



GLOBAL ACCESS TO AFFORDABLE INSULIN UNDERSTANDING THE BARRIERS

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ACCISS Study, Health Action International

Health Action International (HAI)

- Established 1981 in Amsterdam, The Netherlands
- Research and evidence-based advocacy
- Advance policies that enable access to medicines & improved use
- Currently four programmes of work: ACCISS Study, EU projects, Snakebite Envenoming, Health Systems Advocacy (sexual and reproductive health commodities)

Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) Study

- Collaboration between HAI (Marg Ewen & Molly Lepaske), David Beran (University of Geneva), Richard Laing (Boston University School of Public Health) and a large group of international experts in diabetes and access to medicines
- Goal: Improve the life-expectancy and quality of life for people with diabetes requiring insulin by addressing inequities and inefficiencies in the global insulin market
- Phase I of the study focused on identifying the barriers to access to insulin and creating interventions. Phase II focuses on piloting these tools and interventions at a country level while continuing to work globally.
- Started in 2015, funded by The Leona M. and Harry B. Helmsley Charitable Trust and Stichting ICF

ACCISS Expert Advisory Group

- Guido Alarcon, Ecuador
- Mark Atkinson, University of Florida
- Merith Basey, Director, Universities Allied for Essential Medicines
- Carine de Beaufort, ISPAD
- Oumar Diallo, Guinea and USA
- Edwin Gale, International Insulin Foundation
- Hans Hogerzeil, Former head Medicines Dept. at WHO
- Cécile Macé, UNDP
- Christophe Perrin, Independent
- Kaushik Ramaiya, Endocrinologist, Tanzania
- Carla Silva-Matos, Ministry of Health, Mozambique
- Hanne Bak Pederson
- John S. Yudkin, International Insulin Foundation
- Aigerim Zhaparova, Kyrgyzstan

About Insulin

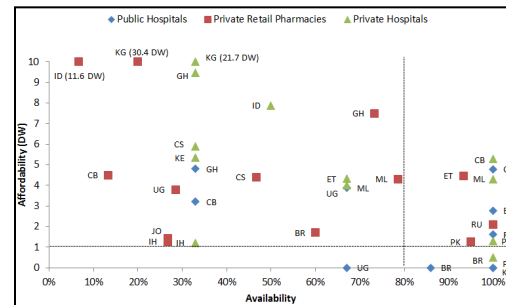
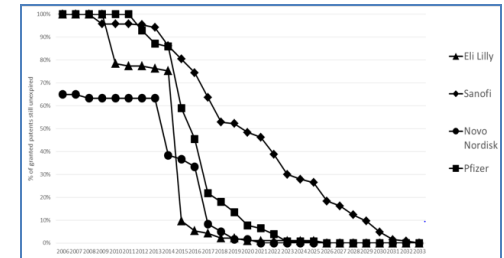
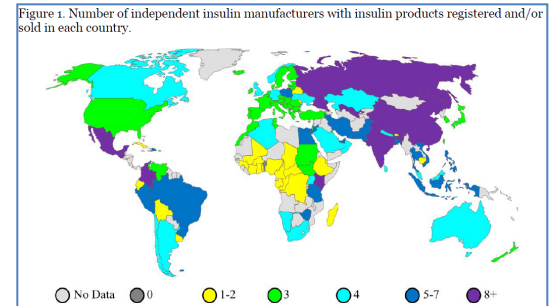
- Biological, first discovered in 1921
- Essential for type 1 diabetes; increasingly being used to manage type 2 diabetes (estimated 63 million people)
- Initially pork and beef extracts; 1982 recombinant DNA (human) insulin (short-acting, intermediate-acting, mixed); mid-1990's analogue insulins (rapid-acting, long-acting, mixed)



ACCISS Research

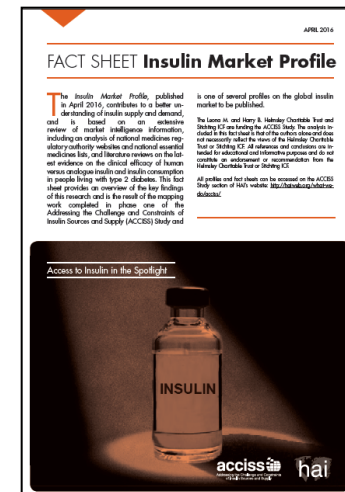
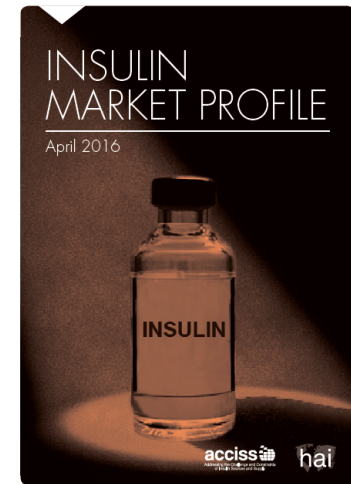
'Angles' looked at by ACCISS starting 2015:

- Market
- Intellectual property
- Trade
- Regulatory
- Perspective of diabetologists, insulin users and manufacturers
- Initiatives
- Need for insulin
- Cost of production
- Availability, prices, affordability, price components



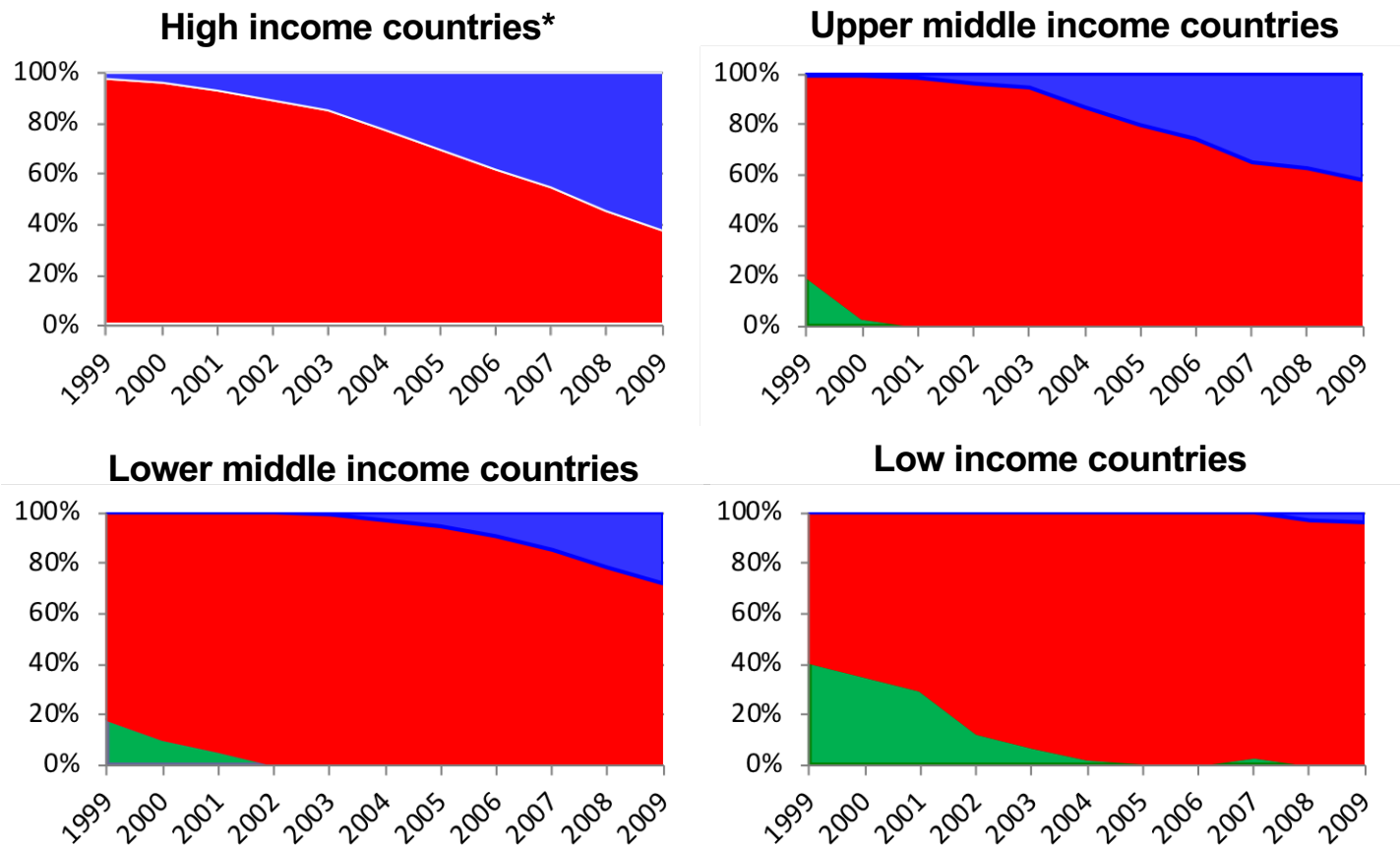
Insulin Market

- Analysis of 100 NEMLs: nearly all countries list both intermediate-acting and short-acting human insulin
- Global insulin market valued at US\$20.8 billion (2012)
- Three major insulin suppliers have >90% global insulin market by value and volume - Eli Lilly, Novo Nordisk and Sanofi
- Of 121 countries, Novo Nordisk products registered in 111 countries, Sanofi -101 countries, Eli Lilly - 94 countries. Sole suppliers of insulin in 55% countries
- 39 smaller insulin manufacturers were identified
 - 23 only sell insulin in one country
 - From discussions, probably only 10 or so are truly independent



Changes in Insulin Use

(red: human; blue: analogue; green: animal)

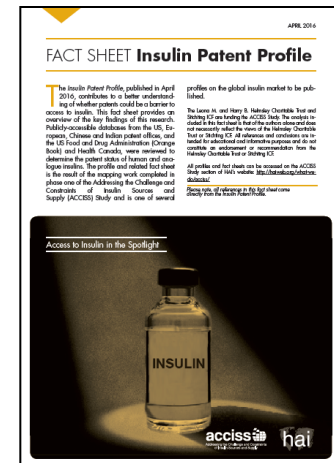
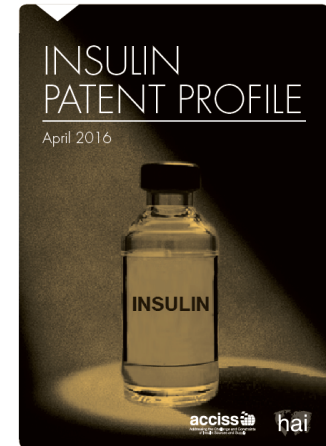


Beran et al. 2016

*USA: According to a 2019 Health Cost Institute, 90% of people with type 1 diabetes now use analogue insulin for their treatment in the US

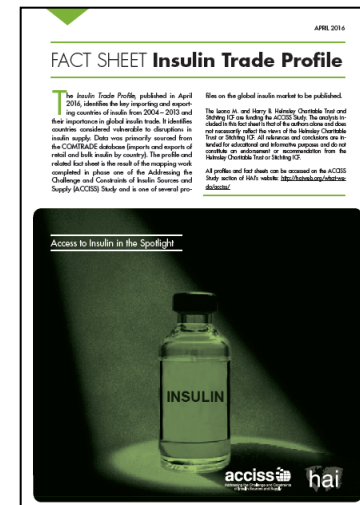
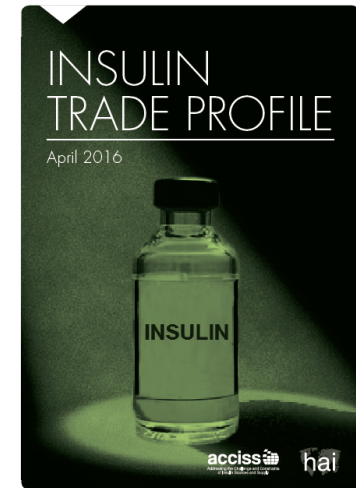
Patents on Insulin

- There are no patents on any formulations for human insulin
- Patents on analogue insulins already on the market in the US and Canada have expired or will soon expire in these countries (based on the filing date and a 20-year patent period)
 - Eli Lilly, Sanofi, Novo Nordisk and Pfizer own these patents
- New ultra analogues are on patent
- Increase of patents on delivery devices (*Luo and Kesselheim 2016*)



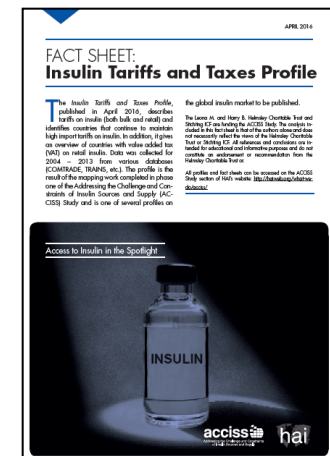
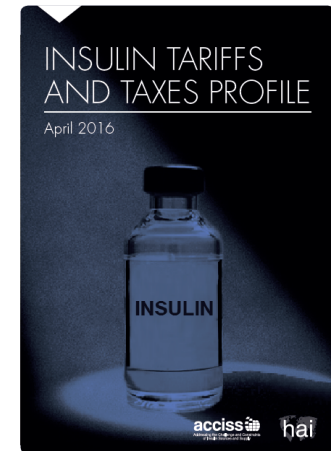
Trade in Insulin

- 10 countries made up 98-99% of the global value of retail insulin *exports* (2004-2013)
 - Germany, Denmark, and France collectively exported between 85-96%
- Approximately 50% of global *imports* of retail insulin were to the US, UK, Germany and Japan (2004-2013)
- Around 60 countries imported insulin from only one country for at least one year (2004-2013)
 - Vulnerable to any disruption in supply



Tariffs and Taxes on Insulin

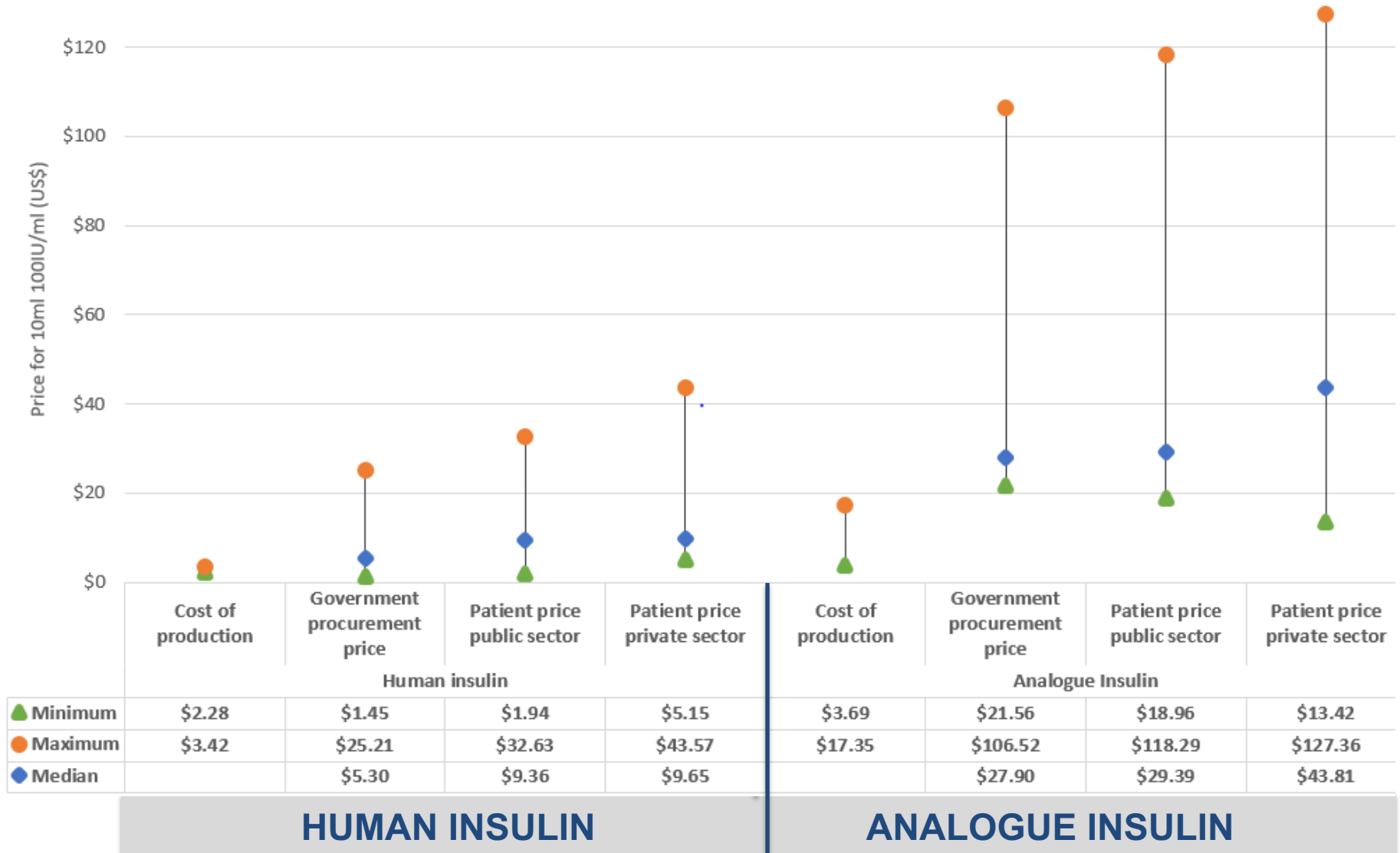
- Majority of countries have no import tariffs on retail insulin
 - Proportion of countries without tariffs has increased since 2004 (52 to 77%)
- Global weighted average import tariff has decreased from slightly less than 3.5% (2004) to about 1.9% (2013)
 - In 2012 and 2013, most of countries with the highest import tariffs were from Latin America
- VAT on insulin ranged from 0-24%
 - Average VAT levels:
 - 8.3% in OECD countries
 - 4.6% in non-OECD high-income
 - 7.0% in all other income groups



The Biosimilar Insulin Market

Income	<ul style="list-style-type: none"> • Size of local market, most seeking new markets
Manufacturing	<ul style="list-style-type: none"> • High cost of investment, underutilised capacity
Challenges expressed by companies & current situation on approvals	<ul style="list-style-type: none"> • Competing with the three large MNCs on price • Marketing • Awareness of biosimilars • Human versus analogue biosimilars. Priority is getting EMA &/or USFDA approval for analogues • Analogues: Abasaglar (Lilly), Semglee (Biocon/Mylan), Admelog (Sanofi) approved. Lusduna (MSD) approved but then withdrew • Currently no biosimilar human insulins have marketing authorisation from a stringent regulatory authority. Told Novartis/Gan&Lee will apply; Julphar?
Biosimilar regulations	<ul style="list-style-type: none"> • Not all countries have regulatory procedures for approving biosimilars • Inconsistent regulatory requirements across national medicines regulatory authorities. Tend to adopted the European Medicines Agency (EMA) regulatory process • The stronger the evidence about structural, biological and formulation similarity between the biosimilar and reference, the less non-clinical and clinical data is needed for approval • EMA stated that clinical data will not be required for biosimilars but it doesn't appear to have been put in practice

Estimated Cost of Production and Insulin Prices in 13 LMICs



Median Prices of Originators vs Biosimilars

Govt. Procurement Prices – biosimilars (vials)

Pakistan: 16% ↓ (regular, isophane, 30/70)

Russia, Kazan: 10% ↑ (regular)

China, Shaanxi: 11% ↓ (30/70)

China, Hubei: 14% ↓ (regular, isophane)

Patient Prices – biosimilars (vials)

Country	Insulin Type	Public sector	Private Pharmacies
Ethiopia	Isophane		26% ↓
Russia, Kazan	Isophane	19% ↓	26% ↑
Brazil	Isophane		3% ↓
Pakistan	Isophane		20% ↓
Pakistan	Glargine		28% ↓
Uganda	Glargine		17% ↓

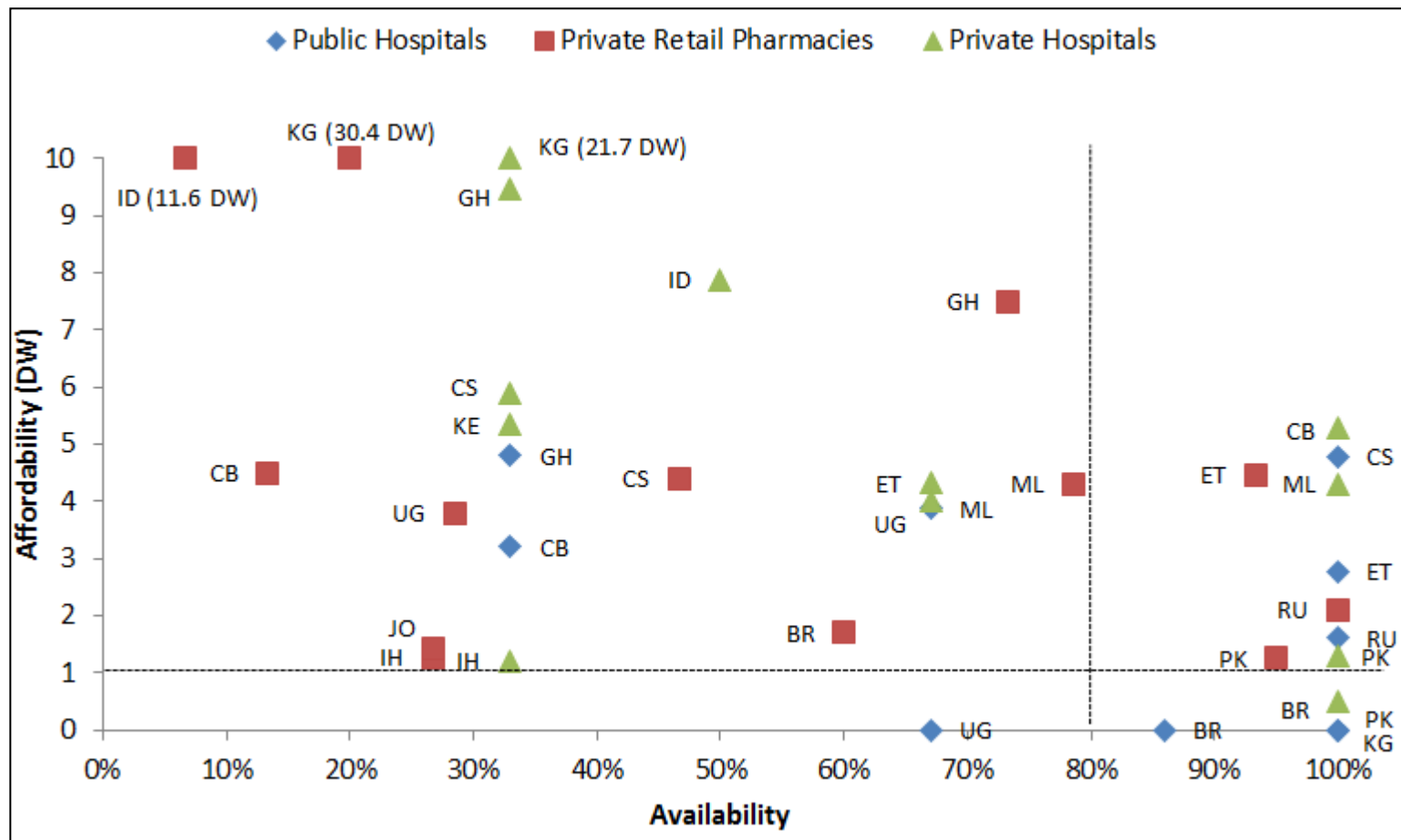
Insulin Affordability in 13 LMICs

Number of days' wages needed for the lowest-paid unskilled government worker to purchase 10ml 100IU/ml insulin

Sector	HUMAN INSULIN		ANALOGUE INSULIN	
	Median days' wages depending on type	Range across insulin types and countries	Median days' wages depending on type	Range across insulin types and countries
Public	3.5 – 3.9	0.3 - 6.8	6.1 – 7.9	2.8 - 17.3
Private pharmacies	2.2 – 4.3	1.2 – 30.4	6.6 – 15.6	2.7 – 94.2
Private hosp/clinics	3.7 – 5.0	0.5 – 22.1	6.7 – 14.3	3.1 – 43.1

Affordability and Availability in LMICs: Isophane

Affordability: number of days wages needed by the lowest paid unskilled government worker to purchase 10ml isophane



Insulin Prices in the US

The Washington Post Magazine

Life, Death and Insulin

THE WALL STREET JOURNAL

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1,963 views | Mar 22, 2019, 11:29am

Insulin Quest: When Lifesaving Drugs Are Out of Reach

Rising Out-Of-Pocket Costs For Insulin Indicates Market Failure

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The human cost of insulin in America

By Ritu Prasad
BBC News

- From 2012 to 2016, US average price increased from 13 cents per IU to 25 cents per IU¹
- Price rapid-acting analogue Humalog® (Eli Lilly) reduced to \$187 for uninsured in March 2019; Sanofi reduced prices for uninsured to \$99 a month
- Much advocacy in US/ Congressional hearings
- Impact on global market yet to be seen

(1) Health Care Cost Institute. Spending on Individuals with Type 1 Diabetes and the Role of Rapidly Increasing Insulin Prices January 2019

Perceptions of People Using Insulin

Questionnaire/interviews with 18 people with type 1, and 16 people with type 2 diabetes, in 11 countries:

- Satisfaction with the insulin they were using
- Respondents (except the UK) struggled to pay for their insulin and/or insulin related supplies and other costs
- Issues with supply reliability and availability
- Members of diabetes associations seem to have more knowledge of types of insulin and manufactures
- Knowledge of brand name versus manufacturer
- Brand loyalty versus company loyalty in changing insulin
- Doctors have a big influence in terms of insulin selection

“I would [have] reservations [about changing insulins] because I’m used to what I use and because I trust it. Anything else would be a risk. The origin doesn’t interest me, it’s what I’m using that’s keeping me healthy.” Canada analogue insulin user, type 1 diabetes

“No preference (on type of insulin). I trust what my doctors say. What they say I should do, I will do.” Mexico analogue insulin user, type 2 diabetes

Perceptions of Healthcare Providers

Questionnaire/interviews with 9 key opinion leaders

- Price of insulin and barriers to access persist
- Human insulin was the main insulin prescribed in LMICs
- Prescribers did not see difference between human and analogue insulin in practice
- Majority of respondents were in favor of pens
- Price of insulin and supplies was a key factor influencing prescribing practices
- Overall issues with health systems and comprehensive diabetes care

Summary

- \$20 billion market (and growing) yet limited competition
- Availability in outlets in LMICs is poor. Where found and not free, insulin is largely unaffordable.
- Biosimilars: inconsistent regulatory requirements, low use (limited understanding & quality perceptions), manufacturing under capacity
- Increasing use of higher-priced analogue insulins over human insulin

Multiple issues require a range of interventions, and pilot their use in different settings

ACCESS TO INSULIN TOOLKIT

Estimation of need for insulin in type 1 and type 2

ABOUT

NEED FOR
INSULIN

INSULIN
MAP

- Country need estimates
- Price data (where available)

- Transition guidelines
- Case studies of countries providing insulin for free
- Cost of care model
- Managing diabetes
- Alternative funding mechanisms for insulin

HEALTH
SYSTEMS

PRICE OF
INSULIN

INSULIN
SELECTION

- Review on the value of insulin
- Guideline on different issues surrounding the use of insulin
- Biosimilar insulin FAQs
- Interchangeability

- Advocacy communications guide
- Insulin FAQs
- Infographics and more

COMMUNICATIONS

- Database: govt. procurement price
- Estimation of cost of production of insulin
- Addressing mark-ups in the supply chain

In-Country Work



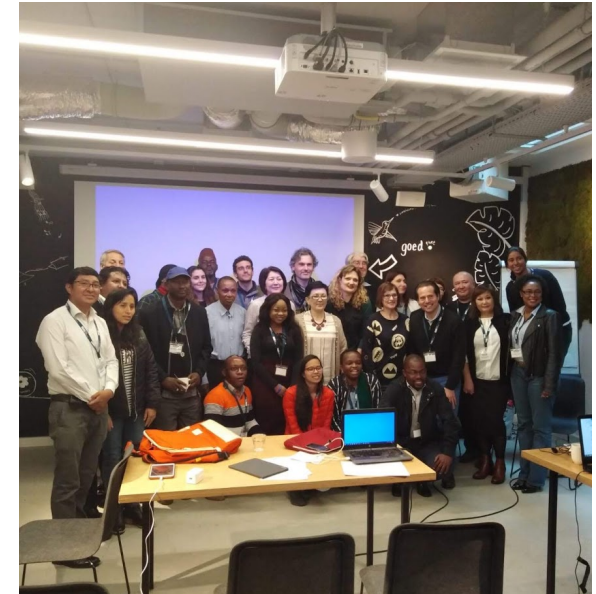
Partnering with Health Policy Analysis Center (HPAC)



Partnering with Santé Diabète



Partnering with CRONICAS



Partnering with Tanzania NCD Alliance

Improving Access to Affordable, Quality-assured Insulin

Discussions with WHO include:

- Inclusion of biosimilar human insulin in their Prequalification Programme
- Expand WHO guidance on the evaluation of biosimilar insulins
- Support regular monitoring of insulin availability and affordability in countries
- Work with countries to regulate mark-ups in the insulin supply chain
- Support the ACCISS Study's insulin price database
- Activities around insulin centenary in 2021

Work with partners on current health system challenges regarding access to insulin and delivery of diabetes care:

- Strengthening supply systems
- Evidence-based standard treatment guidelines
- Improving delivery of care
- Diabetes in UHC



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ACCISS STUDY

Learn more about ACCISS

<http://haiweb.org/what-we-do/acciss>

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