Interventional procedure overview of endoscopic duodenal mucosal resurfacing for insulin resistance in type 2 diabetes

Contents

Table 1 Abbreviations

Abbreviation	Definition
ABPM	Ambulatory 24 h blood pressure monitoring
AE	Adverse event
ALT	Alanine aminotransferase
ASCVD	Atherosclerotic cardiovascular disease
AST	Aspartate aminotransferase
BMI	Body mass index
DIAL	Diabetes lifetime-perspective prediction
DMR	Duodenal mucosal resurfacing
DTSQ	Diabetes Treatment Satisfaction Questionnaire
FPG	Fasting plasma glucose
FPI	Fasting plasma insulin
GI	Gastrointestinal
GLP-1/GLP-1RA	Glucagon-like peptide-1 (receptor agonists)
HDL	High-density lipoprotein
HOMA-IR	Homeostatic Model Assessment Index for Insulin Resistance
IQR	Interquartile range
LDL	Low-density lipoprotein
LS-DMR	Long segment ablation (about 9.3 cm treated) for duodenal mucosal resurfacing
MAP	Mean arterial pressure
mITT	Modified intention-to-treat
PDFF	Proton density fat function
PP	Per protocol
RCT	Randomised controlled trial

SAE	Serious adverse event
SAT	Subcutaneous adipose tissue
SD	Standard deviation
SS-DMR	Short segment ablation (about 3.4 cm treated) for duodenal mucosal resurfacing
T2D	Type 2 diabetes (mellitus)
VAT	Visceral adipose tissue

Indications and current treatment

T2D is a chronic metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in hyperglycaemia. The condition is commonly associated with obesity, physical inactivity, raised blood pressure, periodontitis, disturbed blood lipid levels and a tendency to develop thrombosis. It is recognised to lead to an increased cardiovascular and stroke risk.

Dietary control is the mainstay of T2D treatment. Weight loss and being active are also recommended to help manage the condition. In addition to lifestyle modification, T2D is controlled using metformin, insulin or other medicines, with the aim of keeping a person's blood sugar levels within a healthy range. These treatments have varying efficacy and can sometimes cause side effects, including hypoglycaemia.

What the procedure involves

Endoscopic DMR is a minimally invasive procedure. It involves endoscopic exploration under general anaesthesia or deep sedation. This is followed by submucosal expansion with saline, and then hydrothermal ablation of the duodenal mucosa under direct vision with fluoroscopic guidance. The aim is for mucosal regeneration, and so to treat the duodenal dysfunction that is thought to contribute to insulin resistance.

Outcome measures

The main outcomes included HbA1c levels, FPG), FPI, pancreatic or liver markers, HOMA-IR, treatment satisfaction, weight loss, GI symptoms (for example, diarrhoea, abdominal pain, nausea and oropharyngeal pain), general

symptoms (for example, malaise, fatigue, musculoskeletal pain and rash), hypoglycaemia, hyperglycaemia and cardiovascular outcomes (for example, cholesterol and blood pressure).

HOMA-IR uses fasting insulin and glucose levels to measure insulin resistance. Scores of about 1 or less indicate insulin sensitivity, about 2 indicates early insulin resistance and about 3 or more indicates strong insulin resistance.

ASCVD is an algorithm used to calculate the risk of atherosclerotic cardiovascular disease based on various demographic and blood pressure related domains. Scores equal to and above 20% indicate a patient is at high risk of the disease. 7.5% to 19.9% indicates intermediate risk, 5.0% to 7.4% indicates borderline risk and less than 5.0% indicates low risk.

The DIAL model predicts the cardiovascular disease-free life expectancy (in years) of people with T2D based on various demographic and health factors (for example, BMI, HbA1c, smoking).

The DTSQ is a 6-item questionnaire used in clinical trials and monitoring that gauges the patient's satisfaction with a diabetes treatment regimen. Higher scores indicate greater satisfaction with a treatment and the scores range from 0 to 36.

Evidence summary

Population and studies description

This interventional procedures overview is based on 214 people from 1 RCT, 2 prospective cohort studies (1 study with 2 publications) and 1 proof of concept study. Of these 214 people, 157 people had the procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 5 studies as the key evidence in table 2 and table 3, and lists 4 other relevant studies in table 5.

Mingrone (2022) was a multicentre double-blind sham-controlled RCT for DMR for people with T2D. The study was done across 11 sites in Europe (9) and Brazil (2), with 56 people having the DMR procedure and 52 having the sham version of the procedure. The baseline characteristics of subgroups were broadly similar. The Brazil subgroup was split close to 50% men and 50% women, while men made up around 76% of patients in European centres. Mean age across the study was 58 years and the follow up was 24 weeks.

The study by van Baar (2022) was a prospective single-arm study for DMR for people with T2D with a 2-year follow up. The study was done across 7 sites in the Netherlands, Belgium, Italy, the UK and Chile. Forty-six people were included for the treatment, but the analysis was only done for up to 33 people. From the baseline set of people (n=34), the mean age was 56.2 years and 64.7% were men.

van Baar (2021) was a prospective cohort study for DMR combined withGLP-1 RA) to stop insulin in T2D. It was carried out in the Netherlands and included 16 people with T2D. The median age of this cohort was 61 years and 63% were men. People were followed up for up to 18 months.

Meiring (2022) was based on the same prospective study as van Baar (2021) but with a focus on cardiovascular health. Cardiovascular outcomes were captured at baseline and at 6 months after DMR.

Rajagopalan (2016) was a phase 1 first-in-human non-randomised proof-of-concept study in a single centre in Chile. It investigated the efficacy and safety of DMR in a cohort of 44 people with T2D. The mean age was 53.4 years and 64% were men. Thirty-nine people had the treatment and were followed up for 6 months.

Table 2 presents study details.

Figure 1 Flow chart of study selection

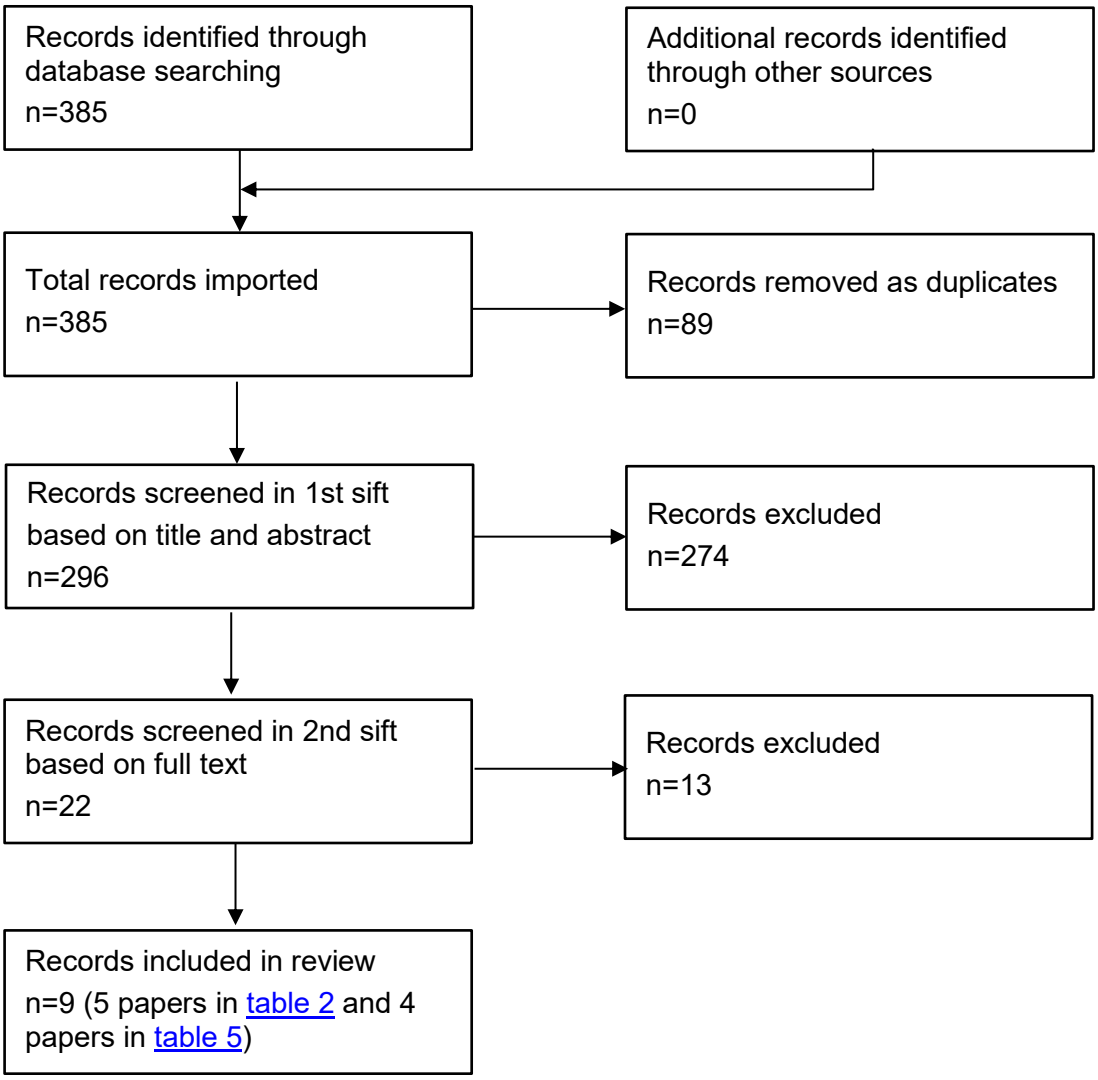

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
1	Mingrone, 2022 Italy, UK, Belgium, Netherlands and Brazil	108 (75:33)	Mean = 58 years	RCT	Aged 28 to 75 years Diagnosed with T2D and evidence of preserved insulin secretion. Fasting insulin greater than 7.0 µU/ml HbA1c levels of 59 to 86 mmol/mol (7.5% to 10.0%) BMI between 24 and 40 kg/m^2 Currently taking 1 or more oral glucose-lowering medications, of which 1 must be metformin, with no changes in medication in the previous 12 weeks before study entry. Able to comply with study requirements and understand and sign informed consent.	DMR versus sham-DMR	24 weeks
2	van Baar, 2022 Multiple	34 (22:12) 46 attempted treatment	Mean = 56.2 years	Prospective cohort study	Aged 28 to 75 years Diagnosed with T2D in the last 10 years BMI between 24 and 40 kg/m^2	DMR	24 months

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
					HbA1c levels of 59 to 86 mmol/mol (7.5% to 10.0%) Stable diabetes treatment with 1 or more oral glucose-lowering medication for at least 3 months at enrolment **Exclusions** Clinical diagnosis of type 1 diabetes, positive glutamic acid decarboxylase antibodies or both Low endogenous insulin production (fasting C-peptide levels <0.333 nmol/litre) Used injectable glucose-lowering medication Had GI surgery that could impact treatment of the duodenum Had chronic or acute pancreatitis Active hepatitis or liver disease Upper GI tract bleeding conditions		
3	van Baar, 2021	16 (10:6)	Median = 61 years	Prospective cohort study	Aged 28 to 75 years BMI between 24 and 40 kg/m^2	DMR, GLP-1RA and	18 months

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
	The Netherlands				HbA1c level of less than or equal to 62 mmol/mol (8%) Adequate beta cell reserve (fasting C-peptide more than 0.5 nmol/litre) Using long-acting insulin **Exclusions** Type 1 diabetes History of ketoacidosis Use of non-insulin injectable glucose-lowering medication	lifestyle counselling	
	Meiring, 2022 The Netherlands	16 (10:6)	Median = 61 years	Prospective cohort study	Aged 28 to 75 years BMI between 24 and 40 kg/m^2 HbA1c level of less than or equal to 62 mmol/mol (8%) Adequate beta cell reserve (fasting C-peptide more than 0.5 nmol/litre) Using long-acting insulin **Exclusions** Type 1 diabetes History of ketoacidosis Use of non-insulin injectable glucose-lowering medication	DMR, GLP-1RA and lifestyle counselling	6 months

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
4	Rajagopalan, 2016 Chile	44 (28:16), 39 treated	Mean = 53.4 (plus or minus 7.5) years	Proof-of-concept study	Aged 28 to 75 years Diagnosed with T2D in the last 10 years BMI between 24 and 40 kg/m^2 HbA1c level of 58 to 108 mmol/mol (7.5% to 12.0%) Using at least 1 oral antidiabetic medication Fasting C-peptide more than 1 ng/mL **Exclusions** Type 1 diabetes (including antibodies to glutamic acid decarboxylase positivity) Current use of injectable antidiabetic medication History of GI surgery or anatomical abnormalities that would preclude the DMR procedure Treatment with antiplatelet drugs that could not be temporarily stopped Pregnancy	DMR	6 months

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Mingrone, 2022*	mITT analysis **HbA1c:** The DMR group had a median absolute change of -10.4 (18.6) mmol/mol at 24 weeks compared with -7.1 (16.4) in the sham group, which was not a statistically significant difference (p=0.147). Similarly, the relative difference (% change) was not statistically significant (p=0.184). In the analysis of the European subgroup (N=75), DMR produced a statistically significant (p=0.033) median improvement of -6.6 (17.5) mmol/mol at 24 weeks compared with -3.3 (10.9) mmol/mol in the sham group. The relative changes were -9.6% and -3.8%, respectively (p=0.034). The absolute and relative differences were larger in the Brazil subgroup (N=33) with more than a 25% median improvement at 24 weeks in both DMR and sham groups, but neither absolute (p=0.104) or relative (p=0.105) changes were statistically significant across treatment groups. **Weight loss:** The median absolute weight loss in the DMR group at 24 weeks was -2.8 (4.5) kg compared with -1.5 (3.3) kg in the sham group, a statistically significant difference (p=0.021).	**SAEs:** In the Brazil subgroup (N=33), 3 SAEs were reported for 2 patients. One patient had haematochezia because of an external haemorrhoid, but the investigator adjudicated it as possibly related to procedure. The other patient had a jejunal perforation needing surgical repair. **AEs within 30 days** **Europe:** • DMR patients (n=39) had instances of abdominal pain (9), diarrhoea (1), nausea (1), vomiting (1) and hypoglycaemia (3). • Sham procedure patients (n=36) experiences instances of abdominal pain (2), diarrhoea (2) and hypoglycaemia (3). **Brazil:** • DMR patients (n=17) had instances of abdominal pain (6), diarrhoea (1), nausea (2), vomiting (1) and hypoglycaemia (11). • Sham procedure patients (n=16) had instances of abdominal pain (2), diarrhoea (1) and hypoglycaemia (21). **AEs after 30 days**

First author, date	Efficacy outcomes	Safety outcomes
	In the Europe subgroup, the DMR group was -2.4 (2.8) kg compared with -1.4 (2.4) kg in the sham group (p=0.012). In the Brazil subgroup, the DMR group was -4.5 (5.6) kg compared with -2.1 (5.7) kg in the sham group (p=0.285). **BMI:** The median absolute change in BMI for the DMR group at 24 weeks was -0.9 (1.5) compared with -0.5 (1.1) in the sham group (p=0.025). In the Europe subgroup, median absolute BMI change in the DMR group was -0.8 (1.2) compared with -0.5 (0.9) in the sham group (p=0.011). In the Brazil subgroup, median absolute BMI change in the DMR group was -1.4 (1.9) compared with -0.8 (1.9) in the sham group (p=0.28). PP analysis **HbA1c:** The data was stratified by baseline FPG level. For people with baseline FPG ≥10 mmol/litre, the median HbA1c change with DMR at 24 weeks was better than sham in the overall group (-14.2 versus -4.4, p=0.002) and the Europe subgroup (-13.1 versus -1.6, p=0.005), but no statistically significant difference in the Brazil subgroup (-17.5 versus -13.1, p=0.448). No statistically significant differences between DMR/sham were seen for HbA1c for people with FPG <10 mmol/litre.	**Europe:** • DMR patients (n=39) had instances of abdominal pain (1) and hypoglycaemia (1). • Sham procedure patients (n=36) had instances of abdominal pain (2) and hypoglycaemia (4). **Brazil:** • DMR patients (n=17) had 53 instances of hypoglycaemia. • Sham procedure patients (n=16) had 52 instances of hypoglycaemia.

First author, date	Efficacy outcomes	Safety outcomes
	Liver MRI-PDFF: The data was stratified by baseline FPG level. For people with baseline FPG 10 mmol/litre or above, the median MRI-PDFF change with DMR at 12 weeks was better than sham in the overall group (-7.6 versus -3.1, p=0.01) and the Europe subgroup (-8.0 versus -2.1, p=0.006), but worse in the Brazil subgroup (-5.4 versus -6.7, p=0.006). No statistically significant differences between DMR or sham were seen for MRI-PDFF for people with an FPG below 10 mmol/litre. **FPG:** There were no statistically significant differences between median FPG change from baseline to 24 weeks across treatment groups in Europe (mITT, p=0.218; PP, p=0.139) or Brazil (mITT, p=0.285; PP, p=0.167) subgroups. **HOMA-IR:** DMR reduced median HOMA-IR at 24 weeks by 1.3 compared with 0.4 with the sham procedure in the Europe subgroup PP analysis (p=0.047). No statistically significant differences in HOMA-IR were seen in the Europe mITT (p=0.06) or Brazil (mITT, p=0.437; PP, p=0.196) subgroup analyses.	
van Baar, 2022	**HbA1c:** Statistically significant reductions in HbA1c from baseline were seen at 6, 12, 18 and 24 months (p<0.05). The mean change of HbA1c at 6 months	**AEs:** Up to 24 weeks after DMR, 24 patients reported 50 procedure-related AEs (mostly GI disorders) and 1 patient had 3 device-related AEs.

First author, date	Efficacy outcomes	Safety outcomes
	after DMR was -10 ± 10 mmol/mol (p<0.001). In PP analysis, the change at 6 months was -12.9 mmol/mol (SD=8.3, n=28) and at 24 months the change was -15.8 mmol/mol (SD=8.5, n=19). **FPG:** Statistically significant reductions in FPG from baseline were seen at 6, 12, 18 and 24 months (p<0.001). The mean FPG change after DMR at 6 months from baseline was -37.3 ± 47.8 mg/dL (-2.1 ± 2.7 mmol/mol) and at 24 months the change was -34.7 ± 36.0 mg/dL (-1.9 ± 2.0 mmol/mol). **Fasting C-peptide:** Statistically significant reductions in C-peptide were seen at 6 and 24 months (p<0.05). The mean C-peptide change after DMR was -0.8 ± 1.1 ng/mL at 6 months and -0.7 ± 1.0 ng/mL at 24 months. **Weight:** Mean weight at baseline was 88.9 ± 11.8kg. The mean weight loss after DMR was -2.6 ± 3.7kg at 12 months (p<0.001) and -3.1 ± 6.0kg at 24 months (p=0.010). **DTSQ:** Treatment satisfaction, given by mean DTSQ (status version), increased from 27.5 ± 6.6 at baseline to 31.1 ± 5.3 at 12 months (p=0.0039) and to 30.1 ± 6.1 at 24 months (p=0.0699). **ALT:**	From 6 months to 24 months, 80% (37/46) of patients reported AEs, including 2 procedure-related AEs: 1 patient reported constipation, and 1 patient reported general malaise and vitamin B12 deficiency. **Serious AEs:** Six patients (possibly of the 37 above) reported SAEs which were neither device nor procedure related.

First author, date	Efficacy outcomes	Safety outcomes
	Statistically significant reductions in (ALT from baseline were seen at 12 months of -10.2 ± 15.8 U/litre (p<0.005) and at 24 months of -8.5 ± 16.8 U/litre (p=0.048). In PP analysis, the change at 6 months was -15.4 (SD=18.2, n=23) and -16.6 (SD=14.2, n=18) at 24 months. **AST:** Statistically significant reductions in AST from baseline were seen at 6 months of -3.7 ± 8.0 U/litre (p=0.033) and at 12 months of -5.7 ± 6.7 U/litre (p<0.001). In PP analysis, the change at 6 months was -7.7 (SD=6.1, n=22) and -9.6 (SD=5.1, n=14) at 24 months. **HOMA-IR:** Statistically significant reductions in HOMA-IR from baseline were seen at 6 and 12 months. The mean HOMA-IR change after DMR at 6 months was -2.9 ± 6.5 (p=0.012) and at 12 months was -3.7 ± 5.4 (p<0.001). **Reduced glucose-lowering medication use:** Medication use was followed up in 34 patients after DMR. At 24 months, patient medication use had reduced (1), remained unchanged (17), increased doses of an existing medication (8), added on 1 oral medication (4), and had insulin added (4).	
van Baar, 2021*	**HbA1c:** Eleven of 16 patients reached adequate glycaemic control (HbA1c ≤7.5%) at 6 months after DMR with	**AEs:** In total, 65 AEs were reported for 15 of 16 patients.

First author, date	Efficacy outcomes	Safety outcomes
	GLP-1RA. They were administered 1.8 mg liraglutide per day and oral glucose-lowering medication remained unchanged. Of these 11 'responders', 9 were still responsive at 12 months and 8 were responsive at 18 months. Five of 11 patients had HbA1c greater than 7.5% at 6 months and switched back to insulin. The median HbA1c was 7.5% at baseline. There were no statistically significant changes at any follow-up point. In the responder subgroup (n=11) median HbA1c reduced from 7.5% (7.1 to 7.9) at baseline to 6.7% (6.6 to 7.0) at 6 months (p=0.008). There was no statistically significant change at 12 or 18 months. **FPG:** Median FPG was 10.1 (8.9 to 12.0) mmol/litre at baseline. It reduced to 8.0 (6.6 to 9.5) mmol/litre at 6 months (p=0.039), 7.1 (6.6 to 9.5) mmol/litre at 12 months (p=0.006) and was 7.3 (6.7 to 8.4) mmol/litre at 18 months (p=0.011). **HOMA-IR:** Median HOMA-IR reduced from 8.4 (4.3 to 12.0) at baseline to 2.5 (1.8 to 3.1) at 6 months (p=0.002). HOMA-IR remained improved at 6 months with a median value of 3.8 (2.4 to 7.9, p=0.015) and also at 18 months with a median of 3.9 (2.0 to 6.0, p=0.006). **FPI:**	Twenty-one procedure-related AEs were reported for 10 of 16 patients: 17 GI symptoms (including diarrhoea, heartburn, abdominal pain and nausea) and 4 general symptoms (including low energy level, orthostatic hypotension). One AE was considered moderate and the other 20 were considered mild. Fifteen study drug-related AEs were reported for 10 of 16 patients with 93% being considered mild. 11 instances were GI symptoms and 4 were general symptoms. Twenty-nine AEs that were not procedure- or study drug-related were reported for 8 of 16 patients. This included GI symptoms (3), general symptoms (9), metabolic symptoms (for example, hypo-hyperglycaemia; 1) and infections (16). No instances of hypoglycaemia or device-related events were reported throughout the follow up. Two patients with 4 treatment-unrelated SAEs were reported: 1 patient with fibula fracture with subsequent thrombosis, 1 patient with asthma exacerbation with subsequent pneumonia needing hospital admission.

First author, date	Efficacy outcomes	Safety outcomes
	Median fasting insulin at baseline was 104 (49 to 178) pmol/litre and some statistically significant changes from baseline were seen. Median fasting insulin was 42 (26 to 64) pmol/litre at 6 months (p=0.001), then 71 (45 to 121) pmol/litre at 12 months (p=0.116), and 63 (34 to 110) pmol/litre at 18 months (p=0.036). **Fasting C-peptide:** At baseline, fasting C-peptide was 0.62 (0.55 to 0.91) nmol/litre. There were no statistically significant changes to fasting C-peptide at any follow up. **Weight loss:** Statistically significant weight changes were seen from the baseline median weight of 87.8 (80.2 to 99.7) kg. At 6 months, median weight was 80.1 (74.6 to 92.3) kg (p=0.001), then 80.8 (73.2 to 95.8) kg at 12 months (p=0.001), then 80.7 (73.8 to 96.8) kg at 18 months (p=0.001). **BMI:** At baseline, median BMI was 28.8 (26.5 to 31.7) kg/m^2. This reduced to a median BMI of 26.5 (24.3 to 29.8) kg/m^2 at 6 months (p=0.001), 27.7 (23.4 to 30.1) kg/m^2 at 12 months (p=0.001) and 26.4 (23.5 to 30.2) kg/m^2 at 18 months (p=0.001). **PDFF:** Median PDFF at baseline was 8.1% (4.0 to 13.5). The median PDFF at 6 months was 5.3% (3.9 to	

First author, date	Efficacy outcomes	Safety outcomes
	11.4,p=0.053) and 5.6% (2.8 to 10.9) at 12 months (p=0.035).	
Meiring, 2022	**Abdominal VAT and SAT:** Median VAT for 14 of 16 patients decreased from 248 (184 to 294) cm^2 at baseline to 188 (156 to 244) cm^2 at 6 months after DMR with GLP1-RA (p=0.002). Median SAT for 13 of 16 patients decreased from 152 (136 to 190) cm^2 at baseline to 121 (93 to 158) cm^2 at 6 months after DMR with GLP1-RA (p=0.002). **ABPM:** ABPM was done in all 16 patients. Median daytime systolic blood pressure reduced from 132 (119 to 148) mmHg at baseline to 127 (115 to 137) at 6 months after DMR (p=0.001). Median daytime diastolic blood pressure reduced from 83 (73 to 89) mmHg at baseline to 79 (72 to 86) mmHg at 6 months after DMR (p=0.037). Median daytime MAP reduced from 104 (95 to 115) mmHg at baseline to 100 (93 to 109) mmHg at 6 months after DMR (p<0.001). Median 24-hour heart rate increased from 78 (67 to 84) bpm at baseline to 81 (73 to 89) bpm at 6 months after DMR (p<0.001). No statistically significant differences were seen for 24 hour or nighttime systole, diastole and MAP.	Not reported.

First author, date	Efficacy outcomes	Safety outcomes
	14 of 16 patients had no change in their blood pressure lowering medication. One patient started amlodipine 5 mg 3 months after DMR and 1 patient stopped hydrochlorothiazide 3 months after DMR. **Postprandial insulin:** Median postprandial insulin was lower at all intervals in the 2 hours after the mixed meal test at 6 months after DMR than it was at baseline. **Fasting lipid panel:** Median total cholesterol reduced from 3.64 (3.34 to 4.89) mmol/litre at baseline to 3.48 (3.18 to 3.97) mmol/litre at 6 months after DMR (p=0.008). Median LDL reduced from 1.92 (1.49 to 2.30) mmol/litre at baseline to 1.79 (1.49 to 2.08) mmol/litre at 6 months after DMR (p=0.044). Median triglycerides reduce from 1.79 (1.15 to 2.66) mmol/litre at baseline to 1.09 (0.91 to 1.89) mmol/Litre at 6 months after DMR (p=0.023). Median HDL reduced from 1.21 mmol/litre at baseline to 1.15 at 6 months after DMR, but this was not a statistically significant difference. **Urine microalbumin:** Median urine microalbumin decreased from 7 (3 to 27) mg/ litre at baseline to 4 (3 to 8) mg/litre at 6 months after DMR (p=0.018). **ASCVD:**	

First author, date	Efficacy outcomes	Safety outcomes
	Median ASCVD risk score reduced from 13.6% (5.7 to 26.0) at baseline to 11.5% (4.2 to 22.5) at 6 months after DMR. The number of patients considered high risk (ASCVD score greater than or equal to 20%) was 6 (37.5%) at baseline which reduced to 4 (25%) at 6 months after DMR. **DIAL:** The DIAL model estimated that ASCVD-free life years increased by 1 year from 82 (81 to 83) at baseline to 83 (81 to 84) at 6 months after DMR.	
Rajagopalan, 2016	**HbA1c:** Mean HbA1c was 9.6% ± 1.4% at screening. Mean HbA1c was reduced by 1.2% ± 0.3% at 6 months after DMR ($p<0.001$). At 3 months, the LS-DMR group had a mean HbA1c reduction of 2.5% ± 0.2%, while the SS-DMR group had a mean reduction of 1.2% ± 0.5% ($p<0.05$ between groups). At 6 months, the LS-DMR group had a mean reduction of 1.4% ± 0.3%, while the SS-DMR group had a mean reduction of 0.7% ± 0.5% ($p=0.3$ between groups). **FPG:** At screening, mean FPG was 187 ± 58 mg/dL. The LS-DMR group had lower mean FPG than the SS-DMR group at 1 and 3 months ($p<0.05$). In the LS-	**AEs:** No GI bleeding, perforation, pancreatitis, severe hypoglycaemia or evidence of malabsorption were reported after the DMR. No patients had any signs of infection. Eight of 40 patients had abdominal pain because of air insufflation, endotracheal intubation, or both after DMR. No patients reported discomfort by 48 hours after DMR. Three patients developed a duodenal stenosis that presented as epigastric pain and vomiting.

First author, date	Efficacy outcomes	Safety outcomes
	DMR group (n=28), most patients had a glucose-lowering response after DMR. **FPI:** There was no observed change in mean FPI from screening (11.7 ± 1.0 ml U/litre) to 3 months (11.8 ± 1.5 ml U/litre) to 6 months after DMR (11. ± 1.3 ml U/litre) in the LS-DMR group (n=28). **Weight:** In the LS-DMR group, there was a weight reduction of 3.9 ± 0.5kg at 3 months ($p<0.001$) and 2.5 ± 0.1kg at 6 months ($p<0.05$). There was no correlation between weight loss and magnitude of HbA1c improvement.	

* Results of Mingrone (2022), van Baar (2021) and Meiring (2022) are median (IQR).

Procedure technique

Of the 4 studies, 1 study detailed the procedure technique and devices used in the paper and 3 studies referred to procedure details in referenced studies.

The procedure involves endoscopic exploration under general anaesthetic or deep sedation, followed by submucosal expansion with saline and the hydrothermal ablation of the duodenal mucosa under direct vision with endoscopic or fluoroscopic guidance. The circumferential ablations are done up to 5 times along the length of the post-papillary duodenum. The aim of the hydrothermal ablation is to cause the mucosa to regenerate and treat duodenal dysfunction, which is thought to contribute to insulin resistance.

The device used for this procedure (the Revita system DMR technology) consists of a console and a novel single-use balloon catheter. The console is used to monitor the procedure, while clinicians use the catheter to access the duodenum and do the DMR procedure in an outpatient setting.

The sham procedure (Mingrone, 2022) involved placing the DMR catheter over the guidewire into the stomach and leaving it in place for 30 minutes before removing it from the patient.

Rajagopalana (2016) did 2 variations of DMR: LS-DMR and SS-DMR. The long version, LS-DMR, ablated about 9.3 cm of duodenum tissue, while the short version, SS-DMR, ablated about 3.4 cm of tissue.

Efficacy

Glycaemic endpoints

HbA1c was reported in all 4 studies. The RCT (Mingrone, 2022) found no statistically significant difference in HbA1c change at 24 weeks between the overall DMR and sham groups. The change from baseline in median HbA1c in

the Europe subgroup was 6.6 mmol/mol after DMR compared with 3.3 mmol/mol after sham at 24 weeks (p=0.033). Median changes in the Brazil subgroup at 24 weeks were not statistically significant (p=0.104). The PP analysis found that DMR reduced median HbA1c in patients with baseline FPG 10 mmol/litre or higher by 14.2 mmol/mol at 24 weeks compared with 4.4 mmol/mol with the sham procedure (p=0.002) in the whole population and by 13.1 mmol/mol compared with 1.6 mmol/mol after sham in the Europe subgroup (p=0.005). There was no statistically significant difference between treatments in the Brazil subgroup or any group in which baseline FPG was less than10 mmol/litre. Mean HbA1c improvements from baseline of -0.9% to -1.2% were seen at 6 months (van Baar, 2022, p<0.001; Rajagopalan, 2016, p<0.001) and remained at 12, 18 and 24 months (van Baar, 2022, p<0.05). One study (van Baar, 2021) found no statistically significant change in median HbA1c up to 18 months, other than a median HbA1c reduction from 7.5% at baseline to 6.7% at 6 months in the PP analysis (p=0.008, n=11). The LS-DMR group (Rajagopalan, 2016) had greater reductions than the SS-DMR group at 3 months (2.5% compared with 1.2%, p<0.05). The differences were not statistically significant at 6 months (1.4% compared with 0.7%, p=0.30).

FPG was reported in all 4 studies. There was no statistically significant difference between median FPG change from baseline across DMR and sham groups in Europe and Brazil subgroups (Mingrone, 2022). Mean reductions in FPG from baseline were seen at 6, 12, 18 and 24 months (p<0.001). There was a mean reduction of 2.1 ± 2.7 mmol/mol at 6 months and -1.9 ± 2.0 mmol/mol at 24 months (van Baar, 2022). Median FPG was statistically significantly different from baseline at 6, 12 and 18 months (van Baar, 2021). FPG was 10.1 mmol/litre at baseline and reduced to 8.0 at 6 months (p=0.039), 7.1 at 12 months (p=0.006) and 7.3 at 18 months (p=0.011). LS-DMR produced lower FPG at 1 and 3 months than SS-DMR (Rajagopalan, 2016; p<0.05).

HOMA-IR was reported in 3 studies. In the RCT (Mingrone, 2022), DMR reduced HOMA-IR by 1.3 compared with 0.4 after sham in the Europe PP analysis (p=0.047). Statistically significant reductions of HOMA-IR of at least 2.9 were seen for median HOMA-IR at 6 and 18 months (van Baar, 2021; p<0.05) and for mean HOMA-IR at 6 and 12 months (van Baar, 2022; p<0.05).

Fasting C-peptide was reported in 2 studies. After DMR, mean fasting C-peptide had reduced from baseline by 0.8 ± 1.1 ng/mL at 6 months and 0.7 ± 1.0 ng/mL at 24 months (van Baar, 2022; p<0.05). van Baar (2021) found no statistically significant changes to fasting C-peptide at any follow up.

FPI was reported in 2 studies. van Baar (2021) found that DMR with GLP1-RA reduced median FPI from the baseline value of 104 (49 to 178) pmol/litre to 42 (26 to 64) pmol/litre at 6 months (p=0.001), 71 (45 to 121) pmol/litre at 12 months (p=0.116) and 63 (34 to 110) pmol/litre at 18 months (p=0.036). Rajagopalan (2016) reported FPI for the LS-DMR group (n=28) and found no statistically significant change from baseline at 3 and 6 months after DMR.

Postprandial insulin was reported in 1 study (Meiring, 2022). Median postprandial insulin was measured at intervals of 15 to 60 minutes for the first 4 hours after mixed meal tolerance testing. The median values at intervals in the 4 hours after the start of the mixed meal test were all lower at the 6 months after DMR test than they were at the baseline test.

Diabetic medication use was reported in 1 study. At 24 months after DMR, 3% (1/34) of patients had reduced their medication usage, 50% (17/34) of patients' medication had remained unchanged and 47% (16/34) had increased their medication dosage, added an oral medication or added insulin (van Baar, 2022).

Metabolic endpoints

Weight was reported in 4 studies. In the RCT (Mingrone, 2022), median weight loss after DMR was -2.8 kg (IQR=4.5) at 24 weeks; a greater weight loss than in the sham group of -1.5 kg (IQR=3.3; p=0.021). Weight loss was greater in DMR groups than sham groups for the Europe and Brazil subgroups but only statistically significantly different in the Europe subgroup (p=0.012). Average weight loss was seen at various time points after DMR. Mean change from baseline after DMR was -2.6 ± 3.7 kg at 12 months (p<0.001) and -3.1 ± 6.0 kg (p=0.010; van Baar, 2022). Median change at 6, 12 and 18 months after DMR and GLP1-RA was about -7 kg (van Baar, 2021; p=0.001). In the LS-DMR group (Rajagopalan, 2016), weight loss of 3.9 ± 0.5kg was seen at 3 months after DMR (p<0.001) and 2.5 ± 0.1kg at 6 months (p=0.05). Rajagopalan (2016) found no correlation between weight loss and magnitude of HbA1c improvement.

BMI was reported in 2 studies. Median BMI reductions from baseline were seen in both studies (Mingrone, 2022; van Baar, 2021). The RCT found a statistically significantly greater reduction in BMI after DMR than after sham at 24 weeks (p=0.025). In the van Baar (2021) study, median BMI reduction was 2.3 kg/m^2 at 6 months, 1.1 kg/m^2 at 12 months and 2.4 kg/m^2 at 18 months (all p=0.001).

Pancreatic or liver markers were reported in 3 studies. PDFF was reported in 2 studies (Mingrone, 2022; van Baar, 2021). Mingrone (2022) found that, for people with a baseline FPG of 10 mmol/litre or more, DMR produced greater reductions in PDFF at 12 weeks than the sham procedure in the overall group (7.6 compared with 3.1, p=0.01) and the Europe subgroup (8.0 compared with 2.1, p=0.006) but not in the Brazil subgroup (5.4 compared with 6.7, p=0.006). For people with a baseline FPG of less than 10 mmol/litre, there was no statistically significant difference between DMR and sham groups. Baseline median PDFF in van Baar (2021) was 8.1%, which reduced to 5.3% at 6 months (p=0.053) and 5.6% (p=0.035) at 12 months. van Baar (2022) reported on AST and ALT. Statistically significant reductions in AST of 3.7 to 5.7 U/litre after DMR were

seen at 6 and 12 months ($p<0.05$). Statistically significant reductions in ALT of 8.5 to 10.2 were seen at 12 and 24 months ($p<0.05$).

VAT/SAT were reported in 1 study. Median VAT reduced from 248 cm^2 at baseline to 188 cm^2 at 6 months after DMR (Miering, 2022; p=0.002). Median SAT reduced from 152 cm^2 at baseline to 121 cm^2 at 6 months after DMR (Meiring, 2022; p=0.002).

Cardiovascular markers

Cardiovascular outcomes were reported in 1 study (Meiring, 2022). Median daytime systolic blood pressure reduced from 132 (119 to 148) mmHg at baseline to 127 (115 to 137) at 6 months after DMR (p=0.001). Daytime diastolic blood pressure reduced from a median value of 83 (73 to 89) mmHg at baseline to 79 (72 to 86) mmHg at 6 months after DMR (p=0.037). Daytime MAP reduced from 104 (95 to 115) mmHg at baseline to 100 (93 to 109) mmHg at 6 months after DMR (p<0.001). Median heart rate increased from 78 (67 to 84) bpm at baseline to 81 (73 to 89) bpm at 6 months after DMR (<0.001). No statistically significant differences were seen for changes in nighttime or 24-hour measures of systole, diastole and MAP between baseline at 6 months after DMR. Fourteen of 16 patients had no change in their blood pressure lowering medication over the 6 months follow up. One patient started amlodipine 5 mg 3 months after DMR and 1 patient stopped hydrochlorothiazide 3 months after DMR.

Median total cholesterol was statistically significantly lower after DMR (p=0.008). Median cholesterol was 3.64 (3.34 to 4.89) mmol/litre at baseline and reduced to 3.48 (3.18 to 3.97) at 6 months after DMR.

Median LDL reduced from 1.92 (1.49 to 2.30) mmol/litre at baseline to 1.79 (1.49 to 2.30) mmol/litre at 6 months after DMR (p=0.044). Median HDL reduced from 1.21 mmol/litre at baseline to 1.15 at 6 months after DMR, but this was not a statistically significant difference.

Urine microalbumin test revealed lowering of albumin after DMR. The median value at baseline was 7 (3 to 27) mg/litre at baseline and reduced to 4 (3 to 8) mg/litre at 6 months after DMR (p=0.018).

The ASCVD scores indicated that DMR reduced the median risk of atherosclerotic cardiovascular disease. At baseline, the median ASCVD score was 13.6% (5.7 to 26.0) and at 6 months after DMR the median score was 11.5% (4.2 to 22.5). The median scores at both time points indicate intermediate risk of cardiovascular disease. The number of patients considered at high risk (ASCVD scores of 20% or above) reduced from 6 at baseline (37.5%) to 4 at 6 months after DMR (25%).

The DIAL model predicted 82 (81 to 83) ASCVD-free life years at baseline. At 6 months after DMR, the predicted value was 83 (81 to 84).

Treatment satisfaction

DTSQ was reported in 1 study (van Baar, 2022). The mean DTSQ score improved from 27.5 ± 6.6 at baseline to 31.1 ± 5.3 at 12 months (p=0.0039), and 30.1 ± 6.1 at 24 months (p=0.0699).

Safety

Safety outcomes were reported in all 4 studies. Across studies, 157 patients were treated with DMR and 229 AEs were reported (including 7 SAEs).

Metabolic symptoms

In the Mingrone (2022) RCT (n=56 for DMR), 68 of 94 AEs were instances of hypoglycaemia. For people in the sham arms (n=52), there were 80 instances of hypoglycaemia out of 89 AEs. One case of hypoglycaemia and 1 case of hyperglycaemia were reported by van Baar (2022; n=46). van Baar (2021)

reported 1 case of either hypo/hyperglycaemia (n=16) and none were reported by Rajagopalan (2016).

SAEs

Three SAEs in 1 paper were haematochezia, haemorrhoid and jejunal perforation (Mingrone, 2022; n=56 for DMR).

GI symptoms

GI-related AEs were described in 4 studies. Mingrone (2022) reported abdominal pain (16), nausea (3), diarrhoea (2) and vomiting (2) for their 56 patients having DMR. van Baar (2022) reported abdominal pain (13), diarrhoea (11), nausea (7), oropharyngeal pain (5), constipation (2), vomiting (2), throat irritation (1) and 1 other GI symptom. One study reported 31 non-specific GI symptoms (van Baar, 2021; n=16). Rajagopalan (2016) reported 8 instances of abdominal pain and 3 instances of duodenal stenosis which presented as epigastric pain and vomiting.

General symptoms

General symptoms such as malaise and fatigue were detailed by 2 studies. van Baar (2022; n=46) reported 3 instances of musculoskeletal pain, 2 instances of malaise and 1 instance for each of fatigue, rash, influenza-like illness, body temperature increase and C-reactive protein increase. The other study reported 17 general symptom AEs and 16 infections (van Baar, 2021; n=16).

Anecdotal and theoretical AEs

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other AEs for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there

were other AEs that might possibly occur, even if they had never happened (theoretical).

They listed the following anecdotal AEs:

- Difficulty swallowing
- Perforation
- Stenosis
- Sore throat
- Stricture
- Bleeding
- Abscess formation
- Anaesthesia complication
- Duodenal perforation/haemorrhage
- Pancreatitis.

They listed the following theoretical AEs:

- Device-related risks, such as:
  - Allergic reaction
  - Device dysfunction
  - Disarticulation of component from the device
  - Device/component lost in GI tract or wall
  - Puncture damage to surrounding structures (for example, liver, pancreas).

Six professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Across studies, the direction of the evidence mostly supports the efficacy of DMR in the reduction of HbA1c and other T2D-associated factors.

- The outcomes differed in measurement (median compared with mean) or units across studies, so comparisons of outcomes between studies should be done with care.
- Across outcomes in the Mingrone (2022) RCT, values differed to support either DMR or the sham procedure across the Europe and Brazil subgroups. The baseline characteristics of the 2 subgroups were broadly similar, but it is believed that the Brazilian population had a more intensive approach to treatment of diabetes and dieting, which explains some of the HbA1c treatment effects.
- van Baar (2022) discussed that changes in insulin resistance in their study were, in large part, driven by reductions in FPG.
- Rajagopalan (2016) found no correlation between weight loss and magnitude of HbA1c improvement.
- The sample sizes of people having DMR ranged from 16 to 56 patients. The procedure is somewhat novel (earliest paper 2016), but these are small samples to draw strong conclusions from.
- The demographic characteristics were similar across studies. They seem somewhat representative of the T2D population in England (National Diabetes Audit), although men are slightly overrepresented as study participants.
- Follow up ranged from 24 weeks to 24 months. Where reductions were seen in the shorter term (3 to 6 months), some papers were able to present sustained reductions from baseline in a given outcome in the longer term (12 to 24 months).
- The 2 most recent studies, Mingrone (2022) and van Baar (2022), included centres in the UK.
- There is overlap in authorship across the included studies.
- All 4 of the included studies included, at least 1 author who has worked for or had connections to Fractyl Laboratories.
- Inclusion criteria were similar across the studies.

- An RCT study NCT04419779 is enrolling up to 560 people for this procedure compared with sham and is due to be completed in January 2025.

Related NICE guidance

Interventional procedures

- NICE's interventional procedures guidance on Implantation of a duodenal-jejunal bypass liner for managing type 2 diabetes (Recommendation: research only IPG518, 2015)

NICE guidelines

- NICE guideline on Type 2 diabetes in adults: management (NG28; 2015, updated June 2022)
- NICE guideline on Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18; 2015, updated May 2023)
- NICE public health guideline on Type 2 diabetes: prevention in people at high risk (PH38; 2012, updated September 2017)
- NICE public health guideline on Type 2 diabetes prevention: population and community-level interventions (PH35; 2011)
- In development:
    - NICE guideline on Type 2 diabetes in adults: management (medicines updates) (publication expected December 2024)

Professional societies

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- British Society of Gastroenterology
- Association of Surgeons of Great Britain and Ireland
- Society for Endocrinology.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was

considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Mingrone G, van Baar AC, Devière J et al. (2022) Safety and efficacy of hydrothermal duodenal mucosal resurfacing in patients with type 2 diabetes: the randomised, double-blind, sham-controlled, multicentre REVITA-2 feasibility trial. Gut, 71(2), 254-264
2. van Baar AC, Devière J, Hopkins D et al. (2022) Durable metabolic improvements 2 years after duodenal mucosal resurfacing (DMR) in patients with type 2 diabetes (REVITA-1 Study). Diabetes research and clinical practice, 184, 109194
3. van Baar AC, Meiring S, Smeele P et al. (2021) Duodenal mucosal resurfacing combined with glucagon-like peptide-1 receptor agonism to discontinue insulin in type 2 diabetes: a feasibility study. Gastrointestinal Endoscopy, 94(1), 111-120
4. Meiring S, Busch CBE, van Baar ACG et al. (2022) Eliminating exogenous insulin therapy in patients with type 2 diabetes by duodenal ablation and GLP-1RA decreases risk scores for cardiovascular events. Cardiovascular Diabetology, 21(1), 1-8
5. Rajagopalan H, Cherrington AD, Thompson CC et al. (2016) Endoscopic duodenal mucosal resurfacing for the treatment of type 2 diabetes: 6-month interim analysis from the first-in-human proof-of-concept study. Diabetes Care, 39(12), 2254-2261

Methods

NICE identified studies and reviews relevant to endoscopic DMR for insulin resistance in T2D from the medical literature. The following databases were searched between the date they started to 22/03/2023: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific AEs that are not available in the published literature.
- Patients with type 2 diabetes.
- Intervention or test: duodenal mucosal resurfacing.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	22/03/2023	1946 to March 21, 2023
MEDLINE In-Process (Ovid)	22/03/2023	1946 to March 21, 2023
MEDLINE Epubs ahead of print (Ovid)	22/03/2023	March 21, 2023
EMBASE (Ovid)	22/03/2023	1974 to March 21, 2023
EMBASE Conference (Ovid)	22/03/2023	1974 to March 21, 2023
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	22/03/2023	
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	22/03/2023	Issue 2 of 12, February 2023

International HTA database (INAHTA)	22/03/2023	Issue 3 of 12, March 2023

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

1 Diabetes Mellitus, Type 2/ 167595
2 ((diabet* or DM) adj4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)).ti,ab. 156433
3 (dm2 or t2d* or mody or niddm).ti,ab. 46927
4 (DM adj4 (keto* or acidi* or gastropare*)).ti,ab. 86
5 ((DM adj4 onset* adj4 (maturit* or adult* or slow*)) or (DM adj4 depend* adj4 (non-insulin* or non insulin* or noninsulin*))).ti,ab. 171
6 or/1-5 207060
7 Intestinal Mucosa/ 93821
8 Duodenum/ 38708
9 7 and 8 5575
10 (duodenal adj4 mucosa*).tw. 3996
11 ((gastric adj4 epithelium) or (gastric adj4 surface adj4 epithelial adj4 metaplasia)).tw. 2161
12 (Duoden* adj4 dysfunct*).tw. 67
13 Insulin Resistance/ 66545
14 (insulin adj4 (sensitiv* or resist*)).tw. 106448
15 6 or 9 or 10 or 11 or 12 or 13 or 14 297290
16 Ablation Techniques/ 3426
17 (((Duoden* or hydrothermal or water) adj4 (resurfac* or ablati*)) or DMR).tw. 1806
18 (thermal adj4 (energy or ablat* or resurfac*)).tw. 7271
19 (organ adj4 edit*).tw. 49
20 (balloon adj4 catheter).tw. and endoscopes/ 49
21 ((balloon adj4 catheter) and endoscop*).tw. 584
22 or/16-21 12622
23 15 and 22 68
24 Revita.tw. 3
25 23 or 24 69
26 Animals/ not Humans/ 5071443
27 25 not 26 62

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed below.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
van Baar AC, Beuers U, Wong K et al. (2019) Endoscopic duodenal mucosal resurfacing improves glycaemic and hepatic indices in type 2 diabetes: 6-month multicentre results. JHEP Reports, 1(6), 429-437	N=94 6 months follow up	Lower mean HbA1c 6 months after DMR (7.9 ± 0.2%) compared with baseline (9.0 ± 0.2%, p<0.001). Lower FPG, AST and ALT at 6 months.	Reviews Rajagopalan (2016) which is included in Table 2 and van Baar (2020) which is superseded by the 2-year follow up, van Baar (2022).
van Baar AC, Holleman F, Crenier L et al. (2020) Endoscopic duodenal mucosal resurfacing for the treatment of type 2 diabetes mellitus: one year results from the first international, open-label, prospective, multicentre study. Gut, 69(2), 295-303	N=46 1 year follow up	Lower mean HbA1c at 24 weeks after DMR and sustained to 12 months. FPG, HOMA-IR and weight improved after DMR.	Superseded by the 2-year follow up, van Baar (2022).
Boškoski I, Orlandini B, Gallo C et al. (2020) Metabolic endoscopy by duodenal mucosal resurfacing: expert	N=92	DMR has shown promising preliminary results in terms of efficacy and safety among the arsenal	Literature review with expert commentary of 2 single case reports, Rajagopalan (2016) which is included in Table 2 and van

review with critical appraisal of the current technique and results. Expert Review of Gastroenterology & Hepatology, 14(5), 375-381		of treatments of T2D.	Baar (2020) which is superseded by the 2-year follow up, van Baar (2022).
de Oliveira GHP, de Moura DTH, Funari MP et al. (2021) Metabolic effects of endoscopic duodenal mucosal resurfacing: a systematic review and meta-analysis. Obesity Surgery, 31, 1304-1312	N=127	Estimated pooled improvements from baseline in HbA1c at 3 and 6 months after DMR. DMR improved FPG, ALT and liver fat, and likely led to reduced weight for patients.	Reviews 2 abstracts, Rajagopalan (2016) which is included in Table 2 and van Baar (2020) which is superseded by the 2-year follow up, van Baar (2022).