%	0.13%	0.17%	2	2	2
Italy	0.13	0.11	0.14	0.05	0.05	0.06	-57.7%	-64.1%	-50.4%	0.22%	0.20%	0.25%	8	7	9
Luxembourg	0.09	0.08	0.11	0.04	0.03	0.05	-58.4%	-65.4%	-48.9%	0.17%	0.15%	0.20%	0	0	0
Malta	0.16	0.13	0.17	0.10	0.09	0.12	-33.6%	-44.3%	-21.9%	0.29%	0.25%	0.33%	0	0	0
Netherlands	0.12	0.11	0.13	0.05	0.04	0.05	-60.2%	-66.2%	-53.5%	0.19%	0.17%	0.22%	2	2	3
Norway	0.34	0.28	0.36	0.15	0.14	0.16	-55.0%	-59.2%	-50.0%	0.64%	0.59%	0.68%	3	2	3
Portugal	0.21	0.18	0.23	0.07	0.06	0.08	-68.4%	-73.2%	-62.7%	0.26%	0.23%	0.30%	2	2	2
Spain	0.12	0.11	0.13	0.03	0.03	0.04	-70.6%	-75.2%	-64.3%	0.15%	0.13%	0.18%	4	3	5
Sweden	0.15	0.13	0.16	0.10	0.09	0.12	-31.2%	-40.7%	-19.9%	0.43%	0.37%	0.50%	3	3	4
Switzerland	0.08	0.07	0.09	0.03	0.02	0.03	-66.2%	-71.7%	-58.6%	0.10%	0.09%	0.12%	1	1	1
United Kingdom	0.18	0.17	0.18	0.09	0.08	0.09	-50.6%	-52.6%	-47.2%	0.28%	0.27%	0.30%	19	18	20
Latin America and Caribbean	**0.66**	**0.63**	**0.70**	**0.43**	**0.41**	**0.46**	**-34.8%**	**-38.1%**	**-30.7%**	**0.3%**	**0.3%**	**0.4%**	**1134**	**1079**	**1197**
Andean Latin America	**0.34**	**0.31**	**0.38**	**0.24**	**0.21**	**0.27**	**-30.1%**	**-39.3%**	**-19.6%**	**0.2%**	**0.2%**	**0.2%**	**70**	**62**	**79**

Bolivia	0.55	0.45	0.67	0.29	0.22	0.36	-47.5%	-61.8%	-31.8%	0.16%	0.12%	0.21%	17	13	21
Ecuador	0.31	0.28	0.35	0.34	0.29	0.39	9.7%	-10.3%	30.9%	0.27%	0.23%	0.33%	28	24	32
Peru	0.29	0.25	0.33	0.16	0.13	0.19	-43.9%	-54.9%	-30.4%	0.15%	0.12%	0.17%	25	21	30
Caribbean	**0.96**	**0.84**	**1.14**	**0.74**	**0.64**	**0.87**	**-23.1%**	**-34.5%**	**-9.5%**	**0.4%**	**0.3%**	**0.4%**	**147**	**128**	**173**
Antigua and Barbuda	0.80	0.70	0.91	0.75	0.65	0.86	-6.1%	-22.8%	13.3%	0.98%	0.81%	1.16%	0	0	0
The Bahamas	0.67	0.59	0.75	0.64	0.55	0.74	-4.4%	-20.6%	13.9%	0.67%	0.57%	0.78%	1	1	1
Barbados	0.99	0.88	1.11	0.83	0.71	0.97	-15.6%	-31.6%	2.9%	1.15%	0.93%	1.40%	1	1	1
Belize	0.97	0.85	1.09	0.80	0.70	0.91	-17.1%	-30.6%	-1.5%	0.63%	0.53%	0.73%	2	1	2
Bermuda	0.41	0.35	0.53	0.19	0.16	0.24	-53.4%	-62.6%	-42.4%	0.49%	0.42%	0.60%	0	0	0
Cuba	0.40	0.37	0.45	0.13	0.11	0.15	-67.8%	-73.2%	-61.6%	0.34%	0.29%	0.40%	5	4	6
Dominica	1.03	0.91	1.18	1.29	1.09	1.50	25.4%	4.1%	51.0%	0.78%	0.63%	0.96%	0	0	0
Dominican Republic	0.99	0.85	1.13	0.70	0.57	0.84	-29.4%	-43.9%	-11.9%	0.42%	0.33%	0.52%	36	29	43
Grenada	1.26	1.11	1.43	0.76	0.65	0.89	-39.6%	-51.1%	-25.9%	1.07%	0.86%	1.30%	0	0	0
Guyana	1.26	1.11	1.41	1.12	0.94	1.31	-11.5%	-26.4%	6.4%	0.72%	0.59%	0.86%	4	4	5
Haiti	2.22	1.66	3.06	1.19	0.93	1.58	-46.4%	-60.4%	-27.3%	0.31%	0.24%	0.41%	75	58	99
Jamaica	0.42	0.37	0.47	0.59	0.48	0.71	41.2%	13.1%	72.5%	0.63%	0.49%	0.79%	8	6	10
Puerto Rico	0.36	0.32	0.40	0.30	0.26	0.35	-14.8%	-28.7%	0.4%	0.29%	0.26%	0.34%	4	3	4
Saint Lucia	1.10	0.96	1.25	0.71	0.62	0.82	-34.8%	-45.5%	-21.1%	0.85%	0.70%	1.03%	1	0	1
Saint Vincent and the Grenadines	0.95	0.84	1.08	1.33	1.14	1.52	39.2%	15.0%	67.0%	1.15%	0.93%	1.38%	1	1	1
Suriname	0.91	0.79	1.04	0.65	0.55	0.75	-28.9%	-40.7%	-14.0%	0.38%	0.32%	0.44%	2	1	2
Trinidad and Tobago	0.56	0.50	0.63	0.49	0.40	0.59	-12.6%	-30.2%	8.4%	0.41%	0.33%	0.50%	2	2	3
Virgin Islands	0.53	0.46	0.61	0.35	0.29	0.42	-34.5%	-47.2%	-17.2%	0.46%	0.39%	0.55%	0	0	0

Central Latin America	**0.68**	**0.64**	**0.71**	**0.48**	**0.45**	**0.52**	**-29.6%**	**-33.5%**	**-24.6%**	**0.4%**	**0.4%**	**0.4%**	**581**	**544**	**628**
Colombia	0.59	0.53	0.65	0.24	0.20	0.30	-58.7%	-66.1%	-49.1%	0.23%	0.20%	0.27%	54	46	66
Costa Rica	0.19	0.17	0.23	0.11	0.10	0.14	-40.5%	-49.9%	-30.2%	0.19%	0.16%	0.23%	2	2	3
El Salvador	0.44	0.36	0.56	0.45	0.36	0.56	1.7%	-26.0%	33.7%	0.39%	0.32%	0.47%	14	11	18
Guatemala	0.39	0.34	0.59	0.75	0.63	0.87	90.8%	11.4%	142.1%	0.38%	0.32%	0.45%	73	61	85
Honduras	0.33	0.28	0.39	0.18	0.13	0.25	-46.1%	-63.2%	-25.1%	0.15%	0.11%	0.20%	10	7	13
Mexico	0.85	0.78	0.89	0.59	0.55	0.65	-31.0%	-35.7%	-23.2%	0.53%	0.49%	0.58%	348	325	382
Nicaragua	0.55	0.47	0.67	0.34	0.29	0.40	-37.9%	-50.9%	-22.8%	0.36%	0.30%	0.44%	11	10	14
Panama	0.22	0.19	0.31	0.27	0.23	0.32	25.0%	-7.8%	53.5%	0.23%	0.20%	0.28%	5	4	6
Venezuela	0.47	0.43	0.53	0.45	0.38	0.53	-5.2%	-21.3%	14.6%	0.29%	0.25%	0.35%	63	54	75
Tropical Latin America	**0.67**	**0.61**	**0.71**	**0.37**	**0.35**	**0.39**	**-44.2%**	**-48.2%**	**-39.2%**	**0.3%**	**0.3%**	**0.3%**	**336**	**319**	**354**
Brazil	0.68	0.62	0.73	0.38	0.35	0.40	-44.6%	-48.7%	-39.5%	0.31%	0.29%	0.32%	326	309	343
Paraguay	0.25	0.21	0.30	0.28	0.23	0.35	13.4%	-14.4%	50.1%	0.30%	0.24%	0.37%	10	8	12
North Africa and Middle East	**0.70**	**0.57**	**0.80**	**0.46**	**0.42**	**0.52**	**-33.7%**	**-44.6%**	**-18.5%**	**0.2%**	**0.2%**	**0.3%**	**1325**	**1188**	**1485**
North Africa and Middle East	**0.70**	**0.57**	**0.80**	**0.46**	**0.42**	**0.52**	**-33.7%**	**-44.6%**	**-18.5%**	**0.2%**	**0.2%**	**0.3%**	**1325**	**1188**	**1485**
Afghanistan	1.64	0.47	2.71	1.39	0.91	1.96	-15.0%	-44.6%	208.1%	0.28%	0.18%	0.40%	307	202	437
Algeria	0.55	0.44	0.68	0.29	0.22	0.38	-46.8%	-61.4%	-32.1%	0.25%	0.18%	0.33%	53	39	70
Bahrain	0.67	0.55	0.83	0.49	0.35	0.64	-26.6%	-48.8%	2.9%	0.98%	0.71%	1.24%	2	2	3
Egypt	0.73	0.61	0.89	0.62	0.49	0.78	-15.1%	-32.5%	12.8%	0.44%	0.34%	0.56%	305	240	382
Iran	0.46	0.40	0.53	0.32	0.28	0.36	-30.9%	-39.6%	-22.7%	0.27%	0.24%	0.31%	100	87	112
Iraq	1.14	0.85	1.42	0.44	0.39	0.51	-61.0%	-69.8%	-48.0%	0.20%	0.18%	0.23%	108	94	123

Jordan	0.51	0.42	0.61	0.19	0.15	0.23	-63.0%	-72.5%	-50.3%	0.18%	0.15%	0.22%	11	9	13
Kuwait	0.95	0.83	1.10	0.33	0.28	0.40	-65.5%	-72.5%	-56.8%	0.61%	0.53%	0.73%	5	4	6
Lebanon	0.63	0.52	0.76	0.31	0.24	0.40	-50.6%	-63.5%	-34.3%	0.51%	0.38%	0.67%	13	10	17
Libya	0.48	0.39	0.60	0.42	0.32	0.53	-13.9%	-35.5%	11.1%	0.35%	0.27%	0.44%	13	10	17
Morocco	0.78	0.63	0.95	0.49	0.38	0.61	-37.5%	-52.9%	-16.9%	0.36%	0.28%	0.45%	77	59	96
Palestine	0.53	0.39	0.72	0.24	0.19	0.29	-55.4%	-68.1%	-39.5%	0.25%	0.21%	0.29%	7	5	8
Oman	0.48	0.36	0.62	0.32	0.26	0.40	-32.1%	-51.8%	-6.8%	0.37%	0.30%	0.45%	6	5	7
Qatar	0.58	0.48	0.72	0.22	0.17	0.28	-62.4%	-71.5%	-51.7%	0.34%	0.28%	0.40%	2	1	2
Saudi Arabia	0.48	0.35	0.63	0.20	0.16	0.26	-57.3%	-71.0%	-35.9%	0.29%	0.24%	0.36%	30	24	38
Sudan	0.72	0.45	1.01	0.43	0.33	0.57	-40.0%	-57.9%	-9.0%	0.13%	0.10%	0.16%	107	81	142
Syria	0.60	0.48	0.74	0.30	0.24	0.36	-50.2%	-61.9%	-33.8%	0.10%	0.08%	0.12%	27	22	33
Tunisia	0.45	0.35	0.57	0.16	0.12	0.20	-64.0%	-75.5%	-50.0%	0.23%	0.18%	0.29%	7	5	9
Turkey	0.87	0.65	1.17	0.24	0.20	0.29	-72.4%	-80.1%	-63.5%	0.27%	0.23%	0.31%	73	61	88
United Arab Emirates	0.18	0.14	0.23	0.14	0.11	0.17	-23.0%	-43.7%	4.3%	0.14%	0.11%	0.18%	2	2	3
Yemen	0.66	0.29	0.97	0.37	0.26	0.53	-43.8%	-62.8%	23.1%	0.11%	0.08%	0.15%	69	47	101
South Asia	**0.44**	**0.38**	**0.51**	**0.36**	**0.32**	**0.41**	**-18.3%**	**-30.3%**	**-4.1%**	**0.2%**	**0.1%**	**0.2%**	**3294**	**2940**	**3685**
South Asia	**0.44**	**0.38**	**0.51**	**0.36**	**0.32**	**0.41**	**-18.3%**	**-30.3%**	**-4.1%**	**0.2%**	**0.1%**	**0.2%**	**3294**	**2940**	**3685**
Bangladesh	0.42	0.31	0.51	0.36	0.28	0.44	-15.5%	-37.8%	18.1%	0.18%	0.14%	0.23%	280	221	346
Bhutan	0.45	0.35	0.57	0.32	0.23	0.41	-28.4%	-47.3%	-2.0%	0.24%	0.17%	0.31%	1	1	2
India	0.44	0.39	0.51	0.28	0.25	0.31	-36.9%	-45.9%	-27.3%	0.13%	0.12%	0.15%	1915	1699	2130
Nepal	0.36	0.24	0.45	0.29	0.22	0.37	-18.6%	-41.9%	28.4%	0.18%	0.13%	0.22%	48	37	61
Pakistan	0.49	0.39	0.60	0.85	0.68	1.05	73.5%	32.1%	136.7%	0.23%	0.18%	0.29%	1049	832	1295
Southeast Asia, East Asia, and Oceania	**0.41**	**0.37**	**0.46**	**0.27**	**0.25**	**0.30**	**-33.2%**	**-38.1%**	**-28.5%**	**0.3%**	**0.3%**	**0.3%**	**2116**	**1930**	**2323**
East Asia	**0.35**	**0.32**	**0.40**	**0.12**	**0.11**	**0.13**	**-67.1%**	**-70.1%**	**-63.8%**	**0.2%**	**0.2%**	**0.2%**	**533**	**489**	**587**
China	0.36	0.32	0.40	0.11	0.10	0.12	-68.8%	-71.7%	-65.4%	0.17%	0.16%	0.19%	482	442	534

North Korea	0.29	0.23	0.37	0.35	0.27	0.45	18.5%	-12.9%	58.3%	0.28%	0.22%	0.37%	34	26	45
Taiwan (Province of China)	0.21	0.18	0.23	0.10	0.09	0.11	-52.3%	-58.9%	-44.0%	0.31%	0.27%	0.35%	7	6	8
Oceania	**0.96**	**0.78**	**1.19**	**0.97**	**0.77**	**1.20**	**0.8%**	**-16.0%**	**22.2%**	**0.3%**	**0.2%**	**0.3%**	**68**	**54**	**85**
American Samoa	0.56	0.47	0.66	0.62	0.50	0.75	9.9%	-12.4%	38.4%	0.69%	0.58%	0.84%	0	0	0
Federated States of Micronesia	0.82	0.63	1.09	0.89	0.62	1.18	8.2%	-22.7%	42.6%	0.62%	0.44%	0.79%	0	0	1
Fiji	1.12	0.90	1.43	1.47	1.20	1.78	31.3%	0.6%	70.1%	0.86%	0.69%	1.04%	6	5	7
Guam	0.26	0.21	0.31	0.26	0.21	0.32	-0.1%	-21.2%	22.4%	0.25%	0.20%	0.30%	0	0	0
Kiribati	1.30	1.06	1.56	1.76	1.38	2.21	35.5%	2.8%	77.8%	0.54%	0.42%	0.68%	1	1	1
Marshall Islands	0.82	0.64	1.05	0.91	0.67	1.19	11.3%	-12.6%	39.1%	0.46%	0.35%	0.62%	0	0	0
Northern Mariana Islands	0.26	0.20	0.33	0.28	0.22	0.34	5.4%	-17.2%	34.4%	0.47%	0.38%	0.58%	0	0	0
Papua New Guinea	1.00	0.77	1.29	0.94	0.71	1.21	-6.1%	-25.9%	20.5%	0.24%	0.18%	0.31%	49	38	64
Samoa	0.55	0.43	0.73	0.47	0.35	0.62	-14.7%	-36.0%	8.5%	0.42%	0.32%	0.53%	1	0	1
Solomon Islands	1.00	0.72	1.33	1.18	0.89	1.52	18.5%	-9.9%	56.1%	0.52%	0.39%	0.66%	4	3	5
Tonga	0.61	0.50	0.75	0.75	0.61	0.92	22.1%	-6.5%	55.3%	0.59%	0.50%	0.71%	0	0	0
Vanuatu	0.65	0.42	0.94	0.83	0.52	1.16	26.6%	-11.4%	80.1%	0.35%	0.25%	0.45%	1	1	2
Southeast Asia	**0.57**	**0.49**	**0.67**	**0.51**	**0.45**	**0.56**	**-10.8%**	**-21.8%**	**-1.0%**	**0.4%**	**0.3%**	**0.4%**	**1516**	**1363**	**1689**
Cambodia	0.44	0.34	0.58	0.27	0.21	0.34	-37.9%	-52.2%	-18.7%	0.13%	0.10%	0.17%	22	18	28
Indonesia	0.68	0.59	0.80	0.60	0.54	0.67	-12.0%	-22.3%	-0.7%	0.42%	0.38%	0.47%	717	642	800
Laos	0.70	0.54	0.94	0.50	0.39	0.64	-28.6%	-44.5%	-8.3%	0.15%	0.11%	0.19%	19	15	24

Malaysia	0.31	0.26	0.37	0.12	0.10	0.15	-61.6%	-70.5%	-48.2%	0.19%	0.16%	0.24%	18	15	22
Maldives	0.56	0.44	0.75	0.12	0.09	0.14	-79.0%	-86.0%	-72.5%	0.26%	0.20%	0.33%	0	0	0
Mauritius	0.39	0.34	0.45	0.77	0.65	0.90	97.4%	60.1%	135.2%	1.11%	0.93%	1.31%	4	3	4
Myanmar	1.47	1.08	1.98	0.85	0.66	1.07	-42.3%	-57.1%	-23.3%	0.36%	0.28%	0.45%	208	167	259
Philippines	0.36	0.31	0.45	0.70	0.59	0.82	95.1%	48.2%	134.3%	0.37%	0.31%	0.44%	373	313	439
Sri Lanka	0.23	0.19	0.27	0.24	0.19	0.30	4.7%	-18.4%	31.8%	0.39%	0.31%	0.48%	21	17	26
Seychelles	0.18	0.14	0.23	0.26	0.21	0.34	47.5%	14.4%	86.8%	0.29%	0.22%	0.37%	0	0	0
Thailand	0.30	0.24	0.39	0.17	0.14	0.21	-43.5%	-54.3%	-28.3%	0.23%	0.19%	0.28%	43	35	53
Timor-Leste	0.42	0.32	0.56	0.30	0.16	0.38	-28.3%	-58.7%	-4.2%	0.14%	0.07%	0.18%	2	1	3
Vietnam	0.27	0.20	0.35	0.21	0.17	0.26	-22.5%	-43.3%	4.5%	0.23%	0.19%	0.29%	86	68	108
Sub-Saharan Africa	**0.62**	**0.51**	**0.72**	**0.49**	**0.44**	**0.54**	**-21.5%**	**-31.1%**	**-7.4%**	**0.1%**	**0.1%**	**0.1%**	**2984**	**2678**	**3337**
Central sub-Saharan Africa	**0.59**	**0.42**	**0.72**	**0.45**	**0.37**	**0.53**	**-24.8%**	**-40.4%**	**6.1%**	**0.1%**	**0.1%**	**0.1%**	**314**	**256**	**376**
Angola	0.64	0.31	0.86	0.43	0.34	0.54	-32.7%	-52.1%	47.2%	0.08%	0.06%	0.10%	68	54	85
Central African Republic	0.77	0.41	1.02	0.67	0.50	0.90	-12.1%	-38.8%	67.7%	0.06%	0.05%	0.09%	18	14	24
Congo (Brazzaville)	0.78	0.59	1.00	0.49	0.36	0.63	-36.9%	-56.2%	-7.4%	0.13%	0.09%	0.17%	12	9	16
DR Congo	0.55	0.35	0.69	0.44	0.33	0.56	-20.8%	-41.1%	18.6%	0.07%	0.05%	0.09%	208	159	264
Equatorial Guinea	0.92	0.69	1.19	0.38	0.25	0.54	-58.2%	-72.3%	-38.9%	0.12%	0.09%	0.15%	3	2	4
Gabon	0.61	0.45	0.78	0.43	0.32	0.56	-29.8%	-48.5%	-4.1%	0.16%	0.12%	0.21%	4	3	5
Eastern sub-Saharan Africa	**0.66**	**0.49**	**0.80**	**0.45**	**0.41**	**0.50**	**-31.5%**	**-43.5%**	**-8.0%**	**0.1%**	**0.1%**	**0.1%**	**1050**	**948**	**1164**
Burundi	0.90	0.70	1.15	0.45	0.36	0.56	-50.1%	-62.1%	-33.5%	0.07%	0.06%	0.09%	28	22	35

Comoros	0.84	0.70	1.00	0.46	0.37	0.56	-45.1%	-57.4%	-29.4%	0.18%	0.14%	0.23%	2	1	2
Djibouti	0.58	0.30	0.79	0.45	0.34	0.62	-22.3%	-47.1%	48.6%	0.17%	0.14%	0.21%	3	2	3
Eritrea	0.81	0.32	1.18	0.65	0.51	0.84	-19.7%	-48.9%	100.9%	0.16%	0.12%	0.21%	23	18	30
Ethiopia	0.87	0.60	1.14	0.40	0.35	0.45	-54.1%	-65.7%	-33.7%	0.10%	0.09%	0.12%	252	221	286
Kenya	0.35	0.28	0.42	0.34	0.29	0.40	-2.6%	-12.4%	8.3%	0.11%	0.09%	0.13%	96	80	111
Madagascar	0.74	0.62	0.87	0.41	0.32	0.52	-44.1%	-57.8%	-27.1%	0.07%	0.06%	0.09%	62	48	78
Malawi	0.52	0.14	0.78	0.48	0.38	0.61	-6.6%	-42.3%	228.8%	0.09%	0.07%	0.12%	49	39	62
Mozambique	0.85	0.69	1.03	0.71	0.57	0.86	-17.2%	-36.8%	10.3%	0.12%	0.10%	0.15%	126	102	154
Rwanda	0.79	0.62	0.99	0.37	0.29	0.46	-53.2%	-66.5%	-36.6%	0.11%	0.08%	0.14%	26	20	33
Somalia	0.70	0.18	1.17	0.64	0.47	0.90	-7.8%	-50.6%	262.2%	0.09%	0.07%	0.12%	65	47	91
South Sudan	0.52	0.15	0.91	0.55	0.40	0.74	5.5%	-37.6%	224.8%	0.06%	0.04%	0.07%	31	23	42
Tanzania	0.50	0.20	0.69	0.46	0.36	0.56	-8.5%	-37.2%	127.9%	0.10%	0.08%	0.13%	148	114	184
Uganda	0.43	0.31	0.57	0.38	0.30	0.48	-11.3%	-35.9%	34.4%	0.08%	0.06%	0.10%	91	73	114
Zambia	0.66	0.36	0.85	0.47	0.38	0.57	-28.8%	-48.7%	32.0%	0.10%	0.08%	0.12%	48	39	58
Southern sub-Saharan Africa	**0.53**	**0.46**	**0.60**	**0.55**	**0.50**	**0.61**	**4.3%**	**-9.7%**	**22.9%**	**0.2%**	**0.2%**	**0.2%**	**209**	**188**	**232**
Botswana	0.45	0.34	0.58	0.37	0.30	0.47	-17.0%	-38.0%	9.9%	0.24%	0.19%	0.31%	4	3	5
Lesotho	0.54	0.41	0.70	0.83	0.64	1.05	54.6%	14.9%	112.4%	0.18%	0.14%	0.23%	9	7	11
Namibia	0.51	0.40	0.65	0.36	0.27	0.48	-29.6%	-48.6%	-5.4%	0.13%	0.10%	0.18%	5	3	6
South Africa	0.51	0.44	0.58	0.38	0.32	0.44	-24.8%	-35.6%	-13.4%	0.17%	0.14%	0.20%	98	83	113
Swaziland	0.69	0.56	0.86	0.95	0.74	1.20	37.2%	0.2%	93.5%	0.27%	0.21%	0.34%	6	5	8
Zimbabwe	0.58	0.48	0.69	1.00	0.81	1.23	73.1%	31.1%	130.1%	0.24%	0.20%	0.30%	87	71	107
Western sub-Saharan Africa	**0.62**	**0.52**	**0.72**	**0.52**	**0.44**	**0.61**	**-15.9%**	**-26.3%**	**-3.1%**	**0.1%**	**0.1%**	**0.1%**	**1412**	**1178**	**1691**
Benin	0.76	0.61	0.93	0.59	0.45	0.76	-22.6%	-43.3%	3.9%	0.11%	0.08%	0.14%	43	32	56

Burkina Faso	0.81	0.62	1.02	0.70	0.52	0.92	-14.0%	-33.8%	14.3%	0.09%	0.07%	0.13%	92	68	124
Cameroon	0.75	0.61	0.91	0.63	0.48	0.81	-15.5%	-36.7%	11.3%	0.14%	0.11%	0.19%	104	79	134
Cape Verde	0.36	0.29	0.45	0.33	0.27	0.39	-10.0%	-31.0%	19.2%	0.26%	0.20%	0.32%	1	1	1
Chad	0.62	0.47	0.79	0.66	0.50	0.84	6.3%	-18.6%	41.7%	0.07%	0.06%	0.10%	67	51	89
Cote d'Ivoire	0.75	0.60	0.93	0.73	0.57	0.92	-2.7%	-24.7%	28.0%	0.13%	0.11%	0.17%	107	83	136
The Gambia	0.60	0.39	0.82	0.57	0.40	0.79	-4.1%	-27.8%	30.0%	0.18%	0.12%	0.24%	8	5	10
Ghana	0.53	0.43	0.64	0.55	0.43	0.70	3.9%	-21.8%	40.3%	0.16%	0.13%	0.20%	95	74	121
Guinea	0.93	0.71	1.17	0.71	0.56	0.89	-23.7%	-44.9%	4.9%	0.11%	0.08%	0.13%	51	40	66
Guinea-Bissau	0.98	0.75	1.26	0.83	0.63	1.10	-15.3%	-36.5%	15.2%	0.15%	0.11%	0.19%	9	7	12
Liberia	0.91	0.70	1.15	0.56	0.44	0.71	-38.0%	-54.3%	-17.8%	0.12%	0.10%	0.15%	16	12	20
Mali	0.98	0.75	1.25	0.73	0.51	1.01	-25.9%	-45.1%	-1.8%	0.09%	0.06%	0.12%	100	69	145
Mauritania	0.56	0.44	0.71	0.49	0.39	0.63	-11.5%	-36.1%	17.3%	0.18%	0.15%	0.23%	11	9	15
Niger	0.86	0.64	1.09	0.51	0.38	0.68	-40.5%	-55.6%	-18.3%	0.07%	0.05%	0.09%	72	53	100
Nigeria	0.47	0.35	0.60	0.39	0.29	0.53	-15.2%	-38.3%	14.2%	0.06%	0.04%	0.08%	521	378	709
Sao Tome and Principe	0.61	0.48	0.76	0.48	0.37	0.60	-22.0%	-41.7%	4.0%	0.23%	0.18%	0.29%	1	0	1
Senegal	0.78	0.61	0.96	0.67	0.51	0.86	-14.0%	-33.1%	11.2%	0.21%	0.17%	0.27%	59	46	77
Sierra Leone	0.86	0.65	1.16	0.69	0.53	0.89	-19.4%	-39.1%	7.7%	0.10%	0.07%	0.12%	33	25	44
Togo	0.67	0.53	0.84	0.49	0.38	0.63	-27.4%	-43.6%	-5.8%	0.11%	0.09%	0.14%	21	16	27