



Comment from Health Action International to the Expert Committee on the application to include long-acting analogue insulins in the WHO Model List of Essential Medicines

For the last two years, the *Addressing the Challenge and Constraints of Insulin Sources and Supply* (ACCISS) Study has been studying the global insulin market to identify barriers to accessing this important medicine. This year we are developing tools for use by governments and others to improve access to insulin. The ACCISS Study is led by Health Action International (Dr Margaret Ewen), Geneva University Hospitals and University of Geneva (Dr David Beran), and Boston University School of Public Health (Professor Richard Laing). The Study includes a large group of international experts on insulin supply and use, and access to medicines. You can read more about the ACCISS Study, and the reports and papers we have published on the insulin market, at <http://haiweb.org/what-we-do/acciss/>

The application to include long-acting analogue insulin on the Model Essential Medicines List concludes that long-acting insulin analogues have a 'slight' therapeutic advantage¹. However, the studies included in the proposal that informed this conclusion are considered to have a 'serious or very serious risk of bias' and should therefore be treated with caution. Moreover, they do not relate to the use of insulin in low- and middle-income countries. The crucial issue not addressed is the unaffordability of long-acting insulins; both to health systems (particularly those in resource-constrained settings) and to individuals (particularly those forced to pay for insulin out-of-pocket). Therefore, our comment is focused on the affordability of long-acting analogue insulin, of limited added-value, in comparison to human insulin, both to health systems and to insulin users

Affordability of long-acting analogues versus human insulin to health systems

A report of insulin prices, published in 2016 by the ACCISS Study, included government procurement (tender) prices and quantities procured in 25 countries², using an adaptation of the World Health Organization (WHO)/Health Action International (HAI) standardised methodology to measure medicine availability, prices and affordability^{3,4}.

¹ Knowledge Translation Program and Li Ka Shing Knowledge Institute of Michael's Hospital. Application for the inclusion of long-acting insulin analogues – glargine and detemir insulins – in the WHO Model List of Essential Medicines, as treatments used for basal insulin support in diabetes type 1. Available at http://www.who.int/selection_medicines/committees/expert/21/en/ Accessed 7 February 2017

² 4 countries were low-income, 11 were lower-middle income, 7 were upper middle-income and 3 were high-income

³ M. Ewen, H-J Joosse, P Ashigbie, D. Beran, R. Laing. Insulin Prices Profile. Accessible at http://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

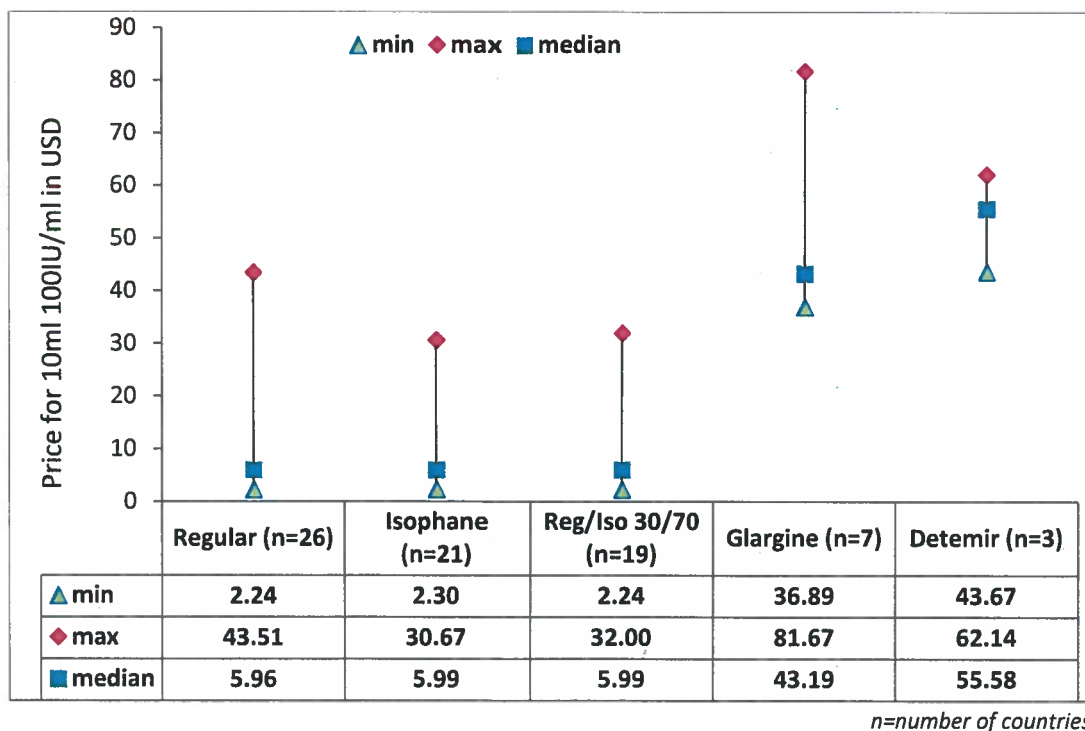
⁴ World Health Organization/Health Action International. Measuring medicine prices, availability, affordability and price components. 2nd edition. Geneva, 2008.

<http://haiweb.org/what-we-do/price-availability-affordability/collecting-evidence-on-medicine-prices-availability/>

The study looked at the median government procurement prices of human insulin (regular, isophane and regular/isophane 30/70) and the two long-acting analogue insulins (glargine and detemir) (see Figure 1 below). The prices are for 10ml 100IU/ml (vials, pre-filled pens or cartridges) in US dollars. The governments in the study were paying approximately \$6 for the three human insulins. Prices were substantially higher (seven to nine times) for glargine (\$43.19) and detemir (\$55.58).

In the few low- and middle-income countries (LMICs) in the study where governments currently buy both human insulin and long-acting analogues, significant savings would result if the government only purchased human insulins. For example, the government of Iran would save \$22 million annually, and the Kyrgyz Republic would save \$221,000. In both countries, savings would be at least double this amount if they did not procure *any* analogues at all.

Figure 1. Median government procurement prices of human and long-acting insulins in USD



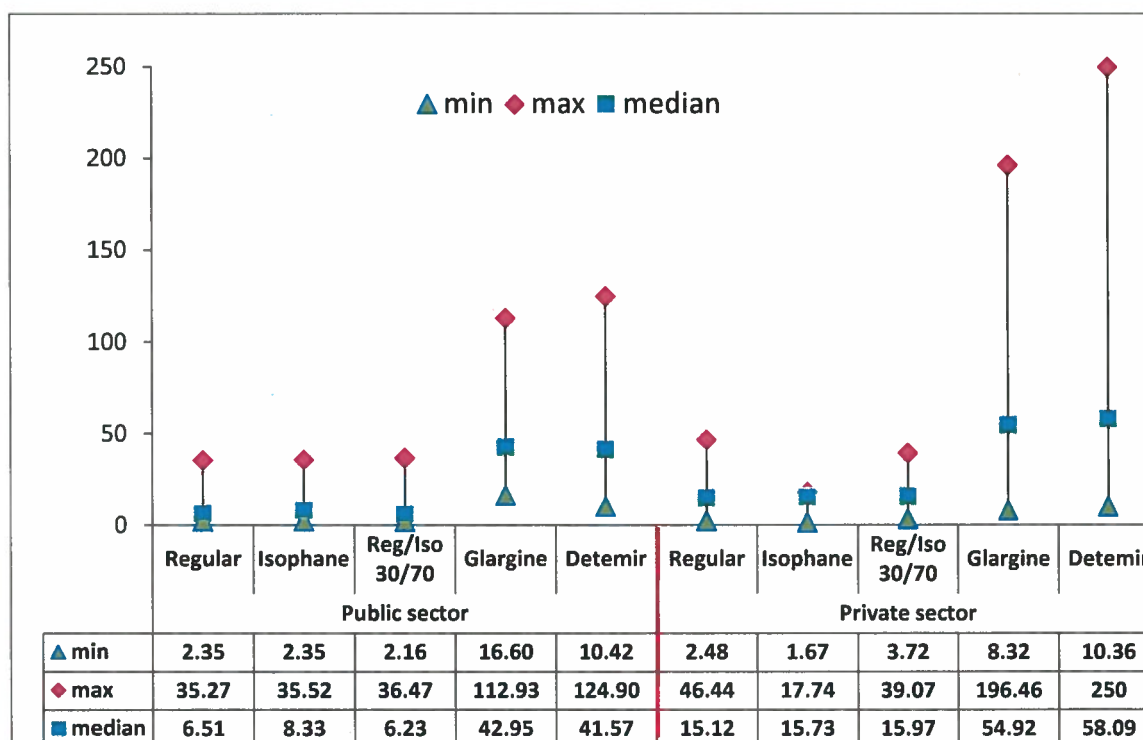
Buying lower-priced human insulins, rather than high-priced long-acting analogues, will result in more people being treated in public hospitals and public health facilities within the existing pharmaceutical budget. For example, based on an average usage of 13 vials annually, an additional 391,111 people in Iran, and 3448 people in the Kyrgyz Republic, could be treated with human insulin from the savings generated from not buying glargine and detemir. Treating more people without additional costs to the government is a welcome outcome in any jurisdiction, but specifically in poorer nations. It will be challenging for governments to bow to pressures from insulin manufacturers, as well as diabetologists and national diabetes associations (many of whom receive funding or other benefits from insulin manufacturers) to buy long-acting analogues if they are included in the WHO Model List.

Affordability of human insulin versus long-acting analogues to individuals

In the same study, patient prices in the public and private sector were collected in 43 countries⁵. In the public sector of countries where people have to pay for insulin out-of-pocket, median prices of the three human insulins ranged from \$6.23 to \$8.33 (Figure 2). Median prices of the long-acting insulins were \$42.95 and \$41.57 for glargine and detemir, respectively. In the private sector, median prices of the three human insulins ranged from \$15.12 to \$15.97. Median prices of the two analogues were \$54.92 (glargine) and \$58.09 (detemir). The selection of insulin type clearly makes a difference in both sectors, with people having to pay on average about four to six times the price for long-acting analogues compared to human insulins.

The national situation can be even more extreme. For example, in the public sector in the Dominican Republic, isophane was \$2.66 whereas glargine was about ten times the price at \$25.83. When insulin availability is poor in public sector outlets, people are forced to buy in the private sector where there can also be large price differences between human insulin and long-acting analogues. For example, in private pharmacies in Zimbabwe, regular insulin cost \$8, detemir was \$68, and glargine was \$120.

Figure 2. Patient prices of human and long-acting insulins in USD



To improve access, insulin needs to be affordable for those having to pay out-of-pocket. The ACCISS Study assessed insulin affordability, which was expressed as the number of days the lowest paid unskilled government worker had to work to buy 10ml insulin, based on median prices. As shown in Table 1, over 8 days' wages would be needed to buy 30 days' supply of glargine or detemir in both

⁵ Eight countries were low-income, 14 were lower-middle income, 11 were upper-middle income and 10 were high-income. Patient prices were collected by HAI and ACCISS Study members, various networks and requests via listservs. Full prices were collected for insulins found in stock in the nearest public hospital/health facility and private pharmacy. These may not be representative of the entire country except in countries where prices are set and WHO/HAI surveys have shown no price variability across outlets.

the public and private sectors. Human insulins were considerably more affordable at 2.5-3.5 days' wages. Paying more than 1 days' wage for 30 days' supply of a medicine to treat a non-communicable disease is considered unaffordable by the WHO and HAI⁶. In all the LMICs in the dataset, long-acting analogues were unaffordable. While human insulins are more affordable than analogues, even they are unaffordable in many countries.

Table 1. Affordability of human and long-acting insulins in days' wages across 43 countries

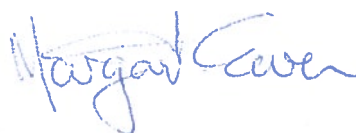
	Mean affordability in days' wages to buy 10ml		
	Human insulins	Glargine	Detemir
Public sector	2.5 <i>(range 0.5-6.2)</i>	10.3 <i>(range 2.6-19.1)</i>	8.6 <i>(range 1.6-17.3)</i>
Private sector	3.5 <i>(range 0.2-48.9)</i>	10.6 <i>(range 0.5-61.0)</i>	18.3 <i>(range 0.5-77.9)</i>

Conclusion

The evidence suggests that the procurement of long-acting analogue insulins is going to put an even greater strain on the pharmaceutical budgets of governments, particularly in resource-constrained settings. In countries where individuals have to pay out-of-pocket for insulin, human insulin is clearly more affordable. By procuring and using human insulins, governments can treat more people without additional funding. The inclusion of long-acting analogues in the WHO Model List will pressure governments to add them to their national essential medicines list, and for both governments and individuals to buy them. The result will be fewer people being treated and more deaths.



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⁶ Gelders S, Ewen M, Noguchi N and Laing R. Price, availability and affordability. An international comparison of chronic disease medicines. Cairo: World Health Organization and Health Action International, 2006