

## LETTER

## Duodenal-jejunal bypass liner for the treatment of type 2 diabetes and obesity: 3-year outcomes in the First National Health Service (NHS) EndoBarrier Service

There is a worldwide pandemic of type 2 diabetes (T2D) and obesity.<sup>1</sup> In clinical practice, many patients fail to achieve adequate glycaemic control despite lifestyle advice and maximal doses of oral and injectable medications.<sup>2</sup> The evidence suggests that Roux-en-Y gastric bypass (RYGB) is more effective than intensive anti-diabetes medical therapy, and this has led to a recent joint statement by international diabetes organizations recommending increased use of metabolic surgery in the treatment of T2D with obesity.<sup>2</sup>

RYGB is, however, a relatively invasive form of treatment compared to endoscopic bariatric and metabolic device called the duodenal-jejunal bypass liner (DJBL), which was developed to mimic the proposed small bowel mechanisms of RYGB.<sup>2,3</sup> DJBL, also known as EndoBarrier, is a 60-cm fluoropolymer liner that is anchored at the duodenal bulb allowing nutrients to pass directly from the stomach into the jejunum.<sup>2,3</sup> DJBL is left in place for up to 1 year and then removed endoscopically and is also not a permanent intervention, which many patients prefer.<sup>4,5</sup> DJBL has been shown to improve many metabolic parameters, in particular weight and HbA1c, in patients with diabetes and obesity.<sup>2-6</sup> However, not being permanent, there is uncertainty over the longevity of any improvements.<sup>2</sup> We, therefore, established a National Health Service (NHS) EndoBarrier service in the United Kingdom, to assess its effect on weight and glycaemic control during the year of treatment and after device removal. The first NHS EndoBarrier implantation was in October 2014 with the last one in November 2017. The last EndoBarrier was removed in November 2018. Thus, by November 2020, all patients were at least 2 years after EndoBarrier removal, and the findings at that time are the subject of this report. As previously described,<sup>4</sup> all patients had T2D, were aged between 28 and 70 years, BMI >30 kg/m<sup>2</sup>, and had tried diet, lifestyle and medications, including GLP-1 receptor agonists and, once available, SGLT2 inhibitors. Thus, the options available for them were to either start insulin, titrate the dose of insulin, if already on insulin, or to have bariatric/

metabolic surgery.<sup>4</sup> Between October 2014 and November 2017, 62 patients received treatment with EndoBarrier, and we have previously reported the outcomes during the year with EndoBarrier<sup>4</sup> and during the year following.<sup>5</sup> Two years after EndoBarrier removal, 45/62(73%) attended for review, and we report here the findings in those patients. The reasons for non-attendance in the non-attenders are shown in Table 1. Among those who did attend, at the time of EndoBarrier implantation, their mean  $\pm$  SD age was 51.4  $\pm$  7.7 years, 53% male, median (inter-quartile range) diabetes duration 14.4 (8–20) years, HbA1c 76.8  $\pm$  20.2 mmol/mol (9.2  $\pm$  1.8%) and BMI 41.7  $\pm$  7.2 kg/m<sup>2</sup>. 30/45 (66.6%) were insulin treated. During EndoBarrier treatment, mean  $\pm$  SD HbA1c fell by 20.8  $\pm$  19.8 mmol/mol (1.9  $\pm$  1.8%), from 76.8  $\pm$  20.2 to 56.0  $\pm$  11.4 mmol/mol (9.2  $\pm$  1.8 to 7.3  $\pm$  1.0%) ( $p < 0.001$ ), weight by 17.3  $\pm$  8.9 kg from 122.5  $\pm$  29.5 to 105.2  $\pm$  30.3 kg (<0.001), BMI from 41.7  $\pm$  7.2 to 35.6  $\pm$  7.6 kg/m<sup>2</sup>, SBP from 138.9  $\pm$  14.1 to 126.1  $\pm$  14.8 mmHg (<0.001) and serum alanine-aminotransferase from 30.2  $\pm$  17.0 to 19.0  $\pm$  11.2 U/L ( $p < 0.001$ ). Median (IQR) total daily insulin dose reduced from 109 (52–167) to 35 (0–63) units ( $n = 30$ ,  $p < 0.001$ ); 10/30(33%) insulin-treated patients discontinued insulin.

Two years after EndoBarrier removal, 33/45(73%) maintained most of the improvement in HbA1c and weight achieved with EndoBarrier, whereas 12/45(27%) reverted to baseline (Figure 1). It is acknowledged that other medications such as SGLT2 inhibitors in those who had not had these before may have contributed to the maintenance of improvement but this would not account for the whole benefit. It is noteworthy that of the 17/62 (27%) who did not attend follow-up of 24 months after removal, there was follow-up data 6–12 months after removal in 8/17 (47%). At 6–12 months after EndoBarrier removal most of the improvements in weight and HbA1c sustained during the year with EndoBarrier were maintained in 7/8 (87%) with only one deteriorating to baseline. In 9/17 (53%) we have no follow-up data. Of those deteriorating, 11/12 (92%) had depression and/or bereavement

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and/or major health problems. 10/62 patients (16%) required early removal (4 for gastrointestinal haemorrhage, two for liver abscess, one for another intra-abdominal abscess and

**TABLE 1** The reasons for non-attendance in the 17/62 (27%) patients who did not attend follow-up

Reason for non attendance at follow up	n (%)
No reason given	7 (41.2)
Too far to travel <sup>a</sup>	6 (35.3)
Does not wish to take time off work to attend	2 (11.8)
Severe depression	1 (5.9)
Patient died 9 months after removal of EndoBarrier <sup>b</sup>	1 (5.9)

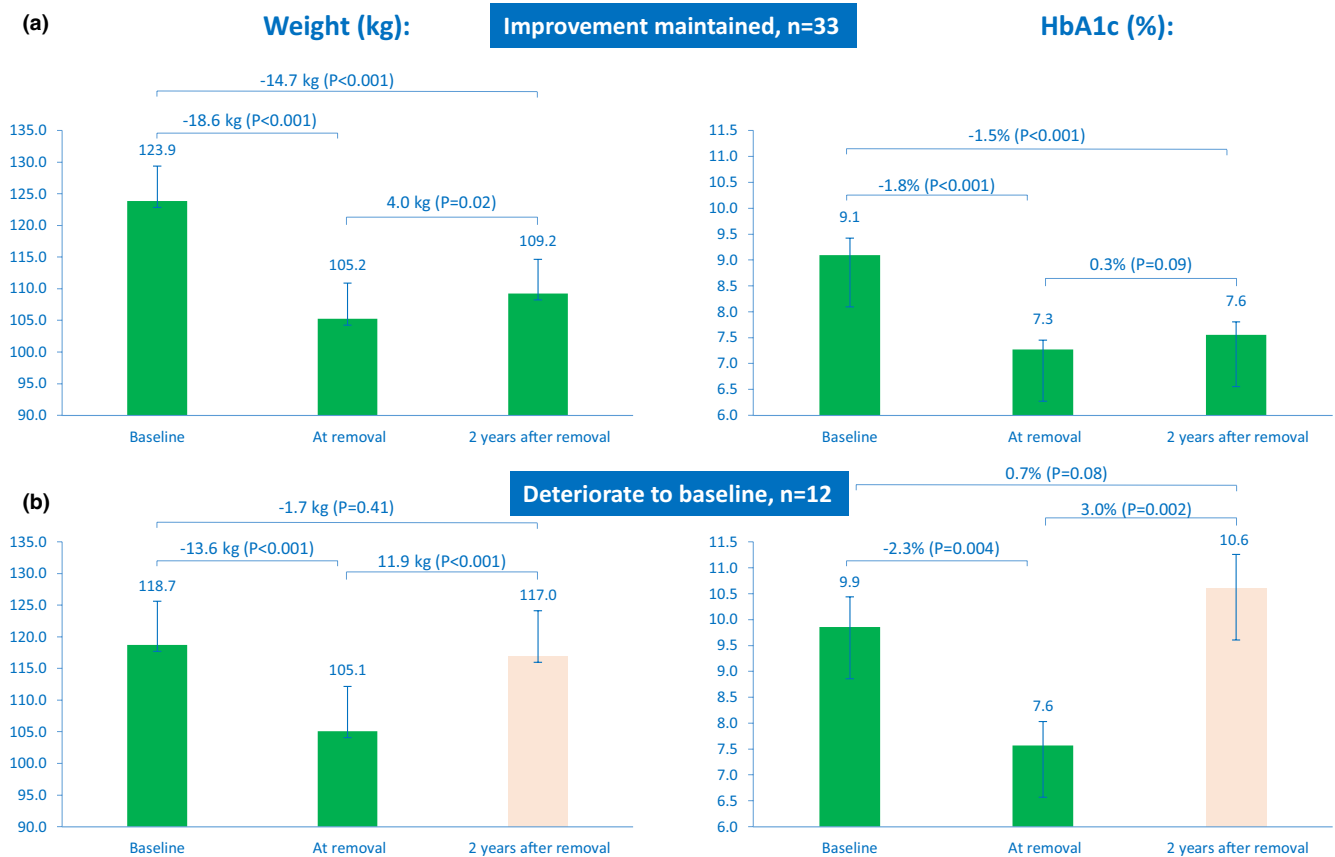
<sup>a</sup>As we were the only NHS service providing EndoBarrier in the UK, we did get some referrals from very far away and it is perhaps understandable that these patients were not prepared to travel so far for follow up.

<sup>b</sup>In memoriam, it is noteworthy that during the year of EndoBarrier treatment her weight fell from 152.4 to 139.6 kg and that in the 6-months after removal, she lost more weight to 124.0 kg. HbA1c fell from 122 to 50 mmol/mol during treatment and was 48 mmol/mol 6-months later. Her insulin requirement was 100 units daily prior to EndoBarrier but she required no insulin 6-months after EndoBarrier.

three for gastrointestinal symptoms). All made a full recovery following device removal and most derived significant benefit despite early removal.<sup>4</sup> We have reported elsewhere the detail of these early removals<sup>4</sup> including the observation that several could have been avoided by patient compliance.<sup>4</sup>

In the largest randomised control trial with EndoBarrier, recently published,<sup>7</sup> EndoBarrier was associated with superior weight loss, improvements in cardiometabolic risk factors and markers of fatty liver disease but not in glycaemia compared with intensive medical care. However, it is important to point out that compared with our patients the patients in that study did not by any means have refractory diabetes. Their median diabetes duration was 7.1 years compared with 14.4 years with our patients, BMI 36.8 compared with our 41.7 and they could not be on insulin, whereas two-thirds of our patients were on insulin. In addition, they did not need to have already tried a GLP-1 receptor agonist and SGLT2 inhibitor as did our patients.

People with longstanding T2D, with poor glycaemic control and obesity, especially those treated with insulin,



**FIGURE 1** Weight and HbA1c at baseline, at removal and two-years after removal in the 33/45(73%) who maintained most of the improvement (a) and 12/45(27%) who deteriorated to baseline (b). (a) Weight (mean  $\pm$  SE): at baseline 123.9  $\pm$  5.5 kg, at removal 105.3  $\pm$  5.7 kg and 2-years after removal 109.2  $\pm$  5.4 kg. HbA1c (mean  $\pm$  SE): at baseline 75.9  $\pm$  3.4 mmol/mol (9.1  $\pm$  0.3%), at removal 56.0  $\pm$  1.9 mmol/mol (7.3  $\pm$  0.2%) and 2-years after removal 59.1  $\pm$  2.7 mmol/mol (7.6  $\pm$  0.2%). (b) Weight (mean  $\pm$  SE): at baseline 118.7  $\pm$  6.9 kg, at removal 105.1  $\pm$  7.1 kg and 2-years after removal 117.0  $\pm$  7.1 kg. HbA1c (mean  $\pm$  SE): at baseline 80.4  $\pm$  5.4 mmol/mol (9.9  $\pm$  0.6%), at removal 56.2  $\pm$  3.6 mmol/mol (7.6  $\pm$  0.5%) and two-years after removal 90.2  $\pm$  7.0 mmol/mol (10.6  $\pm$  0.7%)


find it difficult to lose weight and improve glycaemic control. Many continue to have a high HbA1c and remain obese despite GLP-1 receptor agonists and SGLT2 inhibitors. We need new treatments to help such patients. This is the first study to follow such patients for two years after the removal of EndoBarrier.

The original US Food and Drug Administration (FDA) pivotal study with EndoBarrier was stopped early due to an hepatic abscess rate of 3.5%.<sup>2</sup> In the new FDA pivotal study,<sup>8</sup> the hepatic abscess complication is being carefully addressed by the inclusion of daily temperature monitoring for early detection. Future use of EndoBarrier within the NHS is dependent on restoration of its CE-mark, which was not renewed in November 2017.<sup>9</sup> There is currently an application for restoration of the CE-mark.<sup>10</sup> It is noteworthy that Endoscopy units are ubiquitous in healthcare systems, as are skilled endoscopists. There are also very large numbers of patients with refractory uncontrolled diabetes worldwide and, therefore, should the safety concerns be successfully addressed, it would be relatively easy to make EndoBarrier widely available. The lessons we have learned with regard to measures to minimise serious adverse events would also be useful to future services.<sup>4</sup> Future services might also learn from our experience with regard to those deteriorating often having depression. For example, better depression screening and consideration of mood prior to insertion of EndoBarrier, longer-term psychology input, family support etc. Nevertheless, it needs to be borne in mind that the situation is complex in that many obese patients with poor diabetes control are depressed because of these factors. In our experience the psychological well-being of such patients is greatly helped by the improvements associated with EndoBarrier treatment.

Our data demonstrate EndoBarrier as highly effective in patients with refractory diabetes, with maintenance of significant improvement 2 years after removal in 73%. The benefits to the patients concerned are most readily appreciated from pictorial examples and from interviews with them.<sup>11</sup>

## CONFLICT OF INTEREST

None.

Robert E. J. Ryder<sup>1</sup>   
 Mahi Yadagiri<sup>1</sup>  
 Wyn Burbridge<sup>1</sup>  
 Susan P. Irwin<sup>1</sup>  
 Hardeep Gandhi<sup>1</sup>  
 Tahira Bashir<sup>1</sup>  
 Rachael A. Allden<sup>1</sup>  
 Melanie Wyres<sup>1</sup>  
 Melissa Cull<sup>1</sup>  
 John P. Bleasdale<sup>1</sup>

Edward N. Fogden<sup>1</sup>  
 Mark R. Anderson<sup>1</sup>  
 Piya Sen Gupta<sup>1,2</sup>

<sup>1</sup>Sandwell & West Birmingham NHS Trust, City Hospital, Birmingham, UK  
 Email: bob.ryder@nhs.net  
<sup>2</sup>Guy's and St Thomas' Hospitals, London, UK

## ORCID

Robert E. J. Ryder  <https://orcid.org/0000-0003-4424-355X>

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