NHS Type 2 Diabetes Path to Remission Programme
(formerly the NHS Low Calorie Diet Programme)

Guidance for GP practices and referrers

30 October 2025 (Version 5)

Contents

Background – the clinical trials

- The DiRECT trial (2017) tested a low calorie diet (LCD), total diet replacement (TDR) approach in people with Type 2 Diabetes within 6 years of diagnosis, aiming to achieve weight loss and remission of diabetes. Eligibility criteria included age 18-65 years, BMI > 27 and not being treated with insulin.
- On the first day of starting TDR, all glucose-lowering medications and BP-lowering medications were stopped. People generally received 12 weeks of TDR, followed by further practice nurse / dietician-led support with maintaining weight loss.
- At 1 year, 46% of people in the intervention group achieved remission (as defined in the trial), compared to 4% of controls
- Absolute weight loss (and avoidance of weight re-gain) was strongly associated with achievement and maintenance of remission. The 2 year data showed that 64% of people with ≥10kg loss at 2 years were in remission, compared to 29% of people with 5-10kg weight loss and 5% of people with <5kg weight loss
- While DiRECT used nurses or dieticians to provide behavioural support, the DROPLET trial (2018) showed that similar weight loss could be achieved using a trained workforce of non-healthcare professionals

Background – the NHS programme

- Informed by the clinical trials, the NHS Low Calorie Diet Pilot Programme was launched in 2020 in 10 ICSs and expanded to a further 11 ICSs in 2022
- The pilots tested different delivery models in the real-world and, based on learning from the pilots, a national specification and framework has been developed. This will be rolled out across all ICSs in England in 2023/24
- Informed by user insights, the programme was re-named the NHS Type 2 Diabetes Path to Remission (T2DR) Programme in early 2023
- The programme supports people to lose significant weight, improve glycaemic parameters and potentially achieve remission of Type 2 Diabetes. Even if remission is not achieved, multiple benefits are likely to arise from weight loss
- Data thus far (to the end of 2022) shows uptake from referral to starting TDR of 68%, programme retention of 90% at 3 months and 55% at 12 months, and mean weight loss of 10.9kg at 1 year. Analysis of remission rates will follow once available through linkage with the National Diabetes Audit

What is low calorie, total diet replacement?

- Total diet replacement (TDR) refers to an approach where usual foods are replaced with a micronutrient-replete formulated diet
- The TDR products usually take the form of shakes or soups, however other product forms are available
- There are a number of commercial entities producing TDR products. The composition of such products is regulated by legislation
- Generally, a product is consumed at each meal time. Some TDR regimes also include an additional specially-formulated ‘snack’
- When used as intended and no other foods are consumed, the total daily calorie intake on the 12-week TDR phase of the NHS T2DR Programme is around 800-900 kcals
- Though other approaches such as low calorie diets with ‘real foods’ may be effective for some people, the strongest evidence-base in achieving Type 2 Diabetes remission through non-surgical means is currently with TDR approaches

Aims of the NHS T2DR Programme

- Reduction in weight of Service Users and maintenance of weight loss
- Achievement of remission of Type 2 diabetes / reduction in glycaemia
- Reduction in medication usage
- Further develop evidence for clinical and cost-effectiveness of this intervention in the real world

Overview of the Programme

- Referrals to the NHS T2DR Programme are from GP practices
- Three phases to the intervention:
    - Total Diet Replacement: 12 weeks
    - Food re-introduction: 6 weeks
    - Weight maintenance: 34 weeks (the remainder of the 12-month programme)
- A rescue protocol (with 4 weeks of further TDR and weekly support sessions) will be offered if the participant regains ≥ 2kg weight after the TDR phase
- There is no direct cost to participants (i.e. they do not pay for the TDR products)

Eligibility criteria – part 1

These are aligned to the evidence-base but have been adapted pragmatically. Individuals who satisfy all the following eligibility criteria may be referred to the Service:

- Aged 18 to 65 years (note that individuals aged over 65 years may be referred if clinically appropriate and if potential benefits for that individual are considered to outweigh potential risks associated with rapid weight loss [e.g. exacerbation of pre-existing frailty])
- Diagnosed with Type 2 diabetes within the last 6 years
- BMI ≥ 27kg/m² in people from White ethnic groups (adjusted to ≥ 25kg/m² in people from Black, Asian and other ethnic groups)
    - BMI obtained from self-measured weight is acceptable for referral. If this cannot be obtained, a clinic-measured value within the last 12 months may be used, provided there is no concern that weight may have reduced since last measured such that the individual would not be eligible for the T2DR programme at present
- HbA1c measurement taken within the last 12 months, in line with the following:
    - If on diabetes medication (HbA1c result reflects the effect of glucose-lowering medications), HbA1c 43-87 mmol/mol
    - If not on diabetes medication (HbA1c result does not reflect the effect of glucose-lowering medications), HbA1c 48-87 mmol/mol
    - If there is any concern that HbA1c may have changed since last measured, such that repeat testing may indicate that the individual would not be eligible for the T2DR programme at present, HbA1c should be rechecked before referral is considered
- Must have attended for monitoring and diabetes review when last offered, including retinal screening, and commit to continue attending annual reviews, even if remission is achieved (no need to wait for retinal screening to take place if newly diagnosed)
- Does not meet any exclusion criteria (see next slide)

Eligibility criteria – part 2

If any of the following apply, the individual is unsuitable for the NHS T2DR Programme and referral will not be accepted (exclusions):

- Has been on the NHS T2DR Programme (or NHS LCD Programme) in the last 12 months, unless referred but did not start TDR
- Current insulin user
- Pregnant or planning to become pregnant before the end of the 12-month programme
- Currently breastfeeding
- Has at least one of the following significant co-morbidities;
    - active cancer
    - heart attack or stroke in last 6 months
    - severe heart failure (defined as New York Heart Association grade 3 or 4)
    - severe renal impairment (most recent eGFR less than 30mls/min/1.73m2)
    - active liver disease other than non-alcoholic fatty liver disease (i.e. NAFLD is not an exclusion)
    - active substance use disorder
    - active eating disorder
    - porphyria
    - known proliferative retinopathy that has not been treated (no need to wait for retinal screening before referral if newly diagnosed)
- Previously had bariatric surgery
- Health professional assessment that the person is unable to understand or meet the demands or monitoring requirements of the programme

If ineligible for the T2DR Programme, consider whether the individual would benefit from other weight management support

Definition of remission

- The Expert Advisory Group for the NHS T2DR Programme agreed the below definition of remission:
    - **Remission has been achieved when HbA1c < 48mmol/mol (or FPG < 7mmol/l if HbA1c is not clinically suitable) has been maintained for at least 6 months, off all glucose-lowering medications**
- Using this definition, remission therefore requires checking of HbA1c levels (or FPG if HbA1c is not clinically suitable) at least 6 months apart, with no glucose-lowering medications used during this interval
- An international consensus report has recently proposed a similar definition of remission with glycaemic levels outside the diabetes-range maintained for at least 3 months rather than at least 6 months
- In the absence of a definition within NICE guidance at present, it is recommended that the definition from the Expert Advisory Group (above, in bold text) continues to be used

Remission of type 2 diabetes

- Please make clear that achievement of remission does not equate to ‘cure’ – specifically use the term ‘remission’ and explain that hyperglycaemia may return (and is likely to do so if sufficient weight regain)
- The mechanism of remission is thought to be the removal of excess fat from the liver and pancreas, allowing these organs to return to normal functioning in regulating blood glucose
- Weight regain above an individual’s ‘personal fat threshold for type 2 diabetes’ - the body weight at which disruption of physiology for regulating blood glucose results in diabetes-range glycaemia – is likely to result in a return to hyperglycaemia and the associated risks of developing complications
- It is therefore essential that anyone referred to the NHS T2DR Programme commits to attending diabetes review / monitoring appointments when offered, regardless of whether remission has been achieved
- Ongoing review and monitoring should be offered in line with usual care for people with type 2 diabetes

Coding of remission

- The GP practice is requested to check HbA1c at 6 months and at 12 months after start of the programme
- In line with the definition of remission from the Expert Advisory Group, the earliest point at which remission may be identified is therefore at 12 months
- If remission is achieved, this may be coded as ‘Type 2 Diabetes in remission’ (703138006)
- This code does not remove patients from the Diabetes Register, facilitating ongoing review and monitoring for complications of diabetes, as well as recognition for QOF
- **Please DO NOT use the code ‘Diabetes Resolved’ – this removes the patient from the Diabetes Register, inhibits recall for routine care and is likely to result in loss of applicable QOF attainment**

Coding the NHS T2DR Programme

- Practices will be informed by the provider when a milestone relating to progress on the programme has been reached
- Correspondence from providers will explain which codes to use
- Note that the ‘completion’ code relates to the TDR phase of the programme rather than the entire programme length

Event	SNOMED code	SNOMED code description
Invitation	1239631000000109	Total diet replacement programme invitation
Referral	1239571000000105	Referral to total diet replacement programme
Declined	1239581000000107	Total diet replacement programme declined
Commenced	1239591000000109	Total diet replacement programme commenced
Not commenced	1239621000000107	Did not commence total diet replacement programme
Completed	1239601000000103	Total diet replacement programme completed (relates to 12 week TDR phase)
Not completed	1239611000000101	Did not complete total diet replacement programme
Contraindicated	1239541000000104	Total diet replacement programme contraindicated
Remission achieved	703138006	Type 2 Diabetes in remission

Offering the NHS T2DR Programme

- Pointers for enhancing the offer of a referral:
    - Provided it is clinically appropriate, frame the offer of referral positively as something which you expect will interest the patient. Try not to assume that the programme won't be acceptable
    - Early in the discussion about the programme, make clear that it is free-of-charge (including TDR products)
    - Explain that the person will have a choice of having programme sessions delivered face-to-face at local venues or digitally via apps / websites
    - Make clear that whichever option is chosen, there is support and one-to-once coaching for a full year
    - Feedback from participants is that hunger is generally not a major problem after the first week
    - Explain that the vast majority (90%) of people who start the programme go on to complete the TDR phase. People report that the rapid weight loss they experience during this time is highly motivating
    - On average, people on the Programme lose around 13kg at 3 months and 11kg at 12 months
    - Consider motivational interviewing to help overcome perceived barriers and support readiness to change
- An example script demonstrating discussion of referral to the NHS T2DR Programme has been developed by the Nuffield Department of Primary Care Health Sciences at the University of Oxford. This is available on FutureNHS

Testimonials after a TDR programme

Starting the diet - ‘The first week or so I was probably feeling hungry but after that, absolutely fine. I did think, how am I going to manage on three drinks a day, but absolutely fine.’ (Man, aged 69 years, diabetes duration 3.5 years)

‘I was so surprised, compared to what I was eating to what I have been eating over the last weeks, I really would have thought that I would have been hungry from the moment I opened my eyes to the moment I closed my eyes, but I wasn’t.’ (Woman, 42 years, diabetes duration 1 year)

Regimen and structure - ‘What I found with the diet is that the regimen suits me. I like to know what I’m going to have to eat. If I get choice, if I get here’s a shelf full of food go and choose something and potentially I can choose the wrong foods, so if I plan and know what it is that I’m going to eat then I can do it quite easily.’ (Man, 49 years, diabetes duration 9.5 years)

Physical wellbeing - ‘It was fairly hard to start with but it got easier as the weeks went on and then when I started getting a bit fitter and I could walk further and stand up and sit down and dig the garden it’s great now. I feel great.’ (Man, 44 years, diabetes duration 2.5 years)

Psychological wellbeing - ‘I think as my weight’s gone off I think my mood’s improved quite a bit. I feel quite, I think because I’m enjoying doing the diet and the research project and I’m looking forward to what’s going to happen in the future I think, I don’t know, I just feel more lighter.’ (Woman, 35 years, diabetes duration 1.5 years)

Common adverse effects incl. constipation

- The most common adverse effects experienced during TDR in the DiRECT trial were constipation (46.8%), sensitivity to cold (41.0%), headache (38.1%), dizziness (35.3%) and fatigue (32.4%) (see table on the right)
- The Provider is responsible for supplying a starter pack of fibre supplements to participants, as well as the ongoing supply of these during the programme
- Unless clinically inappropriate, participants should be recommended to commence fibre supplementation at the same time as starting TDR, to reduce likelihood of constipation

Table S9: Adverse effects identified a priori as relevant to the intervention treatment, experienced by intervention group participants during year one at study visits in each phase of the weight management programme. The usual-care control group was seen only at baseline and 12 months.

	TDR phase (12-20 weeks)				FR phase (4-6 weeks)				WLM phase (26-36 weeks)			
	Total (n=139)	Mild	Moderate	Severe	Total (n=124)	Mild	Moderate	Severe	Total (n=94)	Mild	Moderate	Severe
Constipation	65 (46·8)	30 (21·6)	24 (17·3)	11 (7·9)	18 (14·5)	14 (11·3)	4 (3·2)	0 (0·0)	6 (6·4)	2 (2·1)	2 (2·1)	2 (2·1)
Sensitivity to cold	57 (41·0)	37 (26·6)	12 (8·6)	8 (5·8)	30 (24·2)	19 (15·3)	6 (4·8)	5 (4·0)	13 (13·8)	7 (7·4)	2 (2·1)	4 (4·3)
Headache	53 (38·1)	31 (22·3)	13 (9·4)	9 (6·5)	15 (12·1)	10 (8·1)	3 (2·4%)	2 (1·6)	8 (8·5)	5 (5·3)	2 (2·1)	1 (1·1)
Dizziness	49 (35·3)	40 (28·8)	7 (5·0)	2 (1·4)	11 (8·9)	3 (2·4)	6 (4·8)	2 (1·6)	7 (7·4)	4 (4·3)	3 (3·2)	0 (0·0)
Fatigue	45 (32·4)	24 (17·3)	11 (7·9)	10 (7·2)	18 (14·5)	10 (8·1)	3 (2·4)	5 (4·0)	8 (8·5)	2 (2·1)	0 (0·0)	6 (6·4)
Mood change	35 (25·2)	16 (11·5)	12 (8·6)	7 (5·0)	10 (8·1)	4 (3·2)	4 (3·2)	2 (1·6)	4 (4·3)	1 (1·1)	2 (2·1)	1 (1·1)
Nausea	25 (18·0)	15 (10·8)	4 (2·9)	6 (4·3)	3 (2·4)	3 (2·4)	0 (0·0)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Diarrhoea	23 (16·5)	11 (7·9)	10 (7·2)	2 (1·4)	5 (4·0)	4 (3·2)	1 (0·8)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Indigestion	20 (14·4)	15 (10·8)	3 (2·2)	2 (1·4)	4 (3·2)	2 (1·6)	2 (1·6)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Hair Loss	19 (13·7)	10 (7·2)	7 (5·0)	2 (1·4)	13 (10·5)	3 (2·4)	6 (4·8)	4 (3·2)	8 (8·5)	4 (4·3)	3 (3·2)	1 (1·1)

Data reported as N(%)

Adverse effects / events process

- Patients should be advised to contact the Provider directly if experiencing an adverse effect or concurrent event which is not considered an emergency
- To support this process, the Provider has a Medical Director with responsibility for:
    - Responding appropriately to adverse events;
    - Responding and giving advice about concurrent events;
    - Appropriately recording all adverse events and feeding back to the GP practice and NHS England
- The Provider is expected to triage and respond appropriately to concurrent or adverse effects – this may include giving advice, signposting the patient to the GP practice for assessment / medication adjustment or directing the patient to urgent / emergency care services if an urgent medical need is identified
- **If an acutely unwell patient contacts the GP practice directly, they should be assessed and managed appropriately by the GP practice and it would not be appropriate to redirect them to the Provider**
    - e.g. if a patient complains of abdominal pain and has a clinical presentation in keeping with acute cholecystitis, the patient should be admitted to hospital without delay
    - The Provider should be informed, by either the patient or the GP practice, at an appropriate time once urgent action has been taken and they will advise regarding next steps on the T2DR Programme

Responsibilities – GP practice / T2DR Provider

Referring GP Practice

Identify eligible patients and offer referral as appropriate

Provide information on T2DR service and the potential of remission of type 2 diabetes

Discuss medication changes to take place on first day of TDR and provide written confirmation of these changes (including if no changes are needed) to the Provider

Respond to any clinical need to further adjust medications according to capillary blood glucose and blood pressure monitoring by the Provider

Respond to adverse events if patient contacts practice directly with an urgent need or is directed to the GP practice by the Provider

Arrange review of patient at 6 months and 12 months after starting T2DR programme with repeat HbA1c – with further medication adjustment as necessary

T2DR Service Provider

Provide advice / support to referrers regarding required medication changes if this is requested

Contact GP practice if any necessary information (including medication changes) is missing from the referral

Contact patient within 5 working days of referral to provide further information and book Individual Assessment

Confirm medication changes with patient

Arrange supply of TDR products

Provide starter pack and ongoing supply of fibre supplements

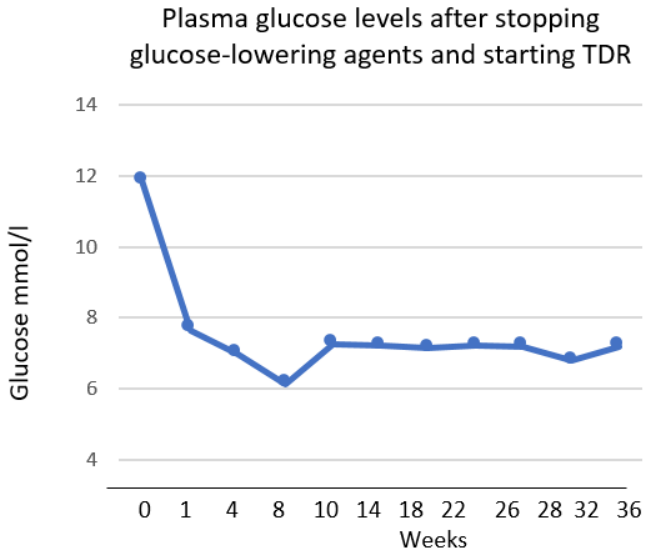
Perform / arrange monitoring of capillary blood glucose and BP and communicate with GP practice as indicated

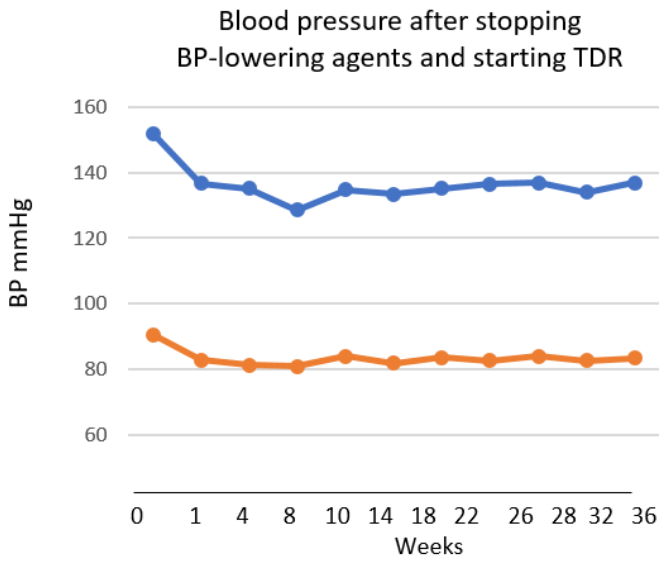
Act as initial contact for patients experiencing a concurrent or adverse event which is not considered an emergency and to triage / respond accordingly

Optimise uptake, retention and programme outcomes

Blood glucose and BP changes on TDR

- We generally tend to be more accustomed to starting medication than stopping medication
- It is recognised that stopping glucose-lowering and BP-lowering medications on the first day of TDR may seem unusual to those less familiar with the intervention
- The graphs on the right demonstrate findings from the Counterbalance study (which informed the DiRECT trial)
- There is a marked reduction in plasma glucose levels within a week on TDR, despite stopping all glucose-lowering medication
- There is a similar, albeit less marked, reduction in blood pressure levels within a week on TDR, despite stopping all BP-lowering medication





Approach to blood glucose and blood pressure

- The approach to managing medication affecting blood glucose and BP in the NHS T2DR Programme is based on the approach used in DiRECT. However, it has been modified to reflect learning and adapted to a ‘real-world’ setting, with a more conservative approach to medication adjustment. Note that adjustment / stopping of statins is not recommended
- Despite stopping all glucose-lowering medications, there were no hyperglycaemia-related adverse events in the DiRECT intervention group
- Hypoglycaemic events should not occur during TDR as the patient MUST stop any drugs prone to causing hypoglycaemia before starting TDR – and will not be able to commence TDR unless this is confirmed
- Though DiRECT stopped all BP-lowering medication on the first day of TDR, referrers to the NHS T2DR Programme are advised to adjust only one BP-lowering medication initially. This is based on data for medication re-starts from the trial as well as evidence for TDR resulting in more marked reductions in blood glucose than for blood pressure
- **At referral, agreed medication changes must be provided in writing to the Provider (on referral form)**
- The medication adjustments recommendations outlined in this slide pack have been agreed by an Expert Advisory Group including the lead investigators of the DiRECT and DROPLET trials, consultant diabetologists and primary care clinicians. The recommendations are designed to be safe, evidence-based and pragmatic. **They constitute guidance only and should not override clinical judgment. Clinical responsibility remains with the referring GP practice**

Monitoring of blood glucose and BP

- A key safety mechanism in the NHS T2DR Programme is the regular monitoring of participants' blood glucose and blood pressure (in those prescribed BP-lowering medication at referral) to detect:
    - clinically significant hyperglycaemia
    - clinically significant high or low blood pressure
- If the programme is delivered remotely, participants will be supplied with equipment and training to undertake self-monitoring by the T2DR Service Provider, with participants communicating readings directly to the Provider
- If the programme is delivered face-to-face, the Provider may perform monitoring directly or arrange self-monitoring
- Capillary blood glucose and blood pressure readings will therefore be received and interpreted by the Provider. Any readings requiring action, including adjustment of medications, will be communicated to the GP practice with appropriate urgency (see next slide)
- When on TDR (the 12-week TDR phase or 4-week 'rescue package'), capillary blood glucose and blood pressure will be checked at least weekly in weeks 1-4 and at least every 2 weeks in weeks 5-12. When not on TDR, capillary blood glucose and blood pressure will be checked at least monthly
- **At 6 months and 12 months after starting the programme, the patient should be reviewed by their GP practice with repeat HbA1c**

Thresholds for communication / action

The provider will monitor capillary blood glucose readings and will communicate with the GP practice as follows:

- Under 15 mmol/l – no additional action required, continue intervention;
- Between 15.0 - 19.9 mmol/l over two sessions / episodes of engagement – the Provider must contact the Service User's GP practice;
- 20.0 mmol/l or higher – there must be same-day contact with the Service User's GP practice (the Provider must contact the GP practice directly and the Service User must also be advised to contact their GP practice same-day)

The provider will monitor BP in people prescribed BP-lowering medication at referral and will communicate with the GP practice as follows:

- 89/59 mmHg or lower (systolic and/or diastolic) or postural symptoms – the Provider must contact the Service User's GP practice. If symptoms are interfering with daily activities, same-day contact with the GP practice must be made (the Provider must contact the GP practice directly and the Service User must also be advised to contact their GP practice same-day);
- 90/60 to 159/99 mmHg – no additional action required, continue intervention;
- 160/100 to 179/119 mmHg over two sessions / episodes of engagement – Provider must contact the Service User's GP practice;
- 180/120 mmHg or higher – there must be same-day contact with the Service User's GP practice (the Provider should contact the GP practice directly and the Service User must also be advised to contact their GP practice same-day);
- For avoidance of doubt, if a blood pressure reading fits into two of the categories described above (e.g. 181/118 mmHg), action should be taken in line with the category prompting the most urgent response (in this example, same-day contact with the GP practice)

Medication adjustments when starting TDR – glucose-lowering medication

NHS England

Discussion at time of referral – stopping glucose-lowering medication on the first day of TDR

- People on 1-2 glucose-lowering medications should stop these on the first day of TDR [it is likely that most patients will be in this category]
- People on ≥ 3 glucose-lowering medications should remain on a single medication which is safe with TDR (preferably metformin if clinically suitable) and stop the other glucose-lowering medications on the first day of TDR

- Counsel the patient about the osmotic symptoms of diabetes and when and how to seek appropriate support
- Medication changes (including if no changes are needed) must be specified in writing to the Provider at time of referral

- (metformin, DPP4 inhibitors and pioglitazone are safe with TDR)
- (GLP-1 analogues are high cost and, although safe with TDR, should generally be stopped on the first day of TDR)
- (Sulfonylureas, meglitinides, SGLT2 inhibitors are not safe with TDR and MUST be stopped on the first day of TDR)

Which glucose-lowering medications are safe with TDR?

NHS England

Class	Examples of medications	Is this safe with TDR?
Biguanides	Metformin	Yes – safe
Sulfonylureas	Gliclazide, Glibenclamide, Glimepiride	No – risk of hypoglycaemia
Meglitinides	Repaglinide, Nateglinide	No – risk of hypoglycaemia
Thiazolidinediones	Pioglitazone	Yes - safe
DPP4 inhibitors (-gliptins)	Linagliptin, Alogliptin, Sitagliptin, Saxagliptin, Vildagliptin	Yes - safe
SGLT2 inhibitors (-flozins)	Dapagliflozin, Canagliflozin, Empagliflozin, Ertugliflozin	No – risk of ketoacidosis
GLP-1 analogues (-tides)	Exenatide, Dulaglitide, Liraglutide, Lixisenatide, Semaglutide	Yes - safe
Alpha-glucosidase inhibitors	Acarbose	Yes – safe
(insulin is not included here as people treated with insulin are not eligible for the NHS T2DR Programme)		

Examples – 1 or 2 glucose-lowering medications

1 glucose-lowering medication time of referral – stop the medication on first day of TDR

- patient is on metformin only at time of referral
    - stop the medication (metformin) on the first day of TDR. This will be the case for any instances of glucose-lowering monotherapy

2 glucose-lowering medications at time of referral – stop both medications on first day of TDR

- patient is on metformin and SGLT2 inhibitor at time of referral
    - stop both these medications (metformin and SGLT2 inhibitor) on the first day of TDR. This will be the case for any instances of glucose-lowering dual therapy
- patient is on metformin and sulfonylurea at time of referral
    - stop both these medications (metformin and sulfonylurea) on the first day of TDR. This will be the case for any instances of glucose-lowering dual therapy

Examples – ≥ 3 glucose-lowering medications

≥ 3 glucose-lowering medications at time of referral – remain on metformin (or, if not clinically suitable, another medication which is safe with TDR, e.g. DPP4 inhibitor or pioglitazone) and stop the other glucose-lowering medications on first day of TDR

- patient is on metformin, SGLT2 inhibitor and DPP4 inhibitor at time of referral
    - remain on metformin and stop the SGLT2 inhibitor and DPP4 inhibitor on the first day of TDR
- patient is on sulfonylurea, SGLT2 inhibitor, and DPP4 inhibitor at time of referral
    - remain on DPP4 inhibitor and stop the sulfonylurea and SGLT2 inhibitor on the first day on TDR
- patient is on SGLT2 inhibitor, DPP4 inhibitor and pioglitazone at time of referral
    - remain on either DPP4 inhibitor or pioglitazone (not both), stopping the other glucose-lowering medications on the first day of TDR
- patient is on sulfonylurea, SGLT2 inhibitor and GLP-1 analogue at time of referral
    - stop all three of these glucose-lowering medications on the first day of TDR (although it would be acceptable to remain on the GLP-1 analogue if clinically indicated)
- patient is on metformin, sulfonylurea, SGLT2 inhibitor and GLP-1 analogue at time of referral
    - remain on metformin and stop sulfonylurea, SGLT2 inhibitor and GLP-1 analogue on the first day of TDR

Rationale for approach to glucose-lowering medication

- It is recommended that people taking 1-2 glucose-lowering medications stop these at the outset to give them the opportunity to achieve remission – which necessitates having stopped all glucose-lowering medications
- The rationale for a different approach for people on ≥ 3 glucose-lowering medications (recommended to stay on metformin or another medication which does not pose harm on TDR) is based on data from DiRECT. This showed a strong inverse association between the likelihood of achievement / maintenance of remission and the number of glucose-lowering medications that the patient was taking at the outset. Though numbers of people taking ≥ 3 glucose-lowering medications at the start of the intervention were small, none maintained remission at 2 years
- There are many factors which may affect the number of glucose-lowering medications that someone is taking – duration of diabetes, glycaemic control, frequency of review, practice processes etc – however, given the data from DiRECT, it is seems reasonable for patients taking ≥ 3 glucose-lowering medications to stay on metformin (or another medication which does not pose harm on TDR) as the data suggests that they are unlikely to achieve remission and, in DiRECT, all such patients had restarted at least one glucose-lowering medication by 24 months
- However, if someone on ≥ 3 glucose-lowering medications is keen to stop all of them on the 1st day of TDR, doing so would still be acceptable. The patient should be made aware that, like all participants, they will be monitored by the provider for hyperglycaemia and that glucose-lowering medications may need to be restarted by the GP practice during the course of the programme

If restarting glucose-lowering medications

- The clinical need to restart medication to control glycaemia may arise during the T2DR programme. This may be flagged by the Provider from monitoring of capillary blood glucose levels or identified by the GP practice (e.g. at the 6 month review with HbA1c)
- Metformin is 1st line and is considered safe in TDR
- Pioglitazone or DPP4 inhibitors are also considered safe in TDR and may be started if clinically appropriate
- GLP-1 analogues are considered safe in TDR but high cost - may be restarted if clinically appropriate, in line with NICE guidance
- Sulfonylureas, meglitinides or SGLT2 inhibitors MUST NOT be used during TDR for safety reasons
    - If the patient is on TDR and there is a need to reduce glycaemia and only these medications are appropriate, the patient MUST be told to stop TDR immediately and the provider MUST be informed straight away if sulfonylureas, meglitinides or SGLT2 inhibitors are restarted
    - If the patient has stopped TDR and there is a need to reduce glycaemia and only these medications are appropriate, the provider MUST still be informed if sulfonylureas, meglitinides or SGLT2 inhibitors medications are restarted
    - Restarting sulfonylureas, meglitinides or SGLT2 inhibitors while the patient is on the T2DR programme will also preclude ‘rescue TDR’ initiation. Therefore consider alternatives while the patient is on the NHS T2DR Programme if possible
- If insulin initiation is deemed clinically necessary at any stage, the patient MUST be told to stop the T2DR programme with immediate effect and the Provider MUST be informed straight away

Supporting information – glucose-lowering medications

- Metformin – safe with TDR but check other contraindications / cautions - 1st line medication to restart if appropriate and control of glycaemia required
- Pioglitazone – safe with TDR but check other contraindications / cautions – can be restarted if necessary and appropriate to further control glycaemia although metformin is 1st line
- The class of DPP4 inhibitors includes alogliptin, linagliptin, saxagliptin, sitagliptin– safe with TDR but check other contraindications / cautions - can be restarted if necessary and appropriate to control glycaemia although metformin is 1st line
- The class of GLP-1 analogues includes exenatide, dulaglitide, liraglutide, semaglutide – these are safe with TDR (check other contraindications / cautions) but high cost - can be restarted if necessary and appropriate, in line with NICE guidance
- The class of sulfonylureas includes gliclazide, glibenclamide, glimepiride, glipizide, tolbutamide – for safety, these MUST not be used with TDR due to high risk of causing hypoglycaemia (stimulate insulin release independent of blood glucose levels). Even if the TDR phase has been completed, consider alternative medications if possible as restarting sulfonylureas while the patient is on the T2DR programme will preclude 'rescue TDR' initiation. The same applies to the class of meglitinides – which includes repaglinide and nateglinide – as, like sulfonylureas, these stimulate insulin release independent of blood glucose levels.
- The class of SGLT2 inhibitors includes dapagliflozin, canagliflozin, empagliflozin, ertugliflozin – for safety, these MUST not be used with TDR due to risk of ketoacidosis (the TDR diet is ketogenic). Even if the TDR phase has been completed, consider alternative medications if possible as restarting SGLT2 inhibitors while the patient is on the T2DR programme will preclude 'rescue TDR' initiation

Medication adjustments when starting TDR – BP-lowering medications

- It is recognised that people may be taking a variety of combinations of medications, at different doses, which affect blood pressure. This guidance makes various assumptions which will not reflect the context and management of every patient
- It is therefore imperative that clinical judgement is used
- Note that a medication may be used in one patient solely for managing blood pressure while, in another patient, it may also be used for another indication, e.g. ACE-inhibitors in heart failure with reduced ejection fraction (HFREF)
- **Medications being used specifically and solely for managing blood pressure, in a particular patient, are the priority for adjustment**

Medication adjustments when starting TDR – BP-lowering medications

BP-lowering medications include medicines used for other indications (e.g. tamsulosin for benign prostatic hypertrophy, candesartan for migraine prophylaxis) as well as medicines used specifically for managing blood pressure

Discussion at time of referral – adjusting BP-lowering medications on the first day of TDR:

- If blood pressure is considered uncontrolled at time of referral (e.g. systolic ≥ 140mmHg or diastolic ≥ 90mmHg), make no changes to BP-lowering medications
- If blood pressure is considered controlled at time of referral (e.g. both systolic < 140mmHg and diastolic < 90mmHg), one BP-lowering medication should be adjusted on the first day of TDR
- It is acceptable to use self-reported blood pressure. If not available, the last clinic-recorded blood pressure may be used, provided there have been no intervening changes to lifestyle or medications affecting blood pressure, there is no history of white-coat hypertension, and there is no concern that blood pressure may have changed significantly since last measured

- The medication changes (including the absence of changes) must be specified in writing to the T2DR provider
- Counsel the patient about symptoms of postural hypotension and advise them of when and how to seek support

Selecting the BP-lowering medication for adjustment

- Identify the medications used for the patient solely for the management of blood pressure (i.e. not also being used for nephropathy, angina, heart failure, BPH, migraines etc) - this must be checked on the records and confirmed with the patient
- Stop the medication would have been added last according to current NICE guidance [at present, this is NICE guideline NG136: Hypertension in adults: diagnosis and management] - unless other clinical factors affect decision making
- If not being used for other indications, this would be (in order of stopping first):
    - Spironolactone or alpha-blocker or beta-blocker
    - Thiazide diuretic (or calcium-channel blocker)
    - Calcium-channel blocker (or thiazide diuretic)
    - ACE-inhibitor or Angiotensin receptor blocker
- If the patient is taking medications which affect blood pressure but all of these are for other indications (none are being used solely to manage blood pressure):
    - use clinical judgement and shared decision making and take into account the blood pressure reading
    - cautiously reduce the dose of this medication rather than stopping it
    - consider arranging early review to monitor clinical response, in relation to the specific indication for the medication
    - in some circumstances, it may be reasonable not to adjust these medications initially but to carefully monitor instead

Examples – ≥ 1 medication used solely for BP

Blood pressure is considered controlled at time of referral – (e.g. systolic < 140mmHg and diastolic < 90mmHg)

- patient is taking ramipril 10mg (for BP solely – no other indications) at time of referral
    - stop the ramipril 10mg on the first day of TDR
- patient is taking ramipril 10mg (for BP solely) and amlodipine 10mg (for BP solely) at time of referral
    - stop the amlodipine 10mg on the first day of TDR
    - the amlodipine would be added last according to NICE guidance for hypertension and is therefore stopped first
- patient is taking ramipril 10mg (previous MI), amlodipine 10mg (for BP solely), indapamide mr 1.5mg (for BP solely) and bisoprolol 10mg (previous MI) at time of referral
    - stop indapamide mr 1.5mg (or, alternatively, the amlodipine 10mg)
    - although bisoprolol would be added last according to NICE guidance for hypertension, it is used here for another indication and should therefore not be adjusted at this time
    - excluding bisoprolol, the indapamide (or amlodipine) would have been added last according to current NICE guidance for hypertension and is therefore stopped first

Examples – no medications used solely for BP

Blood pressure is considered controlled at time of referral – (e.g. both systolic < 140mmHg and diastolic < 90mmHg)

- patient is taking ramipril 10mg (for nephropathy) at time of referral
    - reduce ramipril dose to 5mg rather than stopping
- patient is taking propranolol 40mg bd (for migraine prophylaxis) and doxazosin 2mg (for BPH) at time of referral
    - discuss options, balancing potential impact on migraine frequency / LUTs against risks of hypotension with TDR on these medications
    - given the low doses in this example, it may be reasonable not to make any changes to these medications initially – if so, careful monitoring required
    - if medication adjusted, advisable to arrange review of migraines / LUTs at clinically appropriate interval
- patient is taking ramipril 10mg (HFREF), bisoprolol 10mg (HFREF) and furosemide 60mg (HFREF) at time of referral
    - needs caution – inadvisable to suddenly stop an medication in this example unless strong clinical rationale
    - carefully reduce dose of one medication – use clinical judgement and shared decision making
    - early review, including assessment of fluid status (particularly if adjusting furosemide), should be arranged

Subsequent adjustment of medications for BP

If blood pressure is too low

- If postural symptoms arise or blood pressure is reported by the Provider to be low (systolic < 90 mmHg and/or diastolic < 60mmHg), follow the same process as previously outlined in adjusting BP-lowering medications
- Medications being used specifically and solely for managing BP, in a particular patient, are the priority for adjustment

If blood pressure is too high

- If blood pressure (monitored by the Provider) rises to a threshold where intensification of antihypertensive treatment is clinically indicated, use clinical judgement in restarting or uptitrating doses of medications
- Assess whether any previously-adjusted medications used for other indications (rather than solely for managing blood pressure) should be restarted / up-titrated first
- Follow NICE guidance in restarting antihypertensive therapy (unless other clinical factors affect decision making)

Medications needing adjustment – weight / dietary changes

- Some medications may need to be adjusted due to changes in body weight or dietary intake
- Some of these medicines are likely to be prescribed by the GP practice while others may be prescribed / administered by other services. If prescribed / administered by other services, these may not appear in the record on the GP IT system
- It is therefore important to ask the patient if they are receiving medication or treatment in other settings
- Consider ‘‘if someone lost weight or had a major dietary change, is the dose of this medicine likely to need adjustment?’
- If in doubt, discuss with a clinical pharmacist colleague
- **It is the responsibility of the referrer to ensure that processes are in place for such medications to be adjusted**
- Only refer the patient if safe, robust processes are in place to manage the adjustment of these medicines in line with dietary or weight changes. As a minimum, establish who will be responsible for obtaining weight readings (or other monitoring – e.g. INR for warfarin), the frequency, how this will be recorded, how the prescriber will be notified and how dose changes will be communicated with the patient
- If involving other services, such as specialist clinics, prior discussion with such services must take place to establish feasibility, responsibility and agreement for appropriately frequent patient review and dose adjustment
- **If this cannot be done safely then the patient should not be referred to the T2DR programme**

Medications needing adjustment – weight / dietary changes

- Commonly used oral medications which may require adjustment include:
  - Warfarin
  - Non-vitamin K antagonist oral anticoagulants (NOACs)
  - Digoxin
  - Phenytoin
  - Ciclosporin
  - Antifungals – voriconazole
  - Long-term antibiotic therapy (e.g. isoniazid)
- Many medications administered parentally may require dose adjustment by weight. These include:
  - Low molecular weight heparin
  - Infliximab (and other biologics)
  - Long-term antibiotic therapy (e.g. macrolides, aminoglycosides, fluoroquinolones, beta-lactams)
- This is not an exhaustive list of medications which may need adjustment due to weight / dietary changes

Pre-referral checklist

- ❑ Checked eligibility and made sure no exclusions apply
- ❑ Checked list of medications currently prescribed / taken (including those from other providers such as hospitals) and identified:
  - ❑ Glucose-lowering medications
  - ❑ BP-lowering medications (including those not specifically used to treat blood pressure, e.g. furosemide or tamsulosin)
  - ❑ Medications which may need to be adjusted due to changes in body weight or diet
    - if in doubt, discuss with a clinical pharmacist colleague
    - only refer if safe, robust processes to manage adjustment and review in line with dietary / weight changes
- ❑ Agreed medication adjustments for 1st day of TDR – must be specified in writing to the provider (incl. if no changes are needed)
    - recommended adjustments for glucose-lowering and BP-lowering medications are described in this slide pack
    - use your clinical judgement – if in doubt, discuss with the T2DR service provider
    - patients will not be able to start TDR unless they confirm to the provider that they are stopping / not taking sulfonylureas, meglitinides or SGLT2 inhibitors
- ❑ Confirmed with the patient that they will continue attending reviews / monitoring, regardless of whether remission is achieved
- ❑ Confirmation that patient will notify the GP practice of any unexpected or concerning symptoms which are considered urgent
- ❑ Confirmed with the patient that they will notify the GP practice if they disengage or drop out before programme end. This is particularly important if any medications have been adjusted / stopped on the 1st day of TDR (as may need to be restarted)
- ❑ Counselled the patient appropriately and obtained valid, informed consent to refer