GLOBAL ACCESS TO AFFORDABLE INSULIN
UNDERSTANDING THE BARRIERS

Molly Lepeska and Marg Ewen
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 Lepeska), 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)

High income countries*

Upper middle income countries

Lower middle income countries

Low income countries

*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

<table>
<thead>
<tr>
<th>Income</th>
<th>• Size of local market, most seeking new markets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manufacturing</strong></td>
<td>• High cost of investment, underutilised capacity</td>
</tr>
<tr>
<td><strong>Challenges expressed by companies &amp; current situation on approvals</strong></td>
<td>• Competing with the three large MNCs on price</td>
</tr>
<tr>
<td></td>
<td>• Marketing</td>
</tr>
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<td></td>
<td>• Awareness of biosimilars</td>
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<tr>
<td></td>
<td>• Human versus analogue biosimilars. Priority is getting EMA &amp;/or USFDA approval for analogues</td>
</tr>
<tr>
<td></td>
<td>• Analogues: Abasaglar (Lilly), Semglee (Biocon/Mylan), Admelog (Sanofi) approved. Lusduna (MSD) approved but then withdrew</td>
</tr>
<tr>
<td></td>
<td>• Currently no biosimilar human insulins have marketing authorisation from a stringent regulatory authority. Told Novartis/Gan&amp;Lee will apply; Julphar?</td>
</tr>
<tr>
<td><strong>Biosimilar regulations</strong></td>
<td>• Not all countries have regulatory procedures for approving biosimilars</td>
</tr>
<tr>
<td></td>
<td>• Inconsistent regulatory requirements across national medicines regulatory authorities. Tend to adopted the European Medicines Agency (EMA) regulatory process</td>
</tr>
<tr>
<td></td>
<td>• 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</td>
</tr>
<tr>
<td></td>
<td>• EMA stated that clinical data will not be required for biosimilars but it doesn't appear to have been put in practice</td>
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</tbody>
</table>
Estimated Cost of Production and Insulin Prices in 13 LMICs

Gotham et al. 2018; Ewen et al 2019
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)

<table>
<thead>
<tr>
<th>Country</th>
<th>Insulin Type</th>
<th>Public sector</th>
<th>Private Pharmacies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethiopia</td>
<td>Isophane</td>
<td></td>
<td>26% ↓</td>
</tr>
<tr>
<td>Russia, Kazan</td>
<td>Isophane</td>
<td>19% ↓</td>
<td>26% ↑</td>
</tr>
<tr>
<td>Brazil</td>
<td>Isophane</td>
<td></td>
<td>3% ↓</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Isophane</td>
<td></td>
<td>20% ↓</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Glargine</td>
<td></td>
<td>28% ↓</td>
</tr>
<tr>
<td>Uganda</td>
<td>Glargine</td>
<td></td>
<td>17% ↓</td>
</tr>
</tbody>
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Ewen et al 2019
## Insulin Affordability in 13 LMICs

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

<table>
<thead>
<tr>
<th>Sector</th>
<th>Human Insulin</th>
<th>Analogue Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median days’ wages depending on type</td>
<td>Range across insulin types and countries</td>
</tr>
<tr>
<td>Public</td>
<td>3.5 – 3.9</td>
<td>0.3 - 6.8</td>
</tr>
<tr>
<td>Private pharmacies</td>
<td>2.2 – 4.3</td>
<td>1.2 – 30.4</td>
</tr>
<tr>
<td>Private hosp/clinics</td>
<td>3.7 – 5.0</td>
<td>0.5 – 22.1</td>
</tr>
</tbody>
</table>

Ewen et al 2019
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

• From 2012 to 2016, US average price increased from 13 cents per IU to 25 cents per IU\(^1\)

• Price rapid-acting analogue Humalog\(^\circledR\) (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

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(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
- Transition guidelines
- Case studies of countries providing insulin for free
- Cost of care model
- Managing diabetes
- Alternative funding mechanisms for insulin
- Advocacy communications guide
- Insulin FAQs
- Infographics and more

- Country need estimates
- Price data (where available)
- Review on the value of insulin
- Guideline on different issues surrounding the use of insulin
- Biosimilar insulin FAQs
- Interchangeability

**Database: govt. procurement**
- 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
ACCISS STUDY
Learn more about ACCISS
http://haiweb.org/what-we-do/acciss

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