STRATAFIX™ Knotless Tissue Control Devices and the DERMABOND® PRINEO® Skin Closure System

Value Analysis Brief for Cesarean Section
Executive Summary

22.9 million C-Section procedures were performed globally in 2012\(^1\)

Across the world, nearly 1 in 5 births (18.6%) occur by C-Section\(^2,3\)

- North America: 32.3%
- Europe: 25.0%
- Asia: 19.2%
- Africa: 7.3%
- South America: 40.5%
- Australia: 31.1%

C-Section wound complication rates can be as high as 16% in populations with prominent risk factors\(^4,5\)

- Wound complications are significantly more frequent with metal skin staples (13.0%) versus traditional absorbable subcuticular sutures (4.8%; p<0.01)\(^1,4-8\)

Common wound complications arising from suture-closed C-Sections\(^7\)

- Surgical site infection: 2.9%
- Wound separation: 2.5%
- Hematoma: 1.6%
- Seroma: 1.2%

Ethicon’s wound closure solutions may help reduce the burden of C-Section wound complications\(^9,10\)

**STRATAFIX™ Knotless Tissue Control Devices**

- More security, consistency, and efficiency compared to traditional sutures\(^10\)
- Now available with Ethicon’s Plus antibacterial technology: a triclosan coating that addresses a known risk factor for SSIs\(^a, 21, 22\)
- Exceptional strength for closing high-tension areas\(^b, 13, 17, 23-26\)

**DERMAABOND® PRINEO® Skin Closure System**

- Superior skin holding strength and tension distribution compared to traditional sutures and skin staples\(^27, 28\)
- Provides a flexible barrier to microbial penetration\(^29\)
- No postsurgical dressings may mean easier self-care and greater self-confidence for patients\(^30\)

\(^a\) Specific to STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device, STRATAFIX™ Spiral PDS™ Plus Knotless Tissue Control Device, and STRATAFIX™ Spiral MONOCRYL™ Plus Tissue Control Device
\(^b\) Specific to the STRATAFIX™ Symmetric Knotless Tissue Control Device
22.9 million C-Section procedures were performed globally in 2012

- Over the past 30 years the average global C-Section rate has increased by ~5% each year.
- The global average rate is increasing and greatly exceeded in regions such as North America (32.3%) and China (40.5%).
- C-Section is one of the most common surgical procedures in the US, Canada, and Europe.

1 in 20 C-Sections experience wound complications

- C-Section surgical site infection (SSI) rates can be as high as 19% and 16% in populations with prominent risk factors such as obesity and diabetes, respectively.
- SSI rates are significantly higher in patients undergoing C-Section procedures ≥38 minutes in duration (p=0.026).
  - Many patients may be exposed to this risk because the typical procedure duration is 24-57 minutes.
- The likelihood of C-Section wound separation is 6 times higher in obese patients compared to patients of normal weight (p=0.01).

C-Section wound complications

- Frequency with traditional absorbable suture for skin closure

Risk factors for C-Section SSIs

- The odds ratio is the odds that a wound complication will occur in patients with the risk factor, compared to in those without the risk factor. For example, obese patients are 3.7 times more likely to have an SSI compared to patients of normal weight. *unadjusted odds ratio (adjusted odds ratio not reported)
Wound complications may reduce patient satisfaction\textsuperscript{36}

- Wound complications prolong C-Section recovery time\textsuperscript{37} and may negatively affect a mother’s ability to recover and care for her newborn\textsuperscript{7}.
- Previous C-Section increases the risk of uterine rupture during subsequent pregnancies\textsuperscript{38}, which may worry expecting mothers about the long-term consequences of suboptimal wound healing.

Wound complications increase hospitalization costs\textsuperscript{39-41}

- In China, C-Section hospitalization costs can reach CNY 7,300, with higher costs for longer length of stay (LOS)\textsuperscript{42}.
- SSIs in obstetric and gynecological (OBGYN) procedures, including C-Section:
  - Prolong LOS beyond the typical 2-4 days\textsuperscript{4}.
  - Increase the cost of hospitalization per patient by USD 14,000 or GBP 4,000\textsuperscript{39, 40}.
- Major surgical repairs of separated wounds require readmission and reoperation, costing an additional GBP 1,050 per patient according to a UK estimate\textsuperscript{41, 43}.

SSIs increase LOS and hospitalization costs in OBGYN and C-Section procedures\textsuperscript{39, 40}

In (A), the cost of admission is defined as the cost for a single admission and hospital discharge; in (B), the cost of admission is aggregated for the original admission and linked readmissions. No p-values reported in (A). GBP, Great British Pounds; USD, United States Dollars.
C-Section wound complication rates are as high as 14% using traditional wound closure methods and surgical dressings\(^7,44\)

- Wound complications occur in 4.8% of C-Sections using traditional sutures.\(^7\)
  - Continuous suturing closure can be compromised with a break in the suture.\(^45-47\)
  - Interrupted closure may be stronger and more secure than continuous suturing, but this technique is associated with more knot-related complications.\(^48\)
  - Suture knots can be a site of bacterial colonization for infection and can create inconsistent suture tension, risking tissue gapping between knots.\(^49-51\)
- Skin staples have higher C-Section wound complication rates (13.0%) than traditional sutures.\(^7\)

### C-Section wound complications are more frequent with staples versus traditional sutures\(^7\)

<table>
<thead>
<tr>
<th></th>
<th>Traditional absorbable subcuticular sutures</th>
<th>Non-absorbable metal skin staples</th>
</tr>
</thead>
<tbody>
<tr>
<td>All wound complications</td>
<td>4.8%</td>
<td>13.0%</td>
</tr>
<tr>
<td>SSI</td>
<td>2.9%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Wound separation</td>
<td>2.5%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

- Up to 14% of patients experience C-Section wound complications using a standard surgical dressing.\(^44\)
  - A meta-analysis across surgical specialties found no evidence that traditional surgical dressings can reduce SSI rates compared to leaving the surgical wound exposed\(^52\), highlighting a need for more effective solutions.
- In some British hospitals, women may shower but are advised to avoid bathing for up to 5 days until the dressing is removed\(^53\). This may be frustrating to patients wanting to tend to personal needs.
- Because wound dressings act as a barrier, protecting the wound from bacterial contamination for example when the patient showers or bathes, removing the protective dressing early may risk infection.\(^54\)

### Traditional wound closure methods contribute to the economic burden

- Slow wound closure increases operative duration and places pressure on surgical resource use:
  - Skin closure using traditional absorbable sutures increases C-Section operating time by 7.2 minutes (p<0.01) compared to metal skin staples.\(^7\)
  - Interrupted closure increases procedure time compared to continuous suturing.\(^45,46\)
- Traditional wound dressings do not provide a microbial barrier\(^55\), risking the development of SSIs and the associated increase in LOS and hospitalization costs.
The increasing prevalence of C-Section risk factors\textsuperscript{56-59} may increase the patient burden

- Obesity and diabetes are risk factors for C-Section and C-Section wound complications.\textsuperscript{4, 5, 60, 61}
- The prevalence of these co-morbidities is rising globally,\textsuperscript{56-59} which would be expected to increase the burden of C-Section wound complications.

Traditional suture techniques present trade-offs

- Continuous suturing:
  - Can be compromised with a break in the suture.\textsuperscript{45-47}
- Interrupted closure:
  - Inconsistent tension distribution.\textsuperscript{51}
  - Knot-related complications.\textsuperscript{48}
  - Time-consuming.\textsuperscript{45, 46}

Clinicians and patients need better surgical dressings

- Traditional surgical dressings do not significantly reduce SSI rates compared to leaving the surgical wound exposed.\textsuperscript{52}
- Women may not be able to satisfactorily attend to their personal hygiene until the dressing is removed.\textsuperscript{53}

There is renewed urgency for safe and effective wound closure techniques that:

- Provide an ideal healing environment, with less pain and better cosmesis;
- Limit the rate of wound complications and reduce the clinical and economic burden of current care;
- Enable women to tend to their personal needs as soon as possible following C-Section.
Ethicon’s wound closure solutions address these critical unmet needs

- **STRATAFIX Knotless Tissue Control Devices** are barbed sutures that combine the efficiency of continuous traditional suture closure with the strength and security of interrupted closure, without knot-related complications.\(^{11-13}\)

- **DERMABOND PRINEO Skin Closure System** provides strong, protected wound closure, excellent cosmetic results, and easier self-care after surgery.\(^{10, 30, 62-65}\)

<table>
<thead>
<tr>
<th>STRATAFIX™ Spiral Plus Knotless Tissue Control Device</th>
<th>STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Delivers smooth passage through the tissue, and engages for a secure hold.(^{66})</td>
<td>- Provides exceptional wound-holding strength and security with every pass.(^{23, 24})</td>
</tr>
<tr>
<td>- Unidirectional (single-armed) or bidirectional(^{b}) (double-armed) designs.</td>
<td>- The only knotless tissue control device that provides strong and secure closure appropriate for high-tension areas such as fascia, also suitable for subcutaneous, deep tissue, and organ wound closure.(^{70})</td>
</tr>
<tr>
<td>- Suitable for subcuticular, subcutaneous, deep tissue, and organ wound closure.(^{67, 68})</td>
<td>- Available in the absorbable polymer PDS Suture.(^{70})</td>
</tr>
<tr>
<td>- Available in absorbable polymer PDS(^{a}) (polydioxanone) Suture and MONOCRYL(^{a}) (poliglecaprone 25) Suture, and also in the non-absorbable polymer polypropylene.(^{67, 68})</td>
<td>- Now available with Ethicon’s Plus antibacterial technology.(^{c, 21, 22, 69})</td>
</tr>
<tr>
<td>- Now available with Ethicon’s Plus antibacterial technology.(^{c, 21, 22, 69})</td>
<td></td>
</tr>
</tbody>
</table>
STRATAFIX Knotless Tissue Control Devices and DERMABOND PRINEO Skin Closure System provide strong and secure wound closure

- Compared to conventional sutures, **STRATAFIX Knotless Tissue Control Devices** eliminate the need for compromise, providing improved security, consistency, and efficiency without knot-related complications.\(^{11,20}\)
  - In pre-clinical studies, cutting the STRATAFIX Knotless Tissue Control Device did not result in tissue separation or unravelling of the device.\(^{12,14,17,20}\)
  - STRATAFIX Symmetric Devices show exceptional fascia holding strength compared to traditional suture: 32% stronger than interrupted sutures and 22% stronger than continuous sutures (\(p=0.009\) in a 3-way comparison).\(^{13,19,23-26}\)
  - Fascia separation did not occur when the fascia of pregnant ewes was closed\(^*\) following C-Section with barbed polydioxanone suture.\(^{78}\)

---

**STRATAFIX Symmetric Devices show exceptional fascia holding strength\(^{12}\)**

- **STRATAFIX Symmetric PDS Plus Knotless Tissue Control Device - Size 0**
- **Looped PDS® Plus Antibacterial (polydioxanone) Suture (continuous technique) - Size 0**
- **Coated VICRYL® (polyglactin 910) Suture (interrupted technique) - Size 0**

Pre-clinical study. The \(p\)-value reported is for a 3-way comparison.

*Only the STRATAFIX Symmetric Knotless Tissue Control Device is indicated for fascia closure*
In an ex vivo study, more load in N was required to create a 3 ± 1 mm gap between skin edges approximated with DERMABOND PRINEO System, than with subcuticular 4-0 MONOCRYL Suture or PROXIMATE® Ethicon Endo-Surgery skin staples \( p=0.00 \);

- Study performed ex vivo

**Clinical Value**

- **DERMABOND PRINEO System** was shown to provide significantly greater skin holding strength than skin staples or subcuticular suture.\(^a\)\(^b\)\(^27\)

  - Incisions closed with DERMABOND PRINEO System have been shown to be stronger than other closure methods:
    - > 33% stronger compared to skin staples \( p<0.01 \).\(^b\)\(^64\)
    - > 40% stronger compared to 4-0 sutures \( p<0.01 \).\(^b\)\(^64\)
    - > 32% stronger than DERMABOND ADVANCED Adhesive combined with subcuticular sutures \( p<0.05 \).\(^b\)\(^79\)

- The incidence of C-Section wound separation is:
  - Lower with DERMABOND® Topical Skin Adhesive compared to skin staples (not statistically significant).\(^90\)
  - Lower with cyanoacrylate skin glue compared to Steri-strips \( p=0.03 \).\(^8\)

- Combines the proven strength, flexibility, and antimicrobial protection of DERMABOND ADVANCED® Topical Skin Adhesive with the added support and security of a self-adhering mesh to further facilitate both wound-edge approximation and an optimal healing environment.\(^72\)-\(^76\)

---

**DERMABOND PRINEO System achieves significantly greater skin holding strength versus traditional wound closure methods\(^b\)\(^64\)**

![Graph showing mean max load (N) prior to 3 mm gap compared to DERMABOND PRINEO System, skin staples, and subcuticular suture.](image)

Tension load needed to achieve a 3 mm gap in ex vivo porcine samples closed with DERMABOND PRINEO Skin Closure System (22 cm), surgical staples, or sutures. Incisions closed with DERMABOND PRINEO System required significantly greater loads to create the 3 mm gap.

**The incidence of C-Section wound separation is lower with DERMABOND Adhesive versus traditional skin closure methods\(^8\)\(^90\)**

![Graph showing percentage of patients with wound separation compared to DERMABOND Adhesive or cyanoacrylate skin glue, sutures, skin staples, and Steri-strips.](image)

Patients with wound separation (%)

- Siddiqui et al. (2013): 5% (\( p=0.65 \)), 13% (\( p=0.09 \))
- Westcott et al. (2016): 12% (\( p=0.03 \)), 19% (\( p=0.03 \))

p-values are versus DERMABOND Adhesive (Siddiqui et al. (2013)) or cyanoacrylate skin glue (Westcott et al. (2016)). The patient population studied in Westcott et al. (2016) was obese (average BMI of ~31), and therefore the wound separation rates are high in both cohorts studied\(^8\).

---

\(^a\) In an ex vivo study, more load in N was required to create a 3 ± 1 mm gap between skin edges approximated with DERMABOND PRINEO System, than with subcuticular 4-0 MONOCRYL Suture or PROXIMATE® Ethicon Endo-Surgery skin staples \( p<0.00 \).

\(^b\) Study performed ex vivo.
Appropriate tension leads to better wound healing and cosmetic outcomes

- With significantly more points of fixation than traditional sutures, STRATAFIX Knotless Tissue Control Devices make it easier to manage tension and control approximation during closure.\(^{8,12,16}\)

- DERMABOND PRINEO System redistributes tension away from the wound, gently dispersing tension uniformly across the entire incision area compared to traditional sutures and staples.\(^{6,28}\)

DERMABOND PRINEO System distributes tension more evenly than traditional wound closure methods\(^{6,28}\)

In a head-to-head ex vivo study versus staples and subcuticular suture, incised tissue samples were approximated using 3-0 suture, skin staples, or DERMABOND PRINEO System (22 cm), respectively. Samples were then placed in a device and tensioned mechanically. Digital Image Correlation technology was used to map strain (as measured by tissue movement). Black spacing in mapping image is due to the sensor not being able to capture any readings.

Ethicon’s solutions address known risk factors for C-Section SSIs

- STRATAFIX Knotless Tissue Control Devices with Ethicon’s Plus antibacterial triclosan coating address a known risk factor for SSIs,\(^{9,10}\) providing in vitro protection against bacteria commonly associated with C-Section SSIs, including
  - S. aureus,
  - S. epidermidis,
  - Methicillin-resistant S. aureus (MRSA),
  - Methicillin-resistant S. epidermidis (MRSE),
  - E. coli,\(^{2,6}\)
  - K. pneumoniae.\(^{2,6}\)

  - The use of triclosan-coated sutures are supported by the World Health Organization (WHO), Centers of Disease Control and Prevention (CDC), American College of Surgeons (ACS) and the Surgical Infection Society (SIS).\(^{8,15–84}\)

  - Triclosan inhibits bacterial colonization on the suture surface for >7 days in vitro.\(^{21,22,69}\)

  - Triclosan-coated sutures have been shown to reduce the risk of SSIs in multiple meta-analyses.\(^{85–90}\)

- DERMABOND PRINEO System provides a flexible microbial barrier with 99% protection in vitro for 72 hours against bacteria commonly associated with SSIs, including
  - S. aureus,
  - E. coli,
  - P. aeruginosa,
  - E. faecium,
  - S. epidermis (including MRSA and MRSE).\(^{29}\)

  - Compared to Steri-strips, cyanoacrylate skin glue significantly decreased the composite C-Section wound complication rate (p=0.006) and tended to reduce the SSI rate (p=0.057) in a single study.\(^{8}\)

Triclosan inhibits bacterial colonization on the suture surface\(^{22}\)

<table>
<thead>
<tr>
<th>Log CFU/cm of suture</th>
<th>Poliglecaprone 25 suture with triclosan</th>
<th>Poliglecaprone 25 suture</th>
<th>Silk suture</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>4</td>
<td>6.7</td>
<td></td>
</tr>
</tbody>
</table>

*In vitro colonization by E. coli at 37°C for 24 hours. No p-values reported. CFU, colony-forming units.

Cyanoacrylate skin glue reduces the rate of C-Section wound complications versus Steri-strips\(^{8}\)

<table>
<thead>
<tr>
<th>Patients(%)</th>
<th>All wound complications</th>
<th>SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanoacrylate skin glue</td>
<td>13.9%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Steri-strips</td>
<td>23.3%</td>
<td>23.3%</td>
</tr>
</tbody>
</table>

*Study performed ex vivo. *Triclosan-coated sutures are recommended for the purpose of reducing the risk of SSIs. The CDC, WHO, ACS, & SIS guidelines on reducing the risk of SSIs are general to triclosan-coated sutures and are not specific to any one brand. Among the Ethicon portfolio, specific to STRATAFIX Symmetric, STRATAFIX Spiral PDS Plus, and STRATAFIX Spiral MONOCRYL Plus Knotless Tissue Control Devices, *PDS Plus and MONOCRYL Plus sutures only*
Ethicon’s wound closure solutions can help avoid prolonged recovery times that may potentially affect a mother’s ability to care for herself and her newborn

**Pain**

- Barbed sutures are associated with less itching and irritation compared to traditional sutures, as reported in a single study.91
- Post-operative C-Section pain scores were comparable between traditional sutures and a device of similar material and design to STRATAFIX Knotless Tissue Control Devices.50, 92
- At the time of removal, DERMABOND PRINEO System is associated with less pain than other wound closure devices.10

**Self-care**

- Using DERMABOND PRINEO System, no post-surgical dressings may mean easier self-care and greater self-confidence for patients.30
- Patients may be able to shower immediately after C-Section if directed by their healthcare professional.74
- DERMABOND PRINEO System conforms to the body’s contours and remains securely in place.73

**Cosmesis**

- Patients report less scarring and fewer adverse skin reactions with barbed sutures compared to traditional sutures, as found in a single study.91
- C-Section scar cosmesis scores were similar between traditional sutures and a device of similar material and design to STRATAFIX Knotless Tissue Control Devices.50, 92
- DERMABOND PRINEO System achieved cosmetic results similar to sutures with comparable cosmesis scores at 90 days and throughout the 1-year extension period.73
- In C-Section, patient and observer scar assessments were similar 8 weeks after surgery using DERMABOND Adhesive or sutures.93

---

**Barbed sutures show similar pain scores to traditional sutures**92

<table>
<thead>
<tr>
<th></th>
<th>Pain score (VAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbed sutures</td>
<td>35.5</td>
</tr>
<tr>
<td>Traditional sutures</td>
<td>35.1</td>
</tr>
</tbody>
</table>

The pain VAS scores were reported by patients 3 days following C-Section and range from 0–100, with 0 representing no pain. The p-value was calculated including a 3rd study arm not picture in the graph above (skin staples). ns, not significant; VAS, visual analogue scale

**DERMABOND PRINEO System achieves favorable cosmetic results versus traditional sutures**10

<table>
<thead>
<tr>
<th></th>
<th>Mean Vancouver Scar Scale score</th>
</tr>
</thead>
<tbody>
<tr>
<td>DERMABOND PRINEO System</td>
<td>ns</td>
</tr>
<tr>
<td>Traditional sutures</td>
<td>ns</td>
</tr>
</tbody>
</table>

The Vancouver Scar Scale scores were reported by patients 12 months after abdominoplasty and range from 0–14, with 0 reflecting normal skin. The color of the scar is reflected in the vascularization and pigmentation scores, pliability refers to the scar’s flexibility and resistance to pressure, and height refers to the scar’s thickness. ns, not significant
STRATAFIX Knotless Tissue Control Devices and DERMABOND PRINEO System improve C-section surgical efficiency

- Surgeons report better ease of handling and accuracy of tension application using **STRATAFIX Knotless Tissue Control Devices**, as reported in a single study.  
  - Compared to traditional sutures, barbed sutures significantly reduced closure time and overall surgical time (p<0.05) in studies of gynecological procedures performed world-wide, including in the EU, the Americas, and China.  

- **DERMABOND PRINEO System** may reduce the final layer of skin closure time by as much as 84%.  
  - Significantly decreased skin closure time by 5.2-13.7 minutes versus traditional sutures across various surgical specialties (p<0.05).

### Ethicon’s wound closure solutions reduce suture or overall operative versus traditional sutures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Suture Time (minutes)</th>
<th>Mean suture time (minutes)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine wall closure in laparoscopic myomectomy</td>
<td>Barbed sutures: 115, Traditional sutures: 174</td>
<td>Mean suture time: 158, p&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>Barbed sutures: 118, DERMABOND PRINEO System: 149, Traditional sutures: 162</td>
<td>Mean operative time: 150, p&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>
Ethicon’s wound closure solutions may reduce the utilization of surgical resources

- **STRATAFIX Knotless Tissue Control Devices** can significantly decrease operative resource use and costs, as demonstrated by studies performed across the globe:
  - Barbed sutures significantly reduced materials (32%, p<0.01) and overall surgery costs (16–35%, p<0.001) versus traditional sutures in several surgical specialties.  
  - In a gynecological procedure, barbed sutures significantly reduced LOS compared to traditional sutures (5.17 versus 5.68 days, respectively, p=0.007).

- With **DERMABOND PRINEO System**, there is no need for wound dressings or suture removal by a healthcare professional at a follow-up appointment, reducing costs and time spent on wound management.
  - In one study DERMABOND PRINEO System reduced total operating costs by USD 137 per patient compared to intradermal sutures (p-value not reported).

---

### Ethicon’s wound closure solutions reduce surgical costs versus traditional methods

<table>
<thead>
<tr>
<th></th>
<th>Barbed sutures</th>
<th>DERMABOND PRINEO System</th>
<th>Traditional sutures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysterectomy</td>
<td>$3,701</td>
<td>$4,415</td>
<td>$2,705</td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>$2,705</td>
<td>$2,842</td>
<td></td>
</tr>
</tbody>
</table>

No p-value reported for abdominoplasty. USD, United States Dollars.