Estimation of global insulin use for type 2 diabetes, 2018–30: a microsimulation analysis

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Summary

Background The amount of insulin needed to effectively treat type 2 diabetes worldwide is unknown. It also remains unclear how alternative treatment algorithms would affect insulin use and disability-adjusted life-years (DALYs) averted by insulin use, given that current access to insulin (availability and affordability) in many areas is low. The aim of this study was to compare alternative projections for and consequences of insulin use worldwide under varying treatment algorithms and degrees of insulin access.

Methods We developed a microsimulation of type 2 diabetes burden from 2018 to 2030 across 221 countries using data from the International Diabetes Federation for prevalence projections and from 14 cohort studies representing more than 60% of the global type 2 diabetes population for HbA_{1c}, treatment, and bodyweight data. We estimated the number of people with type 2 diabetes expected to use insulin, international units (IU) required, and DALYs averted per year under alternative treatment algorithms targeting HbA_{1c} from 6·5% to 8%, lower microvascular risk, or higher HbA_{1c} for those aged 75 years and older.

Findings The number of people with type 2 diabetes worldwide was estimated to increase from 405·6 million (95% CI 315·3 million–533·7 million) in 2018 to 510·8 million (395·9 million–674·3 million) in 2030. On this basis, insulin use is estimated to increase from 516·1 million 1000 IU vials (95% CI 409·0 million–658·6 million) per year in 2018 to 633·7 million (500·5 million–806·7 million) per year in 2030. Without improved insulin access, 7·4% (95% CI 5·8–9·4) of people with type 2 diabetes in 2030 would use insulin, increasing to 15·5% (12·0–20·3) if insulin were widely accessible and prescribed to achieve an HbA_{1c} of 7% (53 mmol/mol) or lower. If HbA_{1c} of 7% or lower was universally achieved, insulin would avert 331 101 DALYs per year by 2030 (95% CI 256 601–437 053). DALYs averted would increase by 14·9% with access to newer oral antihyperglycaemic drugs. DALYs averted would increase by 44·2% if an HbA_{1c} of 8% (64 mmol/mol) were used as a target among people aged 75 years and older because of reduced hypoglycaemia.

Interpretation The insulin required to treat type 2 diabetes is expected to increase by more than 20% from 2018 to 2030. More DALYs might be averted if HbA_{1c} targets are higher for older adults.

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Introduction

The prevalence of diabetes worldwide has nearly quadrupled since 1980.[1] Adult diabetes prevalence (type 1 and type 2) reached 425 million people in 2017 (about one in 11 adults).[2] Roughly 12% of overall global health-care expenditures are for diabetes treatment.[2]

Insulin is necessary for all people with type 1 diabetes and a subset of patients with type 2 diabetes to avoid morbidity and mortality from ketoacidosis or hyperosmolar hyperglycaemic states and to reduce long-term microvascular complications. The use of insulin for type 2 diabetes is dependent on treatment algorithms, particularly the target level of HbA_{1c}.[3] Finding an optimal target that maximises disability-adjusted life years (DALYs) averted, while minimising disutility from insulin therapy (eg, from hypoglycaemia), remains an important goal.[4] Insulin treatment is costly,[5] with most insulin produced by three major manufacturers.[2] Hence, a prospective estimation of global insulin requirements and the DALYs averted by improving access might help in the planning of resources required to deliver insulin. Complicating such estimations are the increasing numbers of people with type 2 diabetes, increasing survival of people with type 2 diabetes (which might increase insulin requirements), and increasing availability of newer oral diabetes drugs.

Here, we sought to estimate global insulin use for type 2 diabetes by country and year, worldwide, from 2018 to 2030, and the potential effects of altering insulin treatment algorithms on insulin use and diabetes-related burden of disease.

Methods

Study design

We constructed a microsimulation (figure 1) to simulate the population of adults with type 2 diabetes within each of 221 countries and territories worldwide to estimate the number of adults using insulin and to estimate the

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Research in context

Evidence before this study

We searched PubMed using the keywords "insulin utilization" and "type 2 diabetes" for articles published from Jan 2, 2008, to Aug 31, 2018. We identified seven previous papers on the topic. Three papers reviewed the insulin dosing needs and effectiveness of insulin for people with type 2 diabetes when using basal insulin with or without other antidiabetes medications. Two articles examined the budgetary and cost effect of basal insulin use in the US population. The remaining two papers estimated the low rates of access to insulin and challenges to access in east and south Asia.

Added value of this study

Our current study provides a direct estimate of the anticipated global use of insulin among people with type 2 diabetes, using data from large representative cohort studies, and directly compares the implications of alternative treatment targets for reducing the burden of type 2 diabetes complications.

Implications of all the available evidence

The number of people who require insulin and the amount of insulin required to treat type 2 diabetes worldwide are expected to increase. Substantial improvements in access to insulin in low-income and middle-income countries are needed in order to reduce inequalities in access and complications of diabetes compared with high-income countries.Having a higher threshold of HbA_{1c} of 8% for older adults (age 75 years and older) and HbA_{1c} of 7% for others might avert the greatest number of DALYs from insulin treatment, by balancing the risk of hypoglycaemia against the benefit of reducing microvascular complications.

international units (IU) of insulin used under alternative treatment algorithms. We multiplied International Diabetes Federation (IDF) estimates for type 2 diabetes prevalence by IDF estimates of the proportion of people diagnosed and then by the number estimated to need insulin (appendix). We calculated the proportion estimated to need insulin in two ways: an approach that used current estimates of insulin treatment from cohort studies and an approach based on theoretical comprehensive insulin access (table 1). In both cases, we used weight-based dosing and varied the HbA_{1c} treatment target, then the Risk Equations for Complications Of type 2 Diabetes (RECODe) equations[7,8] to estimate the DALYs averted from microvascular complications by insulin treatment, and a new risk equation to estimate the DALYs caused by hypoglycaemia events requiring medical attention (appendix).

See Online for appendix

Estimates of type 2 diabetes prevalence

Diabetes prevalence (both diagnosed and undiagnosed) among adults in each country and year in the simulation was taken from projections made by the IDF for the period 2018–30.[2] The IDF prevalence estimates were based on a regression model that used data from a systematic review of the medical literature for the individual country or nearest neighbourhood; the reviewed data were used by the IDF to generate smoothed sex-specific and age-specific prevalence estimates for adults aged 20–79 years, which were projected by the IDF into the future using UN population projections and assuming that the age-specific and sex-specific prevalence of diabetes would increase linearly with urbanisation.[9] This conservative assumption produces a lower-bound estimate of future diabetes prevalence. 95% CIs were constructed by the IDF by bootstrapping across study prevalence estimates in the systematic review, for which one study was removed from the data pool at a time. The prevalence estimates were for overall diabetes; based on a systematic review and projections, we estimated that 96·5% of total diabetes among adults could be attributed to type 2 diabetes[10] (varied in uncertainty analyses to the range 92·0–99·0%). The estimate was based on a modelling exercise with extrapolation of ratios of incidence of type 1 diabetes in children to adults from available data applied to country-specific childhood type 1 diabetes incidence estimates.[10]

Estimates of insulin needs

We had two parallel approaches to estimate the number of people using insulin within each simulated country: first, an approach accounting for demographic change but unchanged insulin access, which applied estimated proportions of people with type 2 diabetes currently treated with insulin to the estimated numbers of people with diagnosed type 2 diabetes in the future; second, an approach accounting for demographic change and comprehensive insulin access, which estimated how many more people would be treated if all those estimated to need treatment with insulin under different treatment scenarios were provided with insulin, after appropriate oral antihyperglycaemic therapy, and conditional on a given treatment target for glycaemic control (HbA_{1c}).

In the approach accounting for demographic change alone (with unchanged insulin treatment rates), we multiplied the absolute number of people projected to have diagnosed type 2 diabetes in each year over the period 2018–30 by the proportion of people who are anticipated to be treated with insulin given current estimates of the proportion of people with type 2 diabetes who receive insulin treatment in each country.[2,11] The number of units of insulin required among people given insulin followed current guidelines based on bodyweight, using the distribution of bodyweight among those diagnosed with type 2 diabetes and given insulin from regional surveys (table 1). The estimates of bodyweight-based dosing assumed that 75% of patients given insulin

require only basal insulin at a dose of 0·4 IU/kg per day, while the remaining individuals would require multiple dose injection therapy totalling 0·6 IU/kg per day.[12,13] In a sensitivity analysis, we tested alternative assumptions using 70% and 80% for proportions of people given insulin who require only basal insulin.

In the approach accounting for both demographic change and improved insulin access, we estimated the additional insulin required for the population who do not currently have access. First, we estimated the proportion of people with type 2 diabetes not currently receiving insulin from the geographically closest regional diabetes survey (table 1; appendix) for each simulated country population, concatenating multiple surveys by taking an average if more than one was available (after accounting for survey sample weights from each) for a given country and bootstrapping across all available estimates when a close regional survey was unavailable. The cohort survey data, after using survey weights, represented more than 60% of the global population with type 2 diabetes. Missing data—specifically, missing HbA_{1c} values, bodyweight values, and indicators of whether or not a person was on insulin—were imputed with chained equations assuming data were missing at random,[14] followed by repeated Monte Carlo sampling from uncertainty distributions from each input parameter, done to estimate uncertainty.

Among people not yet on insulin, we estimated whether or not insulin would be necessary after maximum treatment with oral antihyperglycaemic drugs to achieve a given target HbA_{1c} level (detailed below). Following current WHO guidelines and the WHO Essential Medicines List,[15,16] titration was simulated up from 500 mg of metformin once per day to 1000 mg of metformin twice per day, then, if needed, further addition of 80 mg of gliclazide (a sulfonylurea) once per day, which could be titrated up to 160 mg twice per day. We Monte Carlo sampled from the distributions of typical HbA_{1c} reductions for the full dose of each drug (uniform distributions) from a previous meta-analysis,[17] with proportionate linear values for doses less than the maximum, taking into account existing dose levels among those already on oral drugs. Those people still above the target HbA_{1c} after maximum titration of oral drugs were assumed to achieve the target HbA_{1c} only by starting insulin (after discontinuing the sulfonylurea) and setting their insulin use based on their weight (sampling from the weight estimates from the closest regional survey), estimating that 75% of those given insulin require only basal insulin at a dose of 0·4 IU/kg per day (varied from 70% to 80% in sensitivity analyses), while the remaining individuals would require multiple dose injection therapy totalling 0·6 IU/kg per day.[12,13] Among the population already receiving insulin, we estimated total daily insulin needed using these same estimates of total units per kg bodyweight required per day.

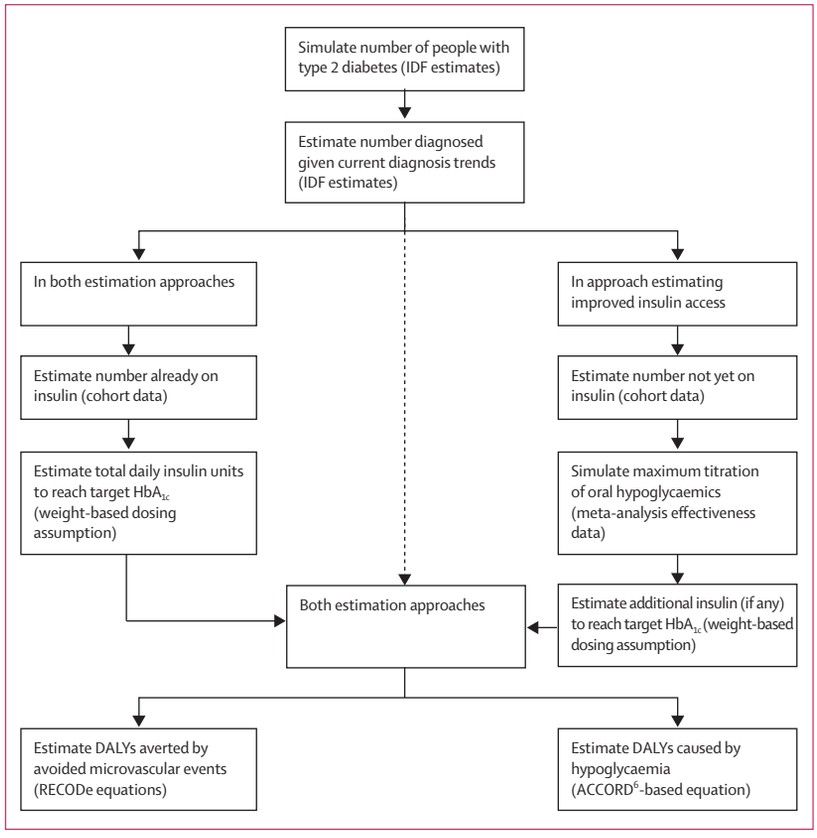

Figure 1: **Study design**
Each cell describes a key input data (with source parenthetically) or outcome estimate (with estimation approach parenthetically). Two approaches were used to estimate the outcomes: (1) an approach incorporating demographic change only and (2) an approach incorporating both demographic change and improved insulin access. IDF=International Diabetes Federation. DALYs=disability-adjusted life-years. RECODe=Risk Equations for Complications Of type 2 diabetes.

Finally, we did a sensitivity analysis to estimate how much less insulin might be required if newer drugs (glucagon-like peptide-1 [GLP-1] receptor agonists, dipeptidyl peptidase-4 [DPP-4] inhibitors, and sodium-glucose co-transporter-2 [SGLT2] inhibitors) were more widely available and were combined with metformin instead of combining a sulfonylurea with metformin; we used the HbA_{1c} reductions estimated in a meta-analysis[18] to estimate the HbA_{1c}-lowering effects of these newer drugs.

Treatment targets

For the scenario accounting for both demographic change and improved insulin access, we simulated five different treatment targets. Recognising that some facilities do not have HbA_{1c} testing, we converted to the nearest average fasting plasma glucose (AFPG) target level.[17] We used the 2018 American Diabetes Association treatment guidelines[19] as a primary clinical reference.

First, we set the target HbA_{1c} to 7·0% (53 mmol/mol) for all diagnosed and treated people (AFPG 8·0 mmol/L). Second, we reduced the target HbA_{1c} to a low of 6·5% (48 mmol/mol; AFPG 7·5 mmol/L). Third, we increased

	People with type 2 diabetes*	Years	Mean HbA_{1c} (95% centiles)	Percentage of people treated with insulin, among those diagnosed	Mean bodyweight, kg (95% centiles)
US National Health and Nutrition Examination Survey	1441	2009–14	7·4% (5·2–12·2)	22·2%	89·5 (53·7–148·2)
US National Institutes of Health Global Health Centers of Excellence surveys from South Africa	1842	2012	9·1% (5·4–14·6)	NA	83·0 (51·0–125·0)
US National Institutes of Health Global Health Centers of Excellence surveys from India	1605	2015	8·7% (5·5–13·4)	NA	67·9 (43·0–98·2)
South Africa National Health and Nutrition Examination Survey	747	2012	7·7% (5·4–12·8)	4·4%	78·0 (44·0–116·6)
UK National Health Service National Diabetes Audit	16 585	2016–17	7·3% (5·1–12·1)	12·5%	80·3 (48·1–133·0)
Indian Jaipur Diabetes Registry	8699	2014	9·0% (6·3–14·8)	9·1%	60·4 (30·6–101·2)
Swedish National Diabetes Register	17 827	2016	8·4% (6·1–10·1)	11·7%	75·6 (48·5–102·7)
Danish Adult Diabetes Registry	11 205	2014–15	7·7% (5·4–12·7)	15·8%	70·9 (33·9–123·5)
Turkish Nationwide survey of Glycemic and Other Metabolic Parameters of Patients with Diabetes Mellitus	4672	2017	7·5% (5·3–12·4)	9·6%	84·7 (52·2–117·2)
China Health and Nutrition Study	1422	1999–2015	7·8% (5·2–12·7)	18·3%	65·5 (45·2–90·0)
DiabCare study of the Philippines	770	2008	8·0% (5·6–13·2)	25·0%	58·5 (36·2–85·9)
Japan National Health and Nutrition Survey	1434	2016	7·2% (5·0–11·8)	7·0%	59·5 (32·2–90·4)
Korea National Health and Nutrition Examination Survey	1341	2010–12	8·2% (5·7–13·5)	3·0%	66·0 (38·5–93·7)
Joint Asia Diabetes Evaluation Registry	28 111	2007–12	7·7% (5·4–12·7)	21·0%	76·8 (58·4–90·0)

References for each cohort dataset are provided in the appendix. NA=not available. *Previous diagnosis, treatment, or laboratory results.

***Table 1*: Input cohort data for estimating reduction in HbA_{1c} necessary to achieve treatment targets, and baseline proportion of people with type 2 diabetes treated with insulin, among those diagnosed**

the target HbA_{1c} to a high of 8·0% (64 mmol/mol; AFPG 9·2 mmol/L). Fourth, we simulated an age-based target, with people younger than 75 years given an HbA_{1c} target of 7% and those aged 75 years and older given a target HbA_{1c} of 8%.[20,21] Fifth, we simulated a risk-based target, with people having 5% or higher risk over 10 years of composite microvascular complications (renal failure or end-stage renal disease, severe vision loss <20/200 on a Snellen chart, or loss of pressure sensation by monofilament testing) estimated from the RECODe equations[7,8] given insulin to an HbA_{1c} of 7%, or the HbA_{1c} level that achieved an estimated risk 5% or less (whichever HbA_{1c} was higher). The threshold was based on previous experiments for risk-based therapy.[22]

Outcomes and statistical analysis

The primary outcome metric we estimated was the number of people with type 2 diabetes estimated to use insulin for each year in each country and each world region (using UN categorisations of countries into regions). The secondary outcome metric was the number of 10 mL vials of U100 insulin (ie, 1000 IU) used per year in the total population of each country and each world region for each year from 2018 to 2030.

For the scenario accounting for both demographic change and improved insulin access, the additional outcome metric was the DALYs averted by achieving the insulin treatment levels simulated. We computed the DALYs averted from each of three microvascular complications (renal failure or end-stage renal disease, severe vision loss <20/200 on a Snellen chart, or loss of pressure sensation by monofilament testing) using the RECODe equations for baseline risk for each complication recalibrated to global DALY estimates from the Global Burden of Disease Study,[7,8,23] the relative risk reduction conditional on HbA_{1c} reduction for each complication from a previous systematic review,[24] and the disability weights provided by a previous international survey (appendix).[25] We also computed the increase in DALYs due to the disutility of daily finger stick glucose monitoring, disutility from injection therapy, and disutility because of hypoglycaemia requiring hospitalisation, emergency care, or other external medical assistance due to severe cognitive impairment, based on a risk equation to estimate the frequency of hypoglycaemia (appendix). The hypoglycaemia risk equation was based on individual participant data from the ACCORD trial[6] and was a multivariable equation incorporating demographics, insulin units used, and related treatment covariates (appendix). We computed DALYs at a standard 3% annual discount rate, integrated over the full life course of all simulated individuals.

Outcomes were computed up to the year 2030 and additionally for the midpoint year of analysis (2024) for comparison.

All estimates were generated in R (version 3·4). The R code has been used shared for reproducibility.

For more on the **R code** see https://github.com/sanjaybasu/insulinestimates

Role of the funding source

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

Results

First, we simulated the approach accounting for demographic change alone (with unchanged insulin access). The numbers of people projected to have type 2 diabetes over the period 2018–30 based on IDF estimates[2] were 405·6 million in 2018 (95% CI 315·3 million–533·7 million) and 510·8 million in 2030 (395·9 million–674·3 million). The estimated number of people with type 2 diabetes in each country was typically proportional to population size, with the largest absolute number in 2018 residing in China (111·9 million [95% CI 97·1 million–146·3 million], 7·9% prevalence) and India (72·5 million [52·8 million– 91·9 million], 5·4% prevalence), followed by the USA, which had a higher prevalence (29·3 million [26·7 million–31·7 million], 9·0% prevalence; appendix). Projections for the year 2030 by the IDF[2] were proportional to anticipated population growth, aging, and urbanisation in less developed countries, with the largest absolute numbers of people with type 2 diabetes projected to be in China (130·2 million [113·4 million–163·3 million], 9·0% prevalence), India (98·0 million [73·7 million–122·9 million], 6·5% prevalence), then the USA (31·8 million [28·7 million–34·5 million], 9·0% prevalence). When we combined data on the number of people with type 2 diabetes with the proportions diagnosed and given insulin,[2,11] we estimated that insulin use would increase from 516·1 million 1000-unit vials (95% CI 409·0 million–658·6 million) to 633·7 million vials (500·5 million–806·7 million) per year between 2018 and 2030. The number of vials used decreased or increased by 2% if the proportion of people given basal insulin only decreased from 75% to 70% or increased to 80%. The absolute number of people estimated to use insulin and the number of U100 insulin vials required would be lowest in Oceania (4·2 million vials in 2030) and highest in Asia (321·6 million vials in 2030) due to population size (table 2). In relative terms, the proportion of people with diagnosed type 2 diabetes using insulin would be lowest in the African region due to low medication access and low prevalence of type 2 diabetes (1·8% of people with type 2 diabetes given insulin in 2030) and highest in the Americas region in the context of greater insulin use and higher type 2 diabetes prevalence (13·6% of people with type 2 diabetes given insulin in 2030).

Second, we simulated both demographic change and improved insulin access. We estimated the proportion of people diagnosed with type 2 diabetes who could receive insulin after maximum oral therapy, if insulin were widely available and if providers aimed to achieve a target HbA_{1c} of 7% (appendix). The distribution of HbA_{1c} among people with diagnosed type 2 diabetes (table 1) had a global mean of 9·1% and 95% centiles extending from 5·1% to 14·8%. The proportion of people with type 2 diabetes who we anticipated to use insulin increased from 7·4% (95% CI 5·8–9·4) to 15·5% (12·0–20·3), on average, when changing from the scenario assuming persistence of current insulin access levels, to the scenario assuming comprehensive insulin access (table 2). The greatest relative increase in number of people anticipated to use insulin between the two scenarios would be in the African region (an increase of 7·1 times from 718 802 if insulin access were at current levels to 5 119 862 under universal access), while the greatest absolute increase would be in the Asian region (an increase of 26·5 million people using insulin from 21·1 million if insulin access were at current levels to 47·6 million under universal access). The ratio of actual use (given current insulin access levels) to estimated use (given comprehensive insulin access) varied from 0·14 in Africa to 0·71 in the Americas; the overall worldwide ratio was 0·48.

We next estimated the net number of DALYs averted as a composite measure, accounting for the DALYs averted with comprehensive insulin access by preventing microvascular complications and subtracting the DALYs caused by insulin-related hypoglycaemia and treatment-related inconvenience. When aiming for a treatment target HbA_{1c} of 7%, we estimated that comprehensive access to insulin would avert 262 884 DALYs in the year 2018, increasing to 331 101 in the year 2030, with 65% of the DALYs averted in Asia alone (table 2). Starting insulin reduced the composite mean lifetime risk of microvascular complications (renal failure, severe vision loss, and pressure sensation loss) from 17·4% to 15·9%, but increased mean lifetime risk of hypoglycaemia requiring medical attention from 11·9% to 20·0%. Nevertheless, due to the greater disutility of microvascular complications than of hypoglycaemia, overall net DALYs were averted through insulin treatment over the life course, after accounting for the delayed onset of microvascular disease and a 3% annual discount rate on DALYs over time.

Changing the target HbA_{1c} produced a proportional change in the number of people estimated to use insulin and in the absolute amount of insulin estimated to be required, though with overlapping CIs based on Monte Carlo sampling (figure 2). A strict glycaemic control target of 6·5% HbA_{1c} increased the global number of people required to be on insulin, and the amount of insulin required, by 38·9% compared with targeting 7% HbA_{1c};

	Demographic change only		Demographic change and comprehensive access to insulin	
	Outcome, 2018	Outcome, 2030	Outcome, 2018	Outcome, 2030
People with type 2 diabetes using insulin				
Africa	502 647 (288 690–798 943) [1·8%]	718 802 (421 154–1 226 177) [1·8%]	3 580 238 (2 056 273–5 690 693) [12·7%]	5 119 862 (2 999 782–8 733 785) [12·5%]
Americas	9 695 648 (7 665 389–11 537 007) [13·7%]	12 235 005 (9 630 417–14 632 677) [13·6%]	13 687 550 (10 821 390–16 287 035) [19·3%]	17 272 413 (13 595 462–20 657 257) [19·2%]
Asia	16 684 889 (13 361 708–21 796 053) [6·4%]	21 093 158 (16 923 703–27 319 674) [6·4%]	37 619 272 (30 126 523–49 143 366) [14·4%]	47 558 556 (38 157 723–61 597 425) [14·3%]
Europe	3 162 812 (2 385 353–4 469 907) [7·5%]	3 372 393 (2 469 168–4 761 120) [7·5%]	7 993 805 (6 028 827–11 297 404) [19·0%]	8 523 506 (6 240 663–12 033 426) [18·9%]
Oceania	183 439 (123 104–240 038) [7·8%]	218 324 (155 957–282 674) [7·7%]	435 532 (292 280–569 911) [18·5%]	518 356 (370 282–671 140) [18·3%]
Global total	30 229 435 (23 824 244–38 841 948) [7·5%]	37 637 682 (29 600 399–48 222 322) [7·4%]	63 316 397 (49 325 293–82 988 409) [15·6%]	78 992 693 (61 363 912–103 693 033) [15·5%]
U100 insulin vials (1000 units each) used per year				
Africa	8 624 782 (4 912 881–13 373 521)	12 305 853 (7 090 162–20 337 229)	61 432 374 (34 993 342–95 256 567)	87 651 814 (50 501 623–144 857 489)
Americas	185 734 884 (148 644 626–218 458 562)	229 389 030 (182 349 618–271 640 903)	262 205 836 (209 844 740–308 402 539)	323 833 311 (257 426 785–383 481 167)
Asia	255 959 077 (206 143 552–334 166 375)	321 604 383 (259 506 395–415 709 828)	577 108 650 (464 790 030–753 441 950)	725 118 538 (585 106 758–937 297 246)
Europe	62 218 758 (46 900 997–88 025 335)	66 228 854 (48 525 714–93 594 458)	157 253 927 (118 539 269–222 478 398)	167 389 188 (122 645 636–236 554 000)
Oceania	3 517 167 (2 388 704–4 588 735)	4 170 065 (2 989 682–5 383 238)	8 350 661 (5 671 400–10 894 840)	9 900 809 (7 098 276–12 781 196)
Global total	516 054 668 (408 990 760–658 612 528)	633 698 185 (500 461 571–806 665 656)	1 066 351 448 (833 838 781–1 390 474 294)	1 313 893 660 (1 022 779 078–1 714 971 098)
DALYs averted by insulin treatment				
Africa	..	..	18 321 (10 517–29 451)	26 585 (15 532–45 613)
Americas	..	..	46 019 (36 477–54 594)	58 216 (45 933–69 554)
Asia	..	..	169 807 (135 827–221 226)	215 179 (172 646–277 939)
Europe	..	..	27 208 (20 524–38 645)	29 282 (21 192–41 539)
Oceania	..	..	1529 (999–2026)	1839 (1298–2408)
Global total	..	..	262 884 (204 344–345 942)	331 101 (256 601–437 053)

Data are n (95% CI) [% of people aged 20–79 years with type 2 diabetes], or n (95% CI). DALYs=disability-adjusted life years.

Table 2: **Outcome measures by world region, with an HbA_{1c} treatment target of 7%**

conversely, a more liberal target of 8% HbA_{1c} reduced the global number of people required to be on insulin, and the amount of insulin required, by 45·0%.

The overall net DALYs averted was related in a complex way to treatment targets (figure 2C). In particular, targets of 6·5% or 7% HbA_{1c} had lower numbers of net DALYs averted than a target of 8% because the lower levels of targeting increased DALYs caused by hypoglycaemia (figure 2D). The highest net DALYs averted was when targeting an HbA_{1c} of 7% for people younger than 75 years and 8% for people aged 75 years and older, because these targets helped to avoid hypoglycaemic events that were concentrated primarily among older adults (figure 2C). This age-stratified cutoff had 44·2% higher net DALYs averted than the universal target of 7%. Additional analyses in which the target HbA_{1c} was risk-based (target of ≤5% for composite microvascular risk) was similar to the target of 8% HbA_{1c} scenario (figure 2C). Net DALYs averted for the midpoint year of 2024 were lower (by about 10%) than for the final year 2030 because of lower rates of diagnosis and lower total numbers of people with type 2 diabetes in 2024 than in 2030 (appendix).

Finally, we did sensitivity analyses to estimate how much less insulin might be used if three types of newer drugs (GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT2 inhibitors) were more widely available and were combined with metformin instead of combining a sulfonylurea with metformin. The absolute number of people requiring insulin, and the units of insulin, did not change meaningfully given the non-significant difference from sulfonylurea in HbA_{1c} reduction.[18] However, the rate of hypoglycaemia was reduced due to avoidance of sulfonylurea treatment, increasing the absolute net DALYs averted by 14·9%. The relative amount of net DALYs averted through each treatment target were not affected (appendix).

Discussion

We estimated global insulin use for type 2 diabetes by country and year, worldwide, from 2018 to 2030, identifying several important findings. First, current levels of insulin access are not only inadequate relative to projected need, but are disproportionately inadequate in the African, Asian, and Oceanic regions. The regions projected to increase insulin use most if access were improved were the African region in relative terms and the Asian region in absolute terms. The finding that Africa has the largest relative unmet insulin need also highlights the importance of availability and affordability improvements to the insulin market. Asia would similarly be expected to use the most insulin whether or not insulin access improved.

Second, we observed that the DALYs averted through insulin therapy would be highest if targeting HbA_{1c} levels of 7% for younger adults (<75 years old) and 8% for those of older age, to balance the risk of hypoglycaemia against the benefit of longer-term reduced microvascular disease (though with overlapping CIs between the alternative approaches simulated). The incremental reduction in microvascular risk by further lowering the HbA_{1c} target from 8% to 7% among those aged 75 years or older was

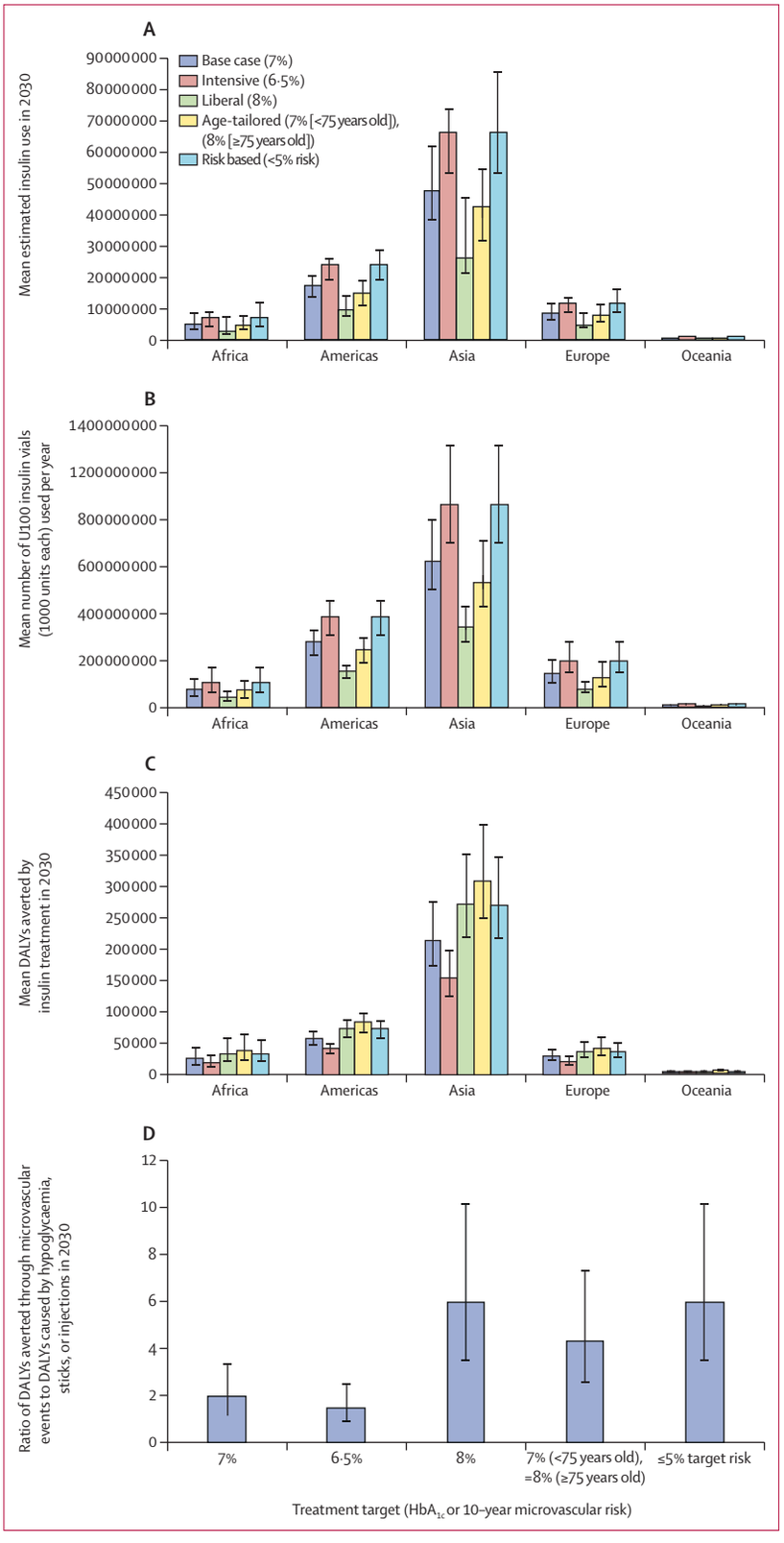

Figure 2: **Variations in insulin treatment and DALYs averted under alternative treatment targets in the year 2030**

People with type 2 diabetes estimated to use insulin (A), number of U100 insulin vials (1000 units each) used per year (B), net DALYs averted by insulin treatment (C), and ratio of DALYs averted by prevention of microvascular events with insulin treatment versus from DALYs induced by insulin treatment (including hypoglycaemia requiring medication attention, daily finger sticks, and injections) (D), worldwide. All estimates accounted for both demographic change and increased insulin access. Error bars represent 95% CIs. Base case: target HbA_{1c} of 7·0% (53 mmol/mol) for all diagnosed and treated people (AFPG 8·0 mmol/L); intensive: target HbA_{1c} of 6·5% (48 mmol/mol; AFPG 7·5 mmol/L); liberal: target HbA_{1c} of 8·0% (64 mmol/mol; AFPG 9·2 mmol/L); age-tailored: for people <75 years target HbA_{1c} of 7% and for those ≥75 years target HbA_{1c} of 8%;[20,21] risk-based: with people having ≥5% risk over 10 years of composite microvascular complications (renal failure or end-stage renal disease, severe vision loss <20/200 on a Snellen chart, or loss of pressure sensation by monofilament testing) estimated from the Risk Equations for Complications of type 2 Diabetes equations[7,8] target HbA_{1c} of 7%, or the HbA_{1c} level that achieved an estimated risk ≤5% (whichever HbA_{1c} was higher).[22] Numerical values corresponding to these figures are provided in the appendix. DALYs=disability-adjusted life years. AFPG=average fasting plasma glucose.

outweighed by the increase in serious hypoglycaemia risk. We found that—for the overall population as a whole—using a more liberal target HbA_{1c} of 8% used half as much insulin with only a 20% decline in DALYs saved. By comparison, intensive treatment to a goal HbA_{1c} of 6·5% dramatically increased insulin use while increasing hypoglycaemia-related harms. Finally, we found that such insulin needs were unlikely to be affected by expanded access to newer oral diabetes drugs because such medicines are generally not more potent than existing drugs in reducing HbA_{1c};[18] however, such drugs might substantially lower the risk of hypoglycaemia and thereby improve DALYs averted through therapy, though their cost might preclude their use in many situations.

Several key assumptions should be noted. First, the projections of type 2 diabetes prevalence from the IDF are based on population projections and the existing relations between age, sex, urbanisation, and diabetes prevalence. Because dietary and physical activity environments can change in both obesogenic and disease-reducing ways, the IDF projections could be either optimistic or pessimistic in unpredictable directions. Second, the RECODe equations we used were previously derived and validated from US samples, though we recalibrated the baseline hazard rates of events here to match GBD estimates.[7,8,23] The use of these equations assumes that the relation between underlying demographics (age, sex), biomarkers (blood pressure, HbA_{1c}), and complications is consistent across countries, which might neglect some ethnic variations. Third, our estimates of hypoglycaemia risk are based on a logistic regression (incorporating risk factors such as age and insulin dose) internally cross-validated in the ACCORD study sample,[6] but not externally validated in another study sample. Fourth, we used the distributions of bodyweight, HbA_{1c}, and insulin use from available cohort studies in the absence of comprehensive longitudinal data of high quality across all countries. The cohort data available nevertheless represent more than 60% of the global population with type 2 diabetes and therefore constitute the largest assembled sample, to our knowledge, of comprehensive diabetes profiles compiled to date. As bodyweight and insulin usage guidelines change, insulin usage quantities are expected to change in turn. We do not know the extent to which insulin initiation might be delayed by improved lifestyle modifications or effective public health interventions. Additionally, we did not have sufficient data to estimate the degree to which different oral antidiabetes drugs have different durability in maintaining HbA_{1c} reductions over time. We assumed similar durability across classes; data from the ADOPT trial suggest that thiazolidinediones might have more durability than sulfonylureas when used as monotherapy,[26] but insufficient data are available regarding durability of add-on therapies to metformin to construct a risk equation for time to insulin initiation.[27–29]

Future research should consider how key barriers to availability and accessibility of diagnosis and therapy, in the African region in particular, might be overcome,[30] and how ministries of health can best prepare for the anticipated large increase in need of insulin in the coming years. Meanwhile, our study has shown that insulin use is likely to rise, particularly in Asia, and that targeting a moderate threshold for control—potentially based in part on age as a proxy for life expectancy and comorbidities—might help to balance the risks of insulin therapy with longer-term microvascular benefit.

Contributors

SB, JSY, and DB contributed to the study design, data collection, data analysis, and writing of the report. SK, JID, SHW, KJL, and JBS contributed to the literature search, study design, data interpretation and writing the report.

Declaration of interests

KJL receives financial support from the US Centers for Medicare and Medicaid Services to develop and evaluate publicly reported quality measures. SHW reports non-financial support for accommodation and subsistence for attendance to the Scottish Study Group for Diabetes in the Young biannual conference from Novo Nordisk. All other authors declare no competing interests.

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EMPLOYMENT

Researcher and Lecturer / Privat Docent since November 2016

University of Geneva, Faculty of Medicine and Geneva University Hospitals, Division of Tropical and Humanitarian Medicine

October 2011-present

Research

- Research focus on 3 areas: Access to medicines, especially insulin; Health systems; and Patient perspective of living with a chronic disease
- On-going research projects include:
    - Mapping of the global insulin market
    - Management of Noncommunicable diseases and Neglected Tropical Diseases in Primary Health Care in Mozambique, Nepal and Peru
    - Adapting of diabetes education approaches to Mozambique and Malawi
    - Improving HIV and Sexually Transmitted Disease care services for indigenous people in the Peruvian Amazon

Projects

- Reform of Medical education in Kyrgyzstan: Technical support to project; Supervision of Monitoring and Evaluation and research components
- Training programme for doctors and nurses on Type 1 diabetes in Nicaragua
- Two G3 (consortium of francophone universities) projects: Online nutrition courses; Web-based resource for qualitative research
- Various work with the World Health Organization: Report on access to essential medicines for Noncommunicable diseases; Report on local production of insulin; Contribution to Global Report on Diabetes; Contribution to report on Noncommunicable disease in Europe
- Discussions on the management of Noncommunicable diseases in Humanitarian emergencies: Development of operational guidelines for UNHCR; Technical support to Médecins Sans Frontières; Discussions with Danish Red Cross and International Committee of the Red Cross on operational research

Teaching

- University of Geneva
    - Undergraduate: Faculty of Medicine: Global Health; Health Systems; Noncommunicable Diseases and Diabetes, Faculty of Medicine (January 2012-present)
    - Supervision of student projects (Bachelor and Masters), Faculty of Medicine (January 2014-present)
    - PhD: Supervision of 3 students, Institute of Global Health (2016-present)
    - Postgraduate: Course organiser and lecturer on health systems for Masters in Global Health, Institute of Global Health (April 2016-May 2017)
- Other teaching responsibilities:
    - University College London: Health Management; Postgraduate (2012-present)
    - Coordination of teaching in Global Health for University of Geneva/Boston University Geneva Exchange Programme for Undergraduate students (January 2012-June 2015); Lecturer (June 2015-present)
    - University of Copenhagen: Research Methods, Noncommunicable diseases and PhD examiner (2012-2014)

Joint positions:
Senior Research Fellow
University College London
Project Coordinator
International Insulin Foundation

November 2002-August 2011

Research
- Development of research protocol and methodology to assess diabetes care
- Implementation: Kyrgyzstan, Mali, Mozambique, Nicaragua, Philippines, Vietnam and Zambia

Communication and dissemination of research
- Project reports and publications including in peer reviewed journals
- National and international advocacy work
- Media interviews on the issue of diabetes and access to insulin
- Building links across stakeholder groups World Health Organization, International Diabetes Federation, Ministries of Health, clinicians, diabetes associations, people with diabetes

Project management
- Development of International Insulin Foundation's vision and policy
- National Diabetes programmes and National Noncommunicable Disease Policies in different countries
- Development and implementation of Diabetes UK "Twinning" Initiative with Mozambique (2007-2009)
- Conducted training of teams in respective countries
- Ownership of budget control for in-country projects

Teaching
- Undergraduate and postgraduate in the areas of diabetes; health systems and access to medicines

CONSULTANCIES

Swiss Agency for Development and Cooperation	Evaluation of national project on Noncommunicable diseases in Ukraine	February-March 2018
World Health Organization	Preparation of report on local production of insulin	February-December 2016
World Health Organization	Preparation of report on access to medicines for Noncommunicable diseases	March-December 2014
Ministry of Health Revolutionary Government of Zanzibar and World Health Organization	Development of a National Strategic Plan for Noncommunicable diseases	December 2013-April 2014
World Health Organization EURO Region	Health system assessment in Hungary on diabetes	June –October 2013
World Health Organization AFRO Region	Preparation of the African Health Report on Noncommunicable diseases	October 2012-March 2013
World Health Organization AFRO Region	Preparation of Regional Strategic plan for Noncommunicable Diseases	February-June 2012
UCL Consulting	Research and preparation of White Paper, Summary documents and presentations on the issue of obesity for a leading food and beverage company	December 2010-April 2011
European Union Funded Project	Evaluation of national diabetes programme in Mali	December 2009

World Health Organization	Development of Rapid Assessment Protocol for Insulin Access into a manual for the World Health Organization	January 2009
Ministry of Health and Social Welfare, Tanzania and Ministry of Foreign Affairs, Denmark	National Strategy on Noncommunicable Diseases for Tanzania	April-October 2008
Handicap International	Diabetes Situation Analysis: Bangkok, Thailand	September-November 2006

POSTGRADUATE EDUCATION

Centre for International Health and Development
Institute of Child Health, University College London

January 2007-December 2011

PhD (part-time): Establishing a hierarchy of needs for Type 1 diabetes – Research carried out in 13 countries

London School of Hygiene and Tropical Medicine

October 2001-August 2002

MSc in Public Health: Dissertation – Prevention of type 2 diabetes in children. Research done in collaboration with World Health Organization Diabetes Group

PROFESSIONAL EXPERIENCE AND OUTREACH

- Member Diabetes Centre at Faculty of Medicine, University of Geneva
- Commissioner, Lancet Diabetes & Endocrinology Commission on diabetes in sub-Saharan Africa
- Editorial Board Member, BMC Health Services Research
- Honorary Lecturer, University College London
- Advisor to the Board, International Insulin Foundation
- Member of the Board, Santé Diabète
- Conference Steering Committee: Creating a healthier future for children and adolescents: A roadmap beyond the UN Summit on NCDs
- Participant Cambridge Diabetes Seminar 2011
- International Diabetes Federation Insulin Task Force: 2006-2009

LANGUAGES

Bilingual: English and French
Working knowledge: German, Portuguese and Spanish

COMPUTER SKILLS

Mac and PC literate, SAP, NVIVO, STATA and Epi-Info

PUBLICATIONS

1. Boulle P, Kehlenbrink S, Smith J, **Beran D**, Jobanputra K. Challenges associated with providing diabetes care in humanitarian settings. ***Lancet Diabetes & Endocrinology***. 2019, 7(8):648-656
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CHAPTERS AND OTHER PUBLICATIONS

1. De Maesseneer J, Borgermans L, **Beran D** and Juan Tello. (2018) Transforming individual health services: towards integrated multidisciplinary primary health care. In: Jakab M, Farrington J, Borgermans L and Mantingh F. Editors. Health systems respond to noncommunicable diseases: time for ambition. Copenhagen. World Health Organization.
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3. **Voko Z, Beran D, Pusztai, Z, Bak Pedersen, H, Evetovits T and Szigeti S.** (2014) Better non-communicable disease outcomes: challenges and opportunities for health systems. Hungary Country Assessment: Focus on diabetes. Copenhagen: WHO Regional Office for Europe.
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GRANTS (last 10 years)

1. Web-based resource for qualitative research – **G3** – € 18,415
2. Improving HIV and STD care services for indigenous people in the Peruvian Amazon **– ESTHER Switzerland –** CHF 100,000 (2018-2019)
3. Addressing the Challenge and Constraints of Insulin Sources and Supply Study – **Helmsley Charitable Trust** – US$ 3,400,000 (2018-2021)
4. EXTending availability of self-management structured EducatioN programmes for people with type 2 Diabetes in low-to-middle income countries (EXTEND) – **UK Medical Research Council** – £578,479 (2017-2018)
5. Medical and nursing education reforms in Kyrgyzstan – **Swiss Agency for Development and Cooperation** – CHF 3,199,985 (2017-2021)
6. Addressing the double burden of disease: improving health systems for Noncommunicable and Neglected Tropical Diseases – **Swiss National Science Fund** – CHF 1,901,714 (2016-2021)
7. Addressing the Challenge and Constraints of Insulin Sources and Supply Study – **Helmsley Charitable Trust** – US$ 1,200,000 (2014-2017)
8. Pre-graduate – postgraduate – continuing medical education reforms in Kyrgyzstan – **Swiss Agency for Development and Cooperation** – CHF 2,549,840 (2014-2017)
9. Barriers and facilitators to access to medicines for Noncommunicable diseases – **World Health Organization** – US$ 25,000 (2014)
10. Management of Chronic Diseases: the perspective of Primary Care doctors in Geneva – **Geneva University Hospitals "Fonds Mimosa"** – CHF 20,745 (2013)
11. Development of an online course on diabetes and nutrition – **G3** - € 20,000 (2013) and € 20,000 (2017)
12. Pilot of the WHO Manual "How to investigate access to care for chronic Noncommunicable diseases in low- and middle-income countries" in Peru and "identifying key lessons learnt from the implementation of the Rapid Assessment Protocol for Insulin Access as a tool for policy change" – **Alliance for Health Policy and Systems Research** – US$ 50,000 (2012)

13. Development of a course on Rapid Assessment Protocols – **University of Copenhagen** – US$ 25,000 (2012)
14. Establishment of the Global Alliance for Chronic Disease Secretariat – **Global Alliance for Chronic Diseases** – US$ 785,000 (2010-2012)
15. The management of people with tuberculosis and diabetes in Kyrgyzstan – **Institute of Global Health** – £5,000 (2010)
16. Implementing the Rapid Assessment Protocol for Insulin Access in Kyrgyzstan and Vietnam **– International Diabetes Federation** – US$ 80,000 (2008-2009)

CONFERENCE PRESENTATIONS AND POSTERS (last 5 years)

1. **12ème Journée de la recherche clinique** (Geneva, Switzerland) Estimating the global need for insulin 2018.2030: a micro simulation. May 2019
2. **Harvard Humanitarian Initiative (Boston, USA)** Access to insulin: a global perspective. 4-5 April 2019.
3. **Prince Mahidol Conference** (Bangkok, Thailand) NCDs in humanitarian settings: reflections from a researcher; and The insulin market, innovation in diabetes and barriers to access. 29 January-3 February 2019.
4. **American Diabetes Association** (San Diego, USA) 9-13 June 2017.
5. **10ème Journée de la recherche clinique** (Geneva, Switzerland) 11 May 2017.
6. **Global ageing: Challenges and opportunities** – Royal Society of Medicine (London, UK) 24-25 April 2017.
7. **Improving care of people with NCDs in humanitarian settings** – London School of Hygiene and Tropical Medicine (London, UK) 2 September 2016.
8. **World Cardiology Congress** (Mexico City, Mexico) 4-7 June 2016.
9. **6ème Congrès Européen de la SETE Education Thérapeutique du Patient** (Geneva, Switzerland) 18-20 May 2016.
10. **World Diabetes Congress** (Vancouver, Canada) 1-4 December 2015.
11. **8ème Journée de la recherche clinique** (Geneva, Switzerland) 8 May 2015.
12. **International Health Economics Association** (Dublin, Ireland) 13-16 July 2014.
13. **Geneva Health Forum** (Geneva, Switzerland) 15-17 April 2014.
14. **International Health Economics Association** (Sydney, Australia) 7-10 July 2013.