
trend UK
TRAINING, RESEARCH AND EDUCATION
FOR NURSES IN DIABETES

Steroids and Diabetes

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Leaning objectives

At the end of this session you should be able to:

- Discuss the implications of steroid use and diabetes
- Review treatments for steroid induced hyperglycaemia
- Identify use in different groups including:

- People with known diabetes
- People not known to have diabetes
- Pregnancy
- End of life care

Case study

- 62 years man. Weight 102kg, BMI 32 kg/m2
- T2DM on Metformin.
- HbA1c 55 mmol/mol
- Background:

- COPD, CVA, IHD
- Respiratory clinic'….progressive dyspnoea

Plan:

Prednisolone 30 mg for 10 days then reduced to 20 mg for one week and then to reduce to 10 mg maintenance for now.

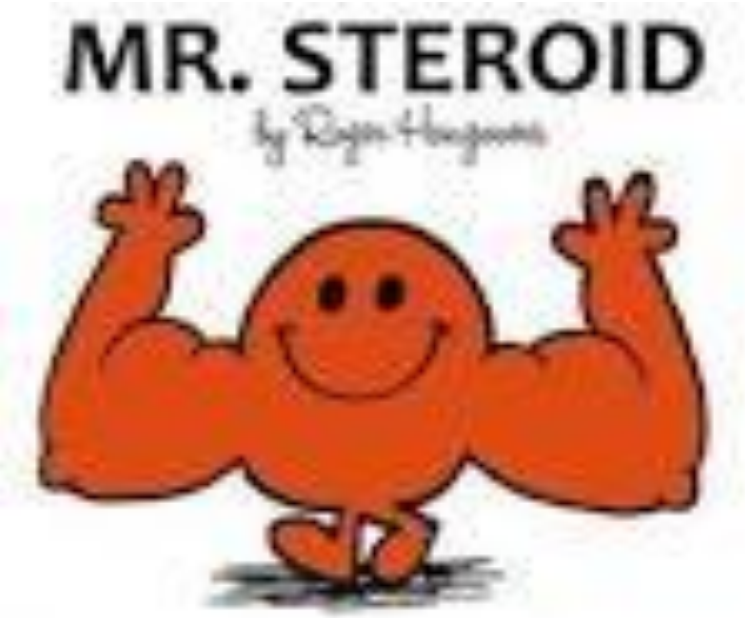
- Follow-up: 2/12

3 weeks later

- Acute admission
- Osmotic symptoms, BG 32 mmol/L
- Hba1c 112 mmol/mol
- 48 hrs in patient stay over weekend
- Gliclazide (SU) , followed by insulin
- 6 months OPD in diabetes clinic discharged OHA, HbA1c 44mmol/mol

Background

- 0.75% use steroids
- 40% for respiratory problems
- Inpatient use >10%
- Most use for <5 days, but 22% is for > 6 months and 4.3% for > 5 years



https://www.nos.org.uk/NetCommunity/Document.Doc?id=422

Fardet L et al Rheumatology 2011;50(11):1982-1990

Background

- There are no reliable estimates for prevalence of glucocorticoid use in hospital/ community
- We don't know if more people in hospital are on steroids, and if so are the doses used usually higher than those used in community?
- The prevalence of undiagnosed diabetes in hospitalised patients may be ~18%

Wexler DJ et al JCEM 2008;93(11):4238-4244

Steroid regimens

- Once a day –short course (Prednisolone 30 mg OD for 5 days)
- Multiple dose (Dexamethasone BD/TDS)
- High dose short duration (methyl prednisolone 3 days/ 5 days)
- High dose infrequent (Oncology)
- Betamethasone x 2 doses (Pregnancy)

People at risk of hyperglycaemia

- Pre-existing type 1 or type 2 diabetes
- People at increased risk of diabetes.
- Impaired glucose regulation - HbA1c 42-47mmol/mol
- People previously hyperglycaemic with steroid therapy

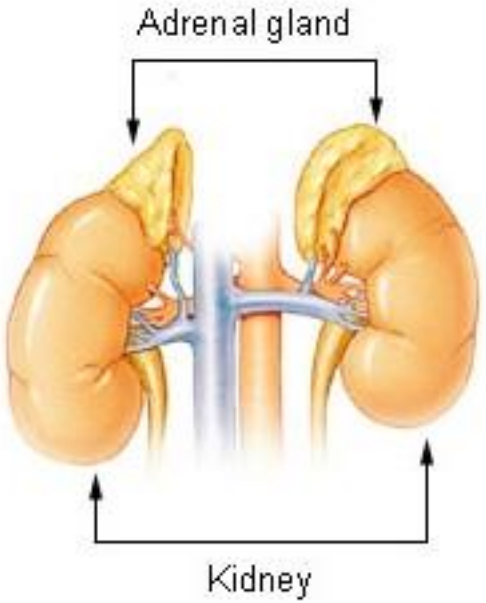
Commonly used steroids

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

Normal physiology

- The adrenal glands produce cortisol that is equivalent to about 7.5mg of prednisolone daily

- Any doses higher than this will lead to problems with carbohydrate metabolism



- Doses > 7.5mg of prednisolone for more than 2 weeks than this causes adrenal suppression
- Too rapid a withdrawal will lead to hypo –adrenalism demonstrated by:

- recurrent hypoglycaemia,
- hypotension
- hyponatraemia, hyperkalaemia

How do “steroids” work?

- Acutely increases hepatic glucose production
- Complex effects on β-cell function and may reduce insulin production
- They promote visceral adipose tissue deposition and enhance lipolysis
- Alter levels of adipose tissue derived hormones and cytokines

Saltiel AR et al Nature 2001;414:799-806
Hollingdal M et al Diabetologia 2002;45:49-55
Boyle PJ Diabetes Reviews 1993;1:301
Lambillotte C et al J Clin Invest 1997;99:414-423
Petersons CJ et al Diabetes Care 2013;36:2822-2829

Glucose inhibition

- Starts very early after steroid ingestion
- In (previously well controlled) patients leads to postprandial hyperglycaemia
- Hyperglycaemia may be a transient rise of blood glucose levels or may result in HHS
- The best predictors of glucocorticoid-induced diabetes are family history of diabetes, increasing age, and glucocorticoid dose

Schacke H et al Pharmacol Ther 2002;96:23-43
Dimitriadis G et al Biochem J 1997;321:707–712
Petersons CJ et al Diabetes Care 2013;36:2822-2829

Now we know the cause, what's the treatment?

- Education and pre-empting the (almost) inevitable
- Letting teams know that when someone starts corticosteroid treatment that blood glucose levels are very likely to rise and to watch for it
- When it happens, treat early

What is the best treatment?

- Glitazones
- DPP-4s
- SGLT2 Inhibitors
- GLP- 1RAs
- Sulphonylureas
- Insulin

Gltizones…..

- Work very slowly – so may have been useful in an outpatient setting
- Several controversies abound regarding the use of glitazones, so their use is declining
  - Increased CV death rates
  - Increased fracture rates
  - Increased rates of macular oedema

Nissen SE NEJM 2007;356(24):2457-2471
Loke YK et al CMAJ 2009;180(1):32-39
Ryan EH et al Retina 2006; 26(5):562-70
Ferwana M et al Diabetic Med 2013;30(9):1026-1032

GLP-1's/ DDP-4s

- SGLT2is
  - Little experience with steroid use
  - Do not have a fast response to reducing hyperglycaemia
- GLP1s - reduce blood glucose but:
  - Little experience/ evidence with steroid use
  - It makes people who are already unwell feel nauseated
  - Not appropriate for people who are NBM
  - Do not have a fast response to reducing hyperglycaemia
- DPP-IV antagonists
  - limited published data on the use with steroids, e.g. Umpierrez using Sitagliptin in 90 hospitalised patients

Umpierrez GE et al Diabetes Care 2013

Sulphonylureas

- SU - Gliclazide
- Titrate from 40 mgs am to 240 mg am
- You may want to contact the specialist team if you are concerned re high Gliclazide doses
- Also add in up to 80 mgs pm (max 320 mgs per day)
- Insulin often required
- Various regimens
- VRII

Insulin

- Insulin is recommended as the drug of choice for the treatment of glucocorticoid-induced hyperglycaemia
- Prandial insulin should minimise the effects of the postprandial rise in glucose
- For patients receiving high-dose intravenous glucocorticoids, an intravenous insulin infusion may be appropriate

Hirsch IB et al Endocr Metab Clin North Am 1997;26:631–645

However!

- How much insulin should be given in the insulin naïve
- What about dose increases in people already on insulin
- Should you give it IV or SC

IV Insulin

Intravenous infusions tend to achieve acceptable blood glucose concentrations quicker than MDI

- An insulin infusion allows appropriate tapering of insulin infusion rates
- Glycaemic control is not compromised
- Hypoglycaemic risks can be minimised – especially with high dose steroids

What About Subcutaneous Insulin?

- IV insulin is not the answer for all – but maybe if the blood glucose is consistently above ~15 mmol/L
- May need a basal bolus regimen
- No work has been done to compare human with analogue insulin in this field

Should “steroid induced” hyperglycaemia always be treated (pre-existing diabetes)

- No clinical studies/ evidence to tell us
- However - hyperglycaemia in a hospital setting (for any cause) is associated with poor mortality, morbidity, and health economic outcomes
- Improving glycaemic control improves these outcomes

Umpierrez GE et al J Clin Endocrinol Metab 2002; 87:978–982

Bruno A et al Diabetes Care 2008;31(11):2209-2210

Which insulin?

- Intermediate acting human basal insulin
- Once a day
- Gradually up titration
- Analogue basal insulin if:

– if hyperglycaemia throughout day

– early morning hypos!

Factors to consider during treatment

- Risk of hyperglycaemia and hypoglycaemia
- Duration of steroid therapy
- Pre-existing diabetes
- Co-morbidities

JBDS targets (UK)

- Inpatient blood glucose readings of 6 - 10 mmol/l recommended but 4 - 12 mmol/l is acceptable
- Avoid wide swings in CBG

Pre existing diabetes

- Type 2

- On non insulin therapies
- Titrate oral medications
- Add Gliclazide and titrate to 240 mgs am/ 80 mgs pm

Type 1 and 2 Insulin treated patients

- Increase morning dose of premixed insulin
- Increase bolus at lunch/tea
- Shift basal to morning

- Test four times a day
- If capillary >12mmol/L on two occasions during 24 hours, then review treatment

Managing 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 daily 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 Insuman Basal, Humulin I or Human Insulatard
- Aim for CBG appropriate to patients' needs

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 (Type 1 and Type 2). 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 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 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 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**

[Version 2.1] 15/10/2014
Design by S.Jamal UHL

Steroid induced diabetes

- Once a day BG monitoring
- Pre lunch or evening meal
- If BG >12 increase frequency to 4/day
- If 2 or more BG >12 mmol/l -TREAT

Glucocorticoid Induced Diabetes

No known diabetes

- Check random glucose before starting on glucocorticoids to identify patient with new onset hyperglycaemia
- If the capillary blood glucose (CBG) is below 12mmol/L consider the patient to be at low risk and record the CBG daily post breakfast or post lunch
- If a capillary blood glucose is found to be greater than 12mmol/L the frequency of testing should be increased to 4 times a day
- If a capillary blood glucose is found to be consistently greater than 12mmol/L (i.e. on 2 occasions during a 24hr period). Then the patient should enter the treatment algorithm below

CBG readings above desired target (6 - 10mmol/L - acceptable range 4 - 12mmol/L)

- Add in gliclazide 40mg with breakfast and increase the dose by 40mg increments if targets are not reached

If no symptoms of hypoglycaemia are experienced by the patient despite being on 160mg of gliclazide in the morning, consider titration to 240mg in the morning. (You may like to seek specialist advice on dose titration at this stage)

If still no improvement on maximum dosage consider

- Adding an evening dose of gliclazide or add morning human NPH insulin e.g. Humulin I / Insulatard / Insuman Basal

Discharge - Monitoring will need to be continued in patients remaining on glucocorticoids post discharge.

- If glucocorticoid treatment is ceased in hospital and hyperglycaemia has resolved CBG can be discontinued post discharge
- If glucocorticoids 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 blood glucose, OGTT or HbA1c)

If glucocorticoids 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

Glycaemic targets:

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

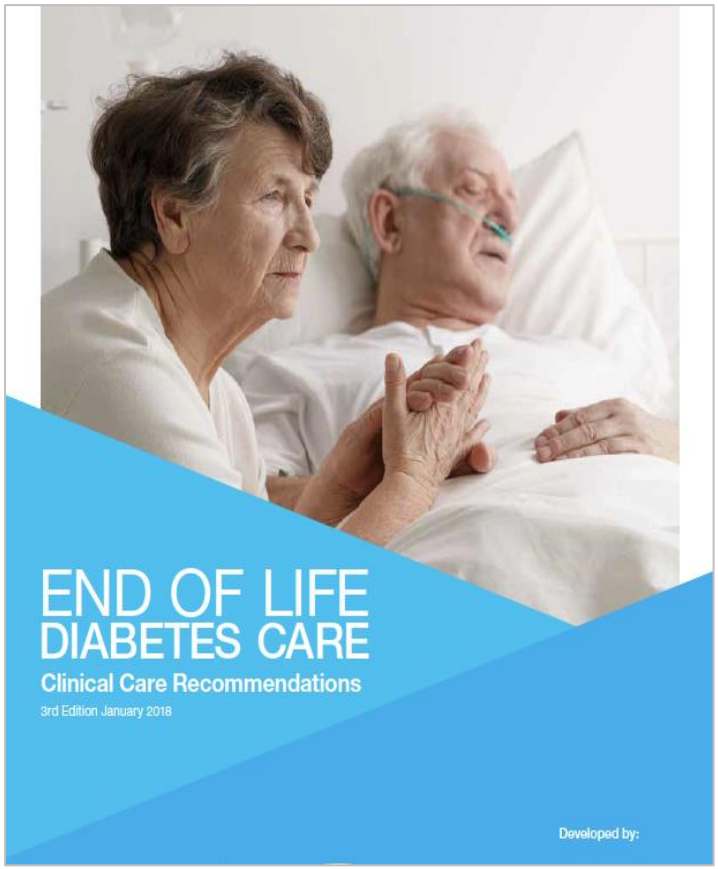
Design by S.Jamal UHL 25/02/2014

Pregnancy

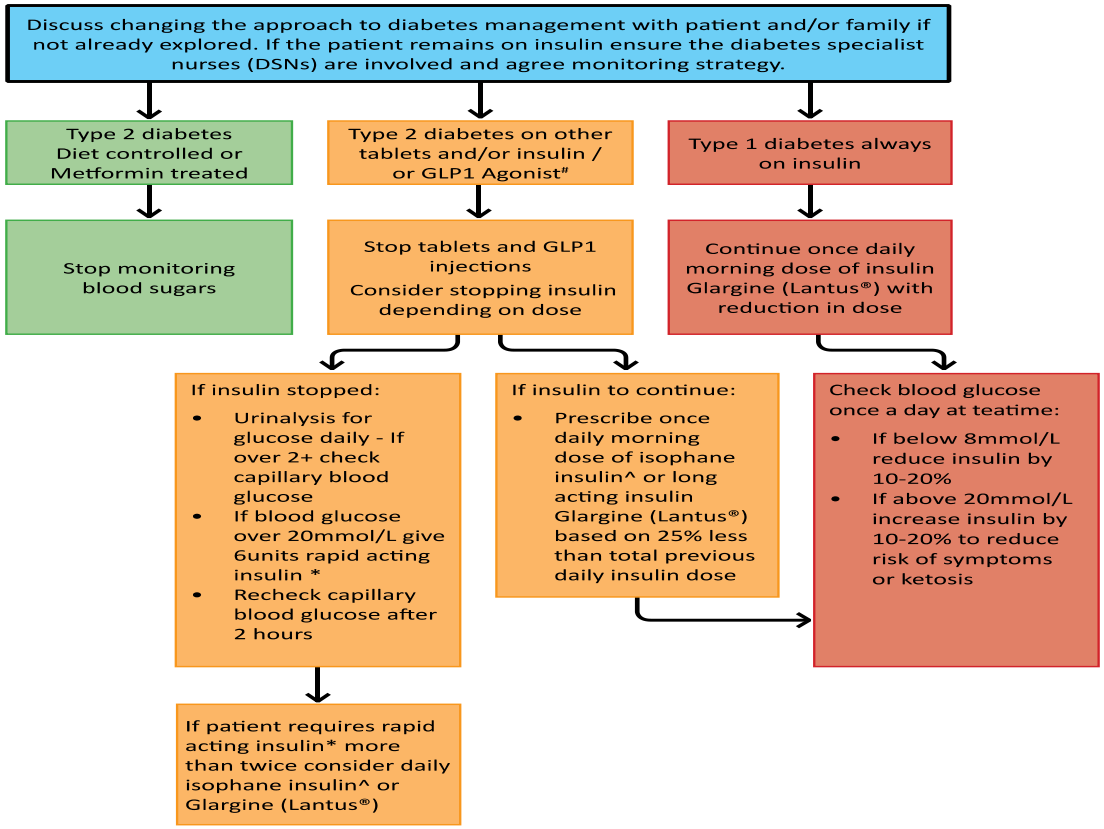
- Betamethasone - lung maturity
- Hyperglycaemia 24 -72 hrs
- Risk - GDM
- Pre-existing diabetes - VRII
- Up to 40% increment in dose

End of life

- Consider stages of end of life
- Hyperglycaemia may be complicated by use of food supplements
- Keep BG 6-15 mmols
- No fasting BG readings
- No HbA1c targets



End of Life Diabetes Management



Key

Bydureon (Exenatide ER), Byetta (Exenatide) / Victoza, (Liraglutide), Lyxumia (Lixisenatide)

* Humalog/Novorapid/Apidra

^ Humulin I /Insulatard/ Insuman Basal

- 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 blood glucose.
- It is difficult to identify symptoms due to "hypo" or hyperglycaemia in a dying patient.
- If symptoms are observed it could be due to abnormal blood glucose levels.
- Test urine or blood for glucose if the patient is symptomatic
- Observe for symptoms in previously insulin treated patient where insulin has been discontinued.

For queries relating to the diabetes flowchart please contact the Diabetes Specialist Nurses
For queries relating to palliative care please contact the Palliative Care Team

Version 5.2 06/14 S.Jamal

Steroids commenced in hospital and patient discharged (No known diabetes)

- Standard education for the individual and carer
- Blood glucose testing once daily (pre or post lunch or evening meal)
- If blood glucose readings greater than 12mmol/L increase frequency of testing to four times daily
- If two consecutive blood glucose readings greater than 12mmol/L in a 24 hour period follow algorithm for management of steroid induced diabetes
- If hyperglycaemia resolved stop CBG testing and arrange definitive test for diabetes

Hospital discharge (Known diabetes)

- Standard education for patient and carer including advice on hypoglycaemia
- Continue CBG monitoring until blood glucose normalises (4 -7mmol/L)
- Review by agreed individual (e.g. GP, Diabetologist, DSN/ PN) at an appropriate juncture to consider down-titration of antihyperglycaemic therapy if necessary

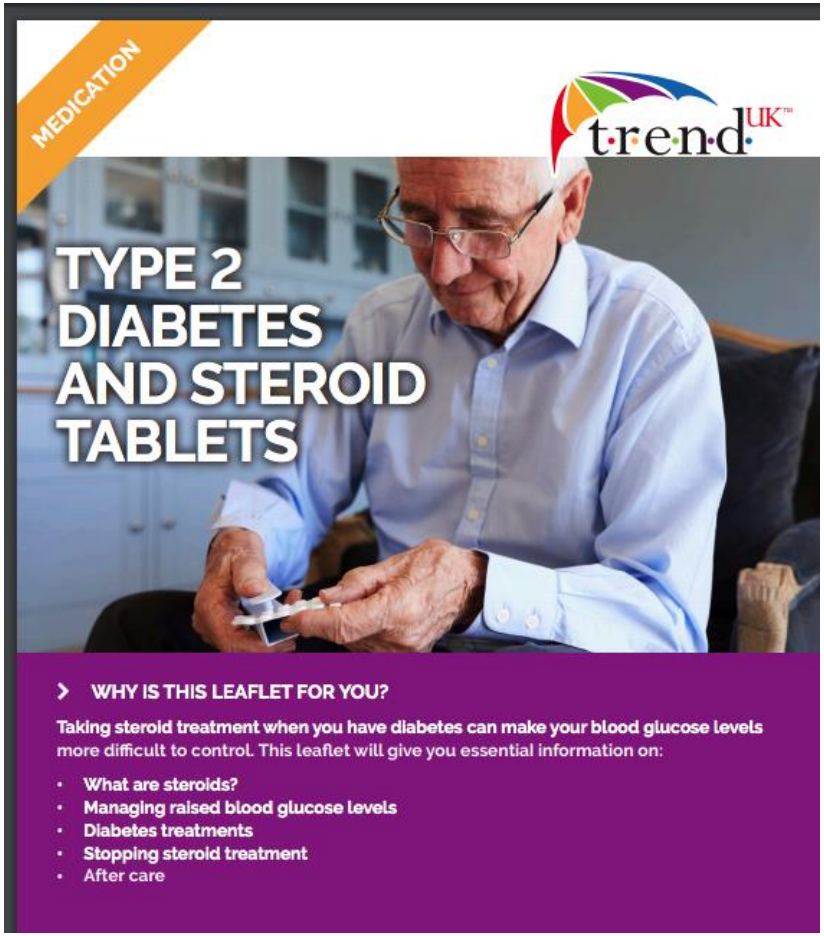
Education

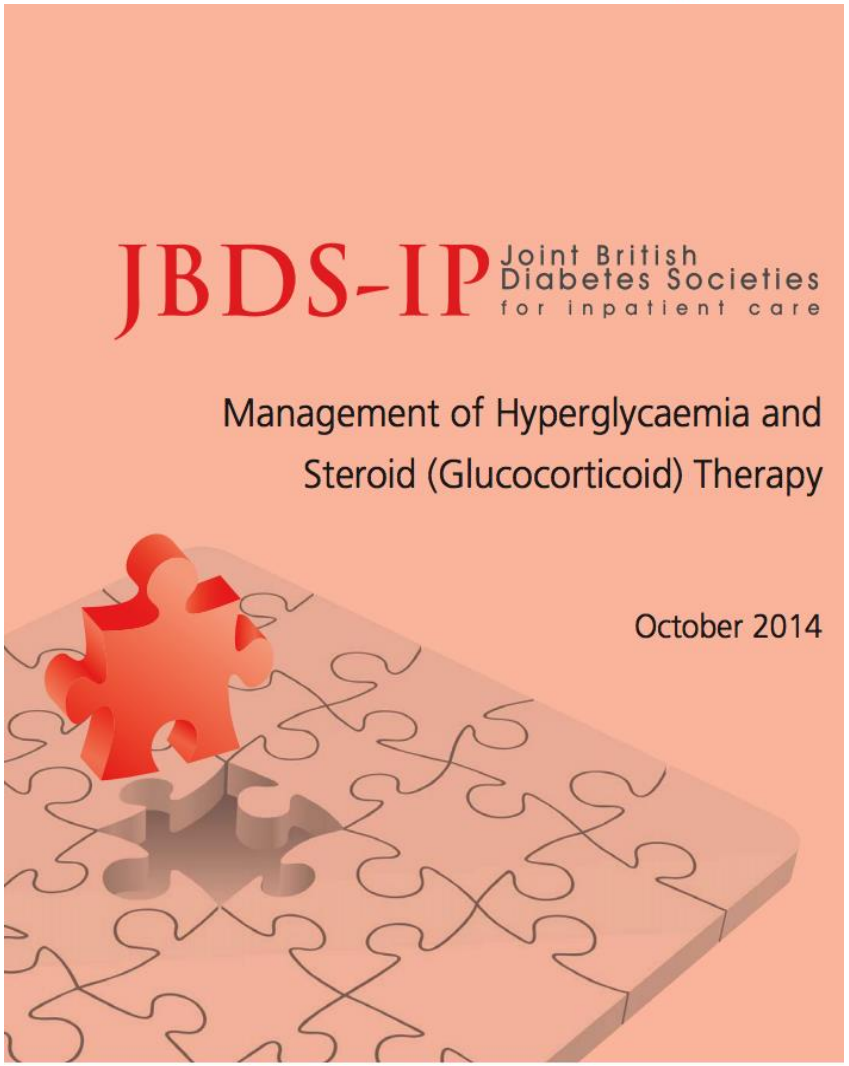
- Steroids are often started by health care professional who may not have experience of managing diabetes
- Patients with or without pre-existing diabetes will need to be aware of the impact steroid therapy makes on glycaemia control.
- Monitoring and treatment

Summary

- Steroid use will result in hyperglycaemia in most cases
- Treatment algorithms are available
- There is consensus guidelines but no real evidence of appropriate treatment pathways
- Those with no previous diagnosis of diabetes will need to undergo screening
- Patient and staff education should be put in place in localities

Resources


MEDICATION
trend UK
TYPE 2 DIABETES AND STEROID TABLETS
WHY IS THIS LEAFLET FOR YOU?
Taking steroid treatment when you have diabetes can make your blood glucose levels more difficult to control. This leaflet will give you essential information on:
What are steroids?
Managing raised blood glucose levels
Diabetes treatments
Stopping steroid treatment
After care


JBDS-IP
Joint British Diabetes Societies for inpatient care
Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy
October 2014