Access to insulin: current constraints and challenges

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Access to NCD medicines on the global agenda

- Sustainable Development Goals
  - NCD targets
    - *"By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being."*
  - Access to medicines
    - *"Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, …."*
  - Universal Health Coverage
    - *"Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all."*
- WHO NCD Global Action Plan
  - *"An 80% availability of affordable basic technologies and essential medicines, including generics, required to treat major NCDs in both public and private facilities"*

Access to NCD medicines on the global agenda, but…

- Different challenges for different medicines:
    1. Generic medicines available cheaply, but problems of access in country including quality (e.g. oral anti diabetic medicines, anti hypertensives, etc.)

    2. Asthma inhalers and insulin available at high cost, and quality assessment is highly challenging

    3. Medicines still under patent and accessible only through expanded access programmes (e.g. certain cancer medicines)

    4. Opioid analgesics for palliative care often limited by excessive regulation

Beran et al. 2014

Insulin: a unique situation

- Discovered in 1921 – but poor access remains today
- Life or death need for type 1 diabetes, increasingly needed to manage type 2 diabetes
- Biological
- Injectable
- High priced compared to other NCD medicines

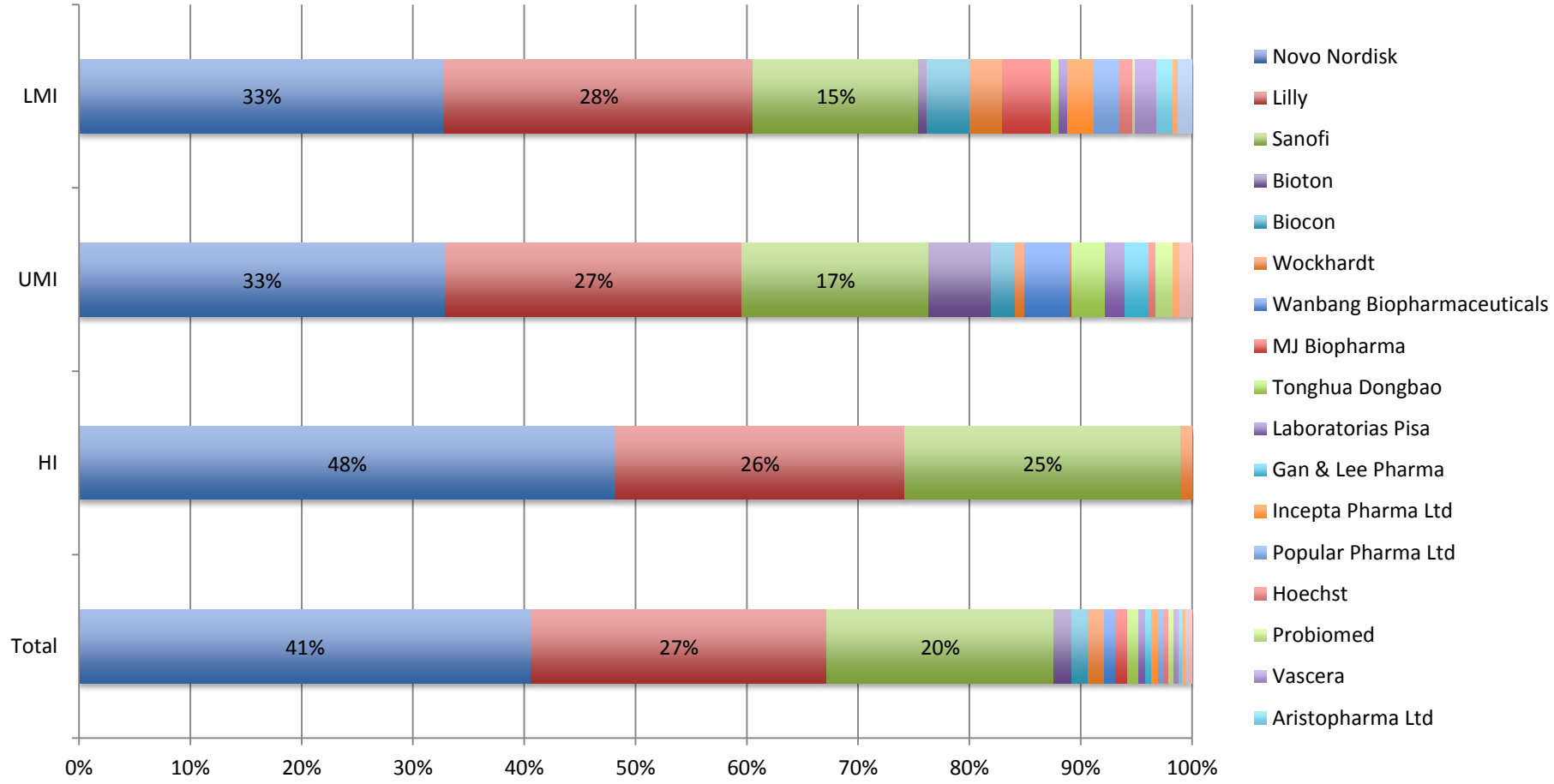
The insulin market

- Domination by 3 large multi-national companies
  - 99% by value
  - 96% by volume
  - 88% by product registrations
- 39 smaller insulin manufacturers identified
  - 23 only sell insulin in one country
  - Probably only 10 insulin manufacturers globally truly independent

ACCISS Study 2016, Perrin et al. 2017

Domination of the market

Percentage of registrations by company and country income group



What about intellectual property?

- 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 and elsewhere
- Increase of patents on delivery devices

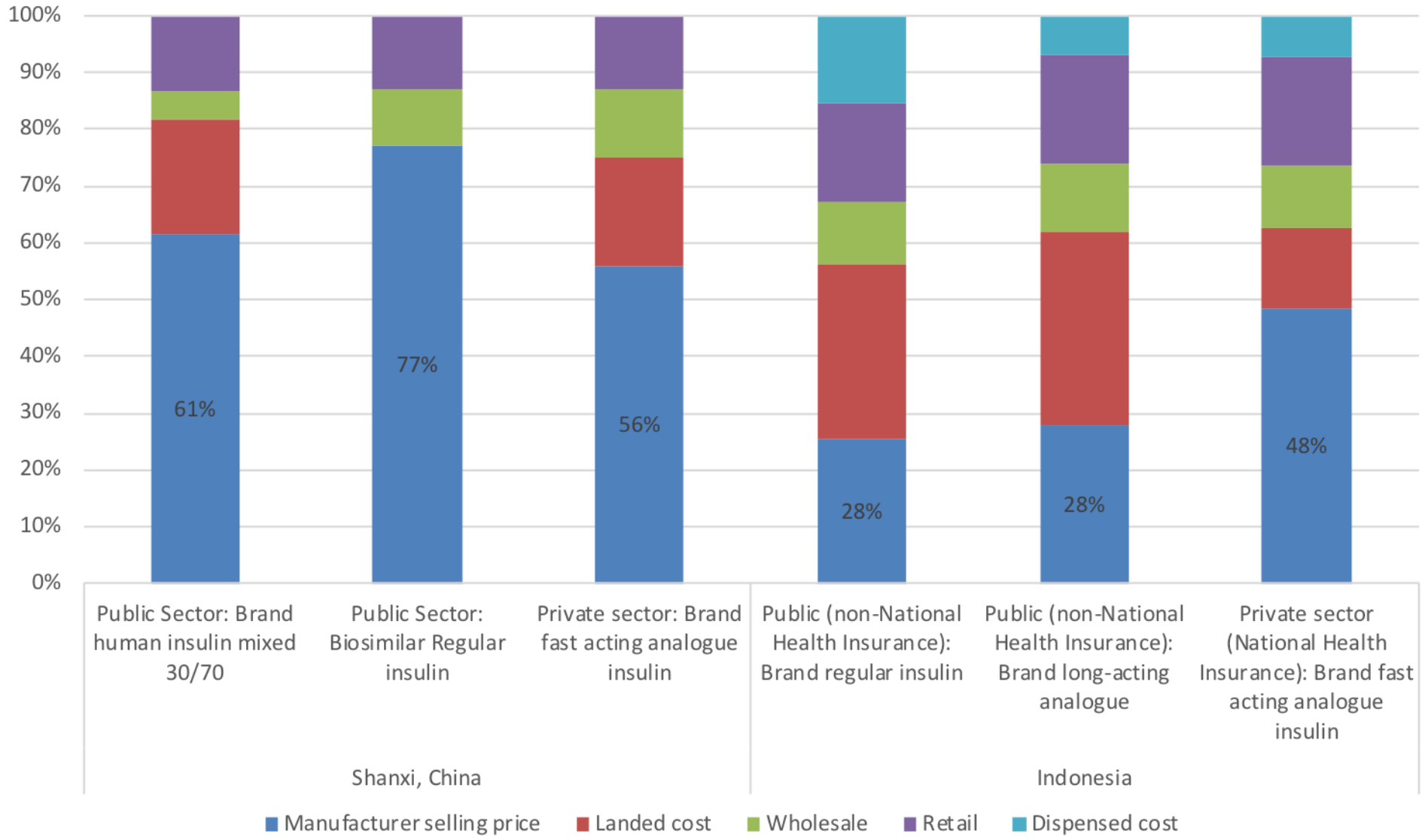
ACCISS Study 2016; *Luo and Kesselheim 2016*

Tariffs and taxes on insulin

- The 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 upper-middle, lower-middle and low-income countries

ACCISS Study 2016

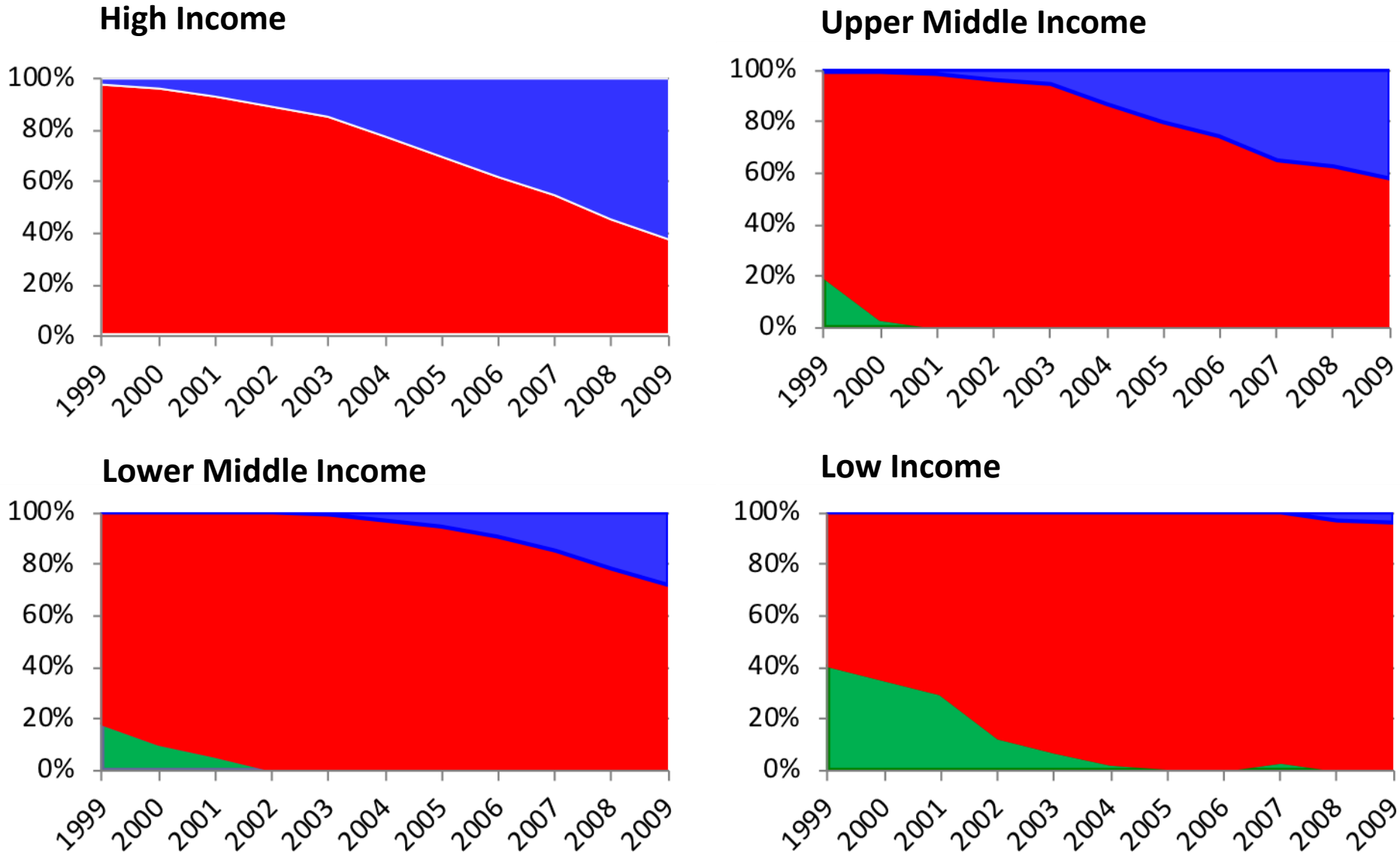
Insulin price components



ACCISS Study 2017 preliminary data

The analogue insulin issue

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



Beran et al. 2016

Guidelines and evidence

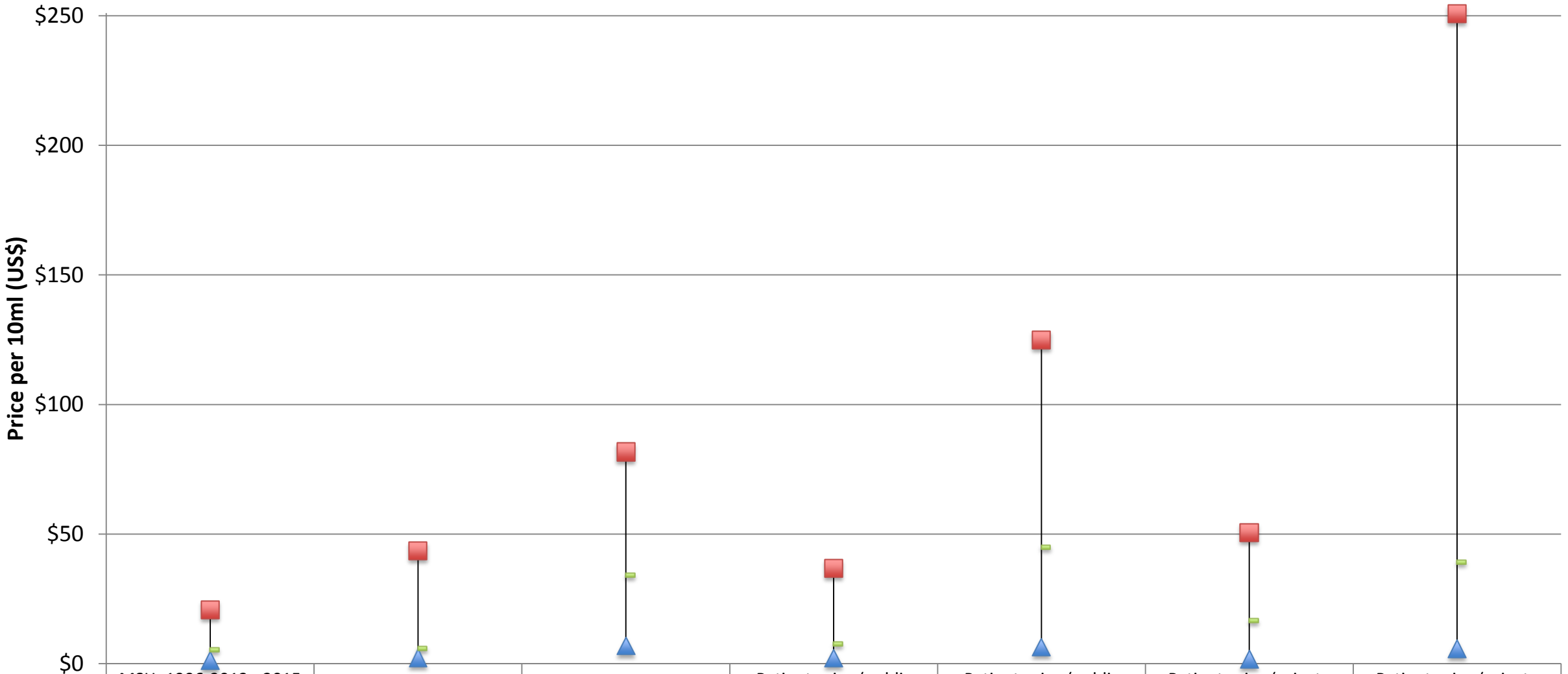
	Year	Review title	Recommendation
Cochrane Reviews	2005	'Human' insulin versus animal insulin in people with diabetes mellitus	"**No significant differences** in metabolic control or hypoglycaemic episodes"
Cochrane Reviews	2007	Long acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus	"only a **minor** clinical benefit of treatment with long-acting insulin analogues … Until long-term efficacy and safety data are available, we suggest a **cautious approach to therapy with insulin glargine or detemir**."
WHO Expert Committee	2011		"insulin analogues currently offer no clinical advantage over recombinant human insulin…"
Cochrane Reviews	2016	Short-acting insulin analogues versus regular human insulin for type 1 diabetes mellitus	"**only a minor benefit** of short-acting insulin analogues…."
WHO Expert Committee	2017		not included in EML and EMLc due to "**small magnitude of benefit and current high price compared to human insulin**."
Cochrane Reviews	2018	Short-acting insulin analogues versus regular human insulin for type 2 diabetes mellitus	"**no clear benefits** of short-acting insulin analogues over regular human insulin …"

The price of insulin

- MSH – Management Sciences for Health - The International Medical Products Price Guide
- Government procurement prices
  - Burkina Faso; Cook Islands; Dominican Republic; El Salvador; Finland; Ghana; Gulf Cooperation Countries; Iran; Jordan; Kyrgyzstan; Lao PDR; Malaysia; Micronesia; Moldova; Mozambique; New Zealand; Pakistan; Philippines; Solomon Islands; South Africa; Sudan; Suriname; Tanzania; Turks and Caicos; Tuvalu; UNRWA; Vanuatu
- Patient prices
  - Argentina; Burundi; Cambodia; Colombia; Dominican Republic; Ecuador; Egypt; El Salvador; England; Ethiopia; Germany; Ghana; Grenada; Guinea; India; India; Indonesia; Iran; Jordan; Kenya; Lao PDR; Malawi; Malaysia; Mali; Mexico; New Zealand; Pakistan; Philippines; Russian Federation; Saudi Arabia; Senegal; South Africa; Spain; Sri Lanka; Sudan; United Arab Emirates; Uganda; Venezuela; Vietnam; Zambia; Zimbabwe
  - Only presented for countries where patients have to pay for insulin

ACCISS Study 2016

The price of insulin



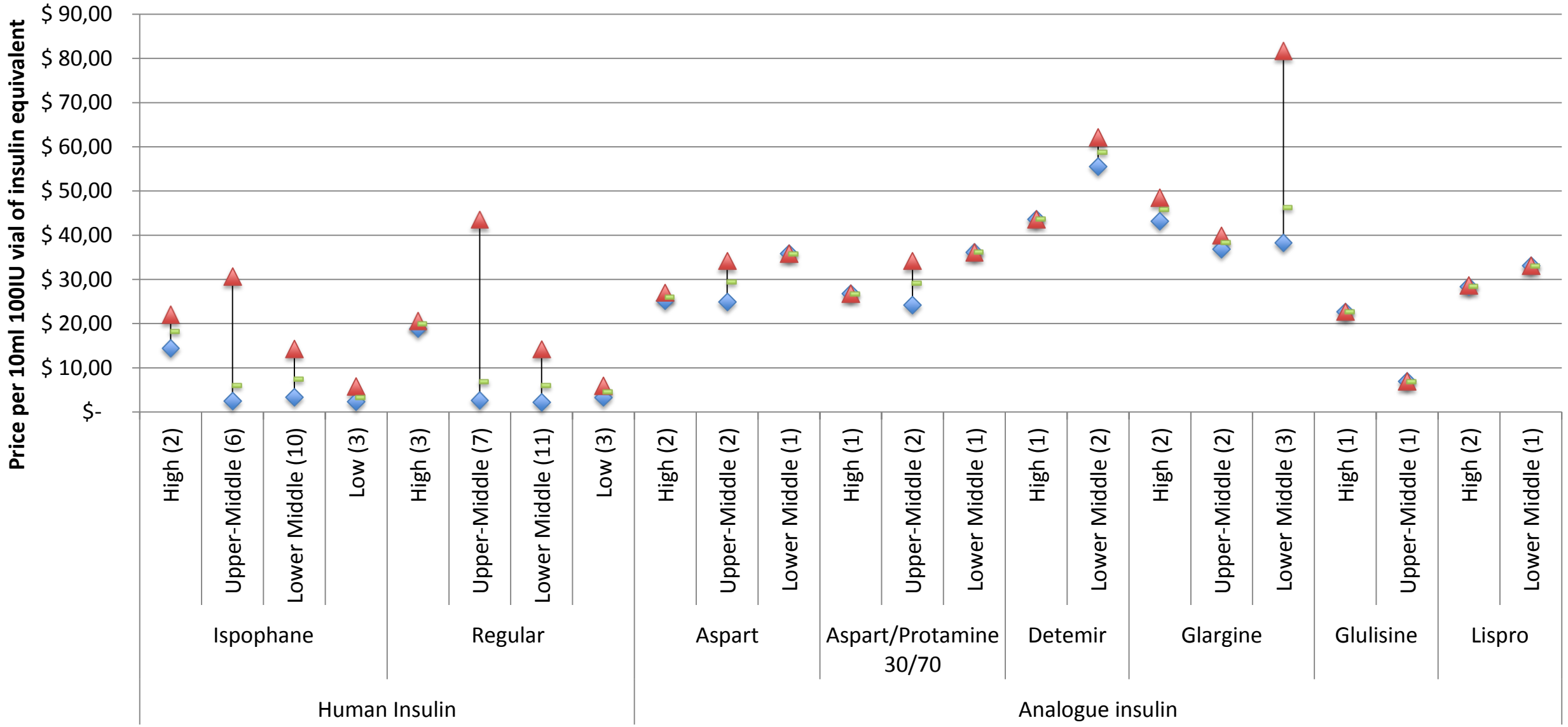
	MSH: 1996-2013 - 2015 prices	Govt price (human)	Govt price (analogue)	Patient price (public sector/human)	Patient price (public sector/analogue)	Patient price (private sector/human)	Patient price (private sector/analogue)
Minimum	$ 1,21	$ 2,24	$ 6,88	$ 2,16	$ 6,41	$ 1,67	$ 5,89
Maximum	$ 20,78	$ 43,51	$ 81,67	$ 36,70	$ 124,90	$ 50,57	$ 250,73
Median	$ 5,48	$ 5,99	$ 34,20	$ 7,64	$ 45,03	$ 16,65	$ 39,35

Price ranges government procurement prices

- Price ranges government procurement prices
  - Brazil, China (Hubei and Shaanxi Provinces), Ethiopia, Ghana, India (Haryana and Madhya Pradesh), Indonesia, Jordan, Kenya, Kyrgyzstan, Mali, Pakistan, Russia (Kazan), and Uganda

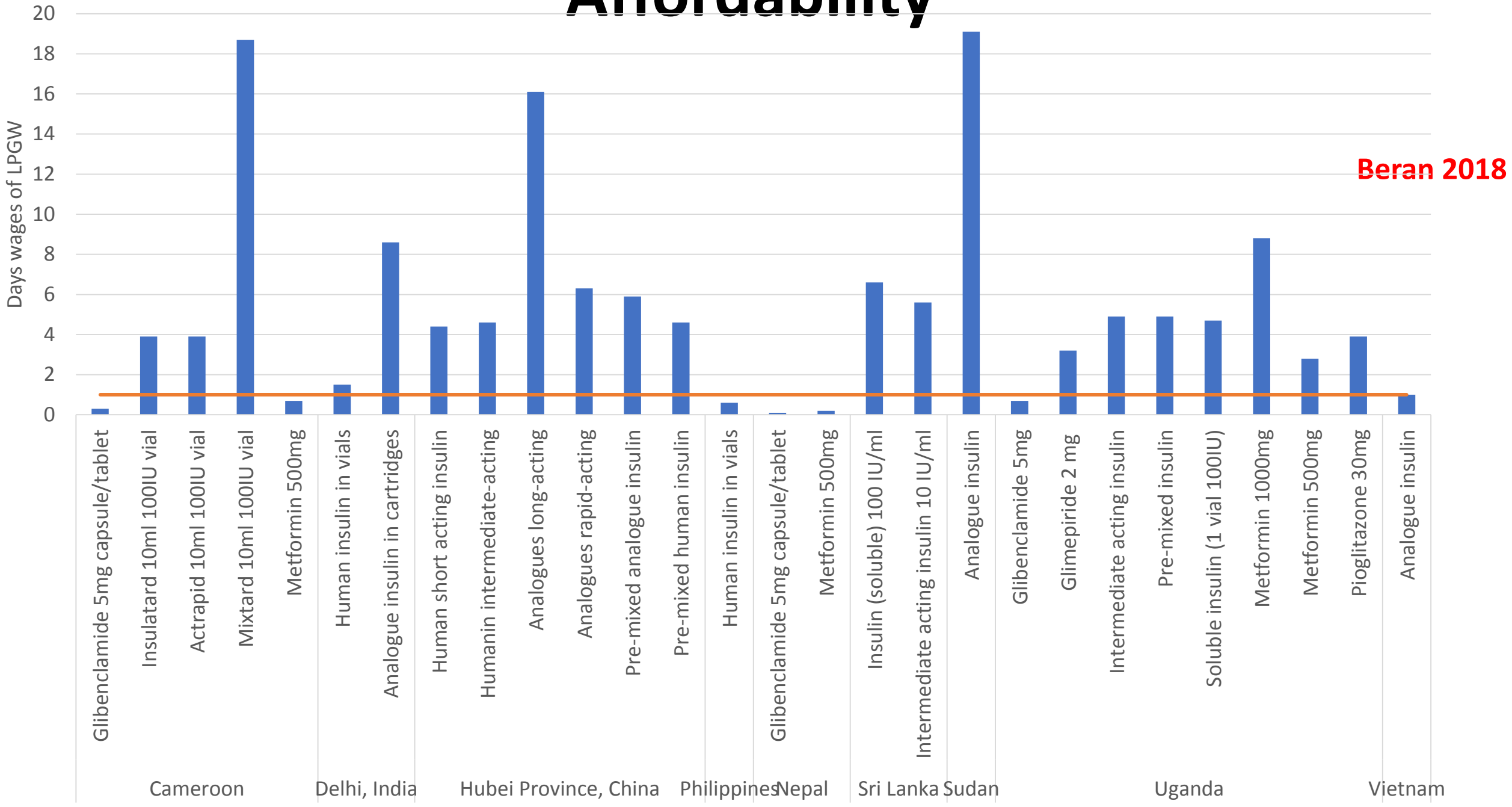
ACCISS Study 2016

Price ranges government procurement prices



ACCISS Study 2017 data for 13 countries

Affordability



Expenditure and potential savings on insulin purchases

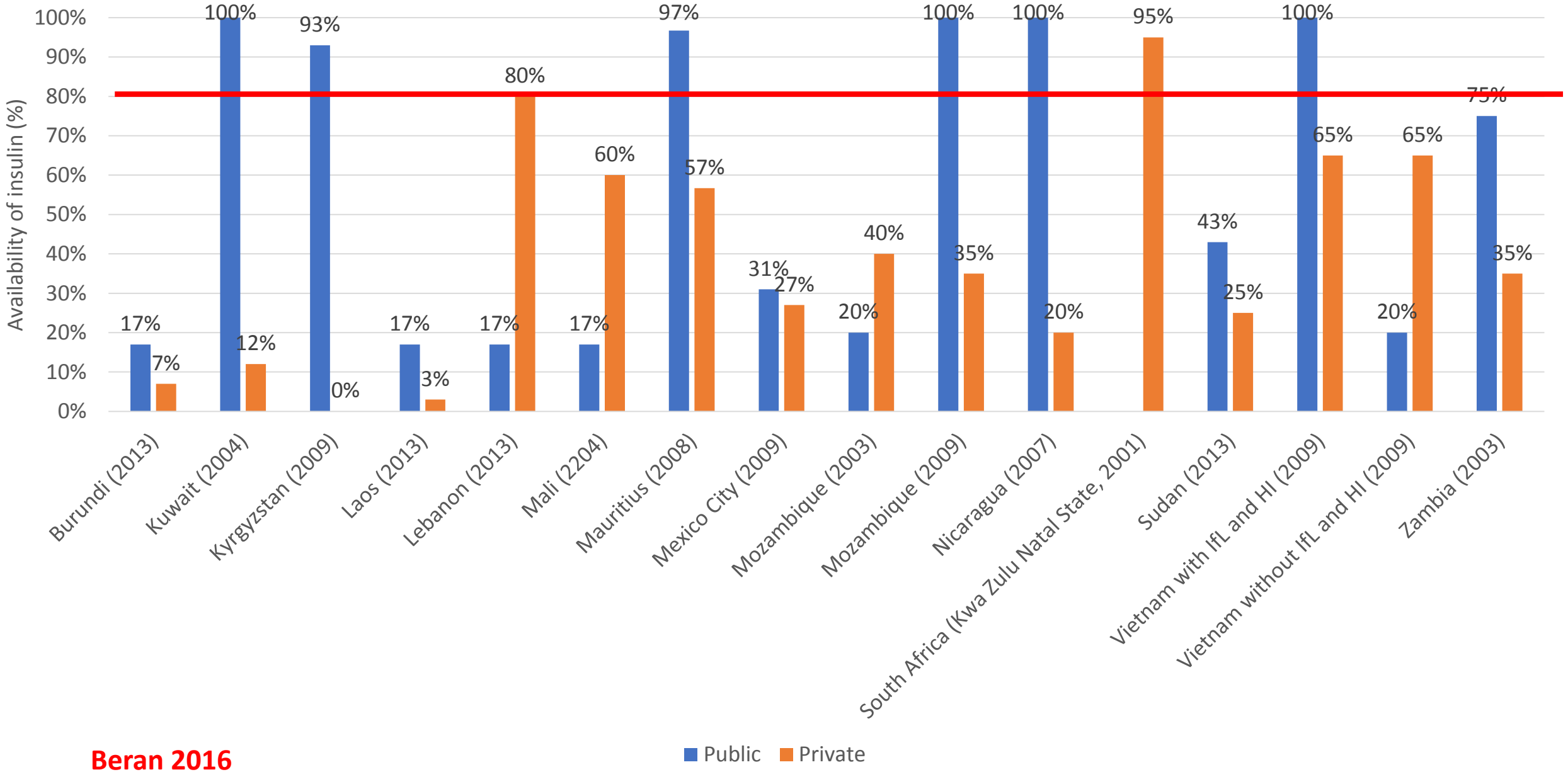
		Iran	Dominican Republic	Moldova	Kyrgyzstan
Human insulin	Volume	4 235 000	200 400	13 104	189 500
	Value (US$)	$18 479 846	$495 405	$94 110	$933 442
Analogue insulin	Volume	1 569 000	5 200	1 333	11 250
	Value (US$)	$56 029 008	$35 786	$58 087	$477 694
Total	Volume	5 804 000	205 600	14 437	200 750
	Value (US$)	$74 508 854	$531 191	$152 197	$1 411 136
Analogue insulin	Percentage of Volume	27%	3%	9%	6%
	Percentage of Value	75%	7%	38%	34%
Only purchasing human insulin	Weighted mean average per vial	$4.36	$2.47	$7.18	$4.93
	Total value (US$)	$25 305 440	$507 832	$103 658	$989 698
	Savings	**$49 203 414**	**$23 359**	**$48 539**	**$421 439**

ACCISS Study 2016

Availability

- Global factors
- National factors
  - Included in National Essential Medicines List and Treatment Guidelines
  - Budget allocation for drugs
  - Adequate buying procedures
  - Quantification
  - Efficient procurement
  - Efficient distribution
  - Rational prescription
  - Proper patient compliance

Availability



Beran 2016

Biosimilar regulations

- Not all countries have regulatory procedures for approving biosimilars
- The authorisation requirements for biosimilars are more challenging than for generics
- Main issue is satisfying the requirements of similarity to the reference insulin product

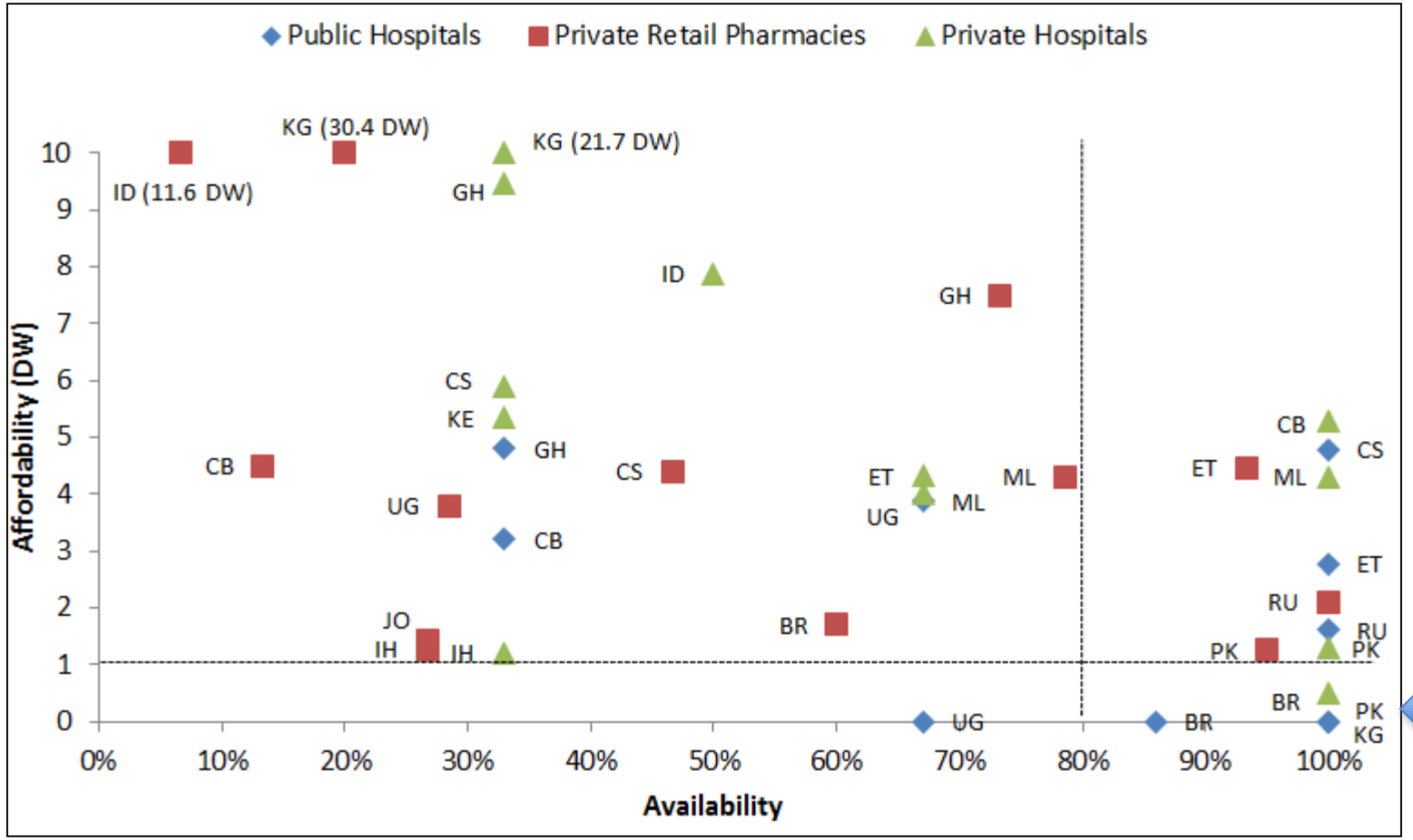
ACCISS Study 2017

Biosimilar companies

- Income
  - Size of local market
  - Existing presence overseas
    - Development of manufacturing capacity
    - Funding of clinical trials and R&D for analogue insulin
- “Ownership” of full manufacturing process
- Manufacturing capacity
  - GMP compliance
  - Overall capacity being used
- Challenges
  - Competing with Big 3 on price
  - Marketing
  - Awareness of biosimilars
  - Human versus analogue insulin
  - Large multi-nationals becoming “biosimilar” manufacturers

Perrin et al. 2017

Affordability and Availability of Isophane Human Insulin



Affordability: number of days wages needed by the lowest paid unskilled government worker to purchase 10ml (approx. 1 month's supply)

ACCISS Study 2017 data for 13 countries

Impact of poor availability and affordability

- Globally 1 in 2 people with Type 2 diabetes do not have access to insulin
  - Europe: 1 in 2.5 people
  - CIS countries: estimated that 3.2 million people currently need insulin
    - How many have problems accessing this medicine?
- Impact on individuals
  - Impoverishment
  - Excess morbidity and mortality

Basu 2018

Key additional challenges

- Increase in prevalence of diabetes
- Increase in use of analogues (and other expensive diabetes medicines) and impact of health budgets
- Wider health system factors needed for diabetes management
- Impact on Universal Health Coverage

Wider health system factors

Accessibility and affordability of Medicines	**Data collection**	**Positive policy environment**
Community involvement/ diabetes association		**Prevention measures**
Patient education and empowerment		**Diagnostic tools and infrastructure**
Healthcare workers		**Adherence issues**
Organised centres for care	**Beran and Yudkin 2006**	**Drug procurement and supply**

Complex constraints and challenges

- Addressing the Challenge and Constraints of Insulin Sources and Supply Study
  - Different tools and resources available
    - Database on insulin prices
    - Toolkit to address mark-ups at various levels of the supply chain
    - Alternative funding mechanisms for insulin
    - Series of positive case studies of countries providing insulin for free
    - Model for improving existing donation programmes
    - Evidence based guideline on different issues surrounding the use of insulin
    - Model to estimate the cost of managing diabetes
    - Collaboration with WHO on biosimilar insulin guideline could be developed
    - Develop a series of tools to improve knowledge of biosimilars
    - Health system guidance

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Addressing the Challenge and Constraints of Insulin Sources and Supply

Complex constraints and challenges

- Addressing the Challenge and Constraints of Insulin Sources and Supply Study
  - Global work
  - Pilot countries
    - Kyrgyzstan

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Addressing the Challenge and Constraints of Insulin Sources and Supply

Thank you for your attention

Any questions?

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http://haiweb.org/what-we-do/acciss/research-findings