Masterclass 4
Insulin dilemmas

Primary Care Diabetes Society 2023

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South Eastern Health and Social Care Trust

South Eastern Health and Social Care Trust

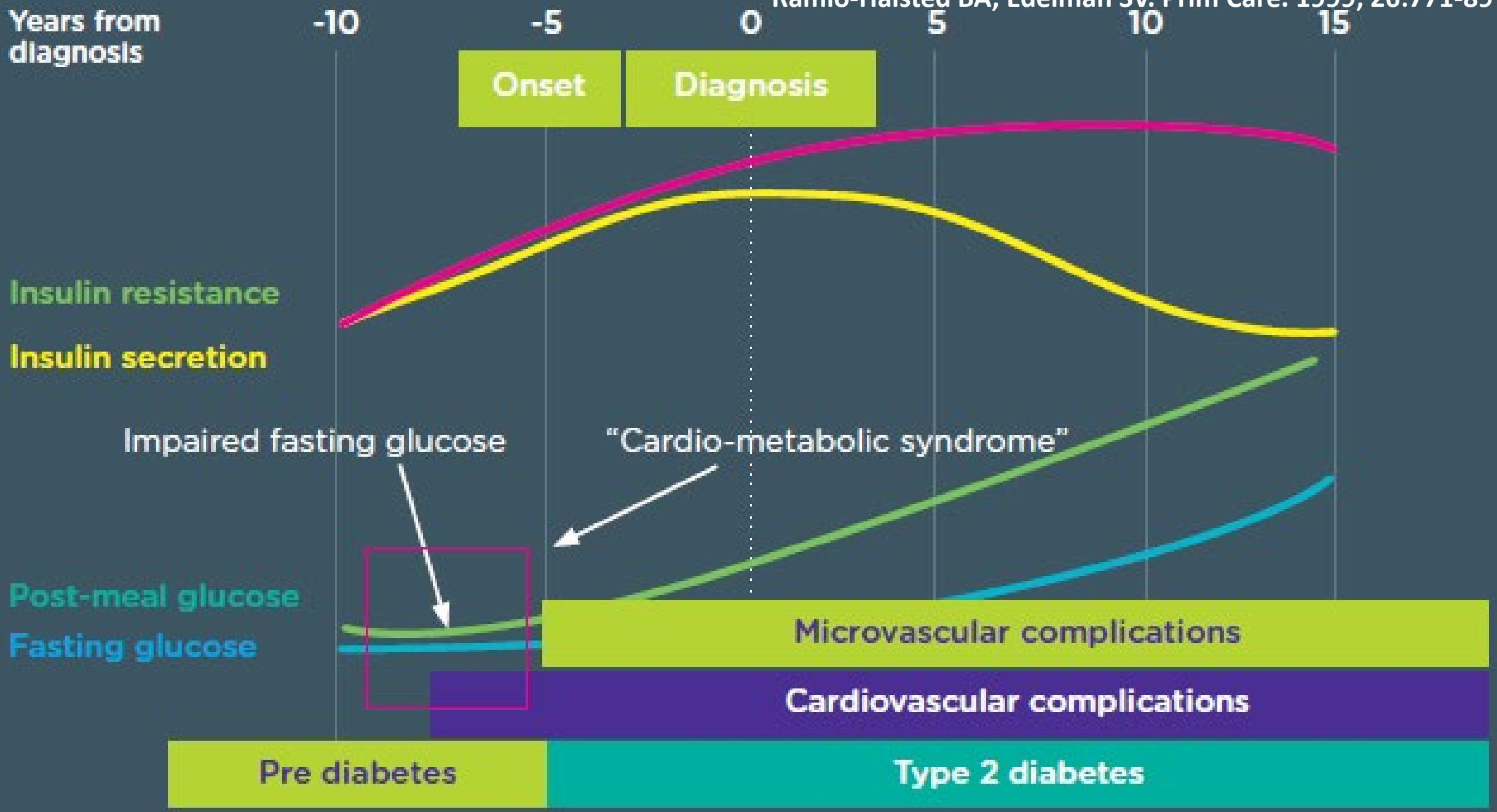
PCDS Primary Care Diabetes Society

Disclosures

I have no disclosures to declare

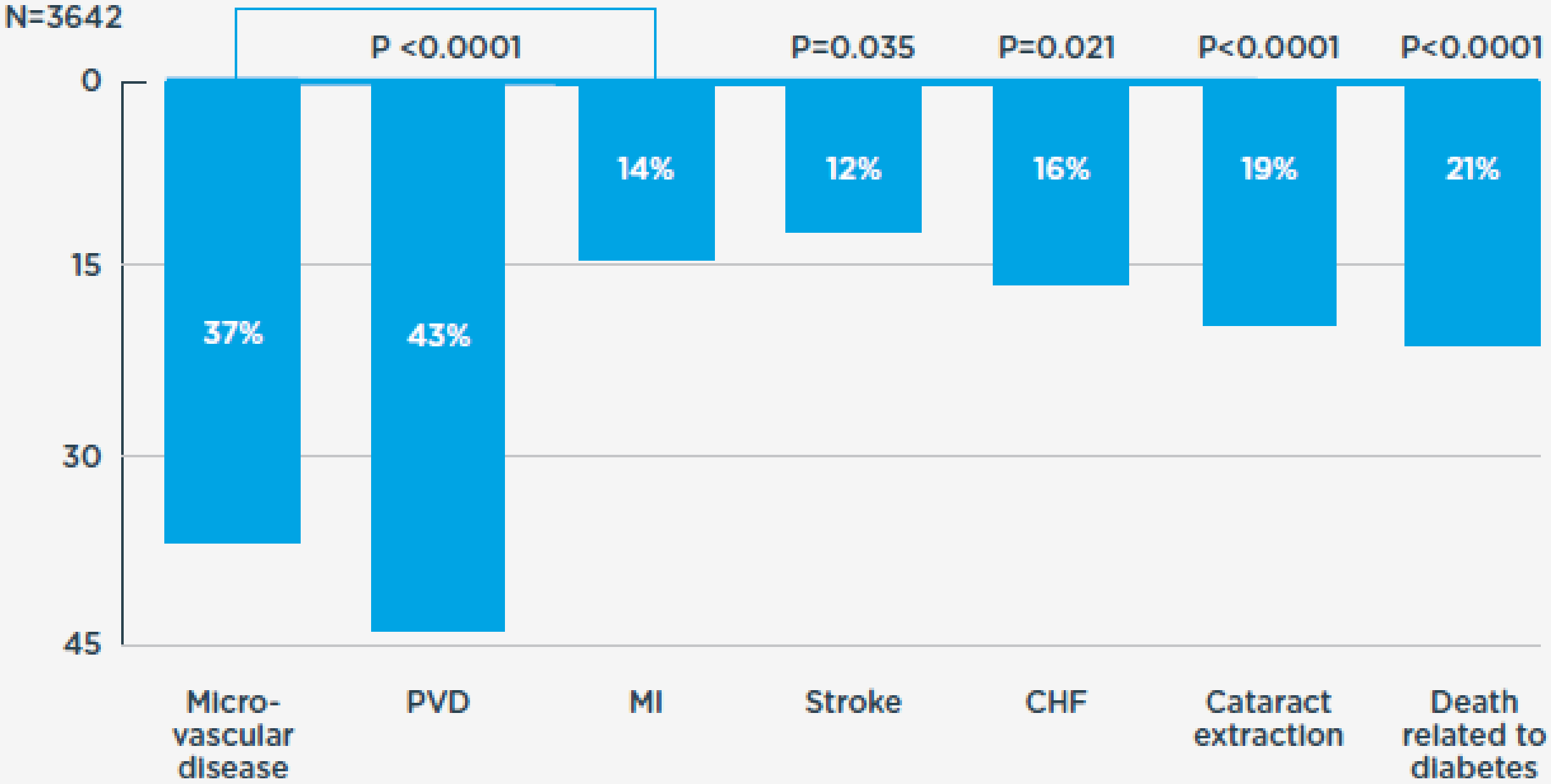
Introduction

Ramlo-Halsted BA, Edelman SV. Prim Care. 1999; 26:771-89



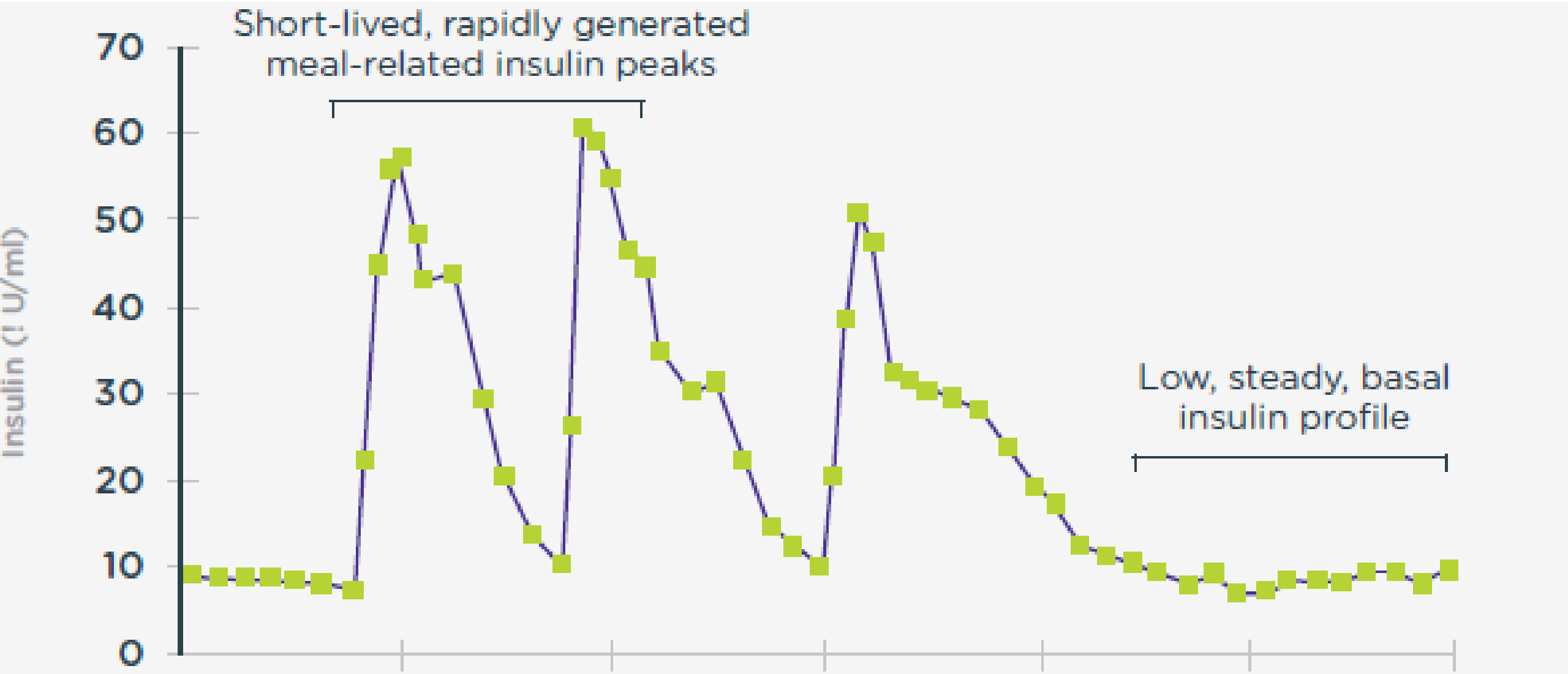
UKPDS 35: Significant risk reduction for T2DM complications with each 1% reduction in mean HbA_{1c}

Stratton IM, et al. BMJ 2000:321:405-412



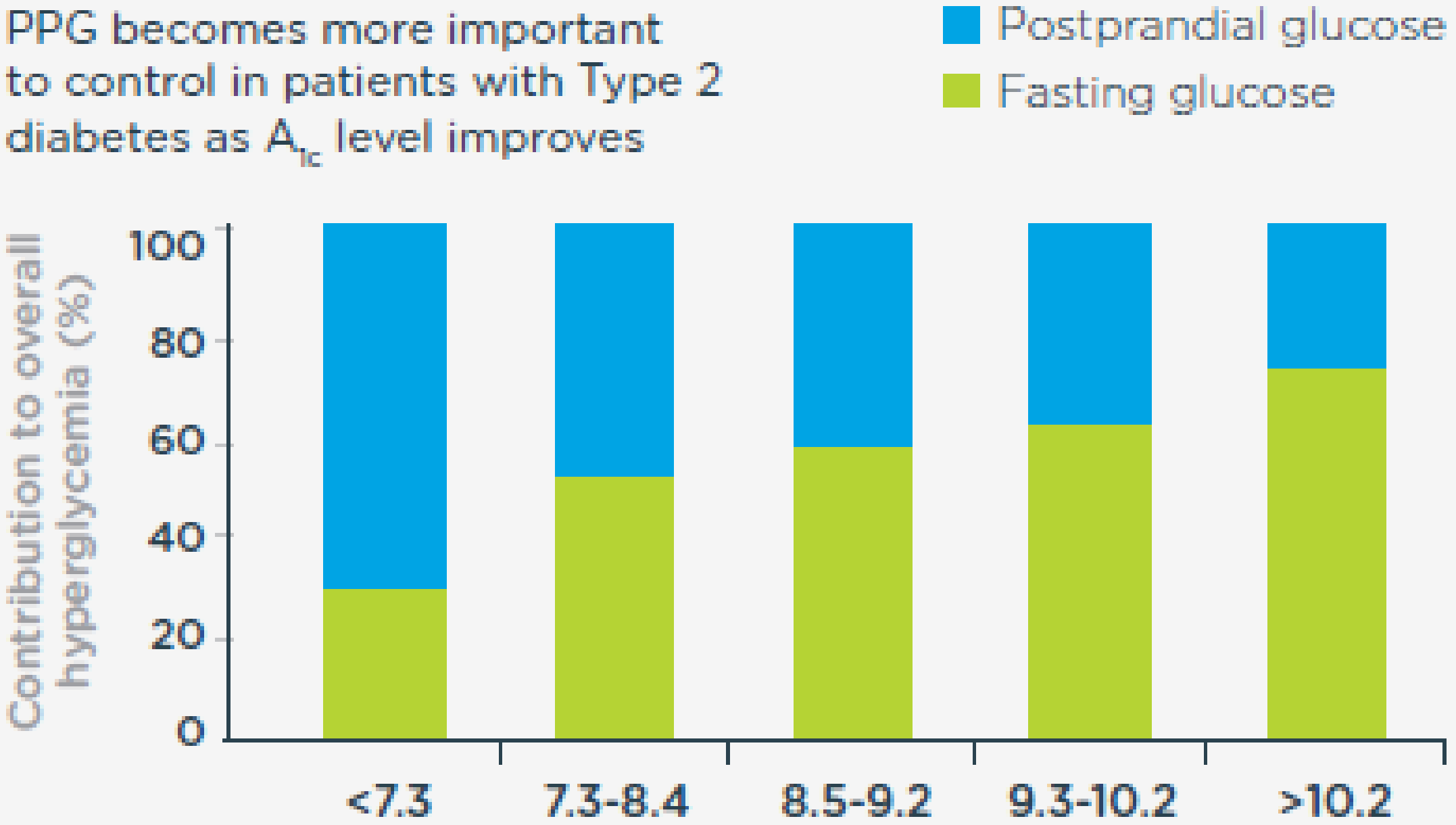
Normal insulin secretion

Polonsky KS et al. J Clin Invest. 1988;81:442-8



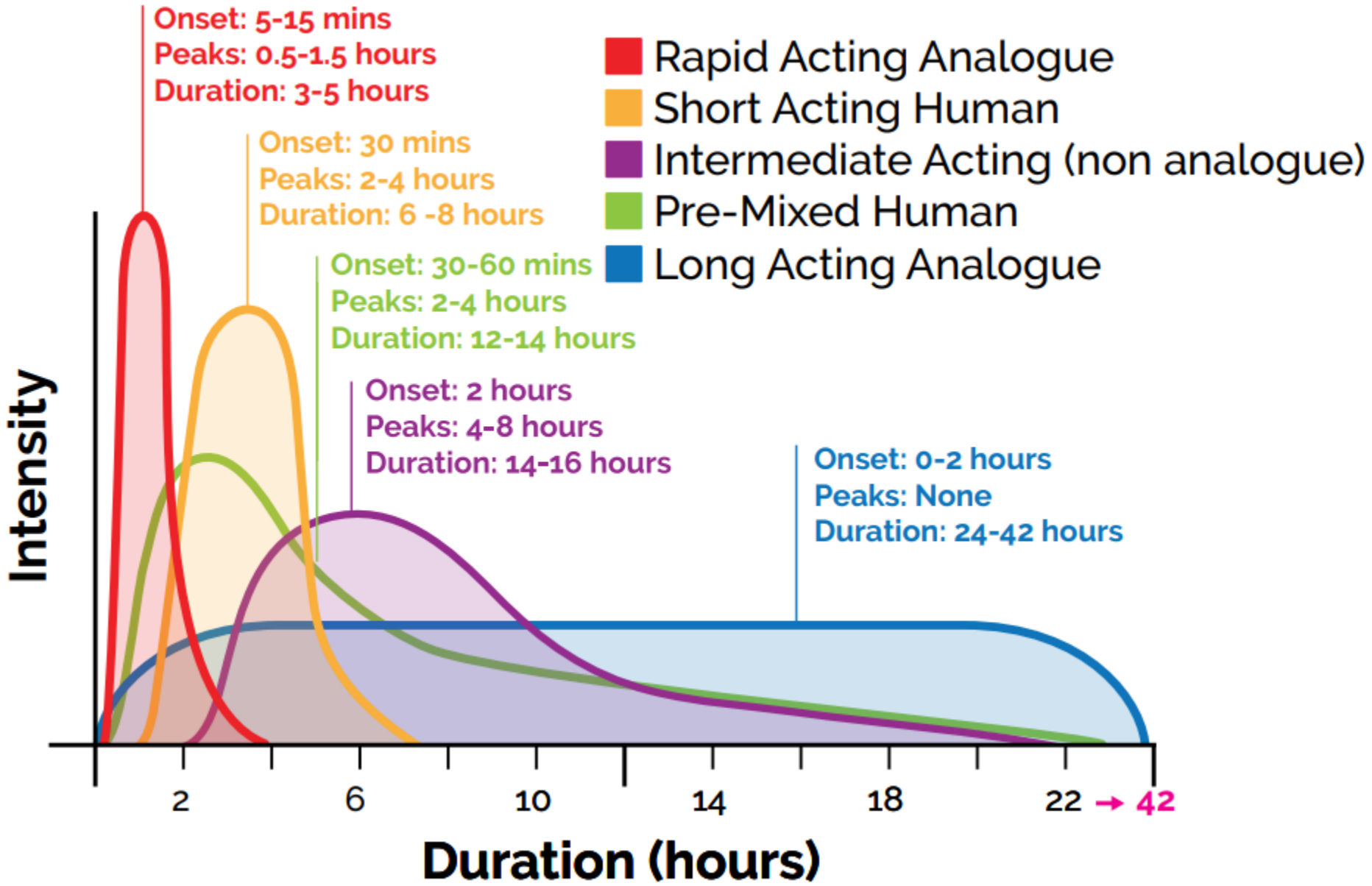
Contribution of postprandial glucose is greater as A_{1c} level improves

PPG becomes more important to control in patients with Type 2 diabetes as A_{1c} level improves



Challenges

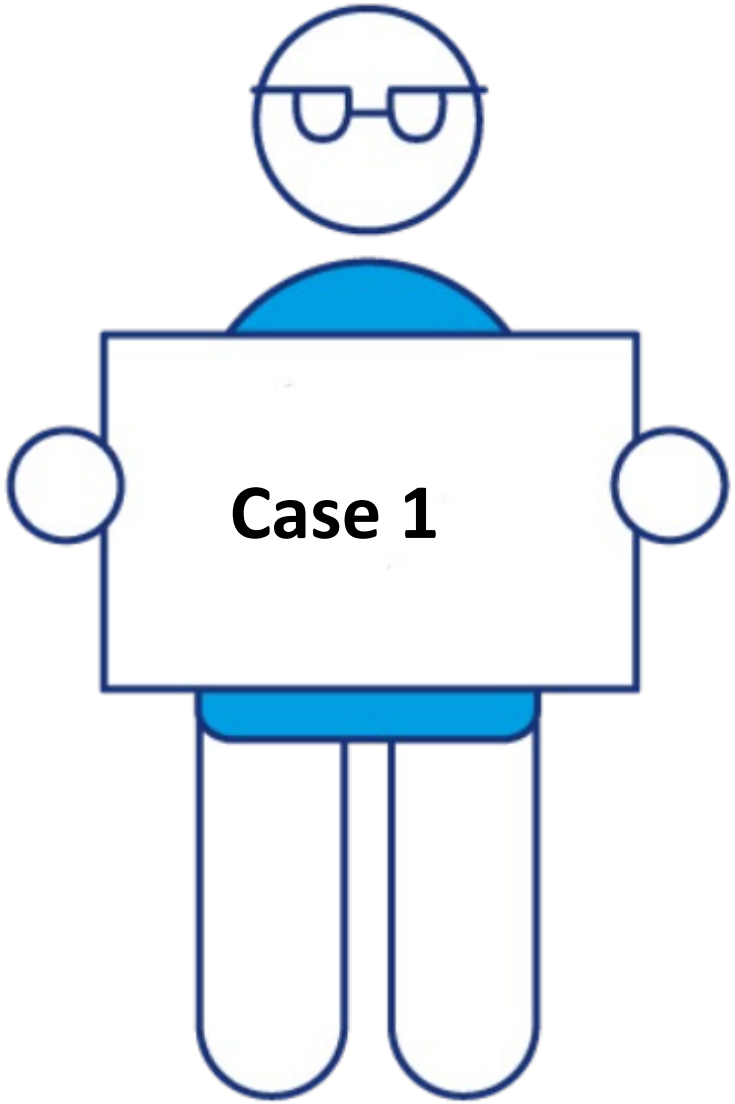

Poor understanding of the benefits of treatment
Worry over impact on lifestyle, ability to drive or employment restrictions.
Concern about associated weight gain
Inconvenience, social embarrassment and impact on quality of life.
Regarded as a sign of personal failure (insulin may have been used as a punishment for poor control)
Influence of external factors (internet, negative or inaccurate media coverage, family & friends experiences).
Fear of hypoglycaemia
Anxiety about injecting and fear of needles
INSULIN


Onset: 5-15 mins
Peaks: 0.5-1.5 hours
Duration: 3-5 hours
Onset: 30 mins
Peaks: 2-4 hours
Duration: 6 -8 hours
Onset: 30-60 mins
Peaks: 2-4 hours
Duration: 12-14 hours
Onset: 2 hours
Peaks: 4-8 hours
Duration: 14-16 hours
Onset: 0-2 hours
Peaks: None
Duration: 24-42 hours
Rapid Acting Analogue
Short Acting Human
Intermediate Acting (non analogue)
Pre-Mixed Human
Long Acting Analogue
Intensity
2
6
10
14
18
22 → 42
Duration (hours)

AIMS

How to manage insulin

1. For steroid induced hyperglycaemia
2. For rescue therapy
3. In palliative care
4. When starting on other drugs



IMAGES FROM DIABETES UK

80 YO

Referred by GI Hub (weight loss)

“ but since May (commencing on steroids and supplement drinks) he has been consistently running high”

Known IBD

Type 2 - 14 years

Canagliflozin 100mg

Gliclazide MR 120mg

Budesonide 6mg

Hba1c 70mmol/mol

POC GLU 13.9mmol/L

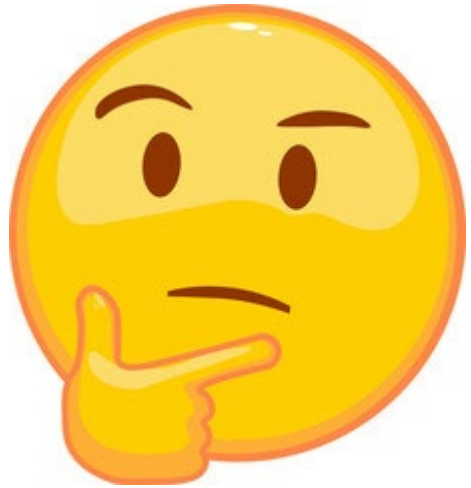
POC KET 0.2

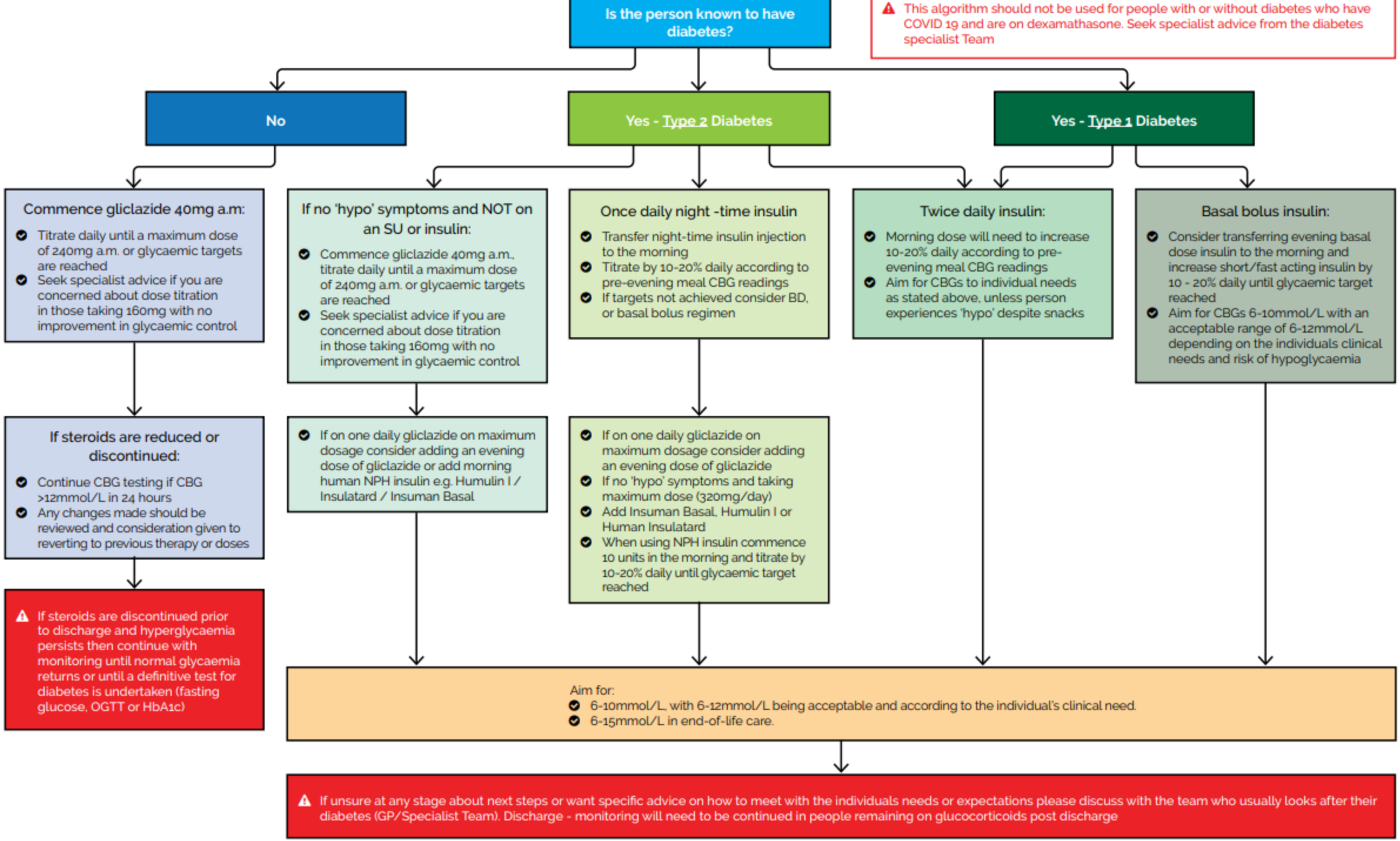
Steroid	Potency (equivalent doses)	Duration of action (half-life, in hours)
Hydrocortisone	20 mg	8
Prednisolone	5 mg	16-36
Methylprednisolone	4 mg	18-40
Dexamethasone	0.75 mg	36.54
Betamethasone	0.75 mg	26-54

N.B. Potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect

Budesonide 1.5mg = Prednisolone 5mg

INSULIN DILEMMA




Is the person known to have diabetes?
This algorithm should not be used for people with or without diabetes who have COVID 19 and are on dexamathasone. Seek specialist advice from the diabetes specialist Team
No
Yes - Type 2 Diabetes
Yes - Type 1 Diabetes
Commence gliclazide 40mg a.m:
Titrate daily until a maximum dose of 240mg a.m. or glycaemic targets are reached
Seek specialist advice if you are concerned about dose titration in those taking 160mg with no improvement in glycaemic control
If no 'hypo' symptoms and NOT on an SU or insulin:
Commence gliclazide 40mg a.m., titrate daily until a maximum dose of 240mg a.m. or glycaemic targets are reached
Seek specialist advice if you are concerned about dose titration in those taking 160mg with no improvement in glycaemic control
Once daily night -time insulin
Transfer night-time insulin injection to the morning
Titrate by 10-20% daily according to pre-evening meal CBG readings
If targets not achieved consider BD, or basal bolus regimen
Twice daily insulin:
Morning dose will need to increase 10-20% daily according to pre-evening meal CBG readings
Aim for CBGs to individual needs as stated above, unless person experiences 'hypo' despite snacks
Basal bolus insulin:
Consider transferring evening basal dose insulin to the morning and increase short/fast acting insulin by 10 - 20% daily until glycaemic target reached
Aim for CBGs 6-10mmol/L with an acceptable range of 6-12mmol/L depending on the individuals clinical needs and risk of hypoglycaemia
If steroids are reduced or discontinued:
Continue CBG testing if CBG >12mmol/L in 24 hours
Any changes made should be reviewed and consideration given to reverting to previous therapy or doses
If on one daily gliclazide on maximum dosage consider adding an evening dose of gliclazide or add morning human NPH insulin e.g. Humulin I / Insulatard / Insuman Basal
If on one daily gliclazide on maximum dosage consider adding an evening dose of gliclazide
If no 'hypo' symptoms and taking maximum dose (320mg/day)
Add Insuman Basal, Humulin I or Human Insulatard
When using NPH insulin commence 10 units in the morning and titrate by 10-20% daily until glycaemic target reached
If steroids are discontinued prior to discharge and hyperglycaemia persists then continue with monitoring until normal glycaemia returns or until a definitive test for diabetes is undertaken (fasting glucose, OGTT or HbA1c)
Aim for:
6-10mmol/L, with 6-12mmol/L being acceptable and according to the individual's clinical need.
6-15mmol/L in end-of-life care.
If unsure at any stage about next steps or want specific advice on how to meet with the individuals needs or expectations please discuss with the team who usually looks after their diabetes (GP/Specialist Team). Discharge - monitoring will need to be continued in people remaining on glucocorticoids post discharge

azide 40mg a.m:

a maximum dose
glycaemic targets

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dose titration
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lycaemic control

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Once daily night -time insulin

- Transfer night-time insulin injection to the morning
- Titrate by 10-20% daily according to pre-evening meal CBG readings
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Twice daily in

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as stated above, unle
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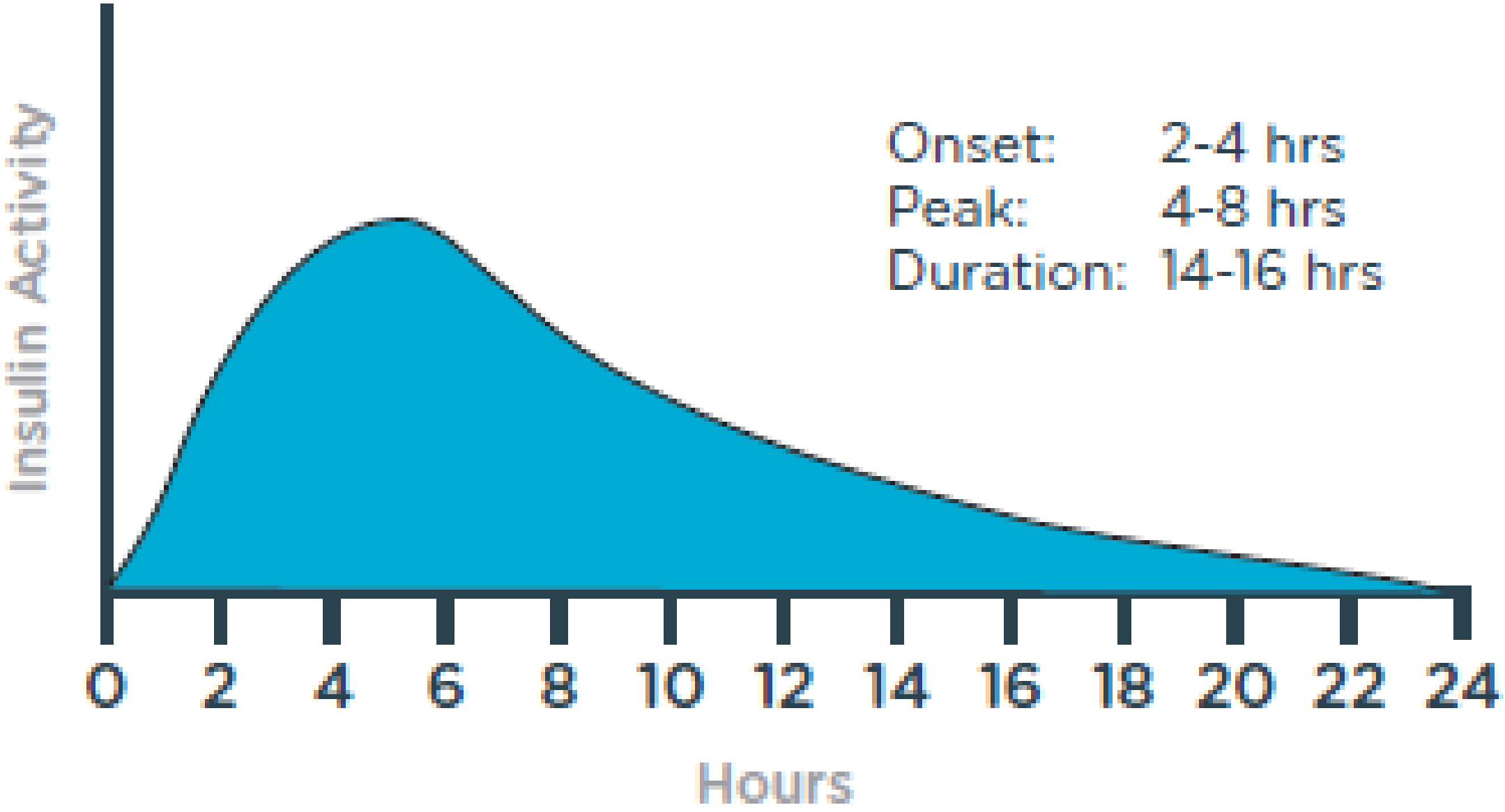
NPH basal insulin (intermediate acting insulin)



ALORGITHM FOR THE MANAGEMENT OF GLUCOSE CONTROL IN PEOPLE WITH KNOWN DIABETES ON ONCE DAILY STEROIDS (GLUCOCORTICOIDS)

KNOWN DIABETES, reassess glucose control and current therapy

- Set target blood glucose e.g. 6-10mmol/L (see glycaemic targets box below)
- Check capillary blood glucose (CBG) 4 times a day and use this flowchart to adjust diabetes medication accordingly
- In Type 1 diabetes also check for ketones if CBG >12mmol/L

Type 2 diet control
OHA +/- GLP1

If no 'hypo' symptoms and NOT on an SU

- Commence Gliclazide 40mg a.m., titrate daily until a maximum dose of 240mg a.m. or glycaemic targets are reached
- Seek specialist advice if you are concerned about dose titration in those taking 160mg with no improvement in glycaemic control
- If on twice daily gliclazide and targets not reached consider referral to specialist care for titration to 240mg morning dose plus 80mg p.m.

- If no Hypo Symptoms and taking maximum dose (320mg/day)
- Add Novomix 30 or Humalog Mix 25 - 10 units at breakfast. Isophane insulin may be used as an alternative, particularly for patients with poor oral intake
- Consider additional insulin at lunch if pre-tea and bedtime CBG's >10mmol/L and titrate

- If CBG remains above desired target before the evening meal
- Increase insulin by 4 units or 10-20%
- Review daily
- If remains above target titrate daily by 10-20% until glycaemic target reached

Insulin controlled (Type1 and Type2)
In Type 1 diabetes always test for ketones. If blood ketones more than 3mmol/L or urinary ketones >++ assess for DKA
In Type 2 Diabetes check for ketones if CBG levels >12mmol/L and the patient has osmotic symptoms

Once daily
Night time insulin - transfer this injection to the morning:

- Titrate 10-20% daily according to pre-evening meal CBG readings
- If targets not achieved consider BD, or basal bolus regimen

Twice daily insulin:

- Morning dose will need to increase 10-20% daily according to pre-evening meal CBG readings
- Aim for CBGs to individual needs as stated above, unless patient experiences 'hypo' despite snacks

Basal bolus insulin:

- Consider transferring evening basal dose insulin to the morning and increase short/fast acting insulin by 10-20% daily until glycaemic target reached
- Aim for agreed CBGs target to patients needs pre-meal unless patient has hypo despite snacks or has long gaps between meals

If steroids are reduced or discontinued

- Blood glucose monitoring may need to be continued in inpatients and, in discharged patients assessed by their GP
- Any changes made should be reviewed and consideration given to reverting to previous therapy or doses

If unsure at any stage about next steps or want specific advice on how to meet with patients' needs or expectations please discuss with the team who usually looks after their diabetes (GP/specialist team)

Glycaemic targets

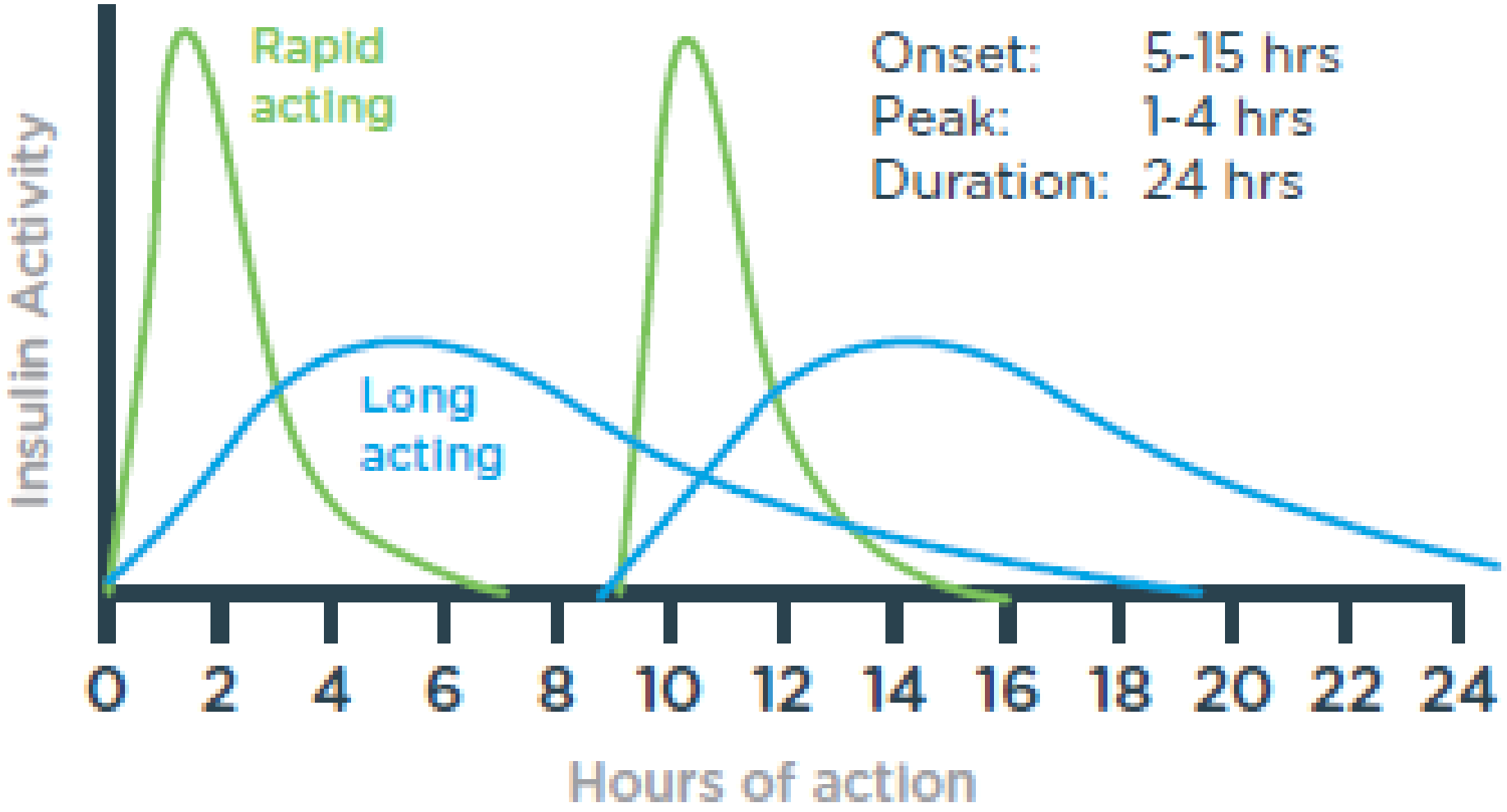
- Aim for 6-10mmol/L (acceptable range 4-12mmol/L)
- **End of life care:** Aim for 6-15mmol/L and symptom relief

FOR DEXAMETHASONE THERAPY IN COVID-19 SEE SEPARATE CONCISE GUIDELINES

STEROID HYPERGLYCAEMIA (SEE SEPARATE GUIDELINE FOR DEXAMETHASONE)

- If no Hypo Symptoms and taking maximum dose (320mg/day)
- Add Novomix 30 or Humalog Mix 25 - 10 units at breakfast. Isophane insulin may be used as an alternative, particularly for patients with poor oral intake
- Consider additional insulin at lunch if pre-tea and bedtime CBG's >10mmol/L and titrate

Pre-mixed Analogues – NovoMix® 30[64], Humalog® Mix25[65], Humalog® Mix50[65]



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POC GLU 13.9mmol/L

POC KET 0.2

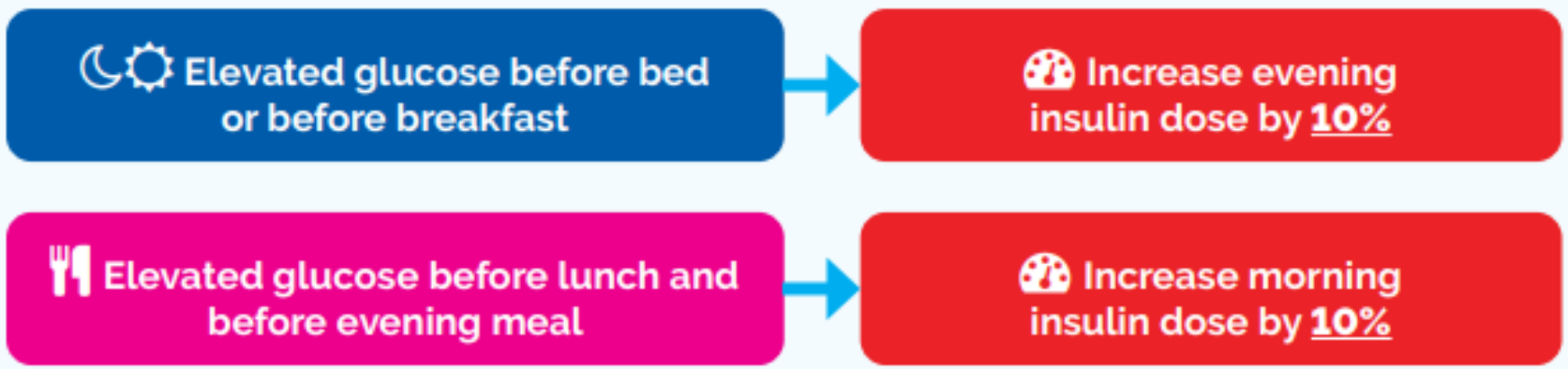
- ❑ Meter /lancet
- ❑ Targets
- ❑ Frequency of testing
- ❑ Glucose diary
- ❑ Insulin profile
- ❑ Insulin storage
- ❑ Demo on insulin administration
- ❑ Injection sites and safe disposal
- ❑ Hypos
- ❑ Driving
- ❑ Duration of steroids

Progress

- Commenced on Humalog mix 25
  - 0.15 - 0.3units/kg
- Titration to 35units OD
  - 30th - 9.5/9.6/4.6/10.1
  - 1st - 8.2/11.9/12.9/13.3
  - 2rd - 6.8/10.9/14.8/11.9
  - 3rd - 9.4

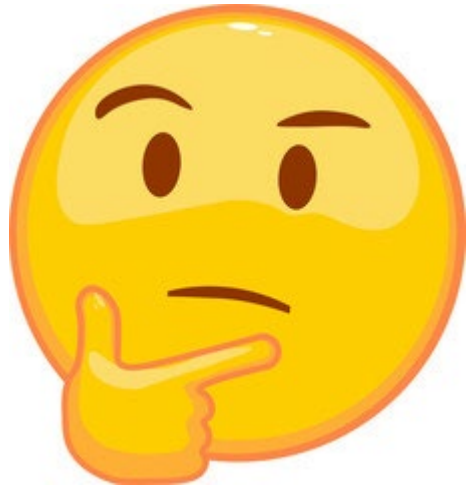
Adjusting **Twice daily** insulin (pre-mixed or intermediate)

These are general rules: always consult product-specific guidelines



For pre-mixed insulin, need to check not hypo at lunch and pre-bed before increasing doses

INSULIN DILEMMA



Progress

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Methylprednisolone	4 mg	18-40
Dexamethasone	0.75 mg	36.54
Betamethasone	0.75 mg	26-54

N.B. Potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect

4/07/2023

- **Reduction of Budesonide to 3mg**
- **Down titration of insulin by 20%**

15/08/23

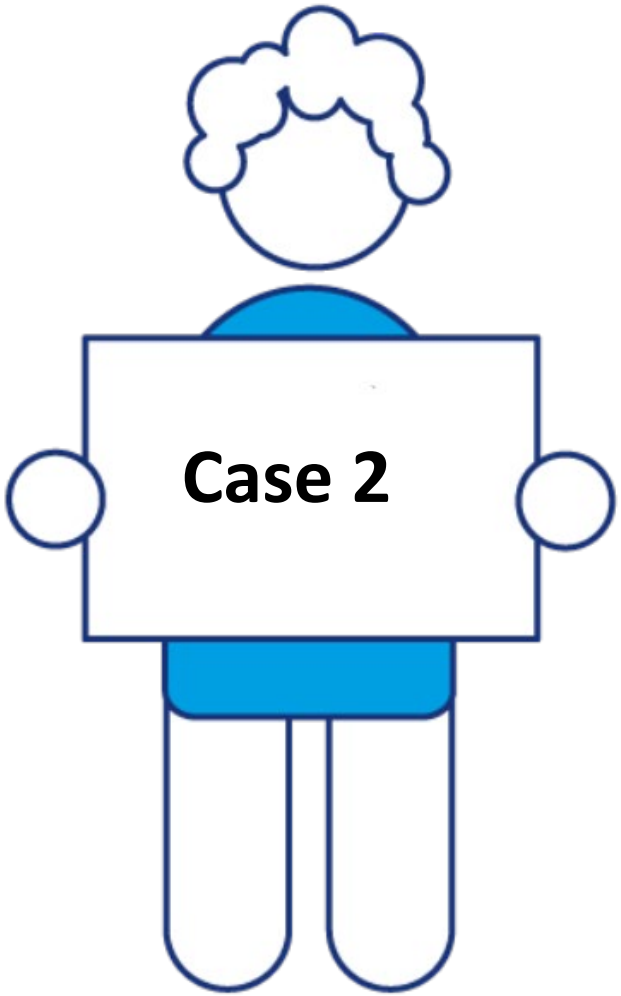
- **Addition of an evening dose of insulin**

23/08/023

- **Stop Budesonide 3mg**
- **Reduction of insulin by 20%**

4/10/23

- **Chemotherapy /Dexamethasone**
- **+50% evening dose**
- **+40% morning dose**



IMAGES FROM DIABETES UK

70 Y.O
GP call “high plasma glucose 37.3mmol/L”
Symptomatic – 2.5L PD/ nocturiax5
Type 2 – 18 years
Metformin and Alogliptin
No SMBG
Weight loss of 20% over 7months
BMI 29

POC GLU 15 - >20
HbA1c 107mmol/mol
Ketones 0.8

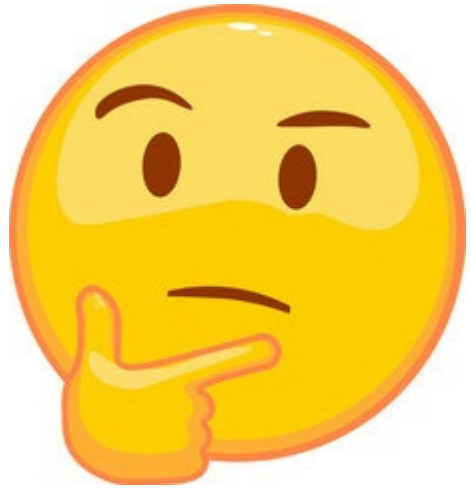
- ❑ SMBG
- ❑ Frequency of testing
- ❑ Safe disposal of sharps
- ❑ Dietary education low GI/portions

Ketones

Less than 0.6 mmol/L	• Normal - check again in 2 hours
0.6 to 1.5 mmol/L	• Risk of developing DKA. • Correct glucose levels (follow advice on insulin adjustment pages 9 and 10), increase fluid intake and retest in 2 hours
1.6 to 2.9 mmol/L	• High risk of developing DKA. • Increase in insulin / or correction dose is required (follow advice on insulin adjustment pages 9 and 10), increase fluid intake and retest in 2 hours
3 mmol/L or higher	• Very high risk of DKA. • Needs urgent medical attention and may need admission to Accident and Emergency department

(Gilles G, 2019)

INSULIN DILEMMA



NICE

"If an adult with type 2 diabetes is symptomatically hyperglycaemic, consider insulin or a sulfonylurea, and review treatment when blood glucose control is achieved"

Progress

- **0.1-0.2units/kg/day (some may need 0.3-0.4units/kg/day)**
- **10units(Davies et al. 2018)**

10 Jan

- HbA1c 107
- Stat of rapid acting insulin
- Commenced on gliclazide

13 Jan

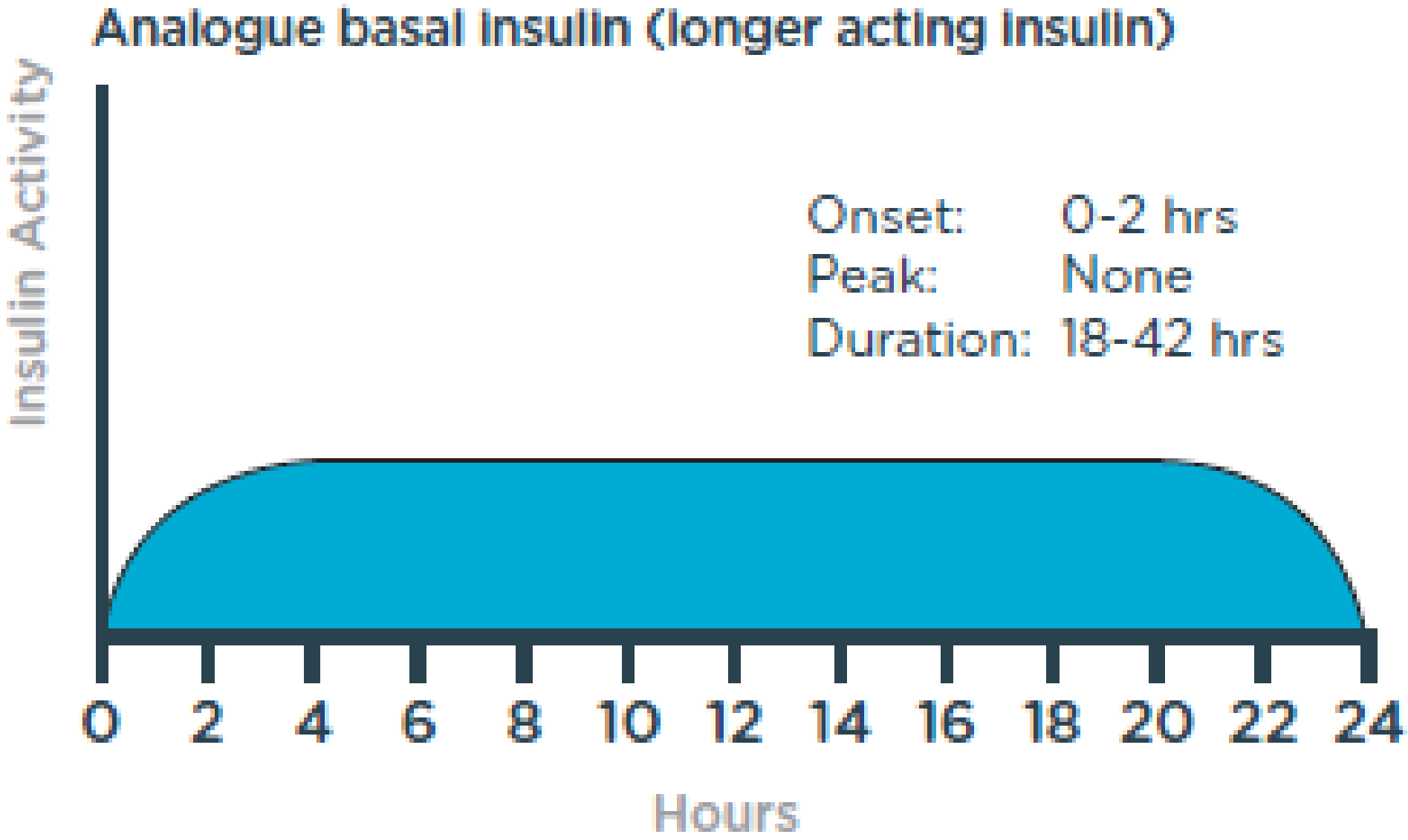
- CBG 27.8
- Attended hub for further stat of rapid acting insulin
- Increase gliclazide
- Commenced on basal insulin at lunch

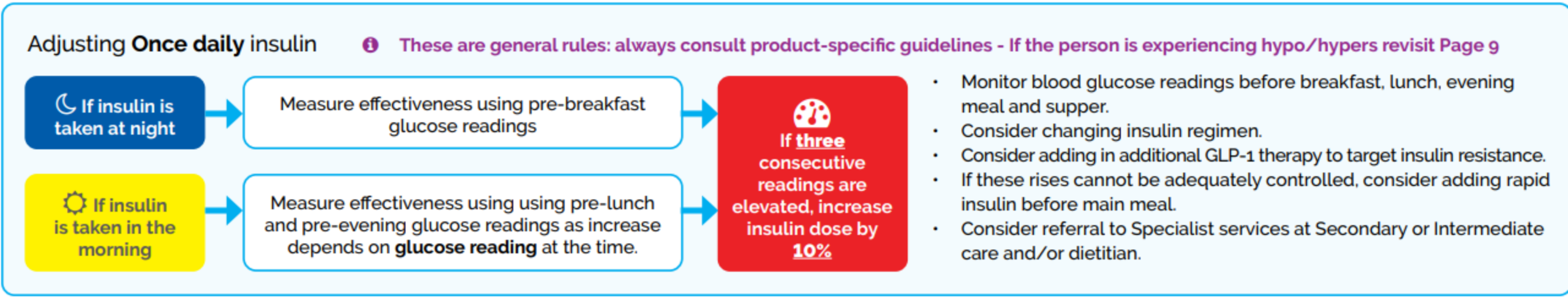
25 Jan

- CBG down to 8
- Down titration of gliclazide and insulin

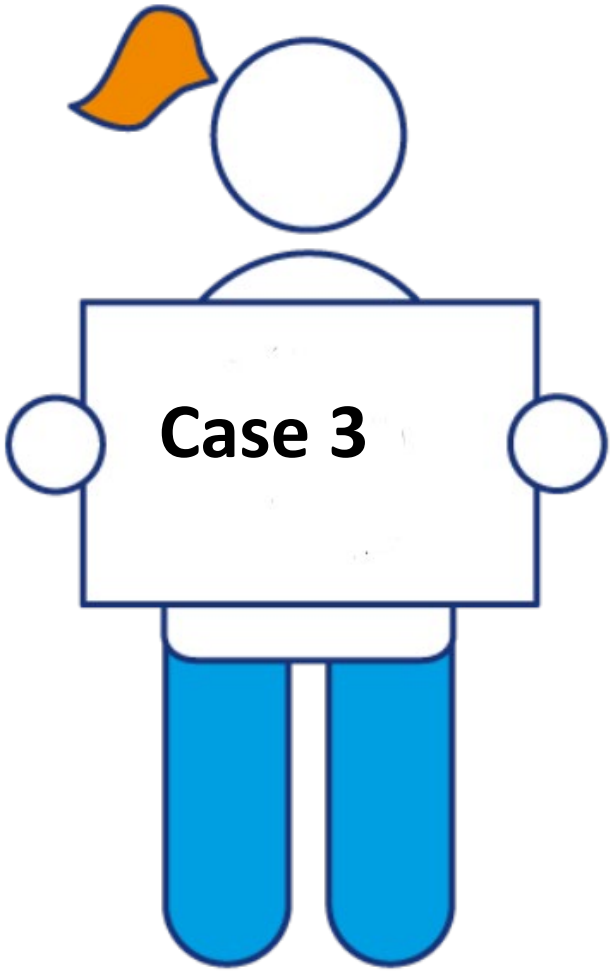
May 23

- CBG <8mmol/L on 10units basal
- Stopped the insulin and commenced on SGLT2 inhibitor
- Hba1c 45mmol/mol


Analogue basal insulin (longer acting insulin)
Insulin Activity
Onset: 0-2 hrs
Peak: None
Duration: 18-42 hrs
0 2 4 6 8 10 12 14 16 18 20 22 24
Hours



For those individuals willing and able to self-titrate an easy to follow method is to advise them to increase the dose by 2 units every 3 days where 3 consecutive fasting glucose levels are above target. (Riddle et al. 2003)



IMAGES FROM DIABETES UK

84 YO
Advance metastatic GI malignancy
Referred by Palliative care team
Type 2 diabetes 20 years
Novomix 30 insulin BD (TDD= 30units)

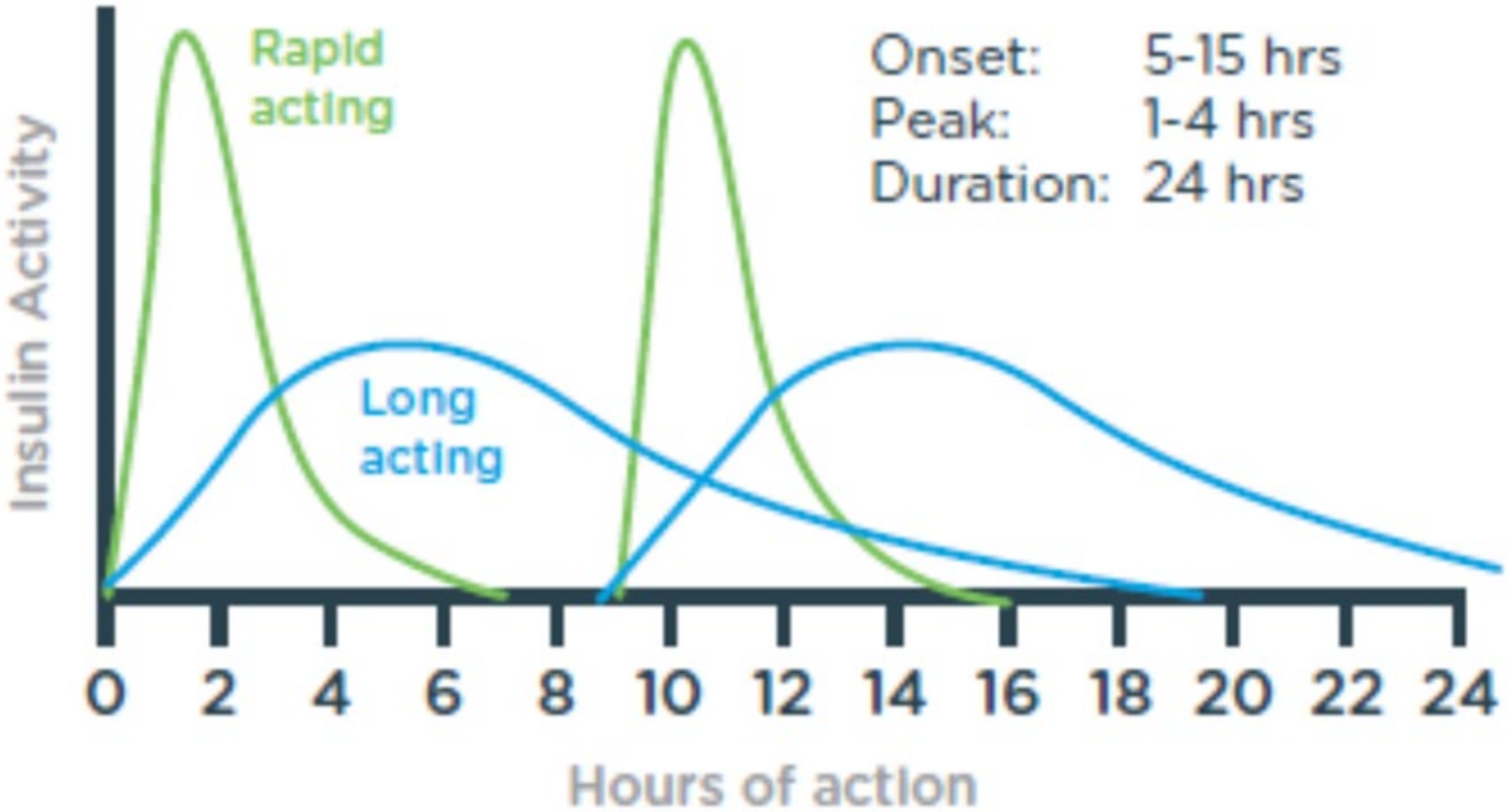
Administered by District Nurse team

Nutritional intake poor

POC GLU 6.8 - 14mmol/L
HbA1c 64mmol/mol

- ❑ Testing/Glucose checks
- ❑ Intake
- ❑ Hypoglycaemia awareness
- ❑ Insulin administration

Pre-mixed Analogues – NovoMix® 30[64], Humalog® Mix25[65], Humalog® Mix50[65]



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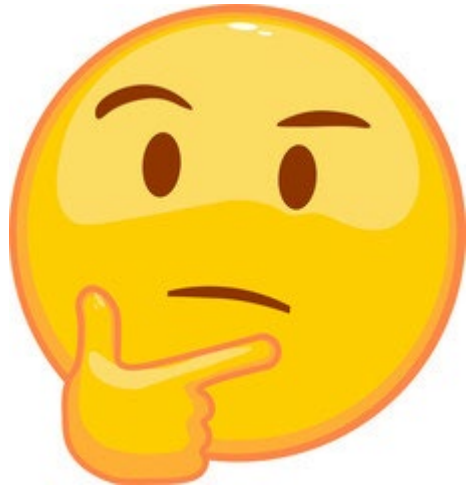

Targets

- **Glucose**
  - no glucose level less than 6 mmol/L
  - no glucose level higher than 15mmol/L

- **Hba1c**
  - Target 53-64mmol/mol
  - up to 70mmol/mol may be appropriate in those who are frail or have dementia

- **End of life**
  - target to avoid symptomatic hyperglycaemia

Adapted Algorithm for the Management of diabetes during the last days of life

Discuss changing the approach to diabetes management with individual and/or family if not already explored. If the person remains on insulin, ensure the Diabetes Specialist Team (e.g. DSN or GP) are involved and agree monitoring strategy

Type 2 diabetes
Diet controlled or Metformin only treatment

Stop metformin
Stop monitoring blood glucose

Type 2 diabetes
On other tablets and/or insulin/or GLP1 RA*

Stop tablets and GLP1 injections
Consider stopping insulin if the individual only requires a small dose (e.g. < 10 units or <0.1units/kg) and the blood glucose readings are less than 10mmol/L.

If insulin stopped:

- If blood glucose over 20mmol/L give 6 units rapid acting insulin such as Novorapid®; Humalog® or Apidra®
- Re-check capillary blood glucose after 2 – 4 hours

If patient requires rapid-acting insulin more than twice on consecutive days

- Consider daily Insulatard® or Humulin I® or an analogue such as Abasaglar®, Lantus® or Levemir®
- Suggested recommended starting dose is 10 units or 0.1units/kg

If insulin to continue:

- Prescribe once daily morning dose of Insulatard®, Humulin I® or analogue Abasaglar®, Lantus®, Levemir®, Tresiba® or Toujeo® based on 25% less than total previous daily long acting insulin dose

Type 1 diabetes

Continue once daily morning dose of insulin Abasaglar®/lantus®/Levemir®/ Tresiba®/Toujeo®
Based on 25% less than total previous daily long acting insulin dose

Check blood glucose once a day at teatime:

- If below 8mmol/L reduce insulin by 10-20%
- If above 20mmol/L increase insulin by 10-20% to reduce risk of symptoms or ketosis

Key:

* Victoza®(liraglutide); Lyxumia® (Lixisenatide), Byetta®(exenatide), Bydureon® (exenatide), Trulicity® (Dulaglutide), Ozempic® (semaglutide)

Note: Xultophy® (iDegLira), Sulqua® (iGlarLixi) – continue as long acting insulin only

Important information

- Aim for capillary blood glucose readings of 6 – 15mmol/L
- Keep tests to a minimum. It may be necessary to perform some tests to ensure unpleasant symptoms do not occur due to low or high glucose.
- It is difficult to identify symptoms due to “hypo” or hyperglycaemia in a dying person.
- If symptoms are observed it could be due to abnormal blood glucose levels
- Test urine or blood for glucose if the person is symptomatic
- Observe for symptoms in previously insulin treated individual where insulin has been discontinued.
- Flash glucose monitoring may be useful in those individual with type 1 diabetes to avoid finger testing

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Type 2 diabetes

On other tablets and/or insulin/or GLP1 RA*

Type 1 diabetes

Stop tablets and GLP1 injections

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Abasaglar®/lantus®/Levemi
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Based on 25% less than total previ
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Check blood glucose once a day at

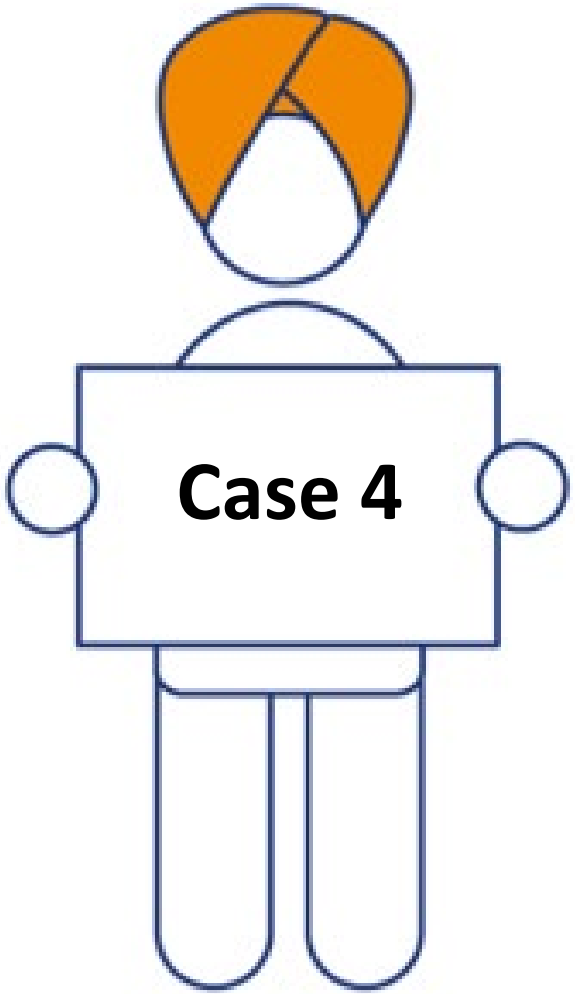
- If below 8mmol/L reduce insul 20%
- If above 20mmol/L increase in 10-20% to reduce risk of symp

Insulin

- Moving from twice daily to once daily

Should be less than the total dose of twice daily pre mixed insulin

75% of total previous dose recommended



IMAGES FROM DIABETES UK

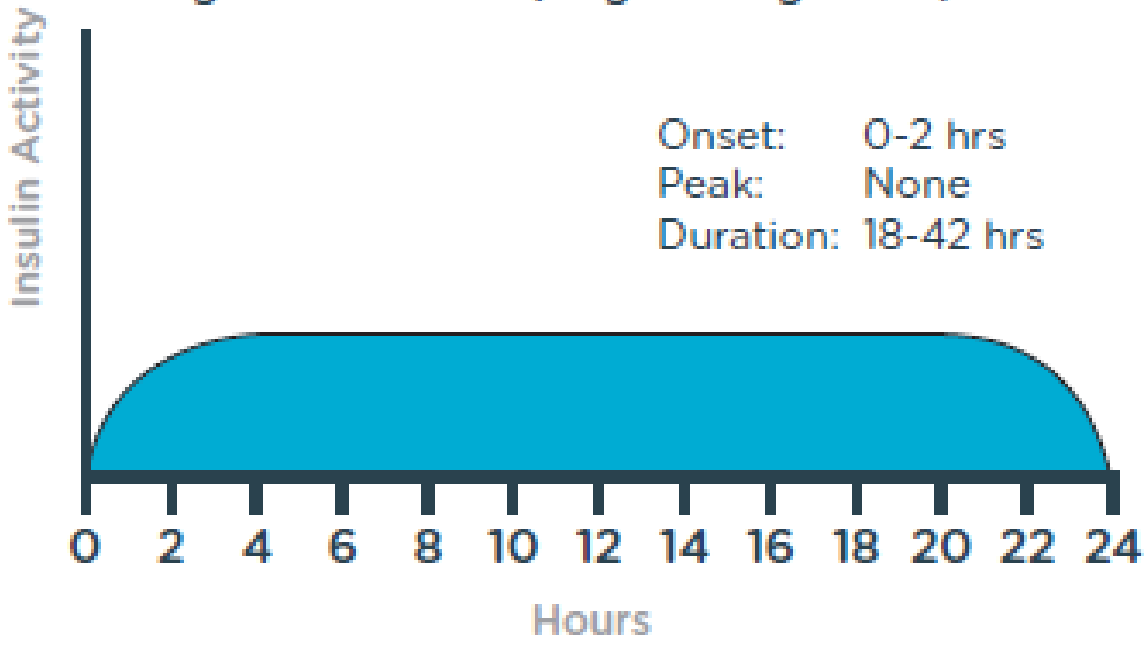
64 YO
Type 2 15 years
BMI 36
OSA, Hypertension
Metformin + SGLT2 inhibitor
Lantus 40 units Novorapid 10 units TDS

- "keen to be considered for GLP1agonist"

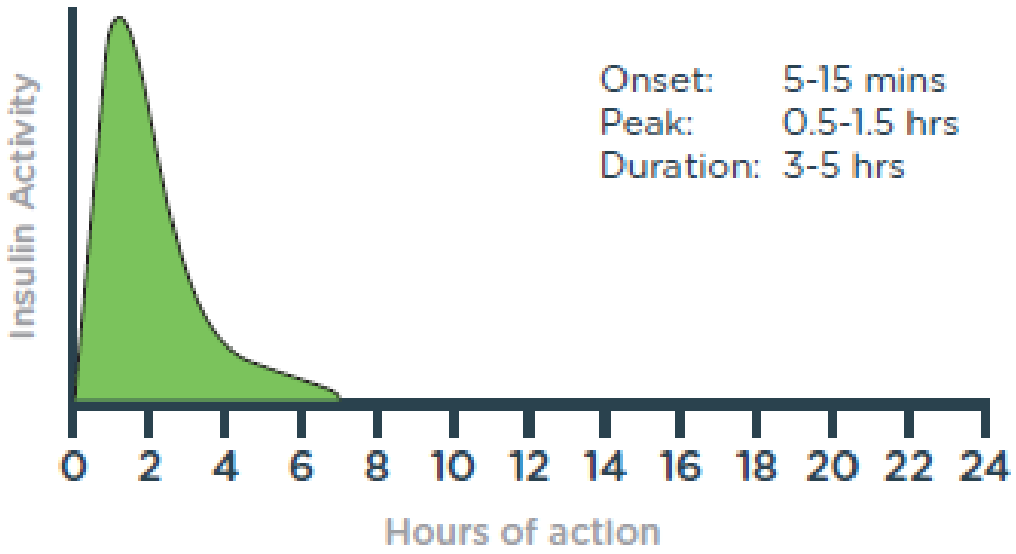
POC GLU 8 - 14mmol/L
HbA1c 64mmol/mol

- ❑ Glucose checks/monitoring
- ❑ Safe disposal of sharps
- ❑ Dietary review
- ❑ Weight targets
- ❑ Additional therapies tried

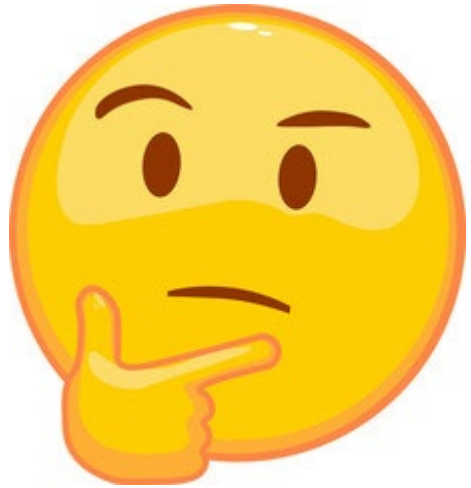
Analogue basal insulin (longer acting insulin)



Rapid Acting Insulin Action – NovoRapid®[66], Apidra®[67,68,69], Humalog®[70]



INSULIN DILEMMA



MEDICATIONS TO CONTINUE, REDUCE OR STOP WHEN INTENSIFYING TO INJECTABLES

METFORMIN (MF)

- Continue treatment with metformin

SULFONYLUREA (SU)

- If on SU, reduce dose by 50% when basal insulin initiated
- Consider stopping SU if prandial insulin initiated or on a premix regimen

THIAZOLIDINEDIONE (TZD)

- Stop TZD when commencing insulin
- **OR** reduce dose

DPP-4 INHIBITORS (DPP-4i)

- Stop DPP-4i if GLP-1 RA initiated

SGLT2 INHIBITORS (SGLT2i)

- If on SGLT2i, continue treatment
- Consider adding SGLT2i if:
  - Established CVD, HF or CKD
  - If HbA1c above target or as weight reduction aid

Beware:

- DKA (euglycaemic)
- Instruct on sick-day rules
- Do not down-titrate insulin over-aggressively

Always check individual product-specific guidelines for contraindications and advice in people with CKD

Recommendations

In people with type 2 diabetes taking insulin a dose reduction of 20% is recommended , if HbA1c < 64 mmols/mol when a GLP-1 injection is added.

For people with a HbA1c >64 mmols/mol you may still need to consider an insulin dose reduction

Summary

How to manage insulin

1. For steroid induced hyperglycaemia ✓
2. For rescue therapy ✓
3. In palliative care ✓
4. When starting on other drugs ✓