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Will pharmacotherapy soon replace bariatric surgery as the gold standard treatment for obesity?

EDUCATION

AUTHOR

Ms Heba Butt
University of Manchster

Dr Louise Hunter
Univeristy of Manchester

Address for correspondence:
Ms Heba Butt
School of Medical Sciences
Stopford Building
University of Manchester
Oxford Road
Manchester, UK
M13 9PL
United Kingdom

Email:
heba.butt@student.manchester.ac.uk

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ABSTRACT

Background: Obesity remains a substantial and growing global health issue, contributing significantly to comorbidities such as type 2 diabetes, cardiovascular disease, and reduced quality of life. As the prevalence of obesity continues to rise, clinicians must help people living with obesity to navigate the increasing range of treatment options. Bariatric surgery has been regarded as the gold standard treatment for severe obesity, due to its consistent and substantial weight loss outcomes. However, recent advancements in pharmacotherapies targeting appetite regulation and metabolic pathways, particularly GLP-1 receptor agonists, have prompted renewed interest in medical management as a potentially effective and more accessible alternative.

Methods: A narrative review was conducted using PubMed, Cochrane, and NICE guideline databases covering studies from 2000 to 2024. Inclusion criteria encompassed clinical trials, meta-analyses, and national health policy reports. Exclusion criteria included non-English sources and case studies with <10 participants. Search terms included "bariatric surgery", "GLP-1", "obesity pharmacotherapy", and "obesity management UK". Data were analysed for treatment efficacy, safety, cost-effectiveness, accessibility, and long-term outcomes. Bias risk and funding sources were noted where applicable.

Results: Evidence indicates that bariatric surgery achieves greater and more sustained weight loss (up to 70% excess weight loss) and improved long-term comorbidity remission, but carries surgical risks and access barriers. New pharmacotherapies such as semaglutide and tirzepatide achieve 15-25% total body weight loss with favourable safety profiles, however long-term outcomes and accessibility remain concerns.

Conclusion: While pharmacotherapy shows promise, especially for less severe obesity or surgery-ineligible patients, it is unlikely to fully replace bariatric surgery in the near future. A combined, patient-centred approach may be the future standard. For clinicians, especially those in training, understanding both approaches is essential for offering tailored treatment strategies based on individual needs and preferences, in order to improve outcomes in obesity management.

1. INTRODUCTION

Obesity poses a serious threat to public health and finances, costing "£6 billion annually, a figure which is expected to rise to over £9.7 billion each year by 2050", according to the UK Government. (1) In addition to increased costs, the rising prevalence of obesity increases demand for specialist services and the need for long-term management of obesity-related conditions, such as type 2 diabetes (T2DM), cardiovascular disease, stroke, arthritis, and certain cancers. (2,3) Offering effective treatment for obesity is thus a priority for healthcare services.

Treatment options for people living with obesity (PLwO) have changed significantly in the past five years. This is largely due to the advent of new, highly effective pharmacotherapies. UK marketing authorisations for semaglutide and tirzepatide for the treatment of obesity were as recent as 2023. This article aims to help today's medical students and resident doctors understand the landscape into which these treatments have arrived. The focus of this review will primarily be for a UK-based readership. However, the broader insights can be applied to other countries' contexts. We discuss bariatric surgery, traditionally the gold standard treatment for severe obesity, offering substantial and sustained weight loss outcomes. (4) We review pharmacotherapies, both new and old, and consider whether pharmacological interventions surpass surgical approaches in efficacy and risk-benefit balance. The newer obesity drugs target pathways related to energy expenditure and appetite management. (5) They offer a non-invasive alternative to surgery, widening their appeal. Furthermore, patients for whom surgery is either contraindicated or less feasible - older adults or people with substantial comorbidities - may find pharmacotherapy more suitable. (6)

2. METHODOLOGY

This review used a structured narrative literature review methodology to synthesise current evidence comparing bariatric surgery and pharmacotherapy in the management of obesity. The process followed elements of systematic review protocols to enhance transparency and reproducibility.

Searches were performed using five databases: PubMed, Cochrane Library, NICE Evidence Search, WHO Global Health Library, and NHS Digital. The review covered literature published from January 2000 to March 2024. Both medical subject headings and free-text terms were used, including: "bariatric surgery", "Roux-en-Y gastric bypass", "sleeve gastrectomy". "GLP-1 receptor agonists", "semaglutide", "tirzepatide", "retatrutide", "SURMOUNT trial", "STEP trial", "obesity pharmacotherapy", "obesity UK guidelines", and "cost-effectiveness of obesity treatment". Boolean operators (AND, OR) were employed to refine results. Relevant literature such as NICE guidance, NHS reports, and WHO data were also reviewed.

Studies were included if they met the following criteria:

- Published in a peer-reviewed journal or official NHS/NICE source
- Focused on the surgical or pharmacological treatment of obesity
- Included data on weight loss, T2DM remission, safety, cost, or access
- Involved adult humans (≥18 years)

Exclusion criteria:

- Animal or in vitro studies
- Case reports with fewer than 10 subjects
- Non-English publications
- Editorials without primary data

The initial search yielded 316 articles. We did not exclude non-UK manuscripts, as many of the important studies in this field have been international clinical trials. After removing duplicates and screening abstracts, 114 full-texts were assessed. Of these, 72 met the inclusion criteria. The selection included randomised controlled trials, systematic reviews, observational cohort studies, and NHS/NICE publications. Studies were evaluated for quality, relevance, and bias, with attention given to funding sources. Over 60% of pharmacotherapy trials were industry-sponsored, while surgical studies were funded by academic or government institutions.

3. RESULTS

3.1 Bariatric Surgery

Most nutrients are absorbed in the small intestine, thus the first bariatric surgery procedures targeted this area. They included malabsorptive small bowel bypass procedures such as the jejunocolic and jejunoileal bypass. (7) However, they were abandoned due to adverse effects such as fatty stools, diarrhoea, and anal complications in patients, which subsequently led to the development of gastric bypass procedures that focused on achieving early satiety and limiting food intake. (7,8) Despite the high-risk nature of patients, bariatric surgery has evolved to achieve better results, reduced hospital stays, and quicker recovery times. (9) Given that many early obesity medications had dangerous side effects (controlled studies comparing benefits and risks were not required until 1962 (10,11), bariatric surgery has been considered the gold standard treatment for obesity ("widely accepted as being the best available" – NICE definition). (12)

3.1.1 Patient selection criteria (UK)

PLwO wishing to undergo bariatric surgery are referred to a multidisciplinary Tier 3 service. Criteria include body mass index (BMI), comorbidities, and a history of weight loss attempts. (13) Significant health conditions such as diabetes, hypertension, and obstructive sleep apnoea are often considered.

According to NICE guidelines, adults with a BMI of ≥40 kg/m^2 or ≥35 kg/m^2 with significant health issues may qualify for surgery. (14) Patients should be in good health, and must be willing to commit to the long-term follow-up care. (15) Absolute contraindications include pregnancy, while relative contraindications involve conditions like Crohn's disease and severe intellectual disabilities. (16)

3.1.2 Current techniques
Modern bariatric surgeries focus on minimally invasive laparoscopic procedures. The three most common are Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy, and laparoscopic adjustable gastric banding (LAGB). (17)

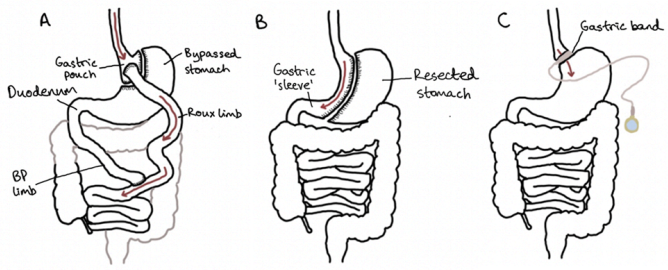

Figure 1: Illustrations of the main endoscopic and surgical procedures for obesity treatment. (Author drawn and adapted from Perdomo et al.). (22) Image A: Roux-en-Y gastric bypass. Image B: Sleeve gastrectomy. Image C: Adjustable gastric banding.

RYGB combines malabsorptive and restrictive procedures to aid weight loss [Figure 1, Image A]. Staples create a small pouch in the stomach, bypassing the larger stomach section, limiting food intake. (18) The procedure involves constructing a gastrojejunostomy and securing mesenteries to prevent complications. (13, 16, 19)

Laparoscopic sleeve gastrectomy (LSG) combines restrictive and resective techniques [Figure 1, Image B]. The aim of LSG is to remove a large portion of the stomach, leaving behind a smaller tube-like 'sleeve'. (19) Reinforcement techniques are used to reduce the risk of leakage and bleeding. (20)

LAGB also combines restrictive and malabsorptive mechanisms [Figure 1, Image C]. A band is placed around the stomach to create a smaller pouch, with an access port permitting adjustments to the band in future. (21) While less invasive, this technique has lower long-term efficacy and higher reoperation rates compared to LSG and RYGB. (22)

3.1.3 Risks and complications
Early complications of RYGB include anastomotic/staple line leaks, haemorrhage, and small bowel obstruction. Late complications include marginal ulceration formation, development of anastomotic strictures, and nutritional deficiencies. (23) Lifelong supplementation is required to manage deficiencies in iron, vitamin B12, and folate. (24)

The most common early complication which occurs after LSG is bleeding in the staple line. This is a life-threatening early complication which occurs in a small percentage of patients. Late complications include the formation of strictures and the development of nutritional deficiencies. A late complication unique to LSG is the development of GORD (gastro-oesophageal reflux disease). Reduced tension in the lower oesophageal sphincter, delayed gastric emptying, and reduced gastric volume leads to increased intragastric pressure. If left untreated, GORD can develop into Barrett's oesophagus, which has the potential to develop into oesophageal cancer. (17, 20, 25)

Complications that can occur after LAGB include band slippage, band erosion, stomach herniation, dysphagia, pouch enlargement, and food intolerance. Port-related complications include infection or port breakage.

3.1.4 Long-term outcomes
RYGB is highly efficacious in achieving weight loss and improving metabolic health. Patients who undergo RYGB achieve a long-term reduction in body weight of 50% or more. (26) RYGB is also associated with improvements in obesity-related comorbidities. (27)Long-term follow up shows that RYGB achieves sustained weight loss, however patients may experience weight regain or complications such as dumping syndrome. (26)

LSG also results in significant weight loss, with patients experiencing a reduction in body weight of 50% or more. (26) Long-term outcomes of LSG are favourable, with studies showing sustained weight loss and improved metabolic health. (28) However, LSG often requires conversion to RYGB due to the development of GORD or weight regain. (29)

Although LAGB is reversible and less invasive compared to other procedures, it is not performed as often due to lower efficacy and higher rates of complications. Many patients require band removal or revision surgery, and studies show that LAGB results in less weight loss compared to RYGB and LSG. (27)

3.2 Pharmacotherapy
3.2.1 Historically available pharmacotherapies
The use of amphetamines such as deoxyephedrine, the first anti-obesity medication, became popular in the 1950s.

Increasing concerns over fatal side effects and the risk of abuse led to these medications being discontinued. (10,11)

Phentermine is a medication still in use today. It was approved in 1996 alongside dexfenfluramine, but the latter was discontinued due to reports of associated cardiac and pulmonary complications. (11, 30) Sibutramine was a serotonin and noradrenaline reuptake inhibitor licensed in the 1990s; however, it too was suspended in 2010 due to concerns regarding its safety. (11, 30)

Some older medications, such as Orlistat (Table 1), are still used in clinical practice. The evolution of pharmacotherapy for obesity reflects a shift towards safer, patient-centred approaches to target weight gain factors. (11, 30)

3.2.2 Current and emerging medications
Liraglutide and Semaglutide
Liraglutide and semaglutide are GLP-1 receptor agonists. GLP-1 is a hormone released from enteroendocrine cells, which decreases blood glucose levels when food enters the gut. These drugs act primarily on GLP-1 receptors in the brainstem and hypothalamus, inhibiting food intake and aiding weight management. GLP-1 receptor agonists also act peripherally, resulting in delayed gastric emptying, increased secretion of insulin in hyperglycaemic conditions, and reduction of blood pressure. (22)

Liraglutide is licensed in the UK under the name 'Saxenda'. It has been authorised for the use of weight loss, with diet and exercise. NICE guidelines state "Liraglutide will be offered to adults with non-diabetic hyperglycaemia who have a BMI of at least 35 kg per m^2 and have a high risk of cardiovascular disease because of risk factors such as high BP or high cholesterol levels." (31) Liraglutide is administered via subcutaneous injections once daily (Table 1). As well as weight loss, liraglutide helps in the prevention of T2DM, and reduces body weight, blood pressure, and HbA1c levels in patients with obesity and obstructive sleep apnoea. (10)

Semaglutide is licensed in the UK under the names 'Wegovy' and 'Ozempic'. Both medications contain the same active ingredient but serve different purposes. Wegovy is approved for weight loss, whereas Ozempic is only approved for the management of T2DM. Semaglutide 2.4 mg administered weekly has demonstrated significant weight loss compared to placebo across various trials. (32) When compared to liraglutide, it has been shown to be more effective when it comes to weight loss. Semaglutide is also better in the maintenance of weight loss. (32) The use of semaglutide has also shown benefits in improved blood pressure, lipid profile, and reduction in HbA1c levels, with a high proportion of patients reaching normoglycaemia. (10)

Liraglutide and semaglutide share common adverse effects (see Table 1). GLP-1 receptor agonists have been linked to an increased risk of medullary thyroid cancer (MTC), contraindicating their use in individuals with relevant medical histories.(33, 34)

3.2.3 Emerging pharmacotherapies
Semaglutide is administered via subcutaneous injection, or a recently available oral version. There are currently many medications undergoing clinical trials which use the same mechanism of agonism of GLP-1 receptors. These include medications like orforglipron and danuglipron, which are taken orally. (35)

There has been a focus on combining GLP-1 agonists with other entero-pancreatic hormones. Gastric-inhibitory peptide (GIP) is a hormone secreted by K-cells in the jejunum. Tirzepatide is a dual GLP-1/GIP receptor agonist which has shown to be highly effective in clinical trials, improving weight and metabolic parameters such as HbA1c and lipid profiles. (35) Results from the 36 week SURMOUNT-4 trial showed that patients on average lost 21% of their body weight from the use of tirzepatide. (36) Recent results from the SURMOUNT-5 trials have suggested that tirzepatide results in greater weight loss in comparison to semaglutide. (37) Side effects experienced with tirzepatide include nausea, diarrhoea, and vomiting. (35)

Glucagon is secreted from alpha cells in the pancreas, and works on the liver to increase glucose production. Glucagon agonism has been trialled in combination with GLP-1 receptor agonists, and as a triple agonist with GIP and GLP-1 agonists. Retatrutide is a triple agonist found to be more effective than dual agonists in increasing weight loss and glycaemic control. (35) It has shown through clinical trials that patients were able to lose up to 25% of their body weight. (38)

Similar to semaglutide, CagriSema (cagrilintide + semaglutide) is a drug which acts as a GLP-1 receptor agonist, with the added benefits of being an amylin receptor agonist using cagrilinitide. Amylin acts by slowing gastric emptying, causing prolonged satiety, thus reducing food intake. CagriSema is currently in Phase 3 trials and is not expected to be on the market until late 2025. (39)

4. DISCUSSION

4.1 Comparative efficacy

Surgery continues to produce the highest and most sustainable weight loss outcomes in PLwO (Table 2), with studies showing up to 60-70% loss of excess body weight within the first year, with long-term maintenance of 50% or more, and T2DM remission rates up to 80%. (4, 40, 41) That being said, not everyone will achieve such a drastic loss in weight. As shown in Table 2, the mean weight loss for the general population would be 25-27% from baseline. Pharmacotherapy, while previously limited to modest reductions, now achieves 15-25% total body weight loss in patients on semaglutide or tirzepatide. (36, 37)

Non-hormonal weight loss drugs				
Drug Name	**Mode of Action**	**Administration**	**Contraindications**	**Side effects**
Orlistat	Inhibition of gastric and pancreatic lipase	Oral medication, taken with meals	Pregnancy Breastfeeding Malabsorption syndrome Cholestasis	Faecal urgency Oily faeces/ steatorrhea Deficiency of fat-soluble vitamins
Phentermine/ topiramate ER	Noradrenaline and GABA agonist, glutamate antagonist	Once-daily oral medication, started at low dose and increased every two weeks	Glaucoma Hyperthyroidism Pregnancy Use of MAOIs in the last 14 days	Tachycardia Insomnia Cognitive impairment Metabolic acidosis Dry mouth
Naltrexone SR/ bupropion SR	Opioid receptor antagonist, dopamine and noradrenaline reuptake inhibitor	Once- or twice-daily oral medication, dose gradually increased	Uncontrolled hypertension Epilepsy Eating disorder Chronic opioid use Use of MAOIs in the last 14 days	Nausea Constipation Headaches Vomiting Dizziness Dry mouth Diarrhoea
Gut-hormone agonist drugs				
Liraglutide	GLP-1 receptor agonist	Once-daily subcutaneous injection, dose increased on a weekly basis	Personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia type 2 (MEN2) syndrome	Nausea Hypoglycaemia Diarrhoea Constipation Vomiting Headache Abdominal pain
Semaglutide	GLP-1 receptor agonist	Once-weekly subcutaneous injection, dose increased on a monthly basis	Personal or family history of MTC or MEN2 syndrome Pregnancy	Nausea Hypoglycaemia Diarrhoea Constipation Vomiting Headache Abdominal pain
Tirzepatide	GIP/GLP-1 dual agonist	Once-weekly subcutaneous injection, dose increased on a monthly basis	Personal or family history of MTC or MEN2 syndrome	Nausea Diarrhoea Vomiting Constipation Dyspepsia Abdominal pain
Retatrutide	Glucagon /GLP-1/GIP triple agonist	Once-weekly subcutaneous injection (currently still under clinical trials)	Uncontrolled hypertension Glaucoma Hyperthyroidism Personal or family history of MTC or MEN2 syndrome	Nausea Diarrhoea Vomiting Constipation

Table 1: produced using references 10, 11, 22, 43, 44. Outlines the mode of action, contraindications, administration, and common side effects of some of the non-hormonal and gut-hormone agonist drugs used in the treatment of obesity.

Long-term efficacy of bariatric surgery vs pharmacotherapy for obesity					
Intervention	**Study/trial**	**Duration of follow-up**	**Mean weight loss (% from baseline)**	**Key findings**	**Common/ notable side effects**
Roux-en-Y gastric bypass	Adams et al., NEJM	12 years	~27% at 2 years, ~26.9% at 6 years, ~27% at 12 years	Sustained weight loss, improved metabolic outcomes, and reduced mortality	Nutrient deficiencies (iron, B12) Dumping syndrome Surgical complications
Sleeve gastrectomy	SLEEVEPASS trial	5 years	~25%	Comparable to bypass for weight loss, but less favourable for comorbidities	GORD Staple line leak Nutrient deficiencies
Semaglutide 2.4mg (weekly)	STEP 5 trial	104 weeks (2 years)	15.20%	77.1% achieved ≥5% weight loss, sustained effect with continued use	Nausea Vomiting Gallbladder disease risk
Tirzepatide	SURMOUNT-4 trial	88 weeks	21.10%	Significant weight regain upon discontinuation, highlighting need for maintenance	GI upset (nausea, diarrhoea) Reduced appetite Fatigue
Retatrutide	Phase 2 trial (Jastreboff et al.)	48 weeks	Up to 24.2%	Promising future candidate with higher efficacy than current agents	GI upset Transient increases in heart rate

Table 2: produced using references 26, 27, 33, 34, 36, 38, 40. Outlines available interventions for obesity and their long-term outcomes.

Notably, pharmacotherapy has a better safety profile and doesn't require hospitalisation or long recovery periods. For patients with moderate obesity, or contraindications to surgery, it is an effective alternative when combined with lifestyle modifications. (5)

However, unlike surgery, pharmacotherapy requires ongoing administration. Discontinuation often results in substantial weight gain, as shown in the STEP-4 trial where participants who switched to a placebo gradually started to regain weight. (42)

This demonstrates the chronic nature of obesity, and suggests that pharmacotherapy may be most effective as part of a long-term management strategy rather than a stand-alone cure.

4.2 Long-term outcomes

Bariatric surgery produces durable weight loss and significant improvement in obesity-related comorbidities. Studies such as the Swedish Obese Subjects study have reported sustained weight loss and reduced mortality over follow-up periods exceeding a decade following bariatric procedures. (26, 38, 39) Additionally, bariatric surgery has shown to improve glycaemic control and reduce cardiovascular risk, with outcomes superior to those achieved through intensive lifestyle or earlier pharmacological interventions. (27, 40). However, the gap in long-term efficacy between surgery and pharmacotherapy is narrowing with the emergence of newer agents.

In the STEP-5 trial, semaglutide 2.4mg administered weekly resulted in a mean weight loss of 15.2% from baseline over 104 weeks, with 77.1% participants maintaining ≥5% weight loss. (33) Similarly, in the SURMOUNT-4 trial, tirzepatide achieved a mean weight loss of 21.1% at 88 weeks in participants who remained on the drug, compared to substantial weight regain in those who discontinued it. (34) Moreover, early phase data on retatrutide demonstrated mean weight reductions of up to 24.2% at 48 weeks, suggesting even greater long-term efficacy. (36) Although continued therapy is required to sustain weight loss, pharmacotherapies are now delivering clinically significant and durable outcomes over multiple years. (31, 43) Longer-term outcome data is continuing to be produced, which will inform treatment choice further.

4.3 Accessibility (UK)

Bariatric surgery is NHS-funded but underutilised due to long wait times, geographic inequalities, and strict eligibility requirements. Less than 1% of those eligible for surgery in the UK receive it annually. (44) As of 2025, semaglutide is available via the NHS only to high-risk patients, and whilst tirzepatide has now been approved for NHS use by NICE, full implementation of its use will take 12 years. (45) Thus many are accessing newer pharmacotherapies through private prescription. This creates a two-tiered system, where wealthier individuals benefit from a variety of options, while others face delayed or unavailable treatment. Such disparities risk widening health inequalities and contradict NHS goals of universal care. (46)

4.4 Economic considerations

Bariatric surgery is initially more expensive than pharmacotherapy due to costs of surgery, hospitalisation, and follow-up care. However, it may be more cost-effective in the long-term if it reduces the need for ongoing treatment.(47)

NICE analyses demonstrate that surgery pays for itself within 2-4 years in high-risk patients. Pharmacotherapy is more cost-effective in the short-term, but the need for ongoing treatment results in cumulative costs over time. The high cost of drugs such as semaglutide (~£2000/year) must be weighed against their benefits. NICE has only approved semaglutide for restricted use based on economic thresholds (typically £20,000-£30.000 per QALY). (48)

4.5 The future of obesity management

Rather than viewing pharmacotherapy and surgery as mutually exclusive, a tiered or integrated treatment model may yield better outcomes. Potential roles for pharmacotherapy include being a first-line option for moderate obesity or early intervention, to reduce BMI pre-operatively to reduce surgical risk, or to be used post-surgery to prevent weight regain. (49) This mirrors the management of conditions such as diabetes and hypertension, where multi-modal care is standard. It also aligns with the understanding of obesity as a lifelong, multifactorial disease requiring sustained management strategies.

4.6 Implications for resident doctors and medical students

Clinicians should be prepared to recognise and diagnose obesity as a medical condition, whilst also understanding the mechanisms, indications, and side effects of available drugs and surgeries, and eligibility criteria, referral pathways and patient counselling.

4.7 Ethical considerations

Many recent pharmacotherapy trials are funded by pharmaceutical companies, raising concerns about bias and selective reporting. (50) Independent and long-term follow-up studies are essential. Ethically, there is concern over promoting expensive, privately-funded treatments in a system designed to offer equal care. Clinicians must be transparent about costs, risks, and expected outcomes, particularly when patients express interest in private options.

5. CONCLUSION

The debate over whether pharmacotherapy will replace bariatric surgery as the gold standard treatment for obesity is complex. While pharmacotherapy offers greater accessibility and reduced invasiveness, it seems unlikely to replace bariatric surgery as the gold standard in the near future. Bariatric surgery is a very effective treatment for morbid obesity, producing significant and sustained improvements in comorbidities and weight loss. However, pharmacotherapy in combination with lifestyle changes may represent an effective option for those with less severe obesity. New pharmacotherapies may also help PLwO who don't want, or are unable, to undergo surgery. Ultimately, the best approach may involve a combination of pharmacotherapy, behavioural therapy, and, when necessary, surgical intervention, tailored to each person's needs.

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