


Navigating the New Options for the Management of Type 2 Diabetes

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Primary Care Diabetes Society of Australia *Diabetes Care For All By All*



Disclosures

- I have previously received speaker's fees, travel support, medical writing grants or served on medical advisory committees for the following companies:


• AstraZeneca Australia	• MSD
• AstraZeneca Global	• Bristol Myers Squibb
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Take Home Messages:

- Selecting anti diabetic medication is based on:**
 - Individualized therapeutic targets
 - Achieving HbA1c target while minimizing side effects, especially hypoglycaemia
 - Individual medication risk benefit analysis:
 - Patient preference
 - Comorbidities and complications
 - Drug characteristics




Take Home Messages 2:

- Selecting anti diabetic medication – ABCD (EFGH) Approach**
Consider:
 - Age
 - BMI
 - CKD
 - Duration of Diabetes
 - Established CVD
 - Financial Considerations
 - Glycaemic Status
 - Hypoglycaemia concern




Overview

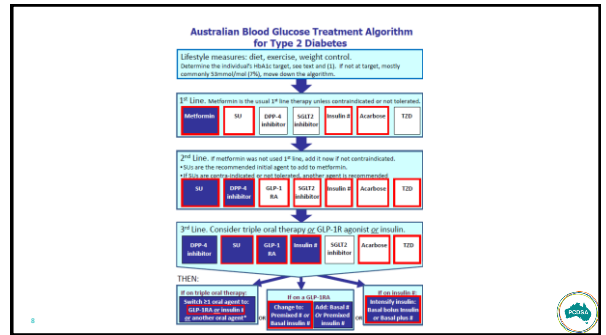
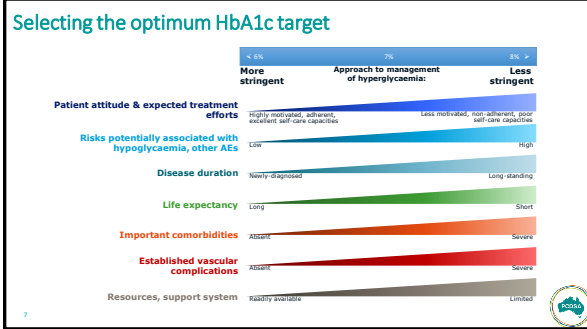
- Setting an HbA1c target
- Therapeutic algorithms
- The ABCD (EFGH) approach
- Case Studies



Set an A1c target - ADS guidelines

Populations	HbA _{1c}	
	%	SI units
General	≤7%	≤53 mmol/L
Diabetes of short duration and no clinical CVD		
• Requiring lifestyle modification ± metformin	≤6.0%	≤42 mmol/L
• Requiring any antidiabetic agents other than metformin or insulin	≤6.5%	≤48 mmol/L
• Requiring insulin	≤7.0%	≤53 mmol/L
Pregnancy or planning pregnancy	≤6%	≤42 mmol/L
Diabetes of longer duration or clinical CVD (any therapy)	≤7.0%	≤53 mmol/L
Recurrent severe hypoglycaemia or hypoglycaemia unawareness (any therapy)	≤8.0%	≤64 mmol/L
Major co morbidities likely to limit life expectancy (any therapy)		Symptomatic





Oral anti-diabetic agents and non-insulin injectables

Class	Generic name	Brand name
Biguanide	Metformin	Glucophage*
Sulfonylureas	e.g. Glibenclamide (glyburide)	Daonil*
	e.g. Gliclazide	Diamicron*
	e.g. Glimepiride	Amaryl*
α-Glucosidase inhibitors	Acarbose	Glucobay*
Thiazolidinediones	Pioglitazone	Actos*
DPP-4 inhibitors	Saxagliptin	Onglyza*
	Sitagliptin	Januvia*
	Vildagliptin	Galvus*
	Linagliptin	Trajenta*
	Alogliptin	Nesina*

Oral anti-diabetic agents and non-insulin injectables

Class	Generic name	Brand name
GLP-1 agonists	Exenatide	Byetta*
	Exenatide	Bydureon*
	Liraglutide	Victoza*
	Lixisenatide	Lyxumia*
SGLT-2 inhibitors	Dapagliflozin	Forxiga*
	Canagliflozin	Invokana*
	Empagliflozin	Jardiance*

Benefits of Diabetic Medications -1

Property	SU	TZD	DPP4i	Glp1a	Acarbose	SGLT2i	Insulin
Efficacy - A1c	✓✓✓	✓✓	✓✓	✓✓✓	✓	✓✓	✓✓✓✓
FBG	✓✓	✓✓	✓	✓	—	✓	✓✓✓
Post-prandial BG	✓✓	✓✓	✓✓	✓✓✓	✓✓	✓✓	✓✓✓
Durability of control	✗✗	✓✓	✓	✓✓	✓✓	✓✓	✓✓✓

Benefits of Diabetic Medications -2

Property	SU	TZD	DPP4i	Glp1a	Acarbose	SGLT2i	Insulin
Use in different duration of DM	Early	All	All	All	All	All	All
Convenience of dosing/delivery	✓	✓	✓	✗✗	✗	✓	✗✗
Affordability	✓	✓	✗	✗✗	✓	✗	✓
Other benefits	Rapid onset	↓ BP Improves fatty liver		↓ BP		↓ BP Empa-Reg	Unlimited efficacy

Risks of Diabetic Medications - 1

Property	SU	TZD	DPP4i	Glp1a	Acarbose	SGLT2i	Insulin
Hypoglycaemia	xx	✓	✓	✓	✓	✓	xxx
Use with CKD	Reduce dose	✓	↓dose	↓dose	✓	↓dose	↓dose
Use with Liver Failure	✓	?x	✓ except Vildagliptin	✓	✓	✓	✓
Use/Risk in CVD	x?	x	✓	✓	✓	✓✓✓ (empagliflozin)	✓
Weight Gain	xx	xxx	-	✓✓✓	-	✓✓	xxx

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Risks of Diabetic Medications - 2

Property	SU	TZD	DPP4i	Glp1a	Acarbose	SGLT2i	Insulin
Fractures	✓	xx	✓	✓	✓	x?	✓
Heart Failure / Oedema	-	xx	x saxagliptin x? alogliptin ✓ sitagliptin	-	-	✓✓✓ (empagliflozin)	-
GIT Symptoms	✓	✓	✓	x	xx	✓	✓
Interactions	x	✓	✓	✓	✓	✓	✓

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Risks of Diabetic Medications - 3

Property	TZD	DPP4i	Glp1a	SGLT2i
Other Possible risks	? bladder cancer Macular oedema	? pancreatitis	? pancreatitis ↑ HR	Thrush DKA Hypovolaemia

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Choosing 2nd and 3rd line agents

- Aim to reduce HbA1c while minimizing side effects
 - Hypoglycaemia
 - Weight gain
- Depends on:
 - Patient preference
 - Comorbidities and complications
 - Drug characteristics

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ABCD (EFGH) Approach

- Age
- BMI
- CKD
- Duration of Diabetes
- Established CVD
- Financial Considerations
- Glycaemic Status
- Hypoglycaemia concern

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A- Age Considerations

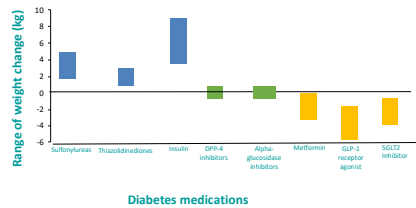
- Age increases risks of:
 - Hypoglycaemia
 - Hypovolaemia
 - Cardiac failure
 - Reduced beta cell function
 - Osteoporosis

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B - BMI Considerations

Range of weight change (kg) in response to diabetes medications



C – Chronic Kidney Disease

- Hypoglycaemia more common in severe CKD
- SU and Insulin dose may need to be reduced
 - Insulin best at end stage renal failure
- DPP4 inhibitors
 - Linagliptin needs no dose adjustment
 - Others need dose adjustment

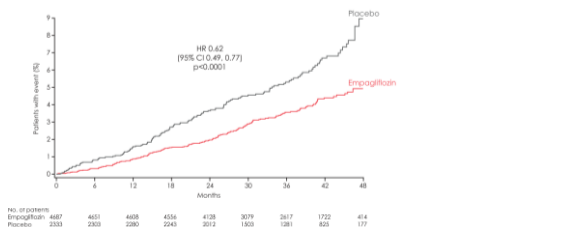
D – Duration of Diabetes

- UKPDS Study showed importance of intensive glycaemic control in early years of T2DM
- Accord Study showed need to loosen targets in diabetes of longer duration
- SUs less effective with longer duration diabetes (as beta cell function declines)

E – Established CVD

- Hypoglycaemia more risky with established CVD
- Empagliflozin reduced CV death by 38% over 3.1 years
- Some concerns from observational studies about CVD safety of SUs

E – Established CVD – Empa-Reg CV death



F - Financial considerations

- In Australia, choices limited by PBS availability more than TGA approval
- Most expensive to prescribe non-PBS are DPP4 inhibitors, GLP-1 analogues and SGLT2 inhibitors

G – Glycaemic Status

- Glycaemic lowering of all agents is greater at higher starting HbA1c
- Efficacy rating:
 - Insulin
 - GLP-1 analogues
 - Sulphonylureas
 - Thiazolidinediones
 - SGLT-2 inhibitors
 - DPP4 inhibitors
 - Alpha-glucosidase inhibitors

H – Hypoglycaemia Concerns

- Sulphonylureas and Insulin main causes of hypoglycaemia
- More prevalent with CKD and longer duration of diabetes
- DPP4 inhibitors, GLP-1 analogues and SGLT2 inhibitors unlikely to cause severe hypoglycaemia and cause minimal hypoglycaemia unless used with Insulin or SU

H – Hypoglycaemia Concerns

- Avoid hypoglycaemia in these groups:
 - Established CV disease
 - Elderly patients
 - Retinopathy (difficult doing SMBG)
 - Living alone
 - Short life expectancy
 - Hypoglycaemia unawareness
 - Previous severe hypoglycaemia
 - Some occupations

Initial Case

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✓
CKD	-	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	-	GLP-1 analogues	✗
Financial	-	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 7.9 %	Insulin	✗
Hypoglycaemia	-		

Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	-	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	-	GLP-1 analogues	✓
Financial	-	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	-		

Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	-	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	-	GLP-1 analogues	✓
Financial	-	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	-		

Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	–	GLP-1 analogues	✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	–		

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Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	–	GLP-1 analogues	✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	–		

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Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	–	GLP-1 analogues	✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	–		

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Case 2 – Poor glycaemic control

Age	48 year old male on Metformin	Sulphonylurea	✓
BMI	29	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	–	GLP-1 analogues	✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 9.6 %	Insulin	✓
Hypoglycaemia	–		

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Case 3 – Morbid Obesity

Age	48 year old male on Metformin	Sulphonylurea	✗
BMI	36	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	1 year	DPP4 inhibitors	✓
Established CVD	–	GLP-1 analogues	✓✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 7.9 %	Insulin	✗
Hypoglycaemia	–		

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Case 4 – Older and CVD

Age	58 year old male on Metformin	Sulphonylurea	✗
BMI	29	Thiazolidinediones	✗
CKD	–	Alpha-glucosidase inhibitors	✗
Duration	11 years	DPP4 inhibitors	✓
Established CVD	YES	GLP-1 analogues	✓
Financial	–	SGLT-2 inhibitors	✓
Glycaemic Status	HbA1c - 7.9 %	empaglifozin (Jardiance)	✓✓✓
Hypoglycaemia	–	Insulin	✓

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Case 5 – CKD

Age	68 year old male on Metformin
BMI	29
CKD	eGFR 52
Duration	21 years
Established CVD	NO
Financial	-
Glycaemic Status	HbA1c - 7.9 %
Hypoglycaemia	-

Sulphonylurea	✘
Thiazolidinediones	✘
Alpha-glucosidase inhibitors	✘
DPP4 inhibitors	✓ (Δ dose)
GLP-1 analogues	✓ (Δ dose)
SGLT-2 inhibitors	+/-
Insulin	✓

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Case 6 – Severe hypoglycaemia

Age	68 year old male on Metformin
BMI	29
CKD	eGFR > 60
Duration	21 years
Established CVD	NO
Financial	-
Glycaemic Status	HbA1c - 7.9 %
Hypoglycaemia	YES

Sulphonylurea	✘
Thiazolidinediones	✘
Alpha-glucosidase inhibitors	✘
DPP4 inhibitors	✓
GLP-1 analogues	✓
SGLT-2 inhibitors	✓
Insulin	+/-

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Case 7 – Terminal breast cancer

Age	78 year old female on Metformin
BMI	29
CKD	eGFR > 60
Duration	31 years
Established CVD	NO
Financial	-
Glycaemic Status	HbA1c - 7.9 %
Hypoglycaemia	-

Sulphonylurea	✘
Thiazolidinediones	✘
Alpha-glucosidase inhibitors	✘
DPP4 inhibitors	✓
GLP-1 analogues	✓
SGLT-2 inhibitors	✓
Insulin	✘

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Take Home Messages:

- **Selecting anti diabetic medication is based on:**
 - Individualized therapeutic targets
 - Achieve HbA1c target minimizing side effects, especially hypoglycaemia
 - Individual medication risk benefit analysis
 - Patient preference
 - Comorbidities and complications
 - Drug characteristics

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Take Home Messages 2:

- **Selecting anti diabetic medication – ABCD (EFGH) Approach**
 - Age
 - BMI
 - CKD
 - Duration of Diabetes
 - Established CVD
 - Financial Considerations
 - Glycaemic Status
 - Hypoglycaemia concern

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Thank You

- **Any Questions:**



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