Department of Endocrinology. Northwestern Medicine, Feinberg School of Medicine

Northwestern Medicine®
Feinberg School of Medicine

# Adding (Ultra-)long-acting Insulin Analogues to the WHO Model List of Essential Medicines

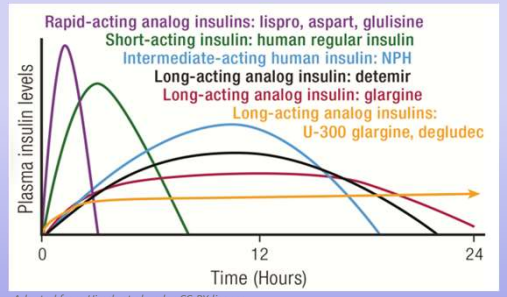
Joshua Katz, MD[1], Brian Godman[2], Sandeep Kishore, PhD[3], Eleonora Allocati[4], Chiara Gerardi[4], Dzintars Gotham, MBBS BSc[5]

[1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2] Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, United Kingdom; Division of Public Health Pharmacy and Management, School of Pharmacy, Sefako; Makgatho Health Sciences University, South Africa; School of Pharmaceutical Sciences, Universiti Sains Malaysia, Malaysia; [3] Brigham & Women's Hospital, Harvard Medical School; [4] Center for Health Regulatory Policies, IRCCS, Italy; [5]Medway NHS Foundation Trust, UK

## Background

- Diabetes affected an estimated 463 million people in 2019, or 9.3% of the global population, of which 79% live in low- and middle-income countries. Cost of insulin is a major barrier to care for many patients with diabetes.
- Only three companies currently control 96% of the insulin market by volume and 99% in terms of value, globally.
- Long-acting insulin analogues offer different pharmacokinetic profiles, adding more flexibility when designing insulin regimens (Table 1). Unfortunately these medications are often more expensive than intermediate-acting insulin.
- The World Health Organization (WHO) defines the Model List of Essential Medicines (MLEM) as "the list of minimum medicine needs for a basic health-care system." Adding a medication to the MLEM helps advocate for lowering cost and increasing access to this vital medication.
- Prior submissions in 2017 and 2019 proposing the addition of long-acting insulin analogues to the MLEM were rejected. The WHO Expert Committee recognized the benefits over human insulin, but reported that the price differences were too great for the documented magnitude of benefit.

## Figure 1. Comparison of time-action profiles for different insulin types




*Adapted from Hirsch et al under CC-BY licence.*

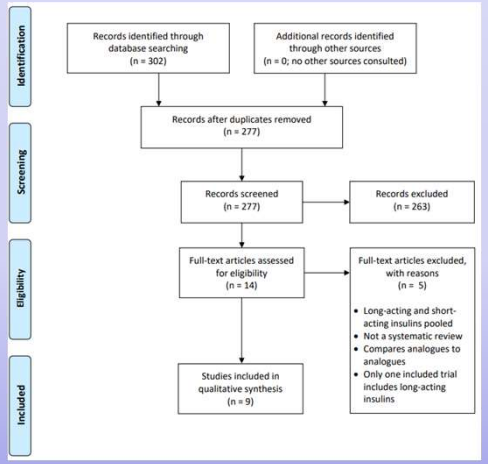
## Research Objective

- To add long-acting and ultra-long-acting insulin analogues (specifically insulin glargine, insulin detemir, and insulin degludec, including similar biotherapeutic products) to the WHO MLEM for type 1 and type 2 diabetes mellitus for adults and children (aged 2 years and above)

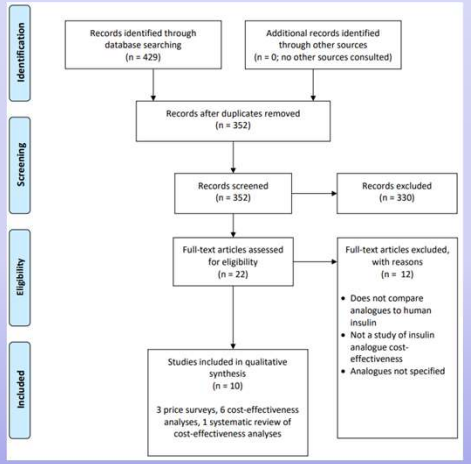
## Methods

- Two literature reviews were performed on both clinical effectiveness / safety and cost-effectiveness.
  - Inclusion Criteria:
    - Published in the past 5 years
    - Compared long-acting insulin analogues to human insulin (including NPH and insulin lente)
- Findings were collated in a report / application that was submitted for review by the WHO Expert Committee

## Figure 2. Flow Diagram for Literature Search on Clinical Effectiveness / Safety




## Figure 3. Flow Diagram for Literature Search on Cost-Effectiveness




## Results

- For Type 1 Diabetes:
  - Compared to intermediate acting insulins, long acting insulins are associated with:
    - Reduction in A1c
    - Improved fasting glucose
    - Reduction in weight
    - Reduction in hypoglycemic events
- For Type 2 Diabetes:
  - Compared to intermediate acting insulins, long acting insulins are associated with:
    - Reduction in hypoglycemic events
- Median price for 1,000 units of long-acting insulin was significantly higher compared to human insulin:
  - Government procurement: US$34.20 vs US$5.99
  - Public Sector: US$45.03 vs US$7.64
  - Private sector: US$39.35 vs US$16.65

## Conclusions

- Despite greater cost, long-acting insulins are cost-effective compared to human insulins due to savings deriving from (assumed/modelled) health benefits such as lower rates of hypoglycemia
- Our application was accepted by the WHO, adding (ultra-)long-acting insulin analogues to the MLEM