A Systematic Review of Cost-Effectiveness Studies of Newer Non-Insulin Antidiabetic Drugs (nNIADS):

Trends in Decision-Analytical Models (DAM) for Modelling of Type 2 Diabetes Mellitus (T2DM)

Henrik V. B. Laursen[1,2], Emmelie P. Jørgensen[5], Peter Vestergaard[2,3,4], Lars H. Ehlers[5]

1) Danish Center for Healthcare Improvements, 2) Steno Diabetes Center North Denmark 3) Department of Endocrinology, Aalborg University Hospital, 4) Department of Clinical Medicine, Aalborg University Hospital, 5) Nordic Institute of Health Economics

Corresponding author: Henrik Vitus Bering Laursen, henrikvitus@gmail.com

INTRODUCTION

As T2DM increases in prevalence globally, and in proportion of all cases of diabetes, it becomes increasingly important to extract information about value for money for the medications, most often nNIADs, used to treat it.

Some of the nNIADs (sodium-glucose cotransporter-2 [SGLT2] inhibitors, glucagon-like peptide-1 [GLP1] receptor agonists) have cardio- and renalprotective effects, which led to a major change in diabetes treatment guidelines. The nNIADs have generally been found cost-effective compared to older pharmaceuticals, but which nNIAD is cost-effective is still unclear. Commonly, cost-effectiveness is evaluated with DAM, as they are able to take into account the complexity and length of T2DM disease progression and their most costly outcome: debilitating diabetes-related complications(DRC) and resulting loss of quality of life and high cost of treatment.

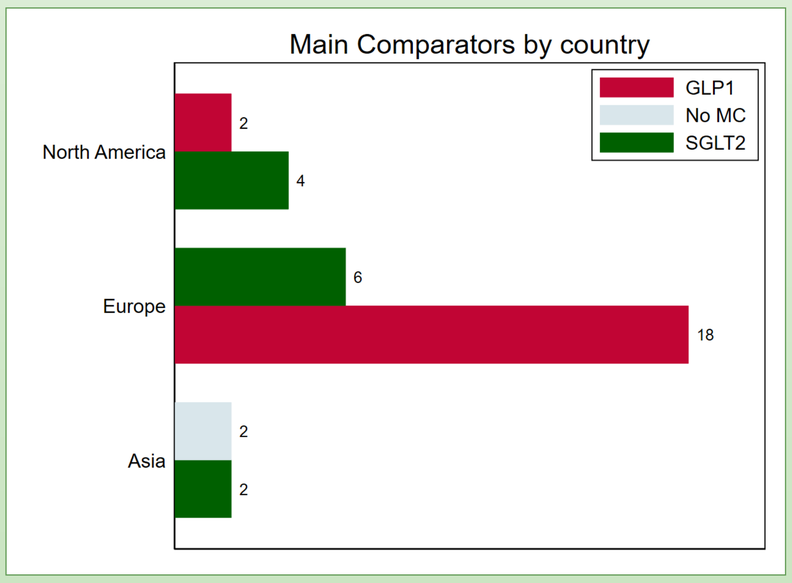
Thus we aim to provide an overview of the cost-effectiveness analyses (CEA) using DAM, comparing nNIADs with other nNIADs, for treatment of T2DM.

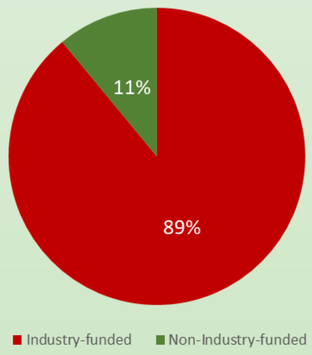
METHOD

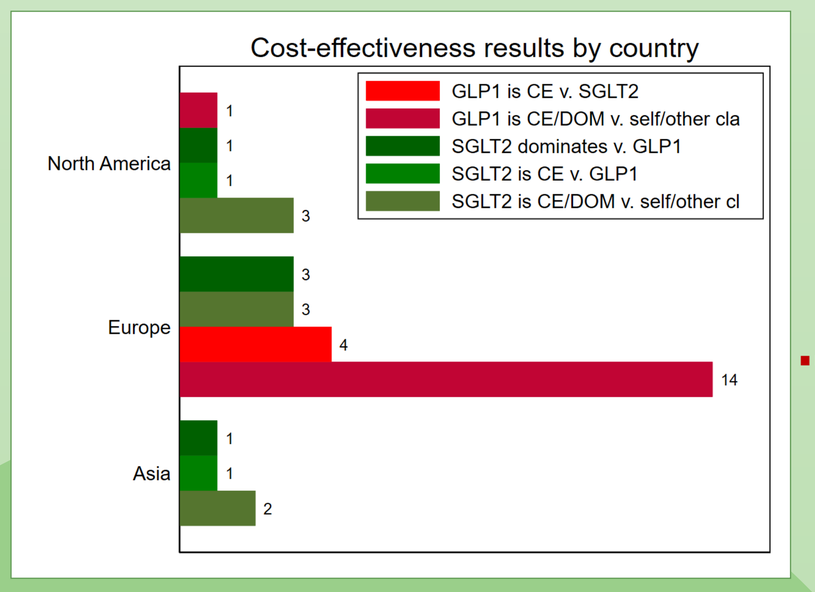
A systematic literature search was performed from start 2018 to august 2021. PubMed, Embase and Econlit databases were used, and the following studies were included: CEAs using DAMs to compare the nNIAD classes and products with other nNIADs.

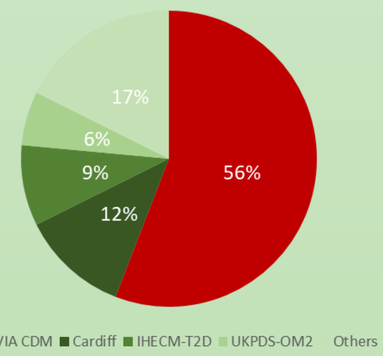
Data was gathered data in a spreadsheet and summary statistics displayed in the form of tables and graphs.

A fraction of the data will be presented here.









CONCLUSIONS:

There is not enough evidence, and too much variation in studies, to conclude anything about cost-effectiveness of the nNIADs.
GLP1 and SGLT2 are most frequently MC.
However, the current trends of the results of direct comparisons can be viewed on a class and product level. The SGLT2 class is more frequently cost-effective or dominant compared to than GLP1. Injectable and Oral Semaglutide, and Empagliflozin, are most frequently cost-effective within their classes.
On the product level, the Semaglutide variants are more frequently cost-effective.
Variation in models make it difficult to draw conclusions.
We need a better practice for evaluating T2DM treatments with DAM, with an emphasis on central clinically relevant model assumptions, parameters, and comparators.

RESULTS

34 Eligible studies was found. Most studies were from Europe (71%), and almost all were industry-funded (89%). Proucts from the GLP1 and SGLT2 classes were main comparators (MC) in 20 and 12 studies, respectively, with two studies comparing several strategies with no discernable MC. DPP4 was not a main comparator, despite being an nNIAD. IQVIAs Core Diabetes Model was used the most (56%).

The most frequently compared products, injectable or oral Semaglutide (n=14) and Empagliflozin (n=8), were cost-effective when compared to products within their own classes. Six studies compared these three products directly. Empagliflozin was more frequently cost-effective against oral Semaglutide, while injectable was more frequently cost-effective against Empagliflozin. There was variation in model assumptions and content which also varied depedent on the class of MC. Assumptions regarding time to switch may be inconsistent with real-world use.

Main differences/similarities in model parameters, assumptions, and sensitivity analysis By Main Comparator Class

	Parameter/ assumption	GLP1	SGLT2
Input	*Basis of cohort characteristics & pre-existing conditions*	• T2DM patients uncontrolled on Metformin • Mainly SUSTAIN, LEADER, PIONEER (only head2head study)	• T2DM patients uncontrolled on Metformin, slightly higher focus on patients with established CVD • Mainly EMPA-REG OUTCOME
	Treatment effect parameters	• Treatment effect added to risk equations	• Treatment effect added to risk equations • CVD reductions added as separate effect in studies with Empagliflozin as main comparator
	Adverse events	• Greater focus on hypoglycemia	• Greater range of adverse events • No Diabetic Ketoacidosis (was only included in 1 study [with GLP1 as the main comparator])
	Risk equations used	• Most frequently used UKPDS 68 (2004) • UKPDS 68 for base case • UKPDS 82 for sensitivity analysis • Reasoning for choice when given: Advice from model proprietors	• Most frequently used UKPDS 82 (2013) • UKPDS 68 less used • UKPDS 82 frequently for base case • Reasoning for choice when given: Model fit
	Treatment switch assumption	• Occurs more at set time • the set time ranged from 2 to 13 years • 90% discontinued drug after a given time within the model	• Occurs more at a HbA1c threshold • the set time ranged from 8 to 13 • 50% discontinued drug after a given time within the model
Output	*Diabetes-related complications*	• Slightly higher focus on hypoglycemia and retinopathy	• Slightly higher focus on heart failure, cardiovascular death, and nephropathy
	*Sensitive factors in sensitivity analysis (**top three**)*	• **Most**: Treatment effect modification, Time horizon, Treatment switch threshold • **2nd most**: Treatment switch threshold, Treatment effect modification, Time to treatment switch • **3rd most**: Time horizon, Treatment effect modification, Drug cost assumption	• **Most:** Drug cost assumption, Time horizon, Treatment effect modification • **2nd most**: Time horizon, treatment effect modification • **3rd most:** Drug cost assumption, inclusion/exclusion of CVD reducing effect

Treatment switch: The time to, and assumptions surrounding, when the comparators are switched out with rescue therapy, or have additional medications added, Treatment switch threshold: The HbA1c level at which the treatment switch occurs, CVD: Cardiovascular disease.

STENO DIABETES CENTER NORDJYLLAND
– i gode hænder

DCHI
DANISH CENTER FOR HEALTHCARE IMPROVEMENTS

BREAKING NEW GROUND
AALBORG UNIVERSITY