Type 2 diabetes mellitus

Guideline for the choice of oral and non-insulin antihyperglycaemic agents in adults

Diabetes Medicines Management Advisory Group (DMMAG)

Contents

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Version history

Version	1.0
Approved	DMMAG January 2019 and BSSE APC (February 2019) with amendments
Version	1.1
Amendments	• Formatting/layout changes and clarification of wording as requested by APC • Addition of warning relating to Fournier's gangrene risk and SGLT2 inhibitors following MHRA alert February 2019
Ratified	Clinical Policies Sub-Group and Quality and Safety Committee, NHS Birmingham and Solihull Clinical Commissioning Group May 2019
Date of publication	June 2019
Review date	2 years after publication, or sooner as needed

Enquiries or questions about the policy document should be directed to the APC Secretary: mlcsu.medicines-management@nhs.net

1 - Scope

These guidelines have been developed to support healthcare professionals with the choice of non-insulin antidiabetic agents for adults with type 2 diabetes. It is intended that future editions will contain additional guidance, for example on insulin prescribing.

The guidelines have been developed taking into consideration the most recent local, national and international publications available at the time of preparation:

1. NICE Guideline NG28: Type 2 diabetes in adults (2015, updated 2017)
2. EASD/ADA Consensus statement (2018)
3. Clinical trials including cardiovascular outcomes data, clinical effectiveness and cost-effectiveness (with publication date up until 22 November 2018)
4. License indications and product availability in the UK market
5. APC Formulary for Birmingham, Solihull, Sandwell and environs
6. Safety advice from the MHRA
7. Cost implications for primary care
8. Local population needs and local clinical expertise

It is recognised that research in the world of diabetes is fast moving, and whilst DMMAG will aim to support prescribers with appropriate clinical guidelines, it remains the responsibility of prescribers to ensure they adhere to the latest guidelines, license changes and product availability.

2 - Local prevalence of diabetes

The prevalence of type 2 diabetes in England is on average 6.8%, but across the Birmingham, Solihull and Sandwell area the prevalence is much higher, ranging from 7.2% in Solihull up to 9.1% across Birmingham and Sandwell (source: Fingertips 2017-18). Spend on antidiabetic drugs across the area totalled £19.2m in 2017-18 (source: OpenPrescribing.net, 2017). It is therefore important that the prescribing of antidiabetic agents is both clinically and cost-effective for the NHS.

3 - Treatment goals in type 2 diabetes and patient-centred care

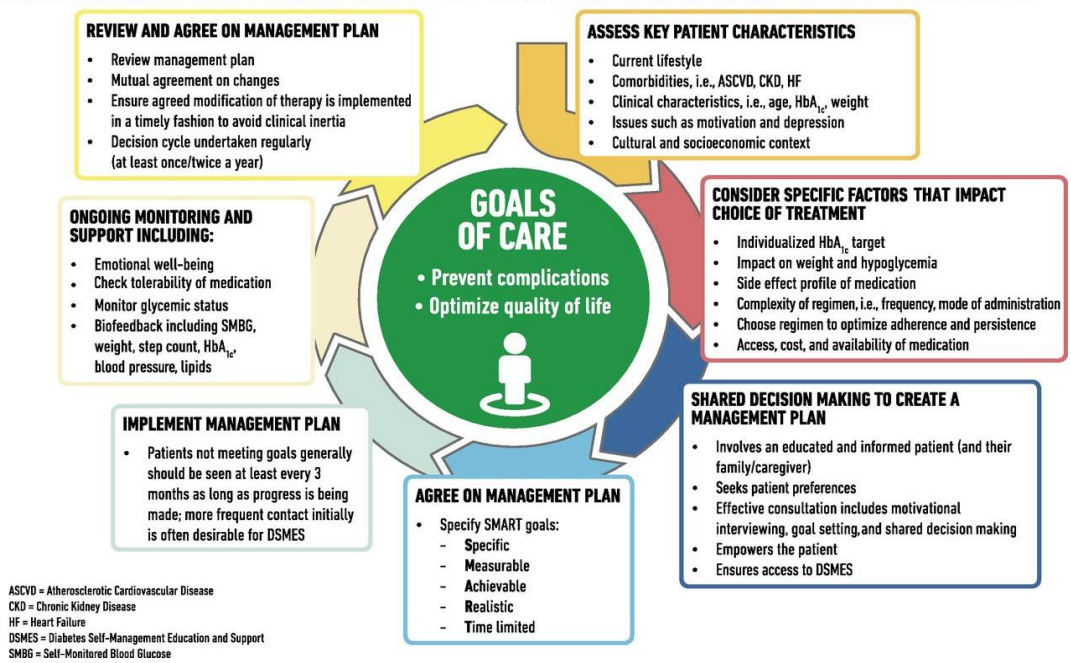
The goals of treatment for type 2 diabetes are to prevent or delay complications and maintain quality of life. People who have type 2 diabetes should be involved in decisions about their care and setting of individual HbA1c target (see figure 1). They should be offered lifestyle advice and drug treatment to support achievement and maintenance of their HbA1c target. HbA1c targets can be relaxed on a case-by-case basis, with consideration for people who:

- Are older or frail
- Have a reduced life expectancy and therefore unlikely to benefit from the prevention of long-term complications
- Are at high risk of the consequences of hypoglycaemia e.g. risk of falling, impaired awareness of hypoglycaemia, drive or operate machinery as part of their job, and

- Who have significant comorbidities and intensive glycaemic management is not appropriate

NICE recommends that if adults with type 2 diabetes achieve an HbA1c level that is lower than their target and they are not experiencing hypoglycaemia, encourage them to maintain it. Be aware that there are other possible reasons for a low HbA1c level, for example, deteriorating renal function or sudden weight loss.

Figure 1: Decision cycle for patient-centred glycaemia management in type 2 diabetes



Source: ADA/ EASD 2018 consensus statement

4 - Managing blood glucose

Dietary and lifestyle interventions are recognised as the cornerstone of diabetes management and should be reinforced at every opportunity. Structured education should be offered to support patients with these. This is particularly important before considering the escalation of treatment.

When dietary and lifestyle interventions alone do not sufficiently manage hyperglycaemia, drug options should be considered. Metformin is the preferred first-line oral agent; on occasion, insulin and sulfonylureas can be considered to manage severe osmotic symptoms and very poor control, once type 1 diabetes has been excluded. After monotherapy, both NICE (2015) and the ADA/EASD (2018) suggest that the choice of medication(s) added to metformin should be based on patient preference and clinical characteristics. Important clinical characteristics include the presence of established cardiovascular disease, frailty, other co-morbidities such as kidney disease, risk of polypharmacy and specific adverse medication effects, particularly hypoglycaemia and weight gain, as well as safety and tolerability. Patient factors can include occupation and health beliefs. The efficacy and cost of treatment should also be considered; NICE recommends choosing medicines with the lowest

acquisition cost if more than one in the same class are appropriate.

The following page outlines a suggested approach to the management of hyperglycaemia using therapies currently available in the UK. These guidelines are intended to support healthcare professionals with prescribing decisions, whilst considering the patient's needs, product licensing and best current evidence. Whilst these guidelines indicate points at which insulin initiation may be useful, a full discussion on insulin prescribing is not currently included.

Throughout the treatment pathway, response to treatment should be regularly assessed. In order to help minimise polypharmacy, ineffective therapies should be discontinued prior to addition of a further agent. If there is improvement in HbA1c but it remains above target, then treatment escalation should be considered. Medication adherence also requires regular reinforcement, particularly when complex regimes are prescribed. For more information about supporting adherence, see the NICE clinical guideline on Medicines Adherence.

5 - Antihyperglycaemic treatment options for adults with type 2 diabetes

Review HbA1c every 3-6 months. If not to target, reassess adherence, doses and treatment effectiveness before treatment intensification.

At diagnosis

Monotherapy if HbA1c < 86 mmol/mol (10%) and type 1 diabetes excluded (screen for ketones, weight loss and osmotic symptoms). Target HbA1c 48 mmol/mol (6.5%), or 53 mmol/mol (7.0%) in risk of hypoglycaemia.

Offer lifestyle intervention: refer to validated structured education programme and encourage physical activity

Monotherapy: Lifestyle/education + metformin

- Add metformin if HbA1c > 48 mmol/mol (6.5%) after 3 months of intensive lifestyle interventions.
- Avoid metformin if eGFR < 30 mL/min/1.73m^2 or any contraindications. Use slow-release metformin if ongoing GI intolerance.
- SU (or insulin) can be used if HbA1c > 86 (10%) or there are osmotic symptoms, after excluding type 1 diabetes.

Monotherapy options if metformin is contraindicated or not tolerated: SU, pioglitazone[3] or DPP4i[8]. Use an SGLT2i[6] instead of DPP4i only if pioglitazone or SU is not appropriate.

First Intensification:

If HbA1c > 58 mmol/mol (7.5%) on lifestyle + metformin, add second agent. Aim for HbA1c < 53mmol/mol (7.0%), or a patient-specific target (see also "section 12 – elderly").

First intensification: lifestyle/education +/- metformin + one agent chosen according to history of CVD

If patient has established atherosclerotic cardiovascular disease (CVD) or heart failure (HF) add in:

- SGLT2i with CVD benefit: (dapagliflozin or empagliflozin)[1] or canagliflozin[2] OR
- If SGLT2i contra-indicated[6], use an agent with CV safety: basal insulin, DPP4i[7,8], SU (gliclazide)[9]

If patient does not have established CVD choose an agent according to individualised patient management plan:

- **To avoid hypoglycaemia[1]**: DPP4i (alogliptin, sitagliptin or linagliptin)[7,8] or pioglitazone[3] or SGLT2i[5]
- **For rapid glycaemic response, or if patient is on steroids**: SU (gliclazide)[9] or insulin (ongoing or rescue therapy)
- **For weight loss:** SGLT2i (dapagliflozin or empagliflozin)[1] or canagliflozin[2]
- **In frail/elderly**: DPP4i (alogliptin, sitagliptin or linagliptin)[7,8]. Avoid drugs causing hypoglycaemia and SGLT2i[6]
- **If all factors are equal**: pioglitazone[3] or SU (gliclazide)[9]

If metformin is contraindicated or not tolerated, consider the following NICE-approved dual therapy options:

- DPP4i + either SU or pioglitazone OR
- Pioglitazone + SU

If any therapy option is not tolerated or ineffective, stop and replace with an alternative prior to intensification.

Key to abbreviations:

SGLT2i – SGLT2 inhibitor
GLP1-RA - GLP1-receptor agonist
SU – sulfonylureas
DPP4i – DPP4 inhibitor ('gliptins')
DKA – diabetic ketoacidosis

5 - Antihyperglycaemic treatment options for adults with type 2 diabetes (continued)

Second intensification

If HbA1c > 58 mmol/mol (7.5%) or patient-specific target on lifestyle + two agents, review treatment. If second agent is effective but HbA1c not to target, add third agent. **Do not use more than 3 agents together.**

Consider insulin

If HbA1c above target, HbA1c > 75 mmol/mol (9%) at any stage, or patient is markedly symptomatic.

Second intensification: lifestyle/education + metformin + two additional agents

Choice will depend on patient factors such as CVD, BMI, eGFR, hypo risk, frailty taking into account existing therapy:

- SU + metformin → consider **pioglitazone** or **DPP4i** or **SGLT2i** or **GLP1-RA**
- DPP4i + metformin → consider **SU** or **pioglitazone**
- SGLT2i + metformin → consider **SU** or **pioglitazone**[4]
- Pioglitazone + metformin → consider **SU** or **DPP4i** or **SGLT2i**[4] or **GLP1-RA**[7]
- Any two agents → consider **insulin**

- Consider **GLP1-RA** if BMI ≥ 35 kg/m^2 (or lower in black, Asian and other minority ethnic groups) or for whom insulin is not recommended due to occupation/comorbidities, in line with NICE NG28: **dulaglutide** (weekly) or **liraglutide** (daily). Consider the CVD benefit of liraglutide when choosing a GLP1-RA[5,7].
- Stop GLP1-RA if there is no reduction in HbA1c of 1% (11 mmol/mol) **AND** no weight loss of 3% within 6 months
- **Avoid co-prescribing** any **GLP1-RA + SGLT2i** or any **DPP4i + SGLT2i** as these carry a high NHS prescribing cost.
- **GLP1-RA + DPP4i** agents should never be co-prescribed, there is no pharmacological basis for this combination.

Insulin based treatment with/without existing treatment

There are multiple insulin regimens which are beyond the scope of this guideline. Specialist advice or referral is available for insulin selection/initiation. Combine **GLP1-RA with insulin** only if HbA1c > 75 mmol/mol (9%) **and** BMI > 35 kg/m^2 (or lower in minority ethnic groups) **and** patient is currently using insulin. The regime must be initiated by a diabetes specialist, with ongoing support from a consultant-led multidisciplinary team (primary/secondary/community care).

Important considerations:

1. Drugs are listed alphabetically. Refer to SmPCs and BNF for full details of prescribing information
2. Canagliflozin is less suitable for prescribing due to increased risk of lower limb amputations. It is not yet known whether this is a class effect.
3. Avoid pioglitazone in bladder cancer, heart failure, elderly, macular oedema, risk of bone fractures (particularly in women); caution with insulin. Doses of 15mg & 30mg may be better tolerated than 45mg.
4. Avoid pioglitazone and dapagliflozin co-prescribing.
5. Liraglutide 1.2mg daily dose is appropriate for most patients; 1.8mg daily dose is restricted to specialist initiation **only**
6. Avoid SGLT2i in elderly >85yr, diabetic foot disease, risk of DKA, risk of Fournier's gangrene, in combination with loop diuretics (or use with caution if used in HF) or eGFR < 45 mL/min/1.73m^2
7. DPP4i and GLP1-RA can both cause pancreatitis. Caution if any risk factors, avoid in history of pancreatitis
8. DPP4i: Use alogliptin first-line (caution in moderate/severe HF)
9. Use gliclazide MR instead of standard release gliclazide to aid compliance

6 - Key considerations to support drug selection

Only drugs currently listed on the BSSE APC formulary are included

DRUG		Hypo risk	Effect on weight	eGFR & dose reduction	Safety Considerations	Cost per 28-tab pack (Prices Jan 2019 Drug Tariff)
Biguanides	Metformin	↔	↔	Caution**	Renal impairment	**Immediate release** 500mg - £0.84, 850mg-£0.68 **Modified release** 500mg - £2.00, 750mg - £3.20, 1000mg - £3.20 **Solution** 500mg/5ml- £6.73 x150ml 1000mg/5ml - £24.00 x150ml
Sulfonyl-ureas	Gliclazide	↑	↑	Caution*	Driving****	**Standard release** 40mg - £1.58, 80mg – £0.78 **Slow release** 30mg - £2.81, 60mg - £4.77
TZDs	Pioglitazone	↔	↑	No caution	CCF Osteoporosis Bladder cancer	15mg - £5.31 30mg - £8.69 45mg - £7.46
DPP4 Inhibitors	Alogliptin	↔	↔	Caution**	CCF (caution NYHA class III-IV) Pancreatitis	6.25mg, 12.5mg, 25mg - £26.60
	Sitagliptin	↔	↔	Caution**	Pancreatitis	25mg, 50mg, 100mg - £33.26
	Linagliptin	↔	↔	No caution^	Pancreatitis	5mg - £33.26
SGLT2 inhibitors	Empagliflozin	↔	↓	Caution***	GU infections DKA, Fournier's gangrene[#]	10mg, 25mg - £36.49
	Dapagliflozin	↔	↓	Caution***		5mg, 10mg - £36.59
	Canagliflozin	↔	↓	Caution***	GU infections DKA, Fournier's gangrene[#] Toe amputations[$] Risk of fractures	100mg, 300mg - £39.20
GLP1 receptor agonist	Liraglutide	↔	↓↓	Caution**	Pancreatitis	£78.48 / 2 pens 0.6mg OD dose - £39.24/ 28d 1.2mg OD dose - £78.48/ 28d 1.8mg OD dose - £117.72/ 28d
	Dulaglutide	↔	↓↓	Caution**	Pancreatitis	£73.25 / 4 pens (28d) 0.75mg/0.5ml and 1.5mg/0.5ml
Insulin	Insulin	↑↑	↑↑↑	Caution*	Driving****	Costs vary depending on insulin and dose–check BNF. NPH (human) insulins are more cost-effective than analogue insulins, use 1st line

*Caution - increased risk of hypoglycaemia in patients with reduced renal function, regular glucose monitoring required
**Dose reduction required in eGFR <45, stop if eGFR < 30 – see BNF or SPC
***Efficacy depends on good renal function. Reduce dose if eGFR<60, stop if eGFR < 45 ml/min
****See DVLA requirements for appropriate advice, occupational hazard may also be an issue
^ Linagliptin requires no dose adjustments in renal impairment, but safety in renal disease is comparable with other DPP4i's
$ It is not known whether this is a class effect. Advise patients on routine preventative footcare in line with NICE guidance
# Fournier's gangrene (necrotising fasciitis of the genitalia/perineum) is a rare side-effect of all SGLT2 inhibitors that may be preceded by urogenital infection or perineal abscess. Advise patients to seek urgent medical attention if they experience severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise. See MHRA Alert Feb 2019.

7 - Addressing cardiovascular risk in type 2 diabetes

People with type 2 diabetes are known to be at high risk of cardiovascular disease (CVD) morbidity and mortality: 2 out of 3 deaths in type 2 diabetes are attributed to stroke, heart failure or myocardial infarction, and every increase in HbA1c of 1% increases the risk of CVD by 10-30%.

This guideline encompasses the emerging evidence around cardiovascular risk reduction, whilst remaining mindful of existing NICE guidelines. Early intensive intervention in diabetes using multiple drug combinations targeting blood glucose, lipids and blood pressure, provides sustained benefits in improving CVD outcomes. Metformin is known to reduce the risk of death and heart attacks in people with type 2 diabetes who are overweight or obesity (UKPDS 34). Some, but not all, SGLT2 inhibitors and GLP1 receptor agonists have been shown to improve HbA1c and also improve CV disease outcomes. However, SGLT2 inhibitors and GLP1-RAs are not currently licensed solely for CVD, they should only be considered for a cardio-protective role in people with both diabetes and existing cardiovascular disease. Structured education, weight loss and dietary interventions also remain central to achieving improved cardiovascular and diabetes outcomes.

8 - Self-monitoring of blood glucose and ketones

People with diabetes prescribed drugs that can cause hypoglycaemia should be offered a blood glucose meter and be taught to self-monitor. Local guidance on blood glucose and ketone monitoring, along with recommendations on the choice of meter, is available via the APC Birmingham, Solihull and Sandwell formulary website.

In general, meters with test strips costing > £10 per 50 strips should be avoided, except where patients are using meters capable of undertaking carbohydrate counting (more expensive strips). Self-monitoring of blood glucose and ketones where not clinically indicated, is discouraged.

9 - Drug dosing in renal impairment

Many of the drugs used in diabetes require dose alterations when prescribed for people with chronic kidney disease. A useful summary table for antidiabetic agents can be accessed at GP Notebook Shortcuts: "The management of hyperglycaemia in those with diabetes and kidney disease"

10 - Sick day rules

Some drugs need to be suspended during intercurrent illness; it is important to also advise patients to restart any suspended medication once they are feeling better and are able to eat and drink. A quick reference guide on 'how to advise patients on sick day rules' has been published in the *Diabetes and Primary Care Journal.* Patient information leaflets '*Type 2 diabetes: What to do when you're ill'* are also available for download at TREND UK (free registration required).

11 - De-escalation of treatment

There are occasions when a dose reduction or discontinuation of treatment is the most appropriate next step for a patient – for example if therapy is ineffective, there is a risk of problematic side effects such as hypoglycaemia, or due to a change in the person's clinical status such as the development of comorbidities or increasing frailty. All guidelines recommend the regular review of HbA1c and treatment; if there is only minimal benefit or it is outweighed by harms then the therapy should be either stopped or the dose reduced.

GLP1-RA should only be continued if a reduction of 11 mmol/mol (1%) in HbA1c and a 3% reduction in initial body weight is achieved within the first 6 months of treatment, in line with NICE guidance. The safety and efficacy of pioglitazone should be reviewed after 3–6 months and pioglitazone should be stopped in patients who do not respond adequately to treatment.

Any patient whose HbA1c level falls below 48 mmol/mol (6.5%), or substantially below the individualized glycaemic target, should have a prompt medication review that involves stopping or reducing the dose of medications that carry any risk of hypoglycemia or weight gain.

12 - Special considerations for the frail elderly

There is increasing evidence that tight control of glucose and blood pressure in frail elderly people with diabetes can be harmful. This group are less likely to benefit from the long-term microvascular outcomes of good glycaemic control and have a marked increase in risk of hospital admissions. There is therefore a need to avoid over-treatment of both blood pressure and glycaemia.

Aims of treatment in the context of frailty should be:

1. To avoid hypoglycaemia
2. To control symptoms of hyperglycaemia
3. To reduce risk of infection
4. To avoid hospital admission
5. To introduce timely end-of-life care
6. To avoid complex regimes

NICE have changed some of the QOF diabetes indicators for primary care in 2019/20. People with moderate or severe frailty can now be excluded from tighter HbA1c and BP control:

NM157 *- The percentage of patients with diabetes* ***without*** *moderate or severe frailty, on the register, in whom the last IFCC-HbA1c is 58 mmol/mol or less in the preceding 12 months*

NM158 *- The percentage of patients with diabetes* ***with*** *moderate or severe frailty, on the register, in whom the last IFCC-HbA1c is 75 mmol/mol or less in the preceding 12 month*

NM159 *- The percentage of patients with diabetes* ***without*** *moderate or severe frailty, on the register, in whom the last blood pressure reading (measured in the preceding 12 months) is 140/80 mmHg or less*

The International Diabetes Federation global guideline for managing type 2 diabetes in older people (IDF, 2013) recommends very specific HbA1c targets (table 1). Active steps must be taken to review this population, including an assessment of their level of frailty, and make appropriate plans.

Table 1: General glycaemic targets for older people, according to functional category*

Functional category	General HbA1c target
Functionally independent	7.0 - 7.5% / 53-59 mmol/mol
Functionally dependent • Frail • Dementia	7.0 – 8.0% / 53-64 mmol/mol Up to 8.5% / 70 mmol/mol Up to 8.5% / 70 mmol/mol
End of life	Avoid symptomatic hyperglycaemia

*Glycaemic targets should be individualised taking into account functional status, comorbidities, especially the presence of established CVD, history and risk of hypoglycaemia and presence of microvascular complications.

Proposed changes in medication and treatment should be discussed with the patient and their carer. The reasons for changes need to be understood in terms of increased risk of therapy and/or low likelihood of benefit. It is important to respond to **falling HbA1c or losing weight** by reviewing and reducing diabetic treatments. A low HbA1c is often overlooked as a desirable target but may result in an admission with hypoglycaemia, particularly where HbA1c is <53mmol/mol (7.0%). Consider treatment de-intensification, starting with drugs that carry a risk of hypoglycaemia.

Poor hydration/oral intake and reduced renal function are also important considerations in older people. Food intake and subsequent medication requirement (including insulin dosage) may reduce with changes in personal circumstances, such as transfer of care settings, and comorbidities. Care home residents who have diabetes need specific review and plans put in place; this is an area that may require focus - Diabetes UK guidance is available.

In the older frail adult, preferentially utilise oral regimes with lower hypoglycaemia risk such as metformin and DPP4 inhibitors. Be wary of sulfonylureas and pre-mixed insulins due to higher hypoglycaemia risk especially in those with renal disease. Insulin should not be with-held if deemed the most appropriate therapy/add-on therapy in those with type 2 diabetes however be aware of the increased risk of hypoglycaemia where tight control is not required. Table 2 represents a consensus view from the guideline authors.

Regular testing of blood glucose is required for any patient where hypoglycaemia is a potential risk. Take into consideration changes in dexterity, vision, and the need for third-party assistance with medicines' administration, particularly injectables, prior to initiation and in ongoing treatment.

Table 2: Antihyperglycaemic agents in older people – advantages and disadvantages

Medication	Advantages	Disadvantages
Metformin	Effective at reducing blood glucose, low hypo risk, preferred first-line agent	Be aware of sick day guidelines in those with poor hydration/oral intake and/or reduced renal function. Risk of lactic acidosis especially in severe CCF, reduce if eGFR<45, stop if <30. Be wary in those with recurrent AKI. GI side effects may reduce tolerability
Sulfonylureas (SU)	Effective. They are an option for older adults who eat consistently and are able to recognize and treat hypoglycaemia. In the elderly, gliclazide M/R may have lower hypo risk than standard release gliclazide (due to gradual increase in plasma levels) where meal patterns are erratic and appetite is poor. Weight gain less of a concern in frailty. Repaglinide works in a similar manner to SUs, but has to be taken with meals so it can be skipped if meals are skipped, thus avoiding hypoglycaemia.	Hypo risk with all SUs, use with caution in older people - can use gliclazide but avoid long-acting SUs with active metabolites (glimepiride and glibenclamide). Higher risk of hypos when SU added to insulin or in people with CKD. Avoid SUs in functionally dependent older people (moderate to severe frailty) due to high hypo risk and inability to treat/recognise hypos. Regular blood glucose monitoring required.
Pioglitazone	Effective, low hypo risk. Weight gain less of a concern in frailty	Use hampered by side effects in older people due to increased prevalence of comorbidities. Risk of peripheral oedema - avoid in heart failure, macular oedema; avoid also in people with fracture risk, and a history or risk of bladder cancer
DPP4i	Moderately effective, safe, well tolerated (e.g. low GI side-effects), low hypo risk. Preferred alternative or add-on to metformin	Dose reduction required in those with deteriorating renal function for some agents in this group. Note risk of pancreatitis

GLP-1 RA	Effective, low hypo risk. Once weekly GLP-1 may be useful in those with administration difficulties.	Injectable therapy may be undesirable e.g. due to poor dexterity, third-party assistance required. Satiety and weight loss effects are not beneficial in frailty. GI side effects may lead to dehydration. Therapeutic experience in those aged >75 years is limited and dose adjustments is required for some agents. Note risk of pancreatitis. Cost/benefit considerations need to be weighed up.
SGLT2i	Effective. Some cardiovascular benefits in people with existing CVD but caution in people with pre-existing low blood pressure	Side effect profile not appropriate in frailty – increased risk of GU infections, diuresis, weight loss. Be aware of sick day guidelines in those with poor hydration/oral intake and/or reduced renal function. Need regular monitoring of kidney function. Avoid in those aged over 85 years due to limited therapeutic experience.
Basal insulin	Effective, simplest regime to use when insulin is clinically indicated, particularly when a third-party is needed to administer the insulin (e.g. carers or district nurses). Best given in morning in those with overnight/early morning hypos, shorter profile of NPH insulins may have benefit in reducing overnight hypos. Useful add-on to oral medication.	Risk of hypos (though less than other insulin regimes). Hypo risk increased when combined with sulfonylureas - use with caution. Higher risk of hypos in CKD. May need dose reduction as appetite/food intake decreases or HbA1c/blood sugars settle to avoid hypos. Requires regular blood glucose monitoring.
Premixed insulin	Fixed dose and time of administration is good for people with regular meal patterns. Fewer injections required than a basal bolus regime, which may be an advantage with third-party administration; simple method of administration in those with post-prandial hyperglycaemia.	Higher risk of hypos compared with other insulin regimes, especially in erratic/poor eaters where mismatch can occur. Higher risk of hypos in CKD. Avoid concomitant use of sulfonylureas. Requires more frequent blood glucose monitoring than basal insulin regimes.

Basal bolus insulin	May be useful in those where tight control isn't required but there is ongoing poor glycaemic control. Sometimes a looser regime based on blood sugar levels may be of benefit in frail/care home residents on a patient-specific basis with specialist input.	Multiple daily injections required, complex regimes may be difficult for functionally dependent people particularly who require third-party assistance. Avoid concomitant use of sulfonylureas. Risk of hypos. Requires intensive blood glucose monitoring.

CKD = chronic kidney disease, GU = genitourinary, Hypo = hypoglycaemia, CCF = congestive cardiac failure, GI = gastrointestinal

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