Hypoglycemic Agents

Dr. Roland Halil, PharmD, ACPR, BScPharm, BSc(Hon)
Clinical Pharmacist, Bruyère Academic Family Health Team
Assistant Professor, Dept of Family Medicine, UOttawa
rhalil@bruyere.org
Twitter: @RolandHalil

July 2022

Disclosures

Relationships with Commercial Interests:

- Consultant with the Foundation for Medical Education at McMaster University (non-profit org)
  - (PBSG module consultant & reviewer)
- Occasional consultant with Rxfiles (non-profit org)

Disclosure of Commercial Support : **None**

Potential for Conflict(s) of Interest: **None**

Objectives

- List the classes of oral antihyperglycemic agents and understand their place in therapy.
  - Determine the relative efficacy, toxicity, cost and convenience of these agents before choosing therapy
  - Rationalize prescribing of oral hypoglycemics
- Describe the current approach to pharmacologic management of type 2 diabetes.

Targets

	A1C	Fasting blood glucose (sugar) (mmol/L)	Post-prandial glucose 2h after eating (mmol/L)
Target for most people with diabetes	≤ 7.0%	4.0 - 7.0	4.0 - 10.0

Diabetes Canada. MANAGING YOUR BLOOD SUGAR
https://www.diabetes.ca/diabetes-and-you/healthy-living-resources/blood-glucose-insulin/managing-your-blood-sugar Accessed July 23/18

Diabetes: complications

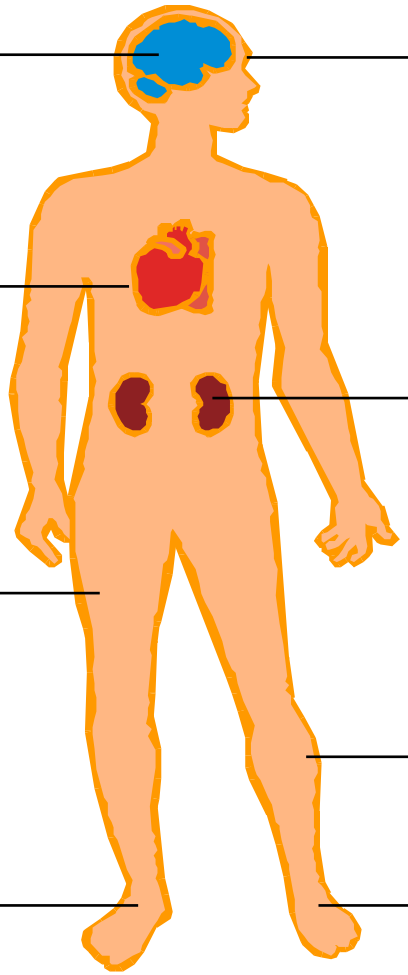
MACROvascular

Stroke

Heart disease & hypertension

Peripheral vascular disease

Foot problems



MICROvascular

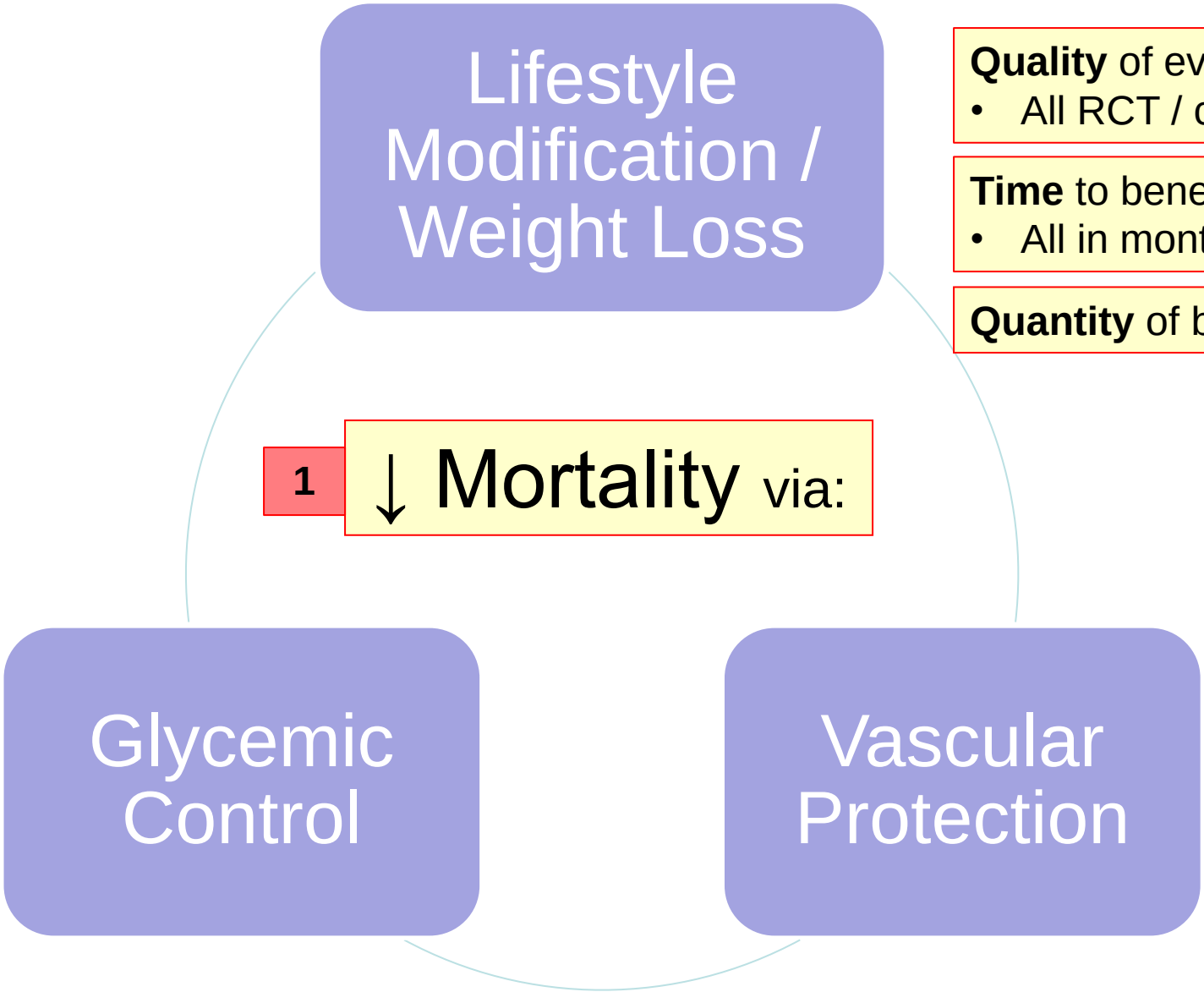
Diabetic eye disease (retinopathy & cataracts)

Nephropathy

Neuropathy

Foot problems

Priorities / Goals of Care



Quality of evidence:
- All RCT / cohort data

Time to benefit:
- All in months

Quantity of benefit?

1 ↓ Mortality via:

Lifestyle Modification & Weight Loss

Finnish Diabetes Trial

- Pre-diabetics (n = 522)
- Moderate wt loss (5%) (esp. abd fat)
- Physical activity
  - ≥ 150 min/week
- **12%** ARR / **58%** RRR for DM2 at 4 years
  - 11% (95% CI 6-15%) vs.
  - 23% (95% CI 17-29%)

N.B. Drugs ~ 30% RRR

DiRECT trial

- Diabetics (n = 306)
  - Specially-formulated 800 calorie liquid diet
  - Consisted of 4 shakes that replaced all meals x 3-5 months
- 15kg wt loss at 1 yr
  - **24%** vs. 0% control (p<0.0001) NNT=5
- DM2 remission at 1 yr
  - **46%** vs. 4% control (p<0.0001, O.R. 19.7, 95% CI 7.8-49.8) NNT=3
  - **36%** remission at 3 yrs

Bariatric surgery

(all types)

ROUX-EN-Y GASTRIC BYPASS

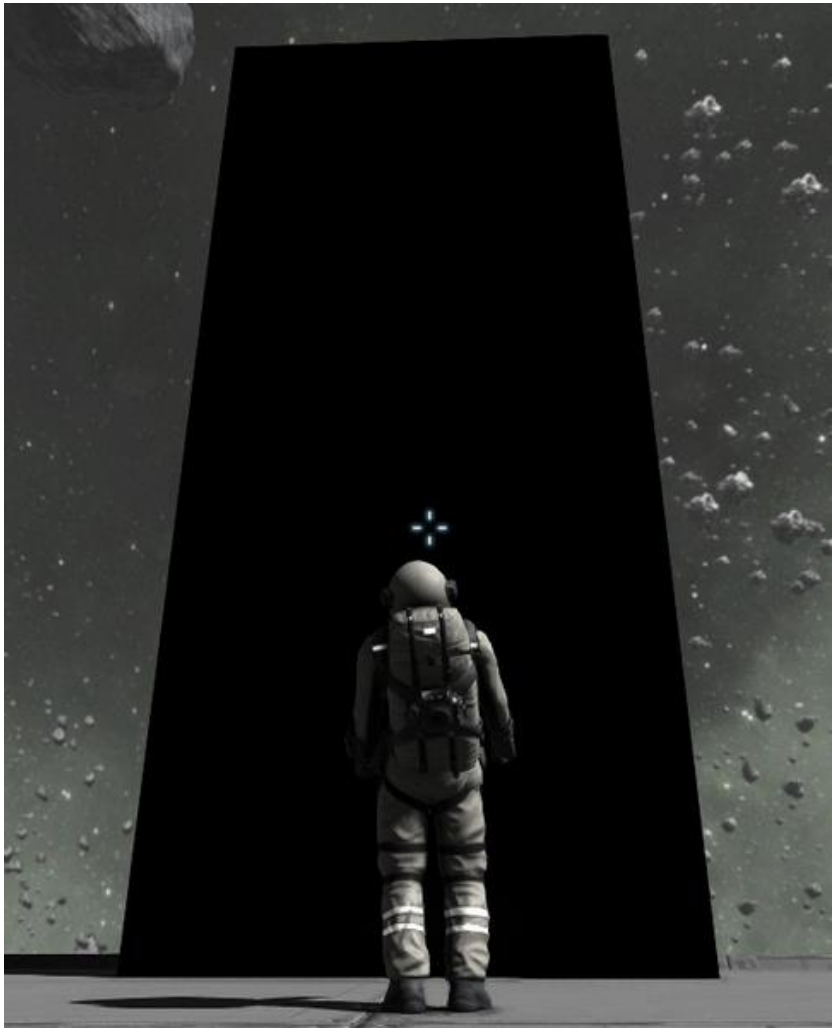
SLEEVE GASTRECTOMY

ADJUSTABLE GASTRIC BAND

DUODENAL SWITCH

- Bariatric surgeries in >135,000 pts found:
- Improved DM2 in **90%**
- DM2 remission in **78%**
  - American Society for Metabolic and Bariatric Surgery (ASMBS)

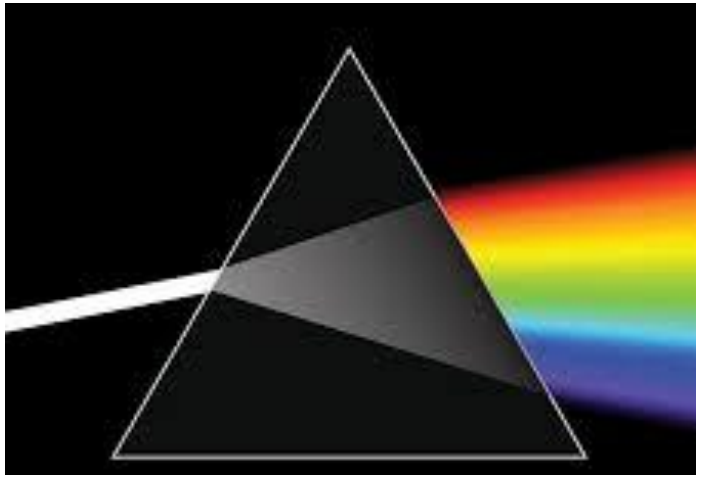
Diabetes



Previously,
DM2 = MI equivalent

- Automatic Rx for:
  - ASA, statin, ACEinh

Currently…



Vascular Protection & Glycemic Control

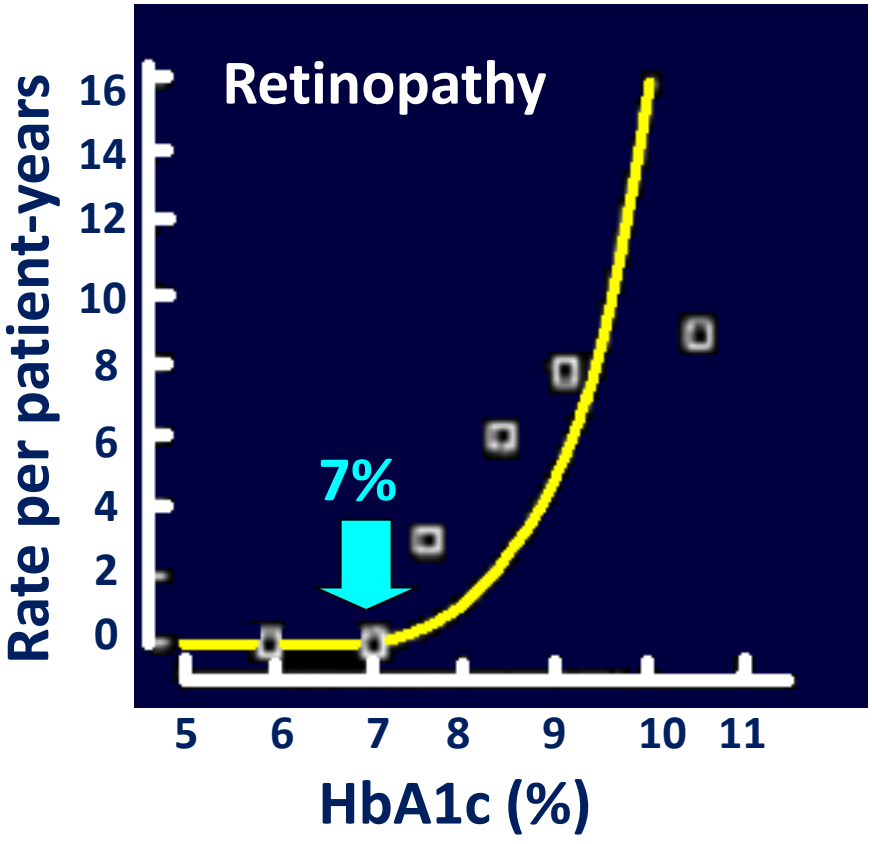
- Any ACEinh or ARB
  - Less clear benefit at lower risk
  - Very clear benefit at higher risk
- Any Statin
  - Less clear benefit at lower risk
  - Very clear benefit at higher risk
- ASA
  - NNT ~ NNH (1' prevention)
  - Only for 2' prevention

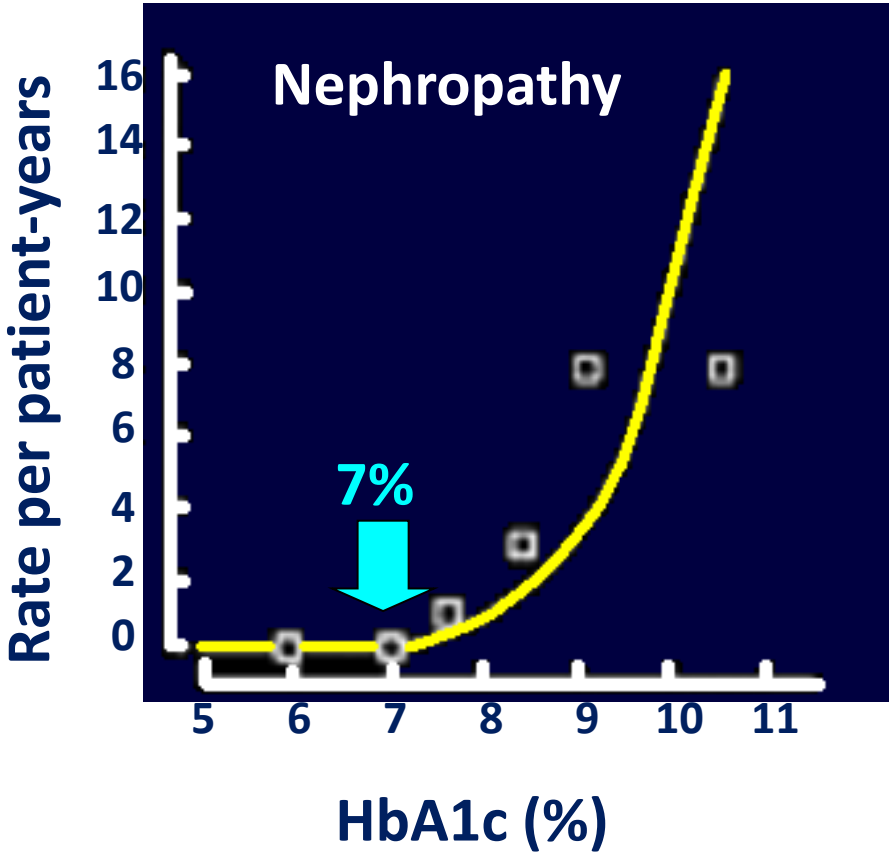
- Metformin
  - UKPDS-34 trial
  - Diabetes-specific mortality
    - (= Death from MI, stroke, PVD, kidney disease, hypo- or hyperglycemia, or sudden death).
    - Metformin vs. intensive:
      - 7.5 vs. 10.3 (P=0.11)
    - Metformin vs. diet:
      - 7.5 vs. 12.7 (P=0.017)
    - **2.8% - 5.2% ARR**
  - All-cause mortality
    - Metformin vs. intensive:
      - 13.5 vs. 18.9 (P=0.021)
    - Metformin vs. diet:
      - 13.5 vs. 20.6 (P=0.011)
    - **5.4% - 7% ARR**

2 ↓ Morbidity via:

Prevention of Microvascular Complications & Hgb-A1C Targets

- Intensive vs Conventional insulin therapy (n=110)
- Median A1c: 7.1% vs 9.4%





Shichiri M et al. Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. Diabetes Care. 2000 Apr;23 Suppl 2:B21-9.

Non-Pharmacologic Tx

Mainstay of therapy!

- Nutrition therapy
  - ↓ A1c 1-2%
  - CDA recommends counseling by a dietician for all type 2 diabetics
  - www.cvtoolbox.com diet for Type 2 diabetes
    - Continuing Medical Implementation Inc. (cvtoolbox.com)
    - http://www.cvtoolbox.com/downloads/diets/type2_diabetes_eating_plan_2010.pdf

Can J Diabetes 2003;27(2);S27

Pharmacotherapy

Comparison of antihyperglycemics

Pharmacotherapy

Drug Classes

Sensitizers

Secretagogues

Other

Drug Classes

Sensitizers

- Metformin
- Glitazones (TZD)
  - Rosiglitazone (Avandia®)
  - Pioglitazone (Actos®)

Secretagogues

- Sulfonylureas
  - Eg. Glyburide, Gliclazide
- Meglitinides
  - Eg Repaglinide (Gluconorm®)

Other

- **Alpha glucosidase inhibitors** (Acarbose)
- **DPP4 inhibitors (Gliptins)**
  - Sitagliptin, Linagliptin
  - Saxagliptin, Alogliptin

SGLT2 inhibitors (Cana- Dapa- Empagliflozin)

Incretin (GLP1) Analogues (sc injection)

* Liraglutide , Dulaglutide, Lixisenatide,
* Exenatide, Semaglutide (**po/sc**)

Pharmacology

Sensitizers

Sensitizers

- Metformin
- Glitazones (TZD)
  - Rosiglitazone (Avandia®)
  - Pioglitazone (Actos®)

- Reduce insulin resistance
- Increase glucose uptake & utilization in muscle and adipose tissue
- Reduce hepatic glucose output

Drug Classes

Sensitizers

- Metformin
- Glitazones (TZD)
  - Rosiglitazone (Avandia®)
  - Pioglitazone (Actos®)

Secretagogues

- Sulfonylureas
  - Eg. Glyburide, Gliclazide
- Meglitinides
  - Eg Repaglinide (GLUCONORM®)

Other

- Alpha glucosidase inhibitors (Acarbose)
- DPP4 inhibitors (Gliptins)
  - Sitagliptin, Linagliptin
  - Saxagliptin, Alogliptin

SGLT2 inhibitors (Cana-, Dapa, Empa-gliflozin)

Incretin (GLP1)Analogues

* Liraglutide , Dulaglutide, Lixisenatide,
* Exenatide, Semaglutide (all sc inj)

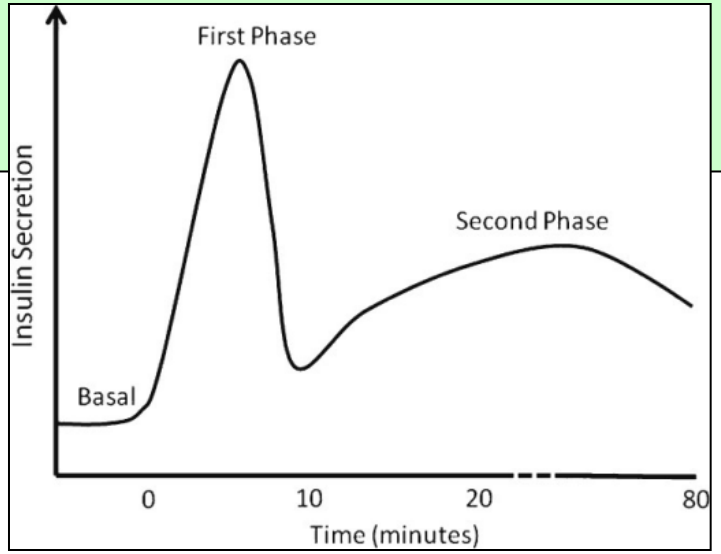
Pharmacology

Secretagogues

- ↑Basal and prandial insulin secretion
  - ↓hepatic gluconeogenesis
- Doesn't correct impaired 1st phase insulin secretion; primarily affects **2nd phase**
- Beta-cell sensitizer – primes glucose mediated insulin secretion (**1st phase**)

Secretagogues

- Sulfonylureas
  - Eg. Glyburide, Gliclazide
- Meglitinides
  - Eg Repaglinide (Gluconorm®)



Lexicomp® 2018

Drug Classes

Sensitizers

- Metformin
- Glitazones (TZD)
  - Rosiglitazone (Avandia®)
  - Pioglitazone (Actos®)

Secretagogues

- Sulfonylureas
  - Eg. Glyburide, Gliclazide
- Meglitinides
  - Eg Repaglinide (GLUCONORM)

Other

- Alpha glucosidase inhibitors (Acarbose)
- DPP4 inhibitors (Gliptins)
  - Sitagliptin, Linagliptin
  - Saxagliptin, Alogliptin

SGLT2 inhibitors (Cana-, Dapa, Empa-gliflozin)

Incretin (GLP1)Analogues

* Liraglutide , Dulaglutide, Lixisenatide,
* Exenatide, Semaglutide (all sc inj)

Pharmacology: Other

- Alpha glucosidase inhibitors (**Acarbose**)
  - Competitive inhibitor of pancreatic α-amylase and intestinal brush border α-glucosidases,

    = delayed hydrolysis of complex carbs & disaccharides and absorption of glucose; Dose-dependent reduction in postprandial serum insulin and glucose peaks; inhibits the metabolism of sucrose to glucose and fructose
- SGLT2 inhibitors (**Canagliflozin**, **Dapagliflozin, Empagliflozin**)
  - Inhibits *sodium-glucose cotransporter 2* (SGLT2) in the proximal renal tubules

    = reduced reabsorption of filtered glucose from renal tubule and lowered renal threshold for glucose (RTG).

    = results in increased urinary excretion of glucose, thereby reducing plasma glucose concentrations.
- DPP4 inhibitors (Gliptins) – (**Sitagliptin, Linagliptin**, **Saxagliptin, Alogliptin)**
  - Prolongs the action of endogenous *incretin* hormones by blocking their breakdown by the enzyme, dipeptidyl peptidase-4 (DPP-4). This leads to more insulin release after eating.
- Incretin (GLP1) Analogues – (**Liraglutide**, **Exenatide, Semaglutide, Dulaglutide**)
  - sc injection (daily or weekly) (New oral, daily semaglutide now available)
  - mimic endogenous incretin hormones:
    - "increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, **slows gastric emptying**; also acts in the areas of the brain involved in **regulation of appetite** and caloric intake."

So Many Options!

How to Choose?

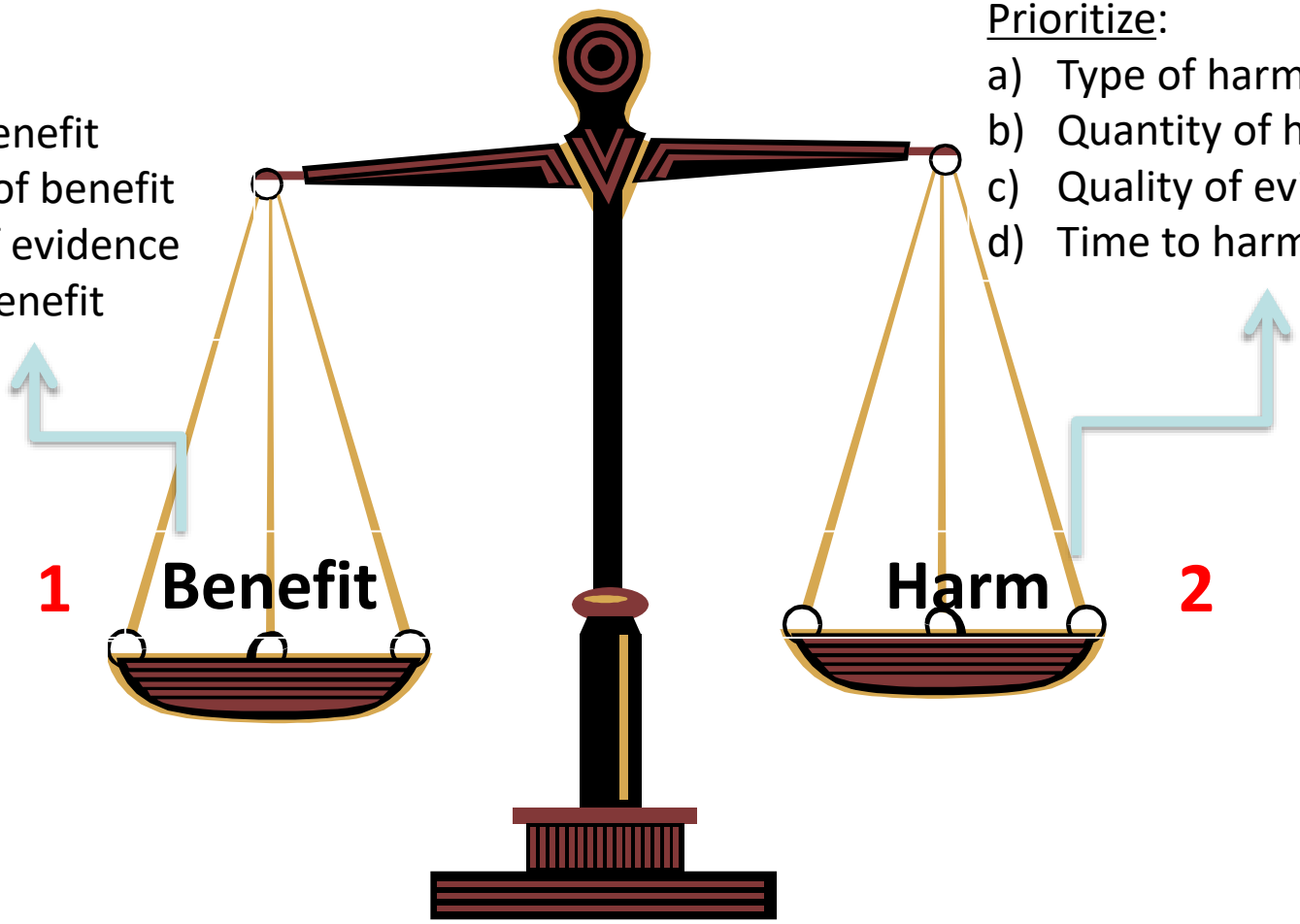
- FOUR steps to Rational Prescribing:

1. **Benefit**
2. **Harm**
3. *Cost*
4. *Convenience*

Rational Prescribing

Prioritize:
a) Type of benefit
b) Quantity of benefit
c) Quality of evidence
d) Time to benefit

Prioritize:
a) Type of harm
b) Quantity of harm
c) Quality of evidence
d) Time to harm



3,4 Cost & Convenience

a) Mortality benefit

- Metformin – UKPDS-34
- GLP1 analogs:
  - Liraglutide – LEADER trial
  - Semaglutide
    - SUSTAIN-6 trial (sc inj)
    - PIONEER-6 trial (po tabs)
      - MACE ns; But lower all-cause death and CV death (?odd)
  - Dulaglutide – REWIND
    - Lowered MACE, (Not mortality, only non-fatal stroke, not MI)
  - Exenatide – EXSCEL - **None**
  - Lixisenatide ELIXA - **None**

- SGLT2-inh:
  - Empagliflozin
    - EMPA-REG trial
    - (2^{o} prevention trial)
  - Dapagliflozin
    - DAPA-HF trial
    - DAPA-CKD trial
  - Canagliflozin
    - CREDENCE trial

- ?Insulin – "legacy effect"
  - 1 yr tight control = reduced M&M 10 yrs later! (UKPDS)

b) Morbidity benefit

(Reduction in microvascular outcomes)

- Older meds have shown a morbidity benefit (SU, etc)
- Newer meds show a reduction in HbA1c

- Metformin
- Acarbose
  - MERIA meta-analysis
  - (Driven by non-fatal MI)

- All GLP1 analogs:
- All SGLT2-inh:
  - Canagliflozin
    - CANVAS & CREEDENCE trials
  - Dapagliflozin
    - DECLARE-TIMI 58 trial
    - Renal Composite (sustained ↓eGFR ≥40% to <60mL/min, new ESRD, or death from renal/CV cause)

Cardiovascular outcome trials

Table 2 HR and 95% CI for CV and kidney endpoints and all death for DPP4 inhibitor, GLP-1RA and SGLT2 inhibitor studies (excludes post-ACS studies)

Study	Medication	MACE[a]	MACE+[a]	MI[b]	Stroke[b]	CV death	Heart failure	All death	Kidney endpoint[c]
DPP4 inhibitor studies									
SAVOR	Saxagliptin	1.00 (0.89, 1.12)	1.02 (0.94, 1.11)	0.95 (0.80, 1.12)	1.11 (0.88, 1.39)	1.03 (0.87, 1.22)	1.27 (1.07, 1.51)	1.11 (0.96, 1.27)	1.08 (0.96, 1.22)
TECOS	Sitagliptin	0.99 (0.89, 1.10)	0.98 (0.88, 1.09)	0.95 (0.81, 1.11)	0.97 (0.79, 1.19)	1.03 (0.89, 1.19)	1.00 (0.83, 1.20)	1.01 (0.90, 1.14)	NG
CARMELINA	Linagliptin	1.02 (0.89, 1.17)	1.00 (0.88, 1.13)	1.12 (0.90, 1.40)	0.91 (0.67, 1.23)	0.96 (0.81, 1.14)	0.90 (0.74, 1.08)	0.98 (0.84, 1.13)	1.04 (0.89, 1.22)
GLP-1RA studies									
LEADER	Liraglutide	0.87 (0.78, 0.97)	NG	0.88 (0.75, 1.03)	0.89 (0.72, 1.11)	0.78 (0.66, 0.93)	0.87 (0.73, 1.05)	0.85 (0.74, 0.97)	NG
SUSTAIN-6	Semaglutide (s.c.)	0.74 (0.58, 0.95)	NG	0.74 (0.51, 1.08)	0.61 (0.38, 0.99)	0.98 (0.65, 1.48)	1.11 (0.77, 1.61)	1.05 (0.74, 1.50)	NG
EXSCEL	Exenatide (MR)	0.91 (0.83, 1.00)	NG	0.97 (0.85, 1.10)	0.85 (0.70, 1.03)	0.88 (0.76, 1.02)	0.94 (0.78, 1.13)	0.86 (0.77, 0.97)	NG
Harmony	Albiglutide	0.78 (0.68, 0.90)	0.78 (0.69, 0.90)	0.75 (0.61, 0.90)	0.86 (0.66, 1.14)	0.93 (0.73, 1.19)	NG	0.95 (0.79, 1.16)	NG
SGLT2 inhibitor studies									
EMPA-REG OUTCOME	Empagliflozin	0.86 (0.74, 0.99)	0.89 (0.78, 1.01)	0.87 (0.70, 1.09)	1.18 (0.89, 1.56)	0.62 (0.49, 0.77)	0.65 (0.50, 0.85)	0.68 (0.57, 0.82)	0.54 (0.40, 0.75)
CANVAS Program[d]	Canagliflozin	0.86 (0.75, 0.97)	NG	0.85 (0.69, 1.05)	0.90 (0.71, 1.15)	0.90 (0.71, 1.15)	0.67 (0.52, 0.87)	0.87 (0.74, 1.01)	0.60 (0.47, 0.77)
DECLARE	Dapagliflozin	0.93 (0.84, 1.03)	NG	0.89 (0.77, 1.01)	1.01 (0.84, 1.21)	0.98 (0.82, 1.17)	0.73 (0.61, 0.88)	0.93 (0.82, 1.04)	0.53 (0.43, 0.66)

HR findings are derived from intention-to-treat analyses

[a] MACE: CV death, MI, stroke; MACE+: CV death, MI, stroke, acute coronary event

[b] Fatal and non-fatal

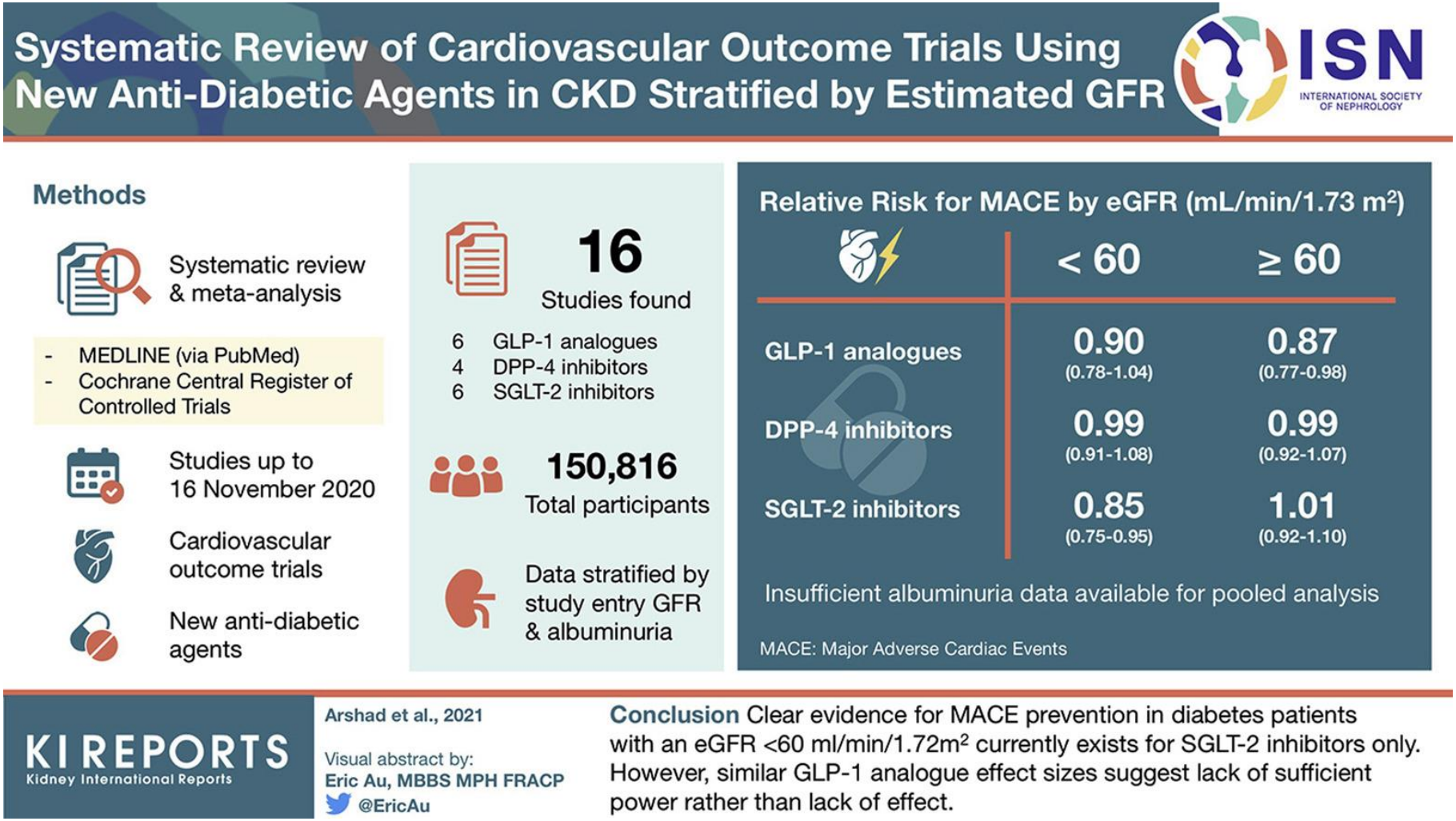
[c] Composite of variables, not including albuminuria

[d] Composed of two studies

MR, modified release (long-acting); NG, not given

Home P. Cardiovascular outcome trials of glucose-lowering medications: an update. Diabetologia. **2019** Mar;62(3):357-369. doi: 10.1007/s00125-018-4801-1. https://link.springer.com/content/pdf/10.1007%2Fs00125-018-4801-1.pdf

Cardiovascular outcome trials



Arshad A. et al. Systematic Review of Cardiovascular Outcome Trials Using New Antidiabetic Agents in CKD Stratified by Estimated GFR. Kidney International Reports. Volume 6, Issue 9, September 2021, Pages 2415-2424 Systematic Review of Cardiovascular Outcome Trials Using New Antidiabetic Agents in CKD Stratified by Estimated GFR – ScienceDirect

Benefit

2nd: SURROGATE Outcomes

c) HbA1c reduction

- Any drug that reduces Hgba1c < 7%
- Blood glucose level reduction
- Fasting or Prandial

d) Insulin Sparing Effects

- Avoidance of hyperinsulinemia and associated risk factors (metabolic syndrome, atherosclerosis, elevated TGs/UA/weight/BP, etc.)

Benefit

2c) **Hb-A1c reduction**

- **~ 1% to 2%**
  - Metformin (1% - 2%)
  - Sulfonylureas (1% - 2%)
  - Repaglinide (1% - 1.5%)
  - Glitazones (TZDs) (0.4% - 1.5%)
  - Canagliflozin (0.8 – 1%)
  - Liraglutide (GLP1 analogs) (1% - 2%)
- **~ 0.5% to 1%**
  - Acarbose
  - DPP4 inhibitors ('Gliptins)
  - Dapagliflozin, Empagliflozin
  - Nateglinide

Nathan DM, et al. *Diabetes Care* 2008 (Dec);31:1-11

Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes. 2018;42(Suppl 1):S1-S325

Benefit

2d) **Insulin Sparing Effect**

= Weight neutral or weight negative

= Reduction of hyperinsulinemia

- METFORMIN
- TZD's (GLITAZONE's)
- ACARBOSE
- DPP4 inh ('gliptins)
- Incretin (GLP1) Analogues (Liraglutide, Semaglutide etc.)
- SGLT2 inh (Empagliflozin etc.)

Consider Harm

Ask yourself…

	Bothersome	**Severe**
Common		Not legal
Rare	Who cares	

- Age?
  - *Newer* agents = **Less** Safety Data
  - *Older* agents = **More** Safety Data

Harm

Serious / Rare

- **Glitazones**
  - CHF
  - Fractures
  - M.I.
    - (rosiglitazone)
  - Bladder Cancer
    - (pioglitazone)

- **Secretatgogues**

  (Sulfonylureas & Meglitinides)

  - Severe Hypoglycemia

Harm

Serious / Rare

- **SGLT2 inhibitors**

(FDA OK **2013**; H.Can. OK **2015**)

  - Euglycemic DKA
    - Risk increased 7x in DM2
    - Estimated incidence ~ 0.1%.
    - **73 cases** (2013 to 2015 in FAERS database)
  - Fournier gangrene
    - **542 cases** by 2020 - necrotising fasciitis in the perineum (FDA warning)
    - reported occurrence = 1.6 out of 100,000 males annually in U.S., most frequently in males 50-79 yo.
  - Urosepsis
    - **19 cases** (2013-2014)(FAERS) database

= ~ Reasonable safety data

- **Incretin (GLP1) Analogues**

(H.Can. approved in 2010)

- **DPP4 inhibitors ('gliptins)**
- ?Heart failure
  - Sitagliptin (Approved in 2008)
    - **No**, per 2015 TECOS trial (n = 14,671)
    - Initially, Yes, per lower quality data [2014 post hoc pooled analysis of 25 RCTs (n = 1261)]
  - Linagliptin – **No** (per CARMELINA tial)
  - Saxoglitpin – **Yes**? (SAVOR-TIMI 53 trial)
  - Alogliptin - **Yes**? (EXAMINE trial)
- ?Pancreatitis – maybe/unlikely
  - Yes per Faillie 2014 (PMID: 2435244) & Lee 2019 (PMID: 31431452)
  - No per Chou 2014 (PMID: 24859164) & Thomsen 2015 (PMID: 25633664)

= ~ Reasonable safety data

Harm

Serious / Rare

- **Metformin**
- ?Risk of Lactic Acidosis
  - 0.03 to 0.06 cases / 1000 pt-yrs
  - ~ 50% fatal
  - When implicated:
    - **Based on case reports**
      - Primarily diabetics w/ significant renal insufficiency, both intrinsic renal disease and renal hypoperfusion, w/ multiple medical/surgical problems and multiple medications.
      - Phenformin pulled from market due to L.A. in 1977
    - **Cohort studies and retrospective reviews**:
      - **Zero** risk of lactic acidosis with metformin

Metformin Dosing

- Dosing recommendations with renal insufficiency:
  - CrCl > 30 mL/min→ full dose
    - 2.5g/day
  - CrCl = 20 – 30 mL/min→ reduced dose
    - 1g/day (If NO other risk factors, else D/C)

- Take home: Assess OTHER RISK FACTORS for lactic acidosis

1) Salpeter SR, et al. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD002967. http://www.cochrane.org/CD002967/ENDOC_risk-of-fatal-and-nonfatal-lactic-acidosis-with-metformin-use-in-type-2-diabetes-mellitus Accessed Sept 24, 2015
2) Nasri, H. et al. Metformin: Current knowledge. J Res Med Sci. 2014 Jul; 19(7): 658–664. PMCID: PMC4214027 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4214027/ Accessed Sept 24, 2015
3) A A Tahrani, et al. Metformin, heart failure, and lactic acidosis: is metformin absolutely contraindicated? BMJ. 2007 Sep 8; 335(7618): 508–512. PMCID: PMC1971167. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1971167/ Accessed Sept 24, 2015
4) Lalau JD. Lactic acidosis induced by metformin: incidence, management and prevention. Drug Saf. 2010 Sep 1;33(9):727-40. PMID: 20701406
5) Lazarus B, Wu A, Shin J, et al. Association of Metformin Use With Risk of Lactic Acidosis Across the Range of Kidney FunctionA Community-Based Cohort Study. *JAMA Intern Med.* Published online June 04, 2018. doi:10.1001/jamainternmed.2018.0292 https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2682516 Accessed June 7, 2018

Risk Factors - Lactic Acidosis

- Severe renal impairment
  - (caution if CrCl $\leq$ 30ml/min)

and

- Hepatic disease
- alcoholism
- CHF
- COPD
- CRF
- Pneumonia
- Ongoing acidosis
  - Lactic, keto etc.

Harm

Common / Bothersome

1) METFORMIN
   - GI upset / diarrhea – **Start low, go slow**!
     - Initial dose 250mg QDaily to BID
   - B12 / folate deficiency / anemia (6 - 8/100)
     - Reduced absorption – so, **supplement**
   - Anorexia – usually **transient**

Harm

Common / Bothersome

2) Sulfonylureas:
   - Sulfa skin reactions
     - Rash / photosensitivity ~1%
   - Weight gain (2-3kg)
   - Mild Hypoglycemia:
     - Most with glyburide. Least w/ glimepiride & gliclazide
     - Requires consistent food intake
     - Major episodes 1-2% (esp. in elderly)

Harm

Common / Bothersome

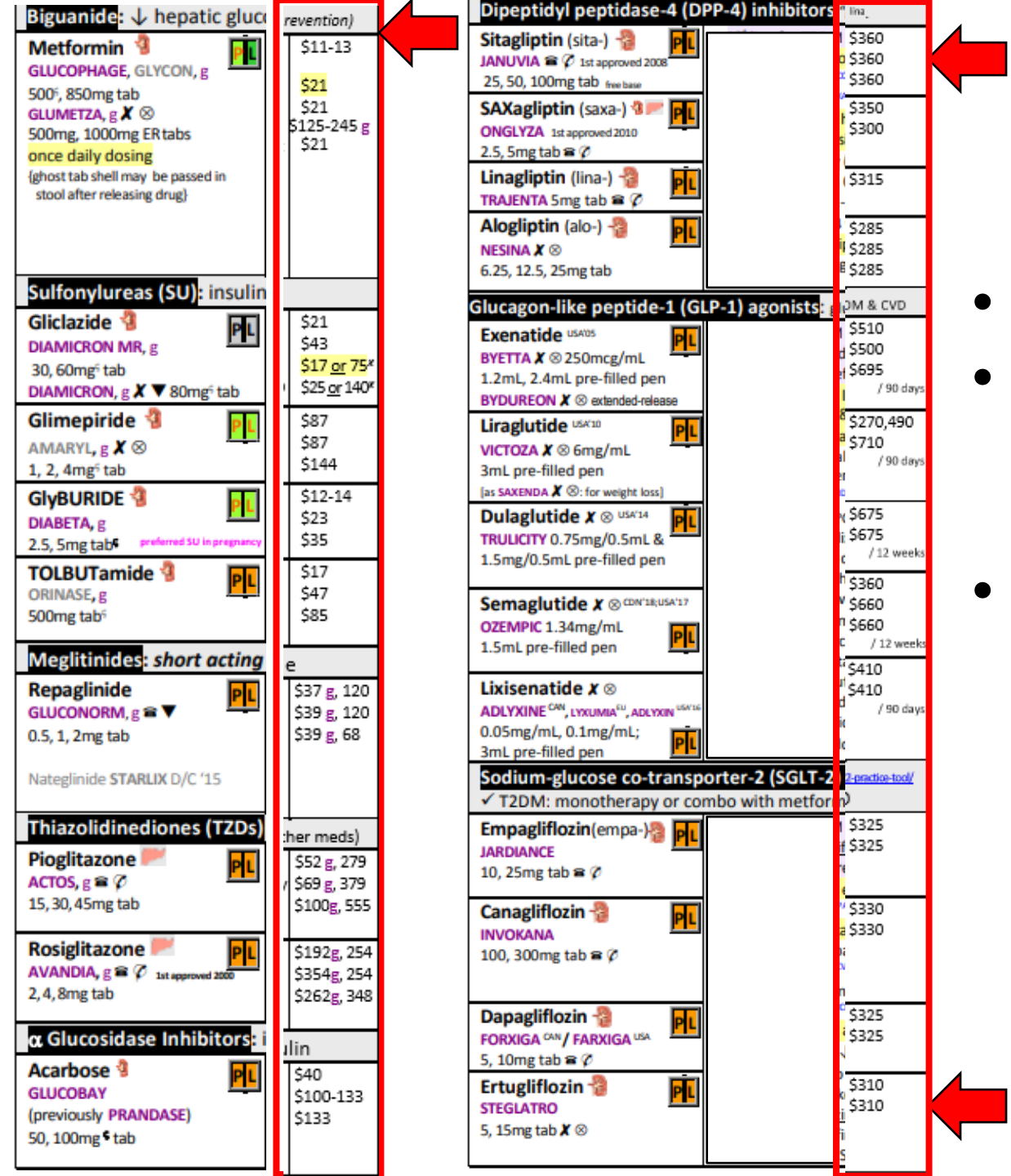
3) Glitazones:
   - Edema
4) Meglitinides:
   - Hypoglycemia
5) Acarbose:
   - GI upset / diarrhea / bloating
6) Gliptins:
   - Generally well tolerated
     - GI upset, edema, ?infection

7) Incretin (GLP1) analogues
   - N/V/D
8) SGLT2 inhibitors
   - HyperK+, AKI
   - UTI (*includes bacteriuria [asymptomatic*], cystitis: 9%; **females**: **4%-18%**; males: 4%),
   - Genitourinary fungal infection (4%; **females**: **5% to 11%** *[includes bacterial vaginosis, cervicitis, vulvitis, vulvovaginal candidiasis, vulvovaginal infection, vulvovaginitis*];
   - males: 2% to 3% *[includes balanitis, balanoposthitis, genitourinary fungal infection, penile infection, scrotal abscess])*

Cost

- Patient cost *vs* Societal cost

- Rx cost?
- ODB coverage?
- Covered under other plans?



Cost

- From Rxfiles Nov 2019
- = **Cost($)/100 days** (in Sask.)
- Alternatively, check ODB e-formulary here:
  - N.B. Not true pt costs
  - Only *comparative* costs

http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-diabetes.pdf

Cost

ODB e-formulary *comparative* costs

Search Results

Therapeutic Classification
68:20:02 ANTI-DIABETIC AGENTS ORAL ANTI-DIABETIC AGENTS

You can sort your results in ascending / descending order by clicking on the column headings, with the exception of Th Notes.

Products found: 154 Ne

DIN/ PIN/ NPN	Generic Name	Brand Name, Strength & Dosage Form	MFR	Drug Benefit Price or Unit Price	Amount MOHLTC Pays	Inter-change-able	Limited Use
02190893	ACARBOSE	Glucobay 100mg Tab	BAY	0.3732	**0.3732**	NO	YES
02425491	CANAGLIFLOZIN	Invokana 300mg Tab	JAN	2.7627	**2.7627**	NO	NO
02443945	EMPAGLIFLOZIN	Jardiance 25mg Tab	BOE	2.6177	**2.6177**	NO	NO
02356422	GLICLAZIDE	Diamicron MR 60mg ER Tab	SEV	0.2529	**0.0632**	YES	NO
02257726	METFORMIN HCL	Act Metformin 500mg Tab	ACV	0.0247	**0.0247**	YES	NO
02303922	SITAGLIPTIN PHOSPHATE MONOHYDRATE	Januvia 100mg Tab	MFC	3.0932	**3.0932**	NO	NO

To roughly estimate pt costs: (add ~10% x No. days) + ~$10 dispensing fee

ODB e-formulary https://www.formulary.health.gov.on.ca/formulary/ Accessed Aug 9, 2018

Convenience

- PO vs IV?
- QD vs QID?
- Lab monitoring?

Convenience

- Gliptin's - QD
- Glitazones - QD
- SGLT2 inh - QD
- DPP-4 inhibitors - QD
- GLP-1 analogs - QD sc inj
- Sulfonylureas – QD to BID
- Metformin - QD to TID
- Meglitinides – QD to TID
- Acarbose – QD to TID

with meals

Summary

1st line – Metformin

CV benefit, renal benefit, very safe, cheap, simple

If obesity or CVD:

- GLP1 analog
- Semaglutide (Ozempic®)
  - CV & renal benefit, wt loss, ODB covered, weekly sc inj

If CHF or CKD:

- Any SGLT2 inh
- **Dapagliflozin** (Forxiga®)
  - CV benefit, renal benefit, CHF specific benefit, ODB covered, combo pill with Metformin (Xigduo®)
  - But, closely monitor SCr, K+, UTI sxs etc
    - Alternative for lower eGFR: **Canagliflozin** 100mg (low dose)

- If no CKD/MI/CVA/CHF: **Anything else**
  - (except TZDs) (never ever)

Review of Basic Concepts

1. Reduce mortality
   - BP control w/ ACEi/ARB
   - Plaque stabilization with statin
   - ASA in 2' prevn
   - Glycemic control with Metformin
     - + GLP1 analogs
     - + SGLT2inh
     - + ?Acarbose
2. Reduce morbidity
   - Glycemic control to prevent microvascular complications
     - A1c < 7%

Summary

- Pathophysiology of disease underscores the key targets for modification
  - Insulin resistance / hyperinsulinemia
- Pharmacology of agents underscores ideal vs. suboptimal combinations of agents
- Rational Prescribing principles underscore priorities for investment in benefit/risk ratios

Questions?

Dr. Roland Halil, PharmD, ACPR, BScPharm, BSc(Hon)
Clinical Pharmacist, Bruyere Academic Family Health Team
Assistant Professor, Dept of Family Medicine, UOttawa
rhalil@bruyere.org
Twitter: @RolandHalil