2017 Summary of findings

Several new studies on Barricaid® were identified, however most of these reported on the same two patient cohorts that were discussed in the original Brief.

Two studies were included in this Update, one randomised controlled trial (RCT) with interim safety results published in a conference abstract and a case series that contained pooled data from two separate multicentre studies. Although the pooled data were reported in the original Brief, this case series was included because it reported 24-month follow-up data for 93 per cent of patients.

In the RCT, fewer serious adverse events, reoperations at the index level and reoperations following recurrence were reported for the Barricaid® plus discectomy treatment, compared with discectomy alone. In the case series study, one symptomatic recurrent re-herniation was reported at 24 months’ follow-up (symptomatic re-herniation rate of 1.5%) and two serious device-related adverse events (mesh dislocation) were reported at 22 and 24 months. Leg and back pain scores were significantly improved from preoperative levels at 6 weeks, and these improvements were maintained for the duration of the 24-month follow-up (p<0.05).

The approval status of the Barricaid® device remains the same as in the 2015 Brief; it has a CE mark and is listed on the Australian Register of Therapeutic Goods, but it has not been approved by the United States Food and Drug Administration. Only one ongoing clinical trial was identified on Barricaid®; this trial was identified and described in the original Brief.

In summary, the evidence base for the safety and efficacy of Barricaid® is still very limited, with the same two patient cohorts still being reported on. Interim results from an RCT due for completion in October 2019 are promising with respect to both safety and effectiveness. Until this trial is complete, the benefit of Barricaid® plus discectomy over discectomy alone remains to be confirmed. No other clinical trials were identified on this technology.

2017 HealthPACT Advice

Currently the Barricaid® prosthesis is in limited use in Australia, mainly in the private sector due to listing on the Prostheses List. High level evidence indicates that it may be suitable for use in a highly selective group of patients, in whom it would reduce pain and re-operation rates.

HealthPACT does not support public investment in the Barricaid® prosthesis in clinical practice until the results of the ongoing RCT are published and reviewed.
Technology, Company and Licensing

Register ID
WP209

Technology name
Barricaid® prosthesis for partial annulus replacement

Patient indication
Partial annulus replacement in patients undergoing spinal disc removal surgery (discectomy)

Reason for assessment
In 2015 a Technology Brief was completed to investigate the Barricaid™ prosthesis for partial annulus replacement. Although small, the studies identified reported promising results for reducing re-herniations. In addition, early analysis indicated that the Barricaid device was cost effective. In light of the developing evidence on this device, HealthPACT recommended that this technology be monitored for further evidence in 24 months. In line with this recommendation, the purpose of the current Update is to consider the evidence that has emerged since 2015 and to determine whether this new evidence may provide additional information to inform policy decisions.

Description of the technology
The Barricaid® prosthesis (Intrinsic Therapeutics, Massachusetts, United States of America) is a small piece of flexible polymer mesh composed of multiple layers of non-degrading polyethylene terephthalate fibres. The mesh, which contains platinum-iridium markers that make it visible on x-ray images, comes in various sizes (8, 10 and 12 mm) and is preloaded in a single-use delivery system. Towards the end of a spinal discectomy procedure, once the herniated disc material is removed, the Barricaid® mesh is placed on the inner surface of the disc annulus using fluoroscopic guidance and secured to the surrounding vertebral bone with an embedded titanium anchor. The mesh expands across the posterior intervertebral space to close the opening created during discectomy. Placement of the mesh takes an additional 5 to 15 minutes just prior to wound closure in a surgery that takes approximately 2 hours.1-4

Figure 1 Barricaid® implant
According to the manufacturer, patients who would most benefit from a Barricaid® mesh implant have the following characteristics: primary, mediolateral disc herniation at the L3 to S1 level (side-to-side bulging of the disc between the third lumbar and first sacral vertebrae); symptoms on only one side of the body; a disc height of more than 5 mm; and, a disc width of between 5 and 12 mm. Additional beneficial characteristics include: herniation at the L1 to L3 level, a central disc hernia, Grade I spondylolisthesis (slippage of one vertebra over another), or, recurrent disc problems. The Barricaid® mesh cannot be implanted in patients who have a disc herniation that is very small, very wide (greater than 12 mm), too tall (greater than 6 mm), a posterior disc height of less than 3 mm, spinal stenosis, osteoporosis, or Grade II or higher spondylolisthesis.5

Company or developer
Intrinsic Therapeutics, Massachusetts, United States of America

2017 Stage of development in Australia
- Yet to emerge
- Experimental
- Investigational
- Nearly established

2017 Licensing, reimbursement and other approval
The approval status of the Barricaid® device remains the same as in the 2015 Brief; it has a CE mark6 and is listed on the Australian Register of Therapeutic Goods,7 but it has not been approved by the United States Food and Drug Administration.

2017 Australian Therapeutic Goods Administration approval
- Yes
- No
- Not applicable

ARTG number (s): 182175

2017 International utilisation

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trials underway or completed</td>
</tr>
<tr>
<td>Australia</td>
<td>✓</td>
</tr>
<tr>
<td>Various European countries including Austria, Belgium, Croatia, France, Germany, Netherlands and Switzerland</td>
<td>✓</td>
</tr>
</tbody>
</table>
2017 Diffusion of technology in Australia

The Barricaid® device has been used in hospitals in Brisbane, Queensland and New South Wales (Personal communication, Brisbane Private Hospital).

2017 Cost infrastructure and economic consequences

The Barricaid® device is listed on the private health insurance Prostheses List (billing code ER305) and has a minimum benefit of $5,900.

2017 Evidence and Policy

Safety and effectiveness

Multiple studies investigating Barricaid® were identified; however, most used the same intervention cohorts reported by Parker et al and Lequin et al, which were included in the original Brief. The included RCT (level II interventional evidence) contained interim safety data and is in the form of a conference abstract (Kursumovic et al). The other included study (Ledic et al) is a case series (level IV interventional evidence) containing pooled data from Parker et al and Lequin et al. Although these data were reported by Bouma et al and included in the original Brief, the outcomes included herein examine a complete 24-month follow-up cohort. Details of the two studies included in this Update are presented in Table 1.

Table 1 Included study characteristics

<table>
<thead>
<tr>
<th>Study details/location</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Number of patients; length of follow-up, losses to follow-up</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kursumovic et al 2014*</td>
<td>6 weeks conservative care, no prior lumbar spine surgery, minimum Oswestry Disability Index and visual analogue leg pain score of 40/100</td>
<td>NR</td>
<td>N = 550</td>
<td>NR</td>
</tr>
<tr>
<td>Prospective level II interventional evidence (RCT) Multicentre Austria, Belgium, France, Germany, Netherlands, Switzerland</td>
<td></td>
<td></td>
<td>Length of follow-up: 12 months: 251 patients; 24 months: 90 patients Losses to follow-up: NR</td>
<td></td>
</tr>
<tr>
<td>Ledic et al 2015†‡</td>
<td>Patients undergoing primary surgical discectomy for symptomatic herniated lumbar discs at one or two levels with at least six weeks of failed conservative treatment prior to surgery²</td>
<td>Spondylolisthesis grade II or higher, back or non-radicularegular pain of unknown aetiology, systemic or local active infection, cauda equina syndrome or neurologic bowel/bladder dysfunction, body mass index &gt;40 kg/m² or weight &gt;100 pounds over ideal body weight</td>
<td>N = 73</td>
<td>NR</td>
</tr>
<tr>
<td>Prospective level IV interventional evidence (case series) Multicentre Croatia, Germany, Netherlands</td>
<td></td>
<td></td>
<td>Length of follow-up: 24 months Losses to follow-up: 12 months: 2/73 (3%); 24 months: 5/73 (7%)</td>
<td></td>
</tr>
</tbody>
</table>

NR: not reported; RCT: randomised controlled trial
*Study reports interim results in the form of a conference abstract
†Study combines data from two prospective, multicentre, single-arm studies on patients treated with Barricaid;
‡The only difference between the protocols of the two included studies that were combined for this case series was that one of them had a lower minimum posterior disc height inclusion criteria (3 mm vs 5 mm)
Kursumovic et al 2014

This conference abstract reported interim safety outcomes from a post-market RCT (NCT01283438) which is due for completion in October 2019. The trial aims to enrol 550 patients into two arms: patients in the intervention arm receive limited discectomy plus Barricaid®, while patients in the control arm receive limited discectomy only. Patients are randomly assigned intra-operatively following discectomy and confirmation of appropriate annular defect size (minimum of 4 mm x 6 mm, maximum of 6 mm x 10 mm). Reported outcomes are from 421 patients who were enrolled prior to September 2013. Of these, 251 had completed 12 months’ of follow-up and 90 had completed 24 months’ of follow-up. The duration of follow-up of the remaining 80 patients was not reported.

Safety

The interim safety outcomes from 421 patients enrolled in the RCT are summarised in Table 2. To date, fewer serious adverse events, reoperations at the index level and reoperations following recurrence have occurred in patients in the Barricaid® group, compared with those in the discectomy group ($p$ values not reported).

Table 2  Interim safety results from 421 patients enrolled in an RCT comparing limited discectomy plus Barricaid® to limited discectomy alone

<table>
<thead>
<tr>
<th>Events</th>
<th>Barricaid® plus discectomy</th>
<th>Control (discectomy alone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>102/210 (49)</td>
<td>112/211 (53)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>40/210 (19)</td>
<td>63/211 (30)</td>
</tr>
<tr>
<td>(6 procedure-related, 1 device-related, 1 both)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reoperations at the index level</td>
<td>14/210 (7)</td>
<td>34/211 (16)</td>
</tr>
<tr>
<td>Reoperations following recurrence, including repeat reoperations</td>
<td>7/210 (3)</td>
<td>27/211 (13)</td>
</tr>
</tbody>
</table>

Ledic et al 2015

This case series pooled data from two separate multicentre, prospective studies of 30 and 45 patients, respectively, that used Barricaid as an adjunct to primary lumbar discectomy. Although both studies were reported in the original Brief, this study reported data from a larger number of patients who had completed the 24-month follow-up (39 of the 43 patients¹ and 29 of the 30 patients²). Outcomes reported included device-related adverse events and Oswestry Disability Index (ODI) and visual analogue scale (VAS) scores for back and leg pain.

Safety

At 24 months follow-up the overall rate of symptomatic recurrent herniation was 1.5 per cent (1/68 patients). Two serious device-related adverse events (2/73 patients; 3%) owing to
mesh dislocation occurred at 22 and 24 months. In both cases the mesh was removed and a further discectomy was performed with full patient recovery.

Effectiveness

At 6 weeks the ODI and VAS scores had significantly improved from preoperative levels (p<0.05). These improvements were maintained for the duration of follow-up. As the values were not reported, the published graphical data have been included (Figure 2 and Figure 3).

![Figure 2](Changes in ODI score over the follow-up period)

![Figure 3](Changes in VAS score over the follow-up period)

2017 Economic evaluation

A poster abstract describing the cost-effectiveness of using Barricaid® in lumbar discectomy surgery in Turkey was published by Tatar et al in 2014. An incremental cost-effectiveness ratio (ICER) was calculated based on using or not using Barricaid®. Resource utilisation data were obtained from expert clinical opinion and included pre-operative, post-operative and follow-up costs. Device costs were derived from the Social Security Institution’s price list. The endpoint used in the calculation was the number of prevented re-herniations. The authors used a value of 18 per cent for the reduction in number of re-herniations achieved using Barricaid®, based on figures in the literature. The reported incremental cost of using Barricaid® was $43,276,145 and the ICER was $9,839. The authors concluded that this ICER

\[1 \text{ AUD} = 2.76 \text{ TRY (XE currency conversion, 28/03/2017)}\]
was within the limits of the thresholds for cost-effectiveness of interventions recommended by the World Health Organization and that Barricaid® is a cost-effective treatment in Turkey.

2017 Ongoing research

Only one clinical trial (ongoing, not recruiting; NCT01283438) was identified from searches of Clinicaltrials.gov and the Australian New Zealand Clinical Trials Registry. This RCT was identified and reported in the original Brief and is due for completion in October 2019. Interim safety results have been described above.

2017 Other issues

The same patient cohorts treated with Barricaid from two separate, multicentre, prospective clinical trials (Parker et al² and Lequin et al¹) have been reported in several publications.

2017 Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies: 2
Total number of Level II studies: 1
Total number of Level IV studies: 1

Date searched
15/11/2016

2017 References


Technology, Company and Licensing

Register ID: WP209

Technology name: Barricaid® prosthesis for partial annulus replacement

Patient indication: For partial annulus replacement in patients undergoing spinal disc removal surgery (discectomy)

Description of the technology

The Barricaid® prosthesis (Intrinsic Therapeutics, Massachusetts, USA) is a small piece of flexible polymer mesh composed of multiple layers of non-degrading polyethylene terephthalate fibres. The mesh, which contains platinum-iridium markers that make it visible on x-ray images, comes in various sizes (8, 10 and 12 mm) and is preloaded in a single-use delivery system. Towards the end of a spinal discectomy procedure, once the herniated disc material is removed, the Barricaid mesh is placed on the inner surface of the disc annulus using fluoroscopic guidance and secured to the surrounding vertebral bone with an embedded titanium anchor. The mesh expands across the posterior intervertebral space to close the opening created during discectomy. Placement of the mesh takes an additional 5 to 15 minutes just prior to wound closure in a surgery that takes approximately 2 hours. 1-4

![Barricaid implant](image)

According to the manufacturer, patients who would most benefit from a Barricaid mesh implant have the following characteristics: primary, mediolateral disc herniation at the L3 to S1 level (side-to-side bulging of the disc between the third lumbar and first sacral vertebrae); symptoms on only one side of the body; a disc height of more than 5 mm; and, a disc width of between 5 and 12 mm. Additional beneficial characteristics include: herniation at the L1 to L3 level, a central disc hernia, Grade I spondylolisthesis (slippage of one vertebra over another), or, recurrent disc problems. The Barricaid mesh cannot be implanted in
patients who have a disc herniation that is very small, very wide (greater than 12 mm), too tall (greater than 6 mm), a posterior disc height of less than 3 mm, spinal stenosis, osteoporosis, or Grade II or higher spondylolisthesis.\textsuperscript{5}

\textbf{Company or developer}
Intrinsic Therapeutics, Massachusetts, USA.

\textbf{Reason for assessment}
Barricaid is an innovative technology that could reduce the number of repeat surgeries required for post-discectomy patients and improve patient outcomes via a quick addition to current disc surgery. At present its use appears to be limited to several European countries.

\textbf{Stage of development in Australia}

\begin{itemize}
  \item [□] Yet to emerge
  \item [□] Experimental
  \item [☑] Investigational
  \item [□] Nearly established
  \item [□] Established
  \item [□] Established \textit{but} changed indication or modification of technique
  \item [□] Should be taken out of use
\end{itemize}

\textbf{Licensing, reimbursement and other approval}
Barricaid spinal mesh was listed on the Australian Register of Therapeutic Goods (ARTG) as a Class IIb device in April 2011. The approved indication is “\textit{as an adjunct to a lumbar discectomy procedure as a means to maintain the relative position of nucleus within the disc space, thereby reducing the risk of a recurrent herniation. The device is not intended for load bearing (i.e., column support of the spine).}”\textsuperscript{6} The device received the European Union CE mark for use in reconstructing soft tissues of the spine in April 2009\textsuperscript{7}, but to date it has not been approved by the United States Food and Drug Administration (US FDA).

\textbf{Australian Therapeutic Goods Administration approval}

\begin{itemize}
  \item [☑] Yes
  \item [□] No
  \item [□] Not applicable
\end{itemize}

\textbf{Technology type} Device
\textbf{Technology use} Therapeutic
**Patient Indication and Setting**

**Disease description and associated mortality and morbidity**

The vertebral discs between adjacent vertebrae are made up of a soft inner core (the nucleus pulposus) surrounded by a tough circular exterior (the annulus fibrosus) that prevents the nucleus from herniating (bulging out). Sometimes called a slipped or ruptured disc, a herniated disc most often occurs in the lower back and is one of the most common causes of low back pain as well as leg pain (sciatica). Low back pain will be experienced by 60 to 80 per cent of people at some point during their lifetime, with the cause often a herniated disc. Risk factors include male gender (particularly ages 30 to 50), repetitive activities that strain the spine, improper lifting, obesity, sedentary lifestyle and smoking. For most people low back pain is the initial symptom. This may be followed by leg pain extending below the knee into the ankle and foot, and numbness, tingling or weakness in the leg, foot or both. Extremely rare is loss of bladder or bowel control caused by compression of the spinal nerves (cauda equina syndrome).

Nonsurgical treatment over several months resolves the symptoms for many people but a small percentage will progress to a recommendation for surgery after about 6 months of conservative treatment. The standard surgical approach, spine discectomy, removes the herniated piece of the nucleus. However, removing too much nucleus may reduce the disc height and lead to back pain, while removing too little nucleus may lead to reherniation.

Surgery generally results in improvements in pain, physical function and disability. Some patients will experience progressive degeneration and loss of height of the operative disc space, same-level recurrent lumbar disc herniation, or both. Such symptoms may require repeat surgery although this may not resolve the symptoms. The incidence of same level recurrent disc herniation following lumbar discectomy varies between 3 and 18 per cent, the range being due to variations in the duration of follow-up, management paradigms, annular disruption and surgical technique. Some authors report even higher reherniation rates of up to 30 per cent.

**Number of patients**

According to a report prepared for the Medical Services Advisory Committee in 2012, there is uncertainty about the prevalence and incidence of back pain and nerve root pain secondary to disc degeneration or prolapse in Australia. In the 2004-05 period, ‘back pain and disc problems’ were reported in 16 per cent of men and 15 per cent of women. With respect to the number of lumbar discectomies performed in Australia, statistics from the Medicare Benefits Schedule indicate a total of 10,327 services for item 40301 (intervertebral disc or discs, microsurgical partial or total discectomy of, fee, $958) and 26 for item 48363 (percutaneous lumbar partial or total discectomy, fee. $809) during the 2013-14 period.
Data from Australian public hospitals between 2011/12 show a total of 2,602 separations, comprised of 84 “Discectomy for recurrent disc lesion” and 2,518 for “Other discectomy”.11

New Zealand patient data for 2011/12 reports a total of 34 cases of “Discectomy for recurrent lesion”; 1,259 cases of “Other discectomy”; and, 176 “Other excision procedures on spinal canal or spinal structures”.12

**Speciality**  
Neurology and neurosurgery OR Orthopaedic Surgery

**Technology setting**  
Specialist hospital

**Impact**

**Alternative or complementary technology**

The Barricaid implant is an additive technology to be used in combination with the current surgical technique of spine discectomy.

**Current technology**

Lumbar discectomy is the most common surgical procedure performed for patients experiencing back and leg pain.8,9 Clinical guidelines from the North American Spine Society (2012) note that “discectomy is suggested to provide more effective symptom relief than medical/interventional care for patients with lumbar disc herniation with radiculopathy whose symptoms warrant surgical intervention”.13

A recent health technology assessment published by the US health insurer Anthem Blue Cross, there are several other closure devices proposed for use in annular repair following a discectomy:

(a) Inclose™ Surgical Mesh System (Anulex Technologies, Inc., Minnesota, USA), which received US FDA 510(k) clearance in 2005 (510(k) # K050969);

(b) Xclose™ Tissue Repair System (Anulex Technologies, Inc.), which received US FDA 510(k) clearance in 2006 (510(k) # K062307);

(c) DART™ System (Magellan Spine Technologies, Inc., California, USA), which has a CE mark but not US FDA clearance.14

The position of Anthem Blue Cross is that closure using devices for annular repair are considered investigational and not medically necessary.9

**Diffusion of technology in Australia**

Global Orthopaedic Technology (NSW, Australia) is the local distributor for the Barricaid mesh in Australia.4,15 According to the distributor, this device is currently used by a small number of Australian surgeons.4,16
International utilisation

<table>
<thead>
<tr>
<th>Country</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td></td>
<td>✔</td>
<td>Likely. Information from the manufacturer states that 3,000 implantations have been done worldwide.³</td>
</tr>
<tr>
<td>Croatia</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>

Cost infrastructure and economic consequences

Overall costs of repeat surgery were calculated by Parker et al (2013)¹⁷ and are described in the Economic Evaluation section of this report. Current information indicates a cost of $5,900 per treatment (personal communication, HealthPACT). Some training appears to be required as described in a study by Lequin et al (2012)¹ where all surgeons received training with the device in a cadaver or an artificial spine. The manufacturer describes a number of educational offerings: (a) symposia held at major medical congresses to outline patient indications, surgical technique and expected clinical outcomes; (b) an instructional cadaver laboratory course provided at European centres or the manufacturer’s Massachusetts facility; (c) a visiting surgeon program where clinical instructors travel to new user sites to provide assistance during the first implantation; and (d) user group meetings.¹⁸

Ethical, cultural, access or religious considerations

No cultural, religious, or access considerations for the Barricaid annular prosthesis were identified.

Evidence and Policy

Safety and effectiveness

Four publications investigated the use of Barricaid.¹⁻³,¹⁹ These publications analysed the experience of only two Barricaid study populations that were initially reported in Lequin et al (2012) and Parker et al (2013). Data from these two primary studies were presented in a combined manner in Bouma et al (2013). In addition a patient subset was subsequently assessed in Trummer et al (2013). The two secondary studies have been included as they provide addition findings. Basic information for each study is presented in Table 1.
### Table 1  Characteristics of included studies

<table>
<thead>
<tr>
<th>Study/ Design</th>
<th>Patients</th>
<th>Outcomes</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parker et al 2013&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Barricaid: 30 consecutive patients (31 discectomies) enrolled between May 2008 and May 2009. Controls: 46 consecutive patients enrolled between January 2003 and May 2006 (control group).</td>
<td>Symptomatic, same-level, recurrent disc herniation; same-level disc height loss.</td>
<td>24 months. 29 of 30 Barricaid patients (97%) were available for outcome assessment at 24 months versus 23 of 46 control patients (50%).</td>
</tr>
<tr>
<td>Croatia (2 sites)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multicentre, prospective, non-randomised comparative study (level III-3 interventional evidence).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lequin et al 2012&lt;sup&gt;1&lt;/sup&gt;</td>
<td>45 patients deemed eligible by the surgeon.</td>
<td>Reherniation, disc height, pain and function.</td>
<td>Reported 40 patients (89%) were available for outcome assessment at 12 months.</td>
</tr>
<tr>
<td>(NCT01534065)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Austria, Germany and The Netherlands (4 sites)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multicentre, prospective, case series (level IV interventional evidence).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bouma et al 2013&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Barricaid: 75</td>
<td>Oswetry Disability Index, Visual Analogue Scale leg, Visual Analogue Scale back</td>
<td>24 months. 40 patients completed the 24 month follow-up period</td>
</tr>
<tr>
<td>Reported combined data from patients previously described in Parker et al (2013) and Lequin et al (2012)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multicentre case series (level IV interventional evidence)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used subset of results from the combined Bouma et al (2013) data set.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multicentre non-randomised comparative study (level III-3 interventional evidence)</td>
<td></td>
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</tr>
</tbody>
</table>

**Parker et al 2013<sup>2</sup>**

From May 2008 to May 2009, an industry-funded, prospective, non-randomised comparative study was conducted at two centres in Croatia (level III-3 interventional evidence). The study’s objectives were to evaluate whether the Barricaid device could be implanted safely, reduce same-level recurrent disc herniation, preserve disc height and improve outcomes after lumbar discectomy. Follow-up extended to 24 months.

Thirty consecutive adults undergoing 31 lumbar discectomies received Barricaid implants during surgery. Their outcomes were compared with those of 46 similar consecutive patients who had undergone lumbar discectomy without Barricaid at the same centres with the same three surgeons from 2003 to 2006. The latter group was initially studied to evaluate the effect of annular defect size and volume of disc removed on recurrent herniation.
Inclusion criteria for both cohorts were: (a) a preoperative magnetic resonance imaging (MRI) study confirming a disc herniation with radicular symptoms and failure of 6 weeks of conservative therapy to relieve symptoms, intolerable sciatica, or severe neurological deficit, including motor loss or symptoms or signs of cauda equina; (b) leg pain of greater than 40 on a 100-point visual analog scale (VAS); and (c) dysfunction of greater than 40 on the 100-point Oswestry Disability Index (ODI). Exclusion criteria were related to anatomy, prior surgery, an active medical or workers compensation lawsuit, and concerns about follow-up compliance. Primary endpoints were symptomatic, same-level, recurrent disc herniation and same-level disc height loss.

The two cohorts were not significantly different with respect to preoperative measures. The Barricaid cohort, in comparison with the control group, had a mean age of 38 years compared with 41 years; mean weight of 83 kg versus 81 kg; disc height of 8.6 mm versus 8.3 mm; and mean ODI score of 63 versus 57. Across both cohorts, the surgical site was primarily L4-5 and L5-S1. The Barricaid cohort had significantly higher mean VAS scores compared with the control group for back pain (66 versus 50) and leg pain (80 versus 69) ($p<0.01$ for both comparisons).

Posterior lumbar discectomy was performed either through the interlaminar space or via a small unilateral laminotomy, and the surgical technique was identical for both study cohorts. All patients had computed tomography scans and MRI scans preoperatively, at 12 and 24 months of follow-up, and with onset of symptoms.

**Safety**

There was no device-related morbidity in the Barricaid group, e.g. durotomy (tear or incision of the dura), nerve root injury during implantation or post-operative device migration. There were no technical failures (for example, inability to place the device). A durotomy unrelated to Barricaid placement occurred in one patient and another patient underwent disc debridement and wound incision and drainage for suspected discitis 56 days after primary surgery (the Barricaid implant was left in). One patient in the control group required a durotomy.

Reherniation at the surgical disc space was considered to be a safety issue. With respect to reherniation at 24 months, there were no cases in the Barricaid group versus three (6.5%) in the control group ($p=0.27$). Of the affected control patients, two had revision discectomy and the third had conservative therapy. Disc height was determined at 12 months for all 30 Barricaid patients and 33 (72%) of the 46 control patients. A trend towards preservation of disc height was observed in the Barricaid patients (7.6 mm, standard deviation [SD] 1.5), compared with the control group 6.9 mm (SD 1.1) ($p=0.054$).
Efficacy

With respect to pain and disability after surgery, patient-reported VAS and ODI scores were available for all 30 Barricaid patients at 12 months and for 29 of 30 (96%) at 24 months. Within this group, significant improvements in all outcome measures were observed compared with baseline values \( (p<0.01) \). In the control group, follow-up data were available for 38 patients (83%) at 12 months and for 23 patients (50%) at 24 months. This group also demonstrated significant improvements in all outcome measures compared with baseline values \( (p<0.01) \). The extent of one-year improvement (change score) was significantly greater in the Barricaid cohort compared with the control cohort. The mean change in leg pain VAS score was 75 (SD 12) for the Barricaid group versus 52 (SD 27) for the control group \( (p<0.001) \). The mean change in back pain VAS score was 53 (SD 22) for the Barricaid group versus 31 (SD 25) for the control group \( (p<0.001) \). The mean change in ODI score was 47 (SD 17) for the Barricaid group compared with 35 (SD 19) for the control group \( (p<0.005) \). Statistically significant differences between the groups persisted at 24 months \( (p<0.05) \).

Lequin et al 2012\(^1\)

Starting in April 2009, an industry-funded, post-marketing surveillance case series study of Barricaid was conducted at four hospitals in three European countries (level IV interventional evidence).

The study prospectively enrolled 45 eligible patients to receive the Barricaid device. Each patient enrolled in the study had sciatica due to MRI-confirmed lumbar disc herniation that had not responded to conservative therapy for at least 6 weeks. Additional inclusion criteria were: (a) a minimum posterior disc height of 3 mm at the index level(s); (b) a leg pain score of at least 40 on a 100-point VAS; and (c) a score of at least 40 on the 100-point ODI. There were multiple exclusion criteria related to symptoms, anatomy, prior surgery, required treatment and obesity. \(^20\)

For patients enrolled in the study the mean age was 42.3 years (SD 11.4), the mean body mass index (BMI) was 26.0 kg/m\(^2\) (SD 4.9) and 53 per cent were men. Smokers made up 49 per cent of the population. The problematic disc was at L4-5 in 22 patients (49%), at L5-S1 in 21 patients (47%) and at L3-4 in 2 patients (4%).

Limited discectomy was performed and the volume of disc material removed was measured. All participating neurosurgeons were experienced in lumbar disc surgery. While none of the surgeons had previously used Barricaid, they all received training with the device in a cadaver or an artificial spine. At the time of the study the implant was available in one size that was capable of blocking a defect up to 10 mm wide. It was prospectively determined that implementation of the Barricaid device would not be attempted if the defect was taller than 6 mm or wider than 10 mm. However, in no case did the surgical defect exceed the size limits.
Safety

Reherniation occurred in one patient (2.4%) within a 12 month follow-up period. The patient was a 40-year-old male smoker with a BMI of 22 kg/m². His primary surgery was an L4-5 discectomy in which the Barricaid was implanted to treat a 4 mm high by 8 mm wide defect. Four months after surgery he reported increased back and leg pain, and recurrent herniation was confirmed on MRI. A spinal fusion was then performed. The operating surgeon and the independent Data Safety Monitoring Board (DSMB) concluded that the implant was placed 3 mm too deep into the disc space, exceeding the recommended range and permitting disc extrusion. Of the remaining 40 patients, 36 (90%) had MRI examinations at 12 months. One patient had a disc protrusion around the implant but was asymptomatic. Two additional reoperations were performed, one for a contralateral herniation 3 weeks after the original surgery and one for excessive scar tissue 5 months after the original surgery. According to the review by the DSMB no device-related adverse events occurred.

Efficacy

The mean duration of surgery was 120 minutes (SD 31) and the mean length of hospital stay was 2.4 days (SD 1.4). In terms of the annulus defect, the mean measurements were: height 4.9 mm (SD 0.7), width 7.8 mm (SD 1.5) and area 38.6 mm² (SD 10.9). The volume of nucleus removed was 1.6 mL (SD 1.1). Of the original 45 patients, 40 (89%) were available at the 12-month follow-up. The remaining five patients were not included due to: failure to implant the Barricaid mesh (1 patient); contralateral reherniation (1 patient, as noted above); failure to return for 12-month follow-up (2 patients); and wrong site of surgery (1 patient).

Preoperative and postoperative mean VAS scores for back pain (60, decreasing to 25) and leg pain (80, decreasing to 18) pain and mean ODI scores (60, decreasing to 18) showed significant reductions (p<0.0001 for all comparisons). The authors noted that these improvements compared favourably to results in the literature for limited discectomy without Barricaid mesh. Radiographic analysis of disc height was available for 30 of the 40 patients (75%). A statistically significant (p<0.01, one sided Student t-test) retention of baseline disc height was identified in 93 per cent (SD 7.9) of barricade patients. This was contrasted by the authors against reports in the literature showing disc height maintenance of less than 75 per cent with standard treatment. Radiography revealed intact implants with no evidence of slippage or migration.

Bouma et al 2013

This study combined the participants and results from Parker et al (2013) and Lequin et al (2012), reporting safety and efficacy outcomes at 12 and 24 months follow-up for 75 patients who had received the Barricaid mesh. At 24 months, follow-up data were available for 11 of the original 45 patients as reported by Lequin et al (2012) and 29 of the 30 patients from Parker et al (2013).
Safety
In the combined population, only the single incidence of reherniation described in the Lequin et al (2012) was reported, with no further mention of adverse events.

Efficacy
Of the total patient population of 40 the significant reductions in mean VAS and ODI scores achieved at 12 months remained at 24 months (data presented graphically).

Trummer et al 2013
Using the participant cohort reported by Bouma et al (2013), this study reported outcomes of a subset of 63 Barricaid recipients with pre-operative and 12-month follow-up images from X-ray computed tomography (CT) scans. Patient selection is not described and may be subject to bias. A control cohort of 137 discectomy-only patients was enrolled; however, the reported analysis used 94 patients that also had pre-operative and 12-month follow-up CT scans. The control patients were similar to the intervention cohort for demographic features, but had significantly lower pain and disability scores in comparison to the Barricaid cohort.

Safety
There were no device-related complications.

Efficacy
Facet degeneration, the movement of a patient to a higher grade of annular degeneration determined by CT scan, was 51 per cent for the control and 24 per cent for the Barricaid cohort \( (p=0.008) \).

Results showed a lower risk of facet degeneration in patients with a smaller annular defect \( (p=0.041) \), and patients who received the Barricaid implant \( (p=0.014) \).

Economic evaluation
An industry-funded post hoc economic analysis was published by Parker et al (2013)\(^ {17} \) based on the non-randomised comparative study by Parker et al (2013)\(^ {2} \) outlined above. As reported earlier, symptomatic, recurrent same-level disc herniation occurred in three of 45 (6.5%) control patients and none of the 30 Barricaid patients \( (p=0.27) \). Two cost estimates for the surgical treatment of reherniation were calculated, one looking at direct costs and the other at indirect costs.

The direct costs were modelled on 2012 USA Medicare national allowable payment amounts based on Diagnostic Related Groups and Current Procedural Terminology codes. Costs were then converted to those of a private payer at 170 per cent of Medicare costs. Indirect costs were calculated based on the number of workdays lost by a patient requiring treatment for
recurrent disc herniation. All cost information (both United States dollars [USD] and Australian dollars) is provided in 2012 dollars.

**Medicare estimated costs:** The mean estimated cost per affected patient to surgically manage recurrent disc herniation included direct costs of USD 17,920 (USD 15,582 for hospital, USD 1,800 for surgeon and radiologist, and USD 538 for radiology). In Australian dollars these costs total $27,758 ($24,137 for hospital, $2,788 for surgeon and radiologist and $833 for radiology). Indirect costs (patient work-day loss of almost 28 days) were estimated to be USD 3,778 ($5,852). The total estimated direct and indirect costs per repeat surgery were USD 21,698 ($33,610). 21

**Private payer estimated costs:** The authors projected that the private payer costs would total USD 34,242 (direct cost USD 30,464 in addition to the indirect cost of USD 3,778). In Australian dollars these costs total $58,893 ($53,041 direct; $5,852 indirect). The cost calculations were extrapolated to annual cost savings of USD 222,573 ($344,764) per 100 primary discectomy procedures performed, or USD $2,226 ($3,448) per discectomy. Annual cost savings were not calculated for the Medicare-associated costs.

**Ongoing research**

**NCT01283438:** a Phase 4, prospective, industry-sponsored, randomised controlled trial (RCT) in 20 European centres located across Austria, Belgium, France, Germany, The Netherlands and Switzerland. The trial started in 2010 and is scheduled for completion by the end of 2016. The goal is to enrol a total of 550 patients evenly into two arms; one arm employing limited discectomy plus Barricaid and the other employing limited discectomy alone. Primary outcomes at 24 months are recurrent disc herniation and a composite of pain, function and safety. Secondary outcomes include back pain improvement, disc height maintenance and improvement in disability. 5, 22

**Other issues**

Two primary Barricaid patient cohorts are reported in several studies.; As reported above, the 30 Barricaid recipients reported in Parker et al (2013a) and the 45 reported in Lequin et al (2012), 1, 2 were combined into a case series study by Bouma et al (2013). 19 Trummer et al (2013) 3 compared a subset of Bouma et al (2013) Barricaid recipients who had undertaken 12-month CT scans with the results of 94 lumbar discectomy only patients.

The research described in all publications located for the Barricaid device was funded by the manufacturer. Two of the seven authors of one clinical study 2 had conflicts of interest related to the manufacturer, i.e. one owned stock options and the other was a paid consultant for the company. For the economic analysis 17, one of the six authors was a paid consultant for the company.
Clinician feedback suggested that there may be the potential for a herniation of the implant that would lead to a greater morbidity than recurrent prolapse alone. This outcome was not examined by any of the included studies.

**Summary of findings**

The evidence base for the safety and efficacy of Barricaid mesh was very limited, including only two patient cohorts and a total of 75 patients. The smaller study of 30 patients compared outcomes with those of historical controls, while the slightly larger study of 45 patients was a case series. The outcomes measured at 12 and 24 months (the latter incomplete) after surgery included reherniation, change in disc height and patient-reported changes in leg and back pain and disability. The smaller comparative study reported no reherniations in the Barricaid group versus three (6.5%) in the control group, although the difference was not statistically significant. Similarly, disc height in the Barricaid group only trended towards height retention.

Measures of pain and disability were more favourable in both groups compared with baseline, although the changes were significantly larger for the Barricaid group compared with the discectomy-alone group. In the larger case series of 45 patients, two reherniations occurred: one symptomatic and one asymptomatic. A small, but statistically significant, reduction in disc height was measured but again, measures of pain and disability were significantly more favourable than baseline values.

The evidence base for Barricaid will be augmented by the results of an industry-sponsored, prospective RCT of 550 patients being conducted in 20 European centres that is estimated to be completed at the end of 2016.

**HealthPACT assessment**

Although studies to date using the Barricaid device have been small, this device may be a useful addition to spinal surgery. Results have been promising with a reduced number of reherniations reported, which may result in better patient outcomes. Successful results may depend on patient selection, with preference for those with single level disease and preserved nucleus height. In addition, early analysis indicates the Barricaid device is cost-effective, thereby potentially resulting in healthcare savings. As the evidence-base for this device is limited, HealthPACT recommends that this device should only be used under the auspices of a clinical trial and that it be reassessed in 24-months.

**Number of studies included**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies 4
Total number of Level III-3 studies 2
Total number of Level IV studies 2

References


