



How to Outfox the Pharma: Providing the Best Diabetes Therapies to our Patients at a Lower Cost to Society

Disclosures

Lectures, advisory boards:

Merck, AstraZeneca, Takeda, Boehringer-Ingelheim, Janssen, Novo Nordisk, Eli Lilly, Sanofi, Abbott, Medtronic, Bayer

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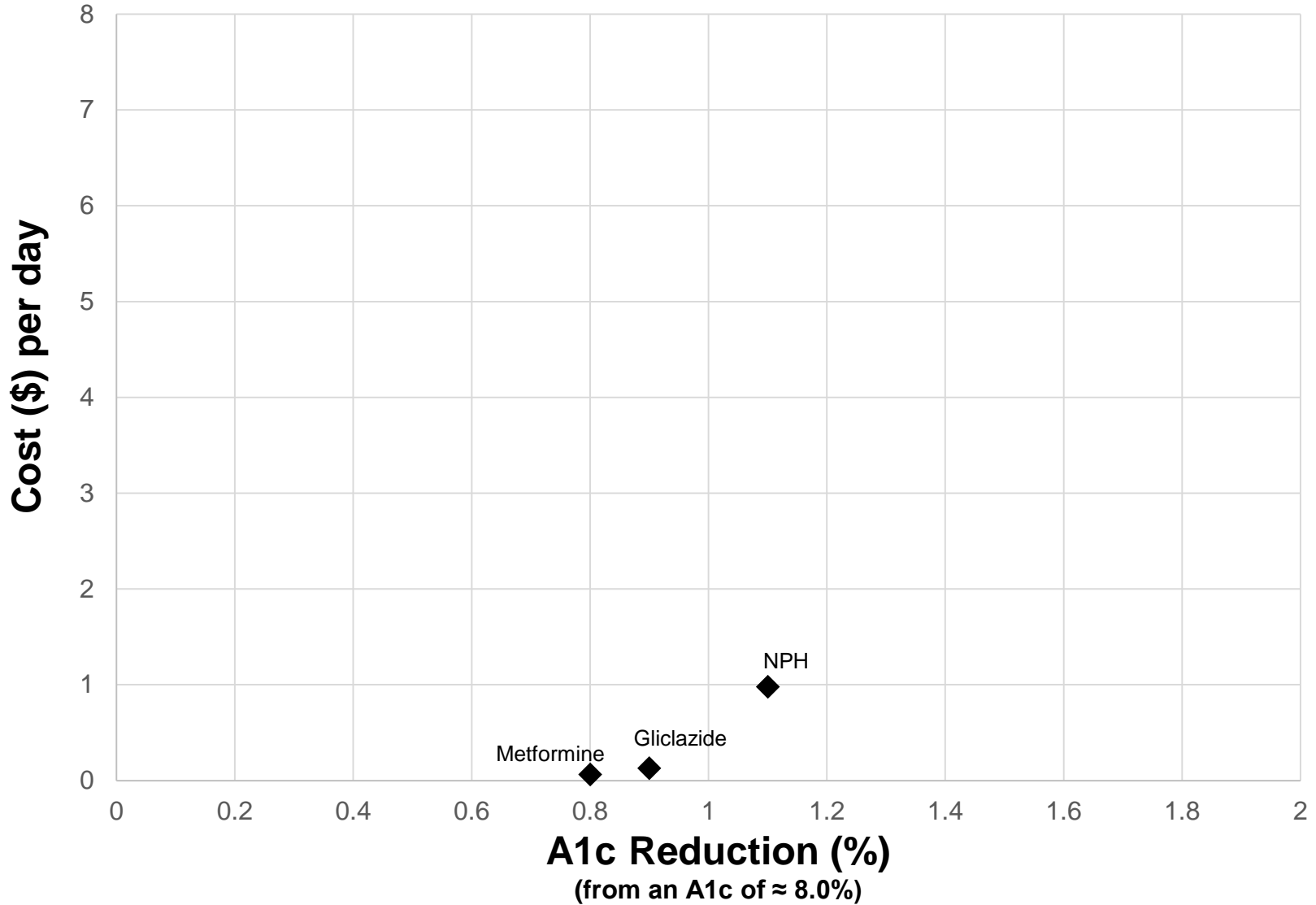
At the end of this presentation, the participant should be able to:

Discuss the place of SGLT2i and GLP-1 RA in the treatment of type 2 diabetes as per national and international guidelines

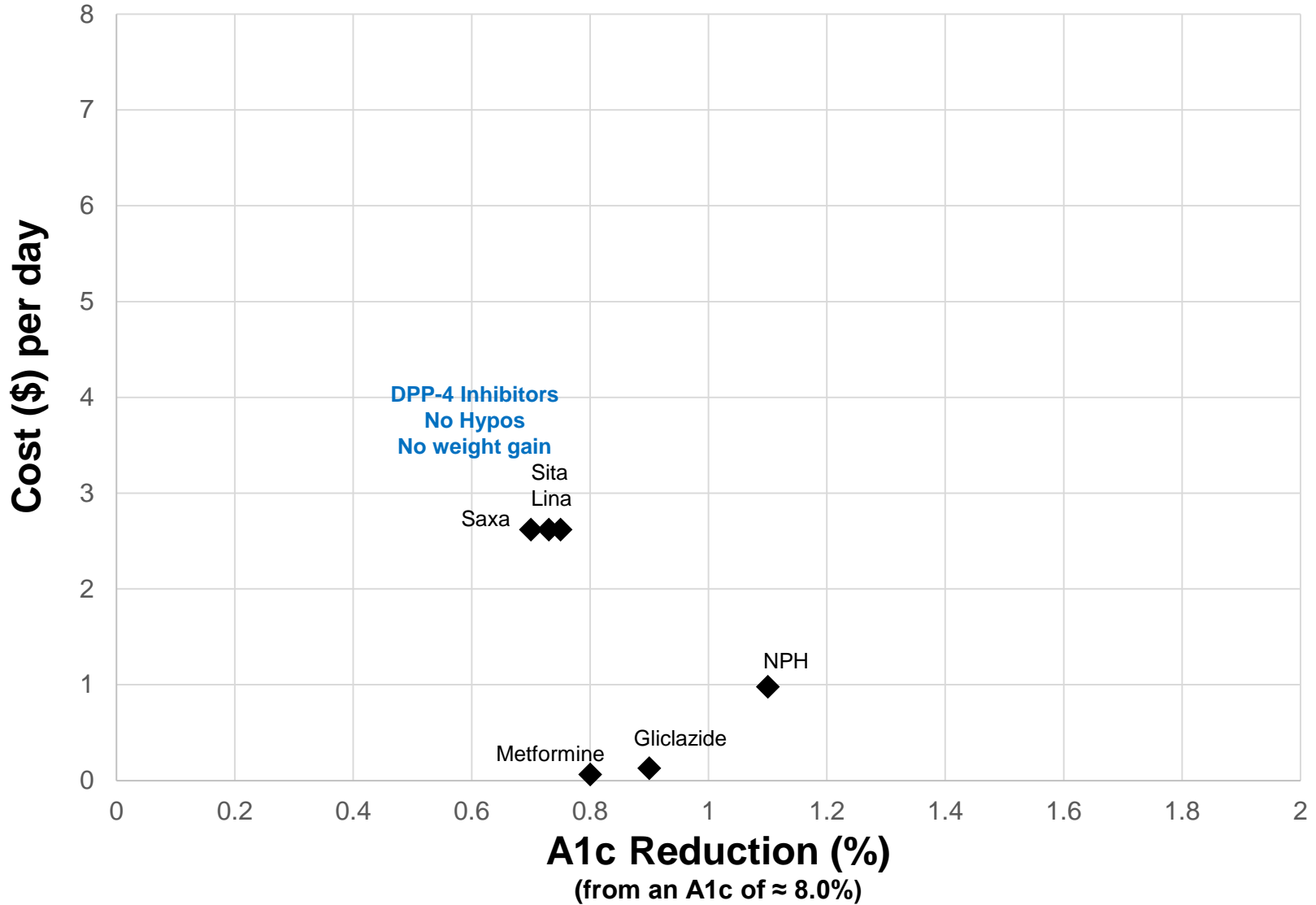
Implement strategies to offer these therapies without significantly increasing the cost to society

Further reduce the cost of therapy by promoting the judicious use of capillary glucose strips

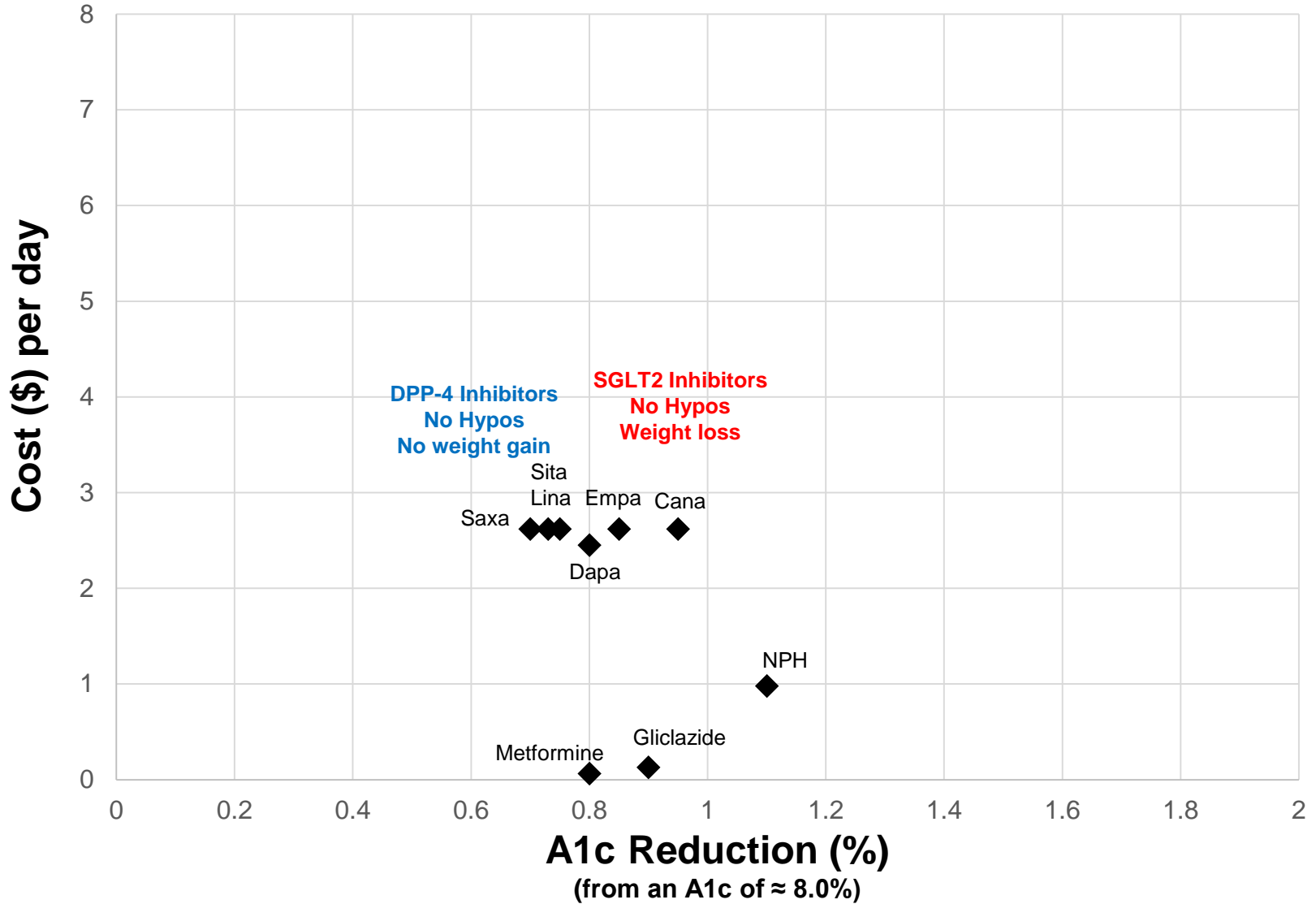
Cost in Function of A1c Reduction



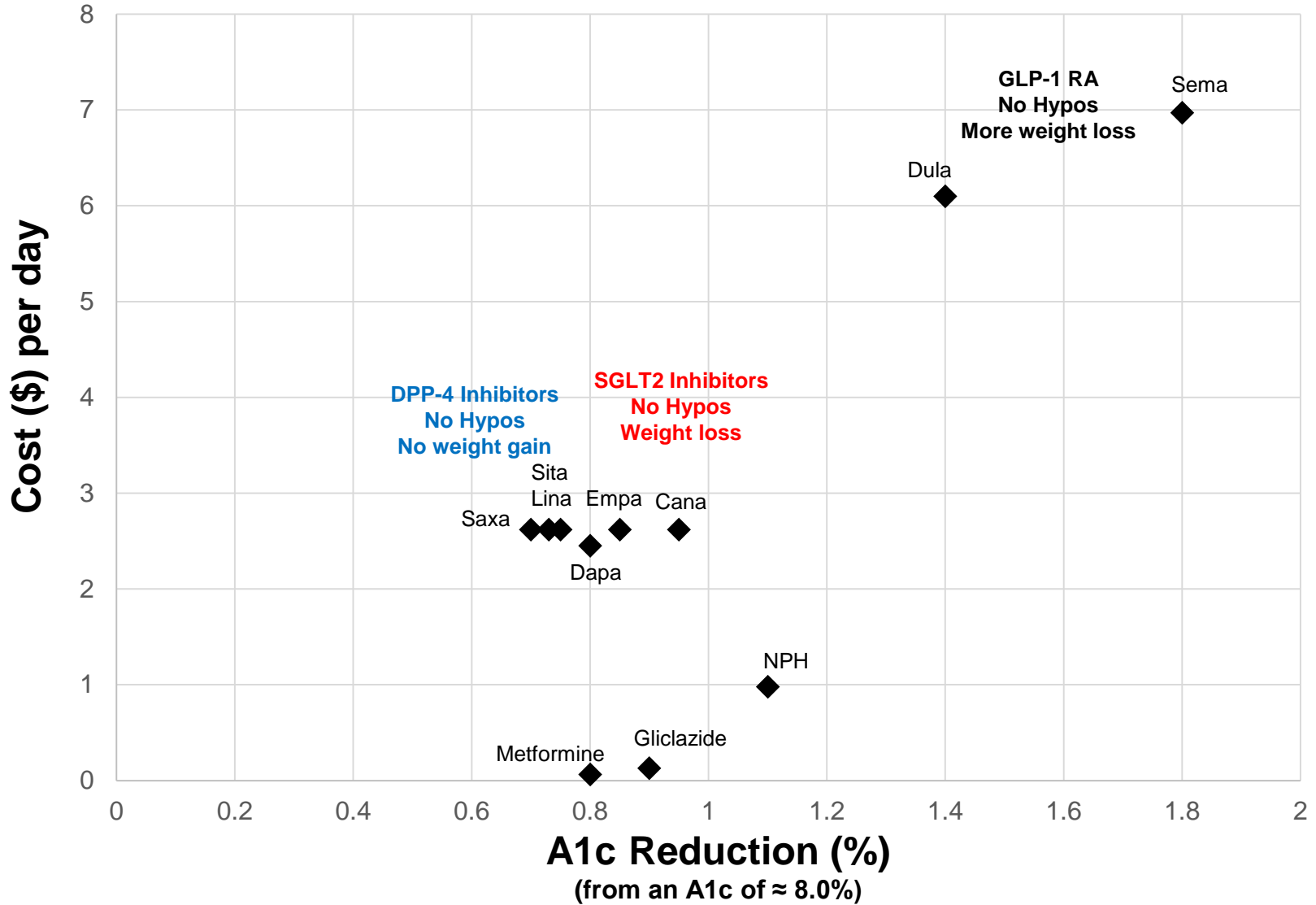
Cost in function of A1c Reduction



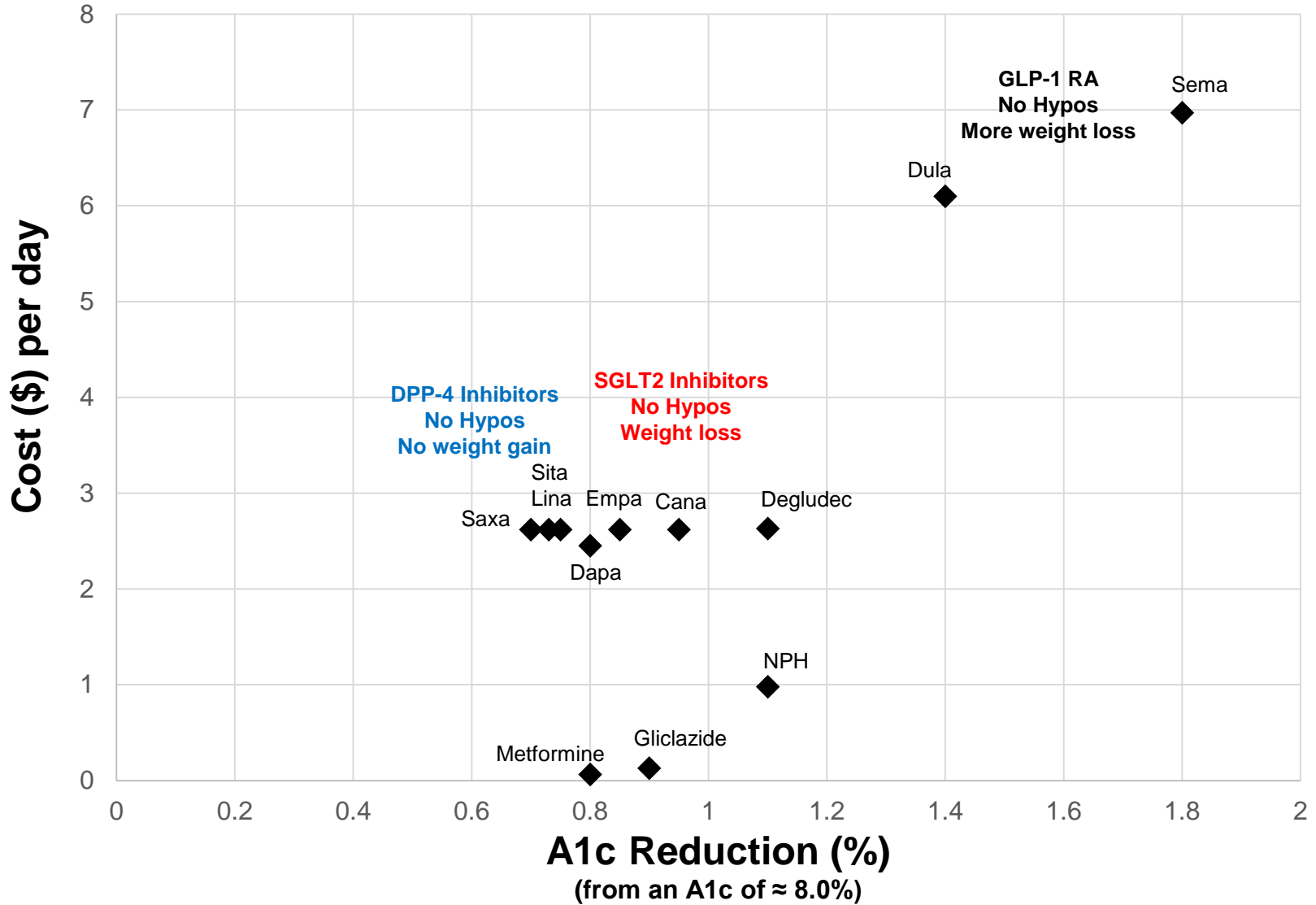
Cost in function of A1c Reduction



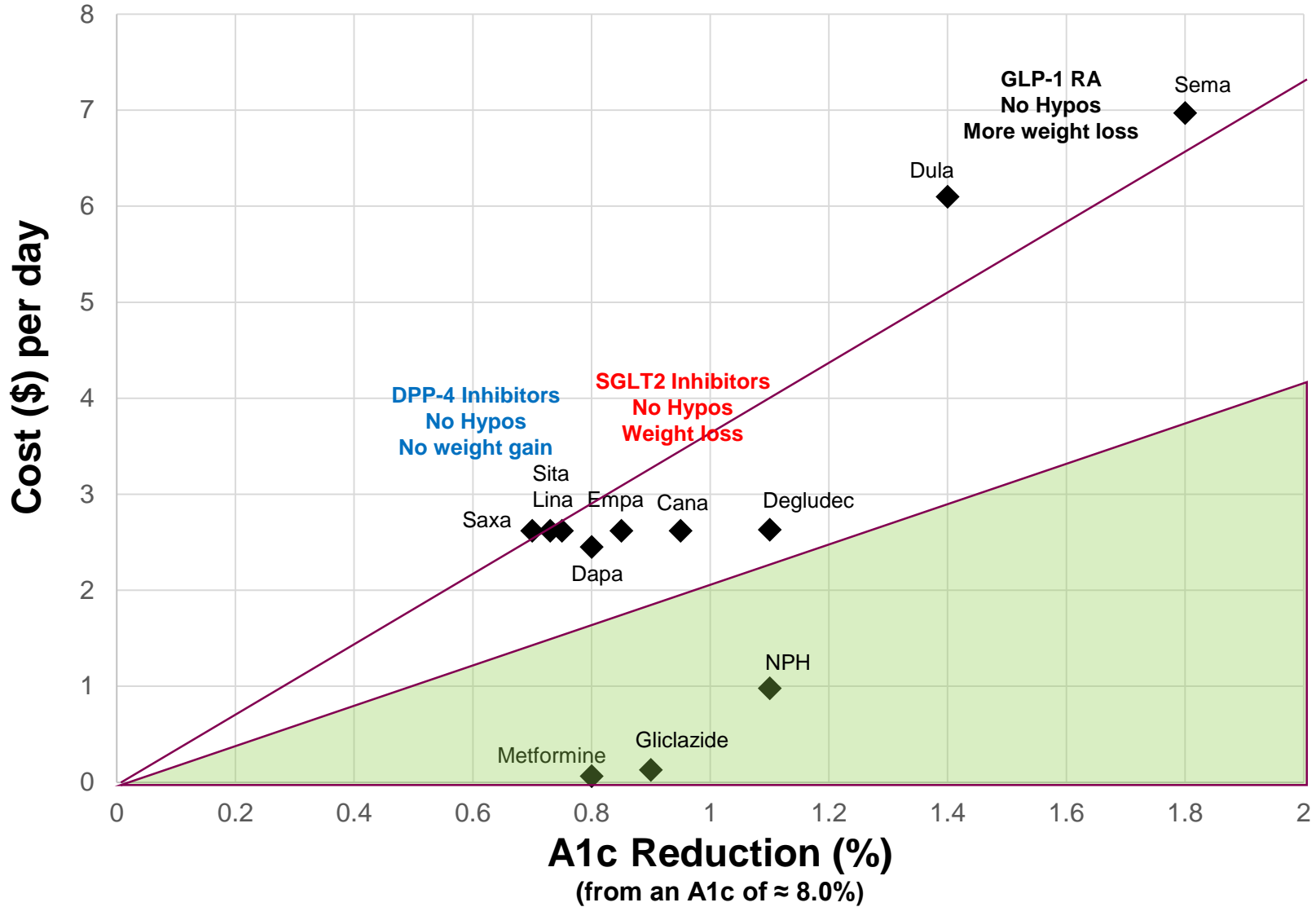
Cost in function of A1c Reduction

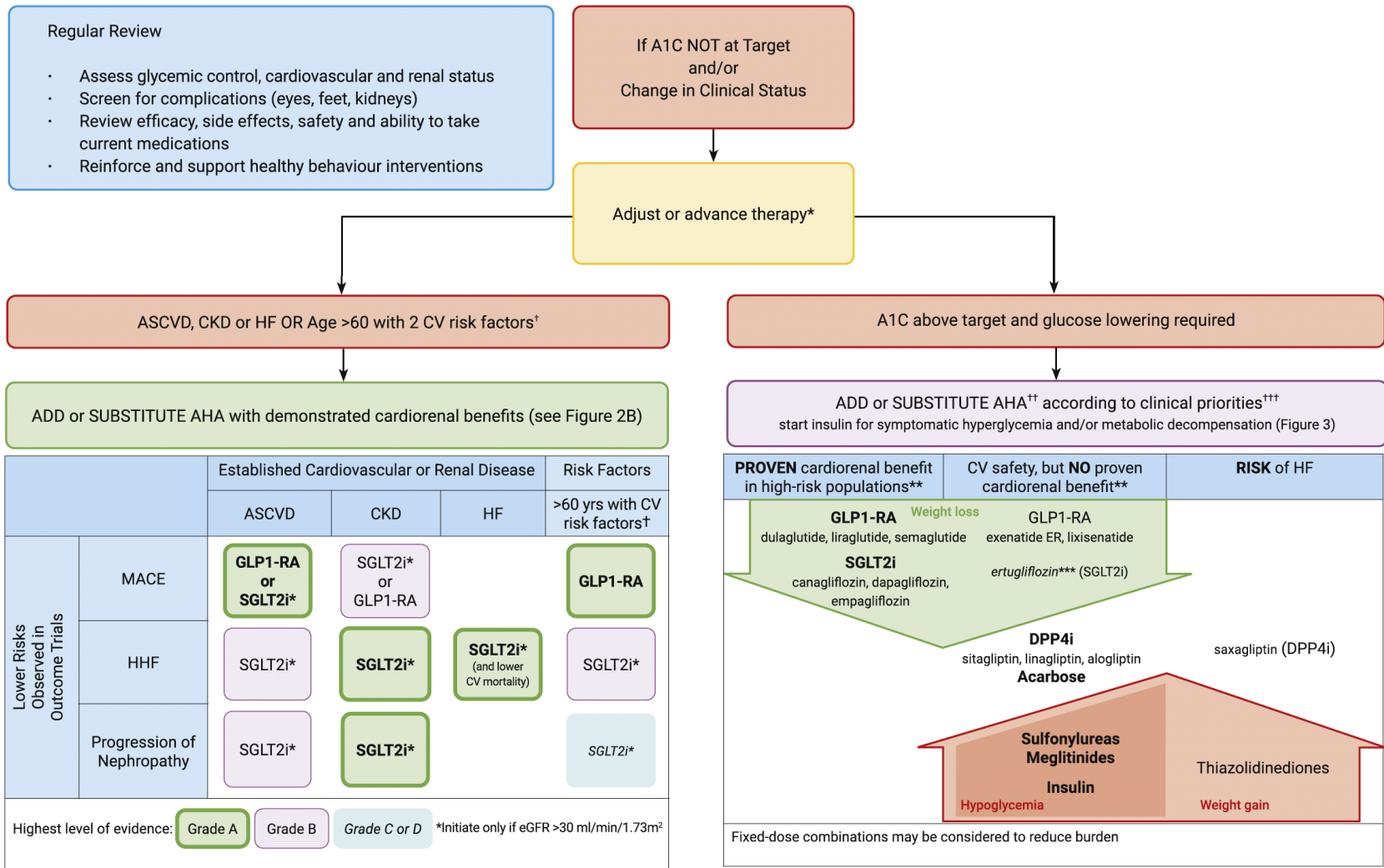


Cost in function of A1c Reduction



Cost in function of A1c Reduction

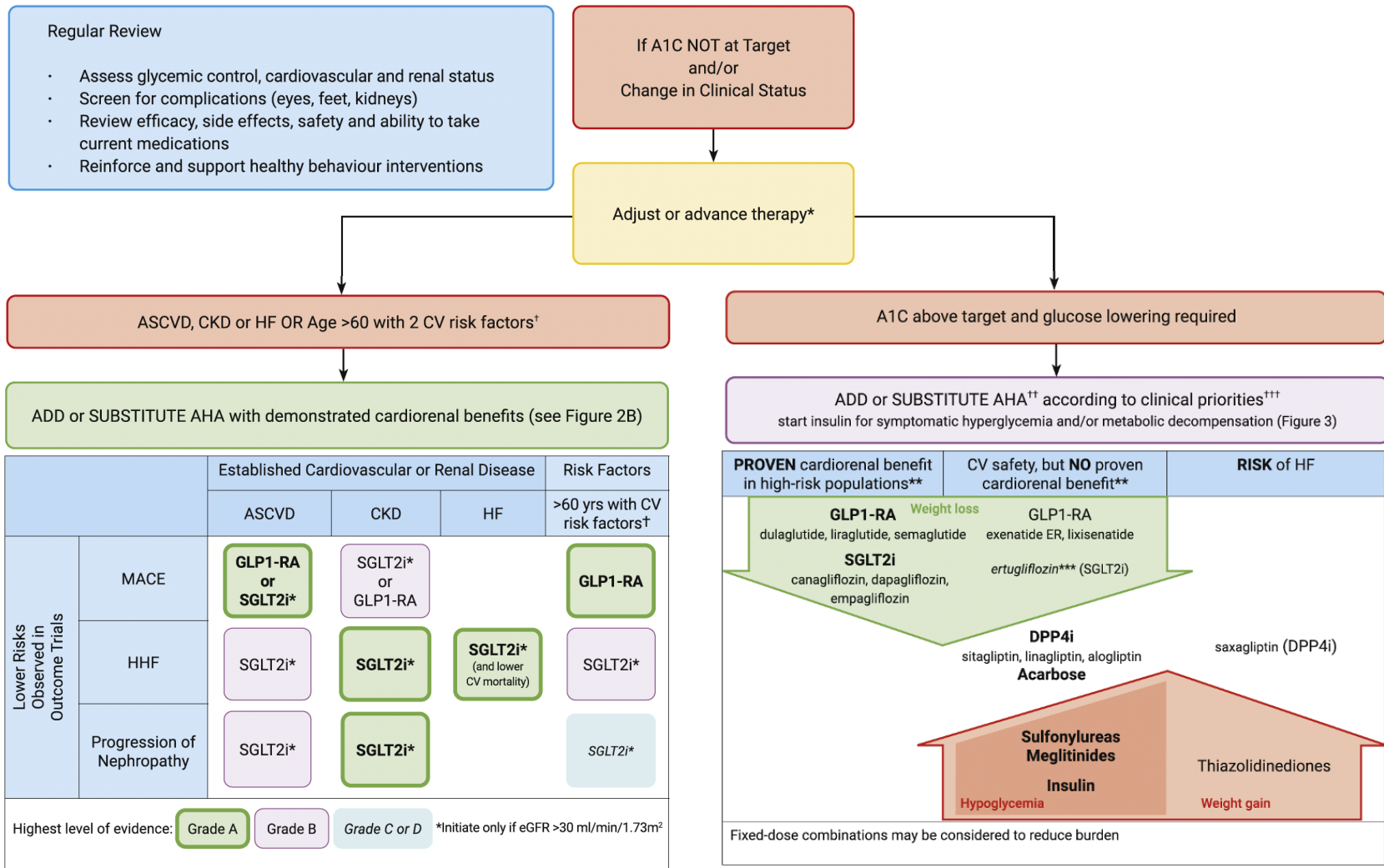




ASCVD, CKD or HF OR Age >60 with 2 CV risk factors[†]

ADD or SUBSTITUTE AHA with demonstrated cardiorenal benefits (see Figure 2B)

		Established Cardiovascular or Renal Disease			Risk Factors
		ASCVD	CKD	HF	>60 yrs with CV risk factors [†]
Lower Risks Observed in Outcome Trials	MACE	GLP1-RA or SGLT2i*	SGLT2i* or GLP1-RA		GLP1-RA
	HHF	SGLT2i*	SGLT2i*	SGLT2i* (and lower CV mortality)	SGLT2i*
	Progression of Nephropathy	SGLT2i*	SGLT2i*		SGLT2i*
Highest level of evidence:		Grade A	Grade B	Grade C or D	*Initiate only if eGFR >30 ml/min/1.73m ²



A1C above target and glucose lowering required

ADD or SUBSTITUTE AHA^{††} according to clinical priorities^{†††}
 start insulin for symptomatic hyperglycemia and/or metabolic decompensation (Figure 3)

PROVEN cardiorenal benefit in high-risk populations**	CV safety, but NO proven cardiorenal benefit**	RISK of HF
GLP1-RA <i>Weight loss</i> dulaglutide, liraglutide, semaglutide SGLT2i canagliflozin, dapagliflozin, empagliflozin	GLP1-RA exenatide ER, lixisenatide ertugliflozin*** (SGLT2i)	
	DPP4i sitagliptin, linagliptin, alogliptin Acarbose	saxagliptin (DPP4i)
	Sulfonylureas Meglitinides Insulin <i>Hypoglycemia</i>	Thiazolidinediones <i>Weight gain</i>

Fixed-dose combinations may be considered to reduce burden

2022 Canadian Cardiovascular Society Guideline for Use of GLP-1 Receptor Agonists and SGLT2 Inhibitors for Cardiovascular Risk Reduction in Adults

Table 1. Summary of relative (hazard ratios) and absolute event reductions per 1000 treated patients for cardiorenal outcomes in study populations with heart failure, chronic kidney disease, or type 2 diabetes

Practice Statement	Strength of Recommendation	Quality of Evidence
In adults with T2D and either ASCVD or multiple risk factors for ASCVD, we recommend use of:		
A. GLP-1RA or SGLT2i to reduce the risk of all-cause, or CV mortality or MACE;	Strong	Moderate
B. SGLT2i to reduce the risk of hospitalization for HF or the composite of significant decline in eGFR, progression to end-stage kidney disease or death due to kidney disease;	Strong	Moderate
C. GLP-1RA to reduce the risk of nonfatal stroke.	Strong	Moderate

IN: Management of Hyperglycemia in Type 2 Diabetes: A Consensus Report by the ADA and EASD

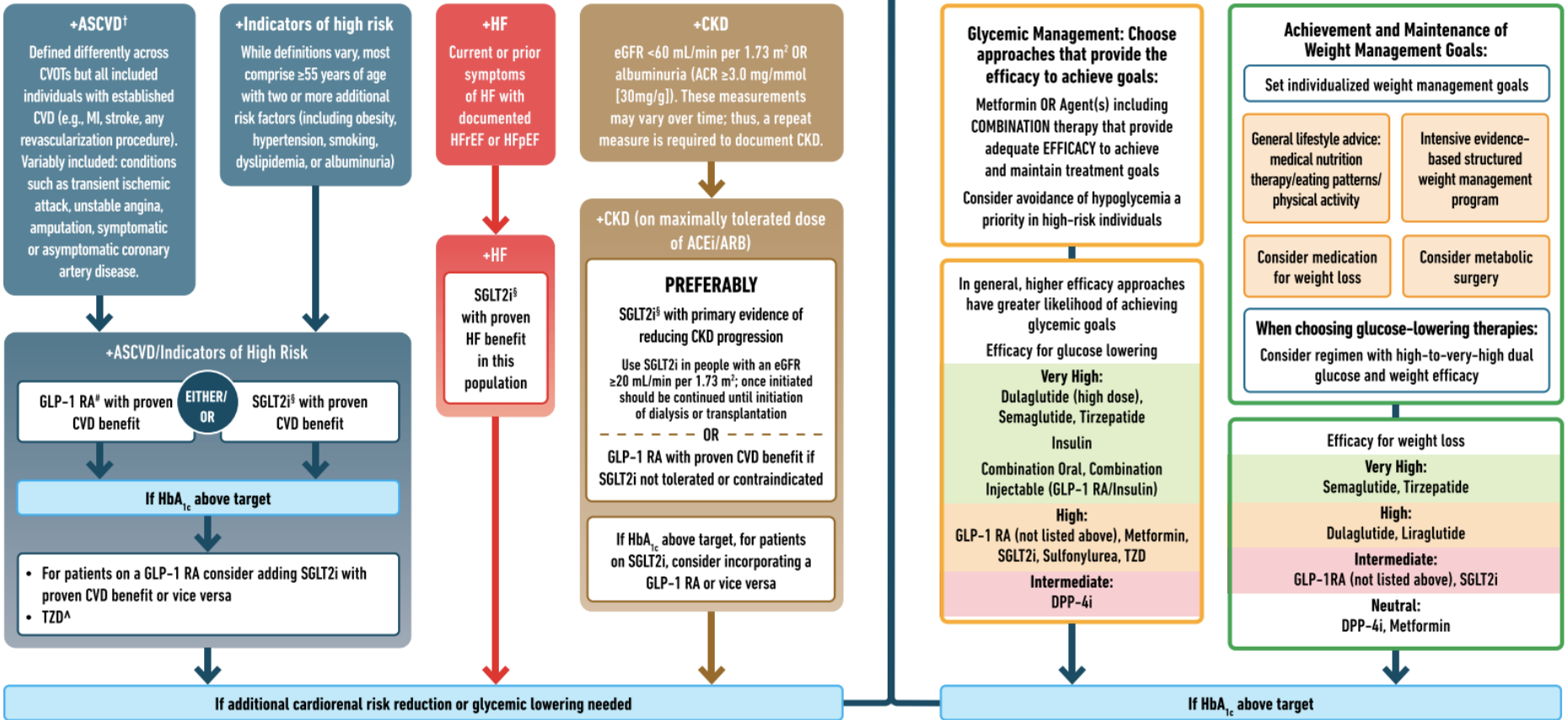
USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)












Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (in addition to comprehensive CV risk management)*

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HFrEF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVDs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Discussion With Patient: Choice of Treatment

	 A1C (%)	 Weight	 Hypoglycemia	 HEART	 KIDNEYS	 Other adverse effects	 Tablet vs Injection	 Public Coverage	 Cost per day \$
Metformin	↓↓↓	0	NO			GI	Tablet	YES	0.06
Sulfonylureas	↓↓		YES				Tablet	YES	0.12
SGLT-2i	↓↓↓	↓↓	NO	GOOD	GOOD	Mycosis	Tablet	Varies	2.62
DPP-4i	↓↓	0	NO				Tablet	Varies	2.62
GLP-1RA	↓↓↓↓	↓↓	NO	GOOD	good	Nausea	Tablet Injection	Varies	6.50
INSULIN	↓↓↓↓		YES				Injection	YES	≈2.63 (40 U)

The choice has to be individualized according to the patient's characteristics:
which of these factors are to be prioritized for THIS patient ?

Antihyperglycemic Coverage by RAMQ

Code CV399
Dapagliflozin:
 if HF class II or III
 on ACEi / ARB

Code EN179
Empagliflozin:
 if CVD and
 A1c > 7%

Form:
Liraglutide
Dulaglutide:
 + metformin
 BMI > 30
 A1c > 6.5%
 despite DPP-4i
 Annual renewal.

Form:
Semaglutide:
 + metformin
 + SU CI, NT or INEFF
 No annual renewal

Class	Medication	\$/day at max dose	MONO if SU and MET NT or CI	+ MET if SU CI, NT or INEFF	+ SU if Met CI, NT or INEFF	CVD	+ MET if DPP4i INEFF, NT or CI and BMI > 30 and high A1c	If other SU CI, NT or INEFF
Biguanides	Metformin (Glucophage)	0.18						
α-Glucosidase Inhibitors	Acarbose (Glucobay)	1.03						
DPP-4 Inhibitors	Alogliptin (Nesina)	2.10	EN167	EN148 (EN150 Kazano)	EN149			
	Linagliptin (Trajenta)	2.25	EN167	EN148 (EN150 Jentaduetto)				
	Saxagliptin (Onglyza)	2.30		EN148 (EN150 Komboglyze)	EN149			
	Sitagliptin (Januvia)	2.62	EN167	EN148 (EN150 Janumet et XR)				
SGLT2 Inhibitors	Canagliflozin (Invokana)	2.62	EN167	EN148	EN149			
	Dapagliflozin (Forxiga)	2.45		EN148 (EN150 Xigduo)	EN149	CV399		
	Empagliflozin (Jardiance)	2.62	EN167	EN148 (EN219 Synjardy)		EN179		
GLP-1R Agonists	Liraglutide (Victoza)	6.85					Form	
	Exenatide (Byetta)	2.49						
	Exenatide QW (Bydureon)	6.85						
	Dulaglutide (Trulicity)	6.85					Form	
	Semaglutide (Ozempic)	6.85					Form	
Thiazolidinediones	Pioglitazone (Actos)	1.05	EN121	EN118	EN119			
	Rosiglitazone (Avandia)	2.87	EN121	EN118 (EN81 Avandamet)	EN119			
Insulin Secretagogues	Gliclazide (Diamicon)	0.50						
	Glimepiride (Amaryl)	0.77						EN23
	Glyburide (Diabeta)	0.23						
	Repaglinide (GlucoNorm)	0.84						

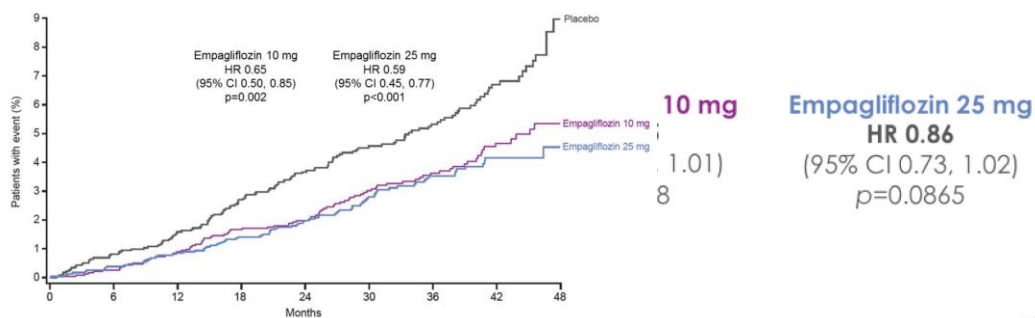
Green = on general list: no code or form required Orange = Médicament d'exception: code or form required
 NT=Not tolerated INEFF=Inefficacious CI=Contraindicated SU=Sulfonylurea MET=Metformin Mono=Monotherapy Form=Médicament d'exception form required

How to use SGLT2 inhibitors and GLP-1RA
without increasing the cost of therapy ?

Impact of SGLT2i Dose

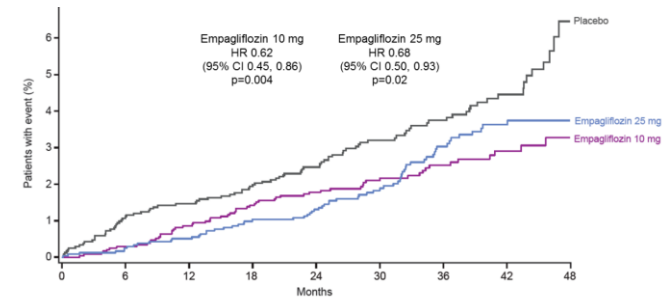
Ex: Empagliflozin in EMPA-REG

Cardiovascular Deaths



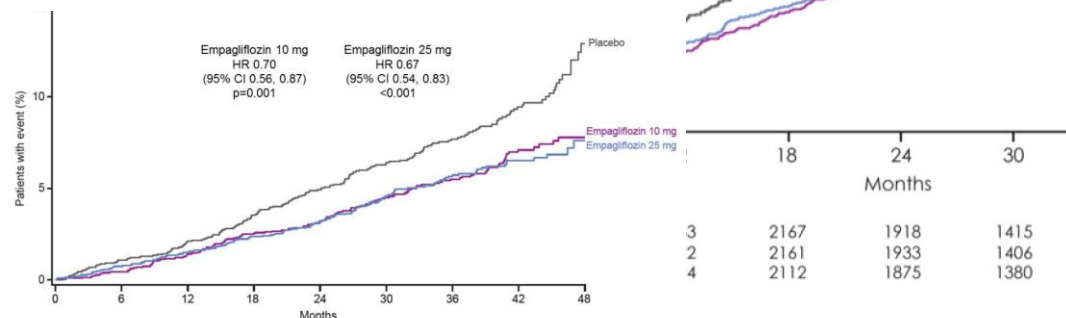
No. of patients	0	6	12	18	24	30	36	42	48
Empagliflozin 10 mg	2345	2327	2305	2274	2055	1542	1303	847	201
Empagliflozin 25 mg	2342	2324	2303	2282	2073	1537	1314	875	213
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

Hospitalizations for HF



No. of patients	0	6	12	18	24	30	36	42	48
Empagliflozin 10 mg	2345	2306	2256	2204	1981	1473	1240	804	188
Empagliflozin 25 mg	2342	2308	2267	2223	2007	1477	1247	830	207
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

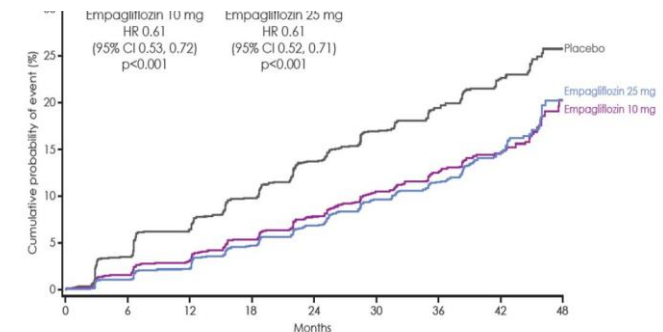
Total Mortality



No. of patients	0	6	12	18	24	30	36	42	48
Empagliflozin 10 mg	2345	2327	2305	2274	2055	1542	1303	847	201
Empagliflozin 25 mg	2342	2324	2303	2282	2073	1537	1314	875	213
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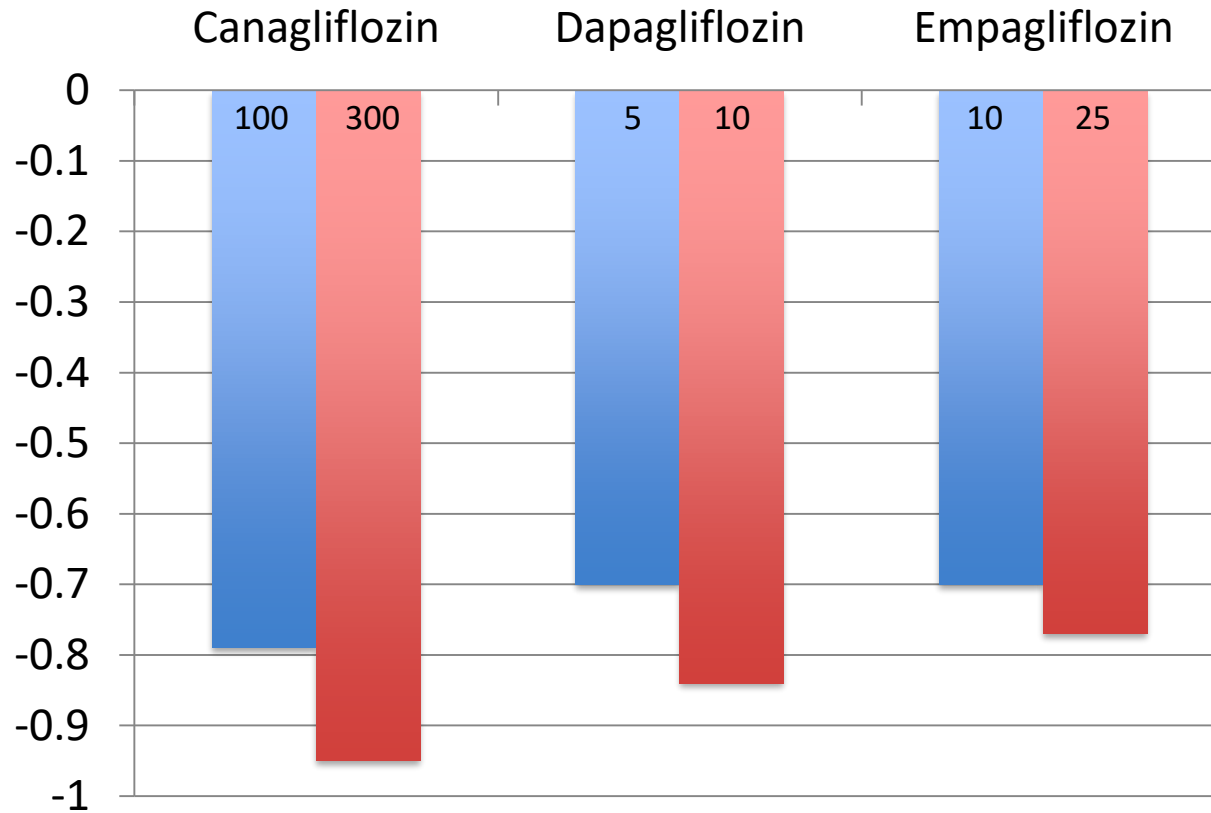
Adverse Cardiovascular Event; HR, hazard ratio

Worsening of nephropathy



No. of patients	0	6	12	18	24	30	36	42	48
Empagliflozin 10 mg	2055	1991	1912	1825	1571	1122	922	593	136
Empagliflozin 25 mg	2069	2003	1936	1844	1600	1157	965	626	154
Placebo	2061	1946	1836	1703	1433	1016	833	521	106

Impact of SGLT2i Dose on A1c Reduction



Decreasing SGLT2i Cost

**\$493 savings
per patient per year**

Canagliflozin 100 mg 2.62/day
Canagliflozin 300 mg 2.62/day



Empagliflozin 10 mg 2.62/day
Empagliflozin 25 mg 2.62/day



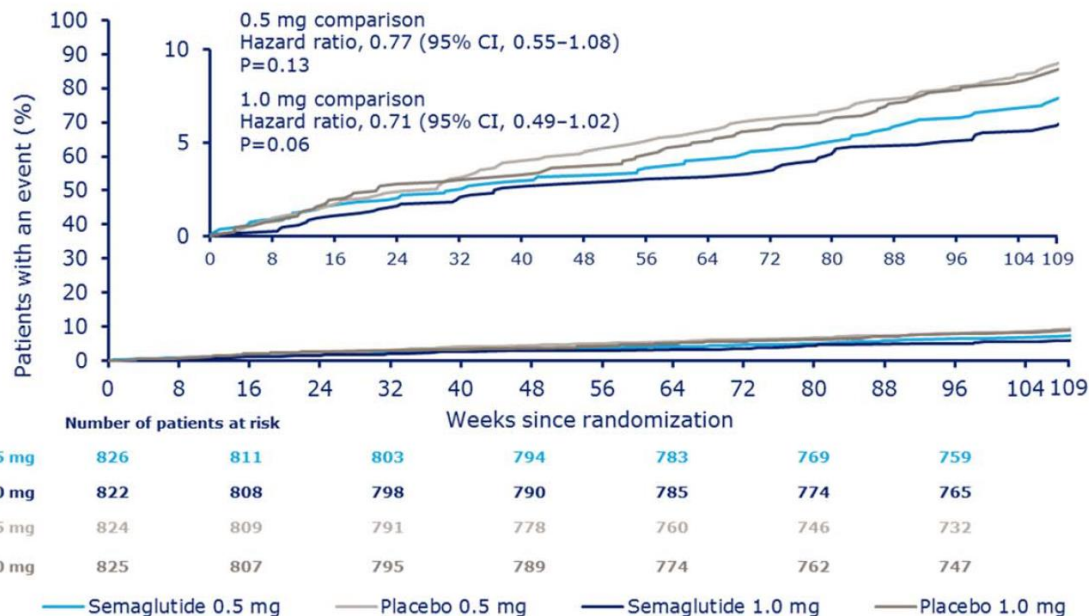
Dapagliflozin 5 mg 2.45/day
Dapagliflozin 10 mg 2.45/day



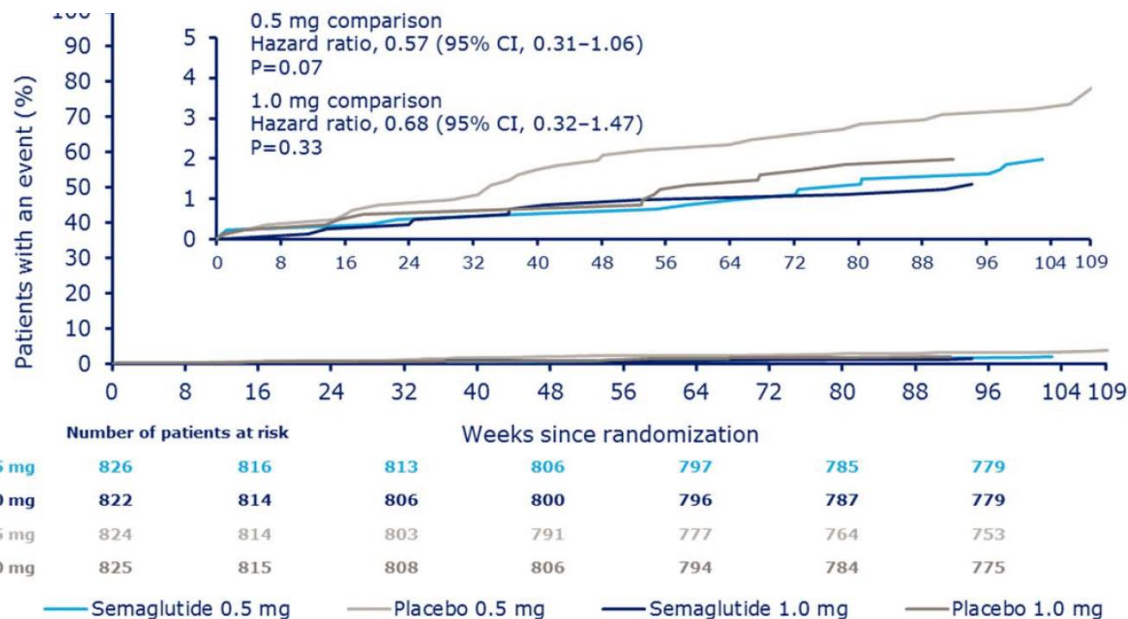
Impact of GLP-1 RA dose on cardio-renal benefits

Ex: Semaglutide in SUSTAIN-6

Primary Outcome

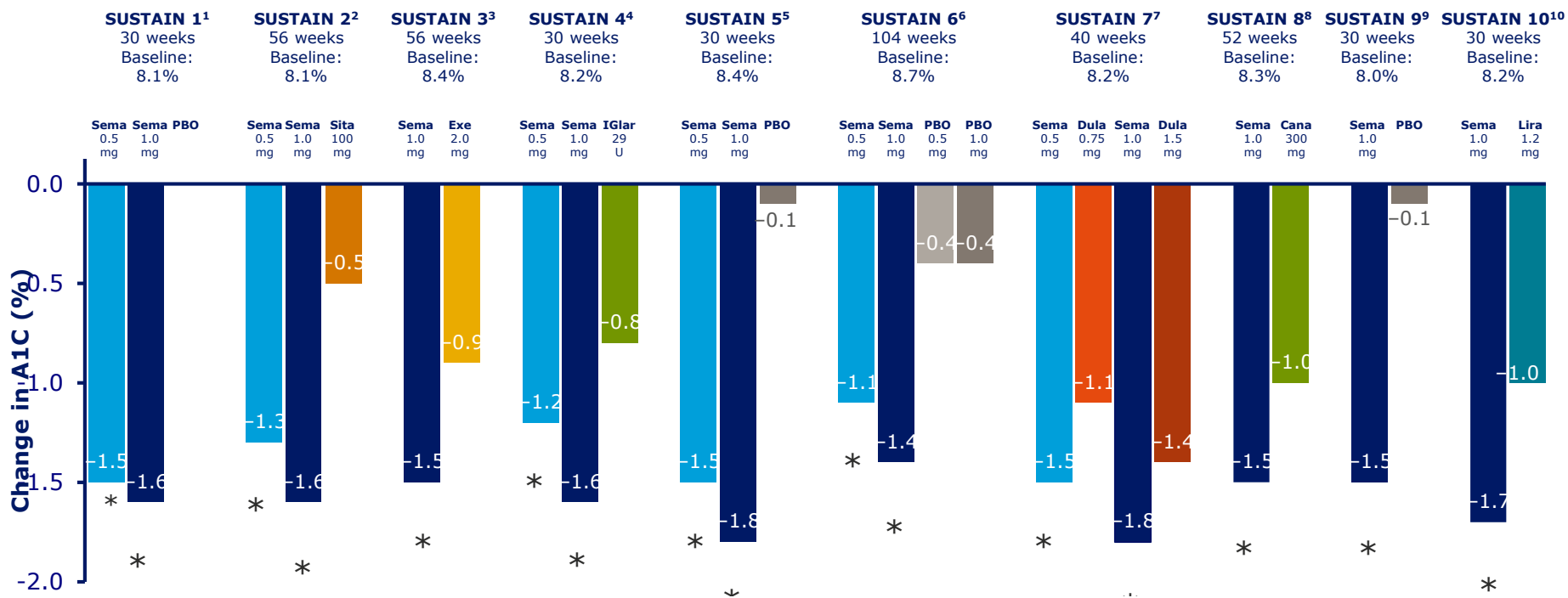


Non fatal Stroke



Impact of GLP-1 RA Dose on A1C Changes

Semaglutide: SUSTAIN Program



% of 1mg:

94%

81%

75%

83%

79%

83%

* p<0.0001 vs comparator.

Dula, dulaglutide; Cana, canagliflozin; Exe, exenatide extended release; IGlar, insulin glargine; Lira, liraglutide; PBO, placebo; Sema, semaglutide; Sita, sitagliptin. 1. Sorli C et al. Lancet Diabetes Endocrinol 2017;5:251-60;

2. Ahrén B et al. Lancet Diabetes Endocrinol 2017;5:341-54; 3. Ahmann AJ et al. Diabetes Care 2018;41:258-66; 4. Aroda VR et al. Lancet Diabetes Endocrinol 2017;5:355-66;

5. Rodbard HW et al. J Clin Endocrinol Metab 2018;103:2291-301; 6. Marso SP et al. N Engl J Med 2016;375:1834-44; 7. Pratley RE et al. Lancet Diabetes Endocrinol 2018;6:275-86; 8. Lingvay I, et al. The Lancet Diabetes & Endocrinology. 2019 [epub ahead of print]; 9. Zinman B et al. Lancet Diabetes Endocrinol 2019. [Epub ahead of print]. 10. Capehorn M, et al. Diabetes & Metabolism. 2019 [epub ahead of print].

Semaglutide Pens



0.25/0.5 mg pen



0.5 mg per week = 6.97 CAD per day
2 mg pen = 195.06\$

**\$1274 savings
per patient per year**

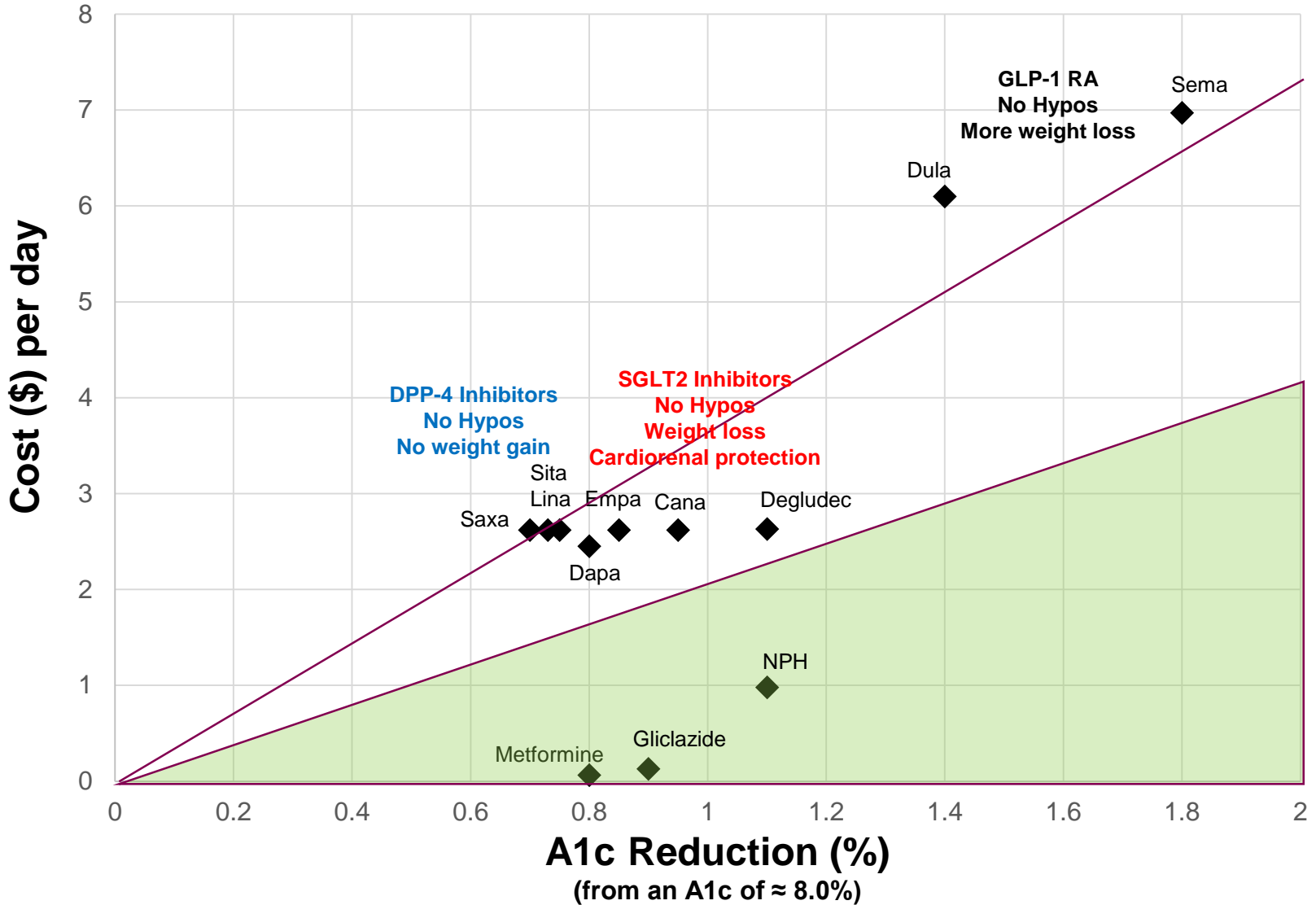
1.0 mg pen



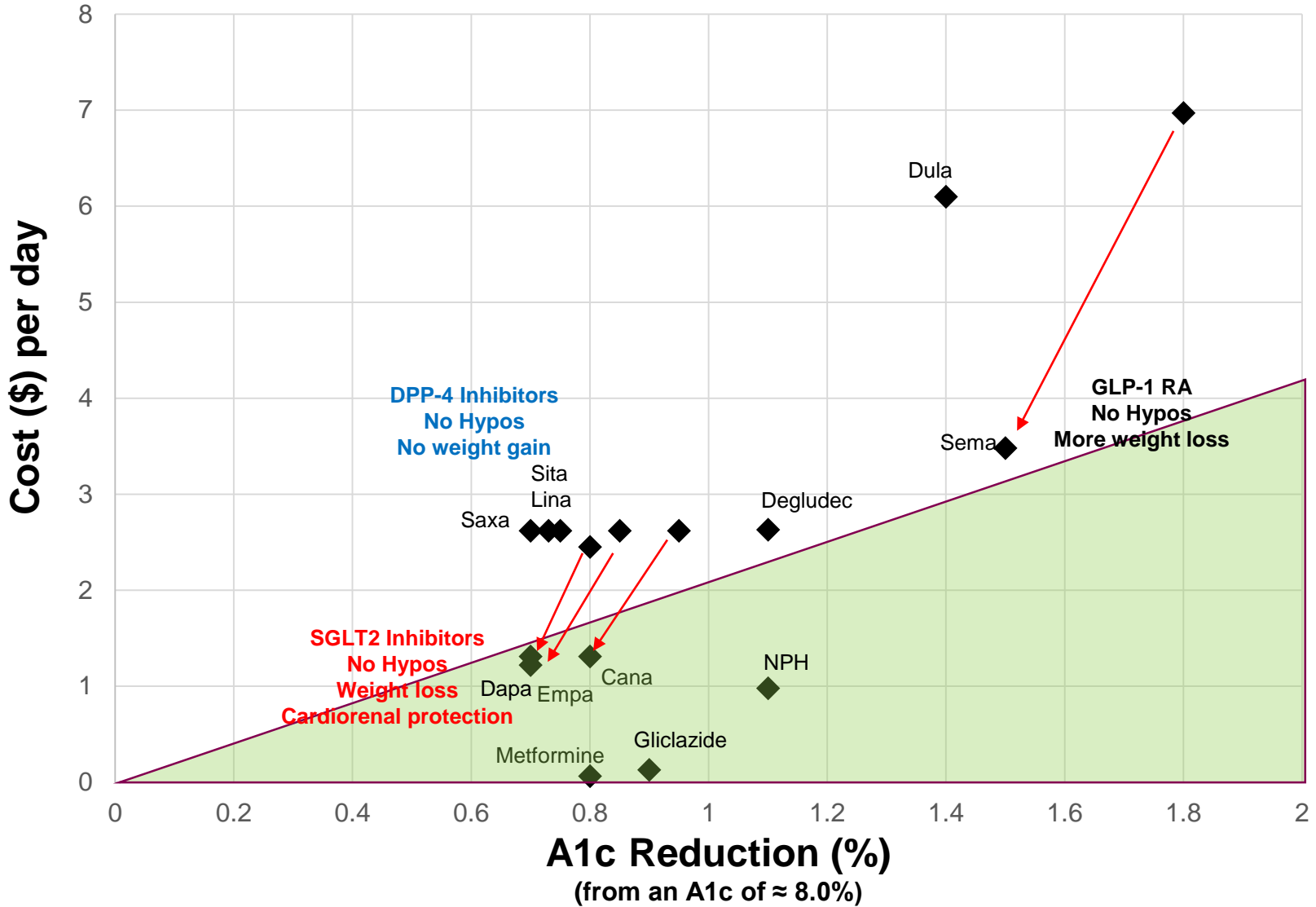
1.0 mg per week = 6.97 CAD per day
4 mg pen = 195.06\$

Using this pen to give 0.5 mg per week
brings the cost down to 3.48 per day
But you have to count the clicks... 36 clicks
0.5 mg = 36 clicks
0.25 mg = 18 clicks

Cost in function of A1c Reduction



Cost in function of A1c Reduction



Classical Approach		
Agent	Cost \$/d	A1c Drop
Metformin 850 bid	0.06	-1.1
Gliclazide MR 120 die	0.12	-0.8
Sitagliptin 100 die	2.62	-0.7
1 strip / day	0.70	
Total Cost	3.50	

Guidelines Approach		
Agent	Cost \$/d	A1c Drop
Metformin 850 bid	0.06	-1.1
Empagliflozin 10 die	2.62	-0.7
Semaglutide 0.5/wk	6.97	-1.3
0 strip / day	0	
Total Cost	9.65	

How to decrease the cost of new medications

\$4.79 x 365 = Savings of \$1748 / year

Even Lower Cost Approach		
Agent	Cost \$/d	A1c Drop
Metformin 850 die	0.03	-1.1
Empa/met 12.5/1000	1.35	-0.7
Semaglutide 0.25/wk	1.74	-0.9
0 strip / day	0	
Total Cost	3.12	

Guidelines Low Cost Approach		
Agent	Cost \$/d	A1c Drop
Metformin 850 die	0.03	-1.1
Empa/met 12.5/1000	1.35	-0.7
Semaglutide 0.5/wk	3.48	-1.3
0 strip / day	0	
Total Cost	4.86	

Potential Cost Savings add up....

- \$ 1748.00 savings per patient per year
- If each of you applies these tips on 10 patients this year
- \$ 17480.00 savings per physician listening today
- If 800 participants are connected today...
- Potential savings of \$13,984,000.00

Further Potential Savings: Capillary Glucose Test Strips

1 strip (\$0.70) a day = \$ 255.50

If on a secretagogue, 400 strips covered by RAMQ = \$280.

Testing every morning is not very useful...

Could do 4 tests a week on the same day (before meals and hs)

208 strips a year = \$145.60

Savings of \$134.40 per patient per year

If not on a secretagogue/insulin, 200 strips covered by RAMQ = \$140.

Could do 4 tests a month on the same day

4 tests a month = 48 tests a year = \$ 33.60

Savings of \$106.40 per patient per year

The End

A photograph of a modern university building with colorful facades (yellow, blue, orange, and grey) and a large, spherical sculpture made of metal rods in the foreground. The sky is blue with scattered white clouds. The text 'The End' is overlaid in white on the upper part of the image.

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