

Polydioxanone implants: a systematic review on safety and performance in patients

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BACKGROUND: Medical devices made of polydioxanone (PDO) (a synthetic biodegradable polymer) have been available since the early 1980's. However, no review regarding their performance and safety has been published.

OBJECTIVE: This systematic review intends to review and assess commercially available PDO implants and their safety and performance in patients.

METHODS: We searched for approved PDO implants in several FDA databases. Then, we performed a literature search for publications and clinical trials where PDO devices were implanted in patients. This search was performed on MEDLINE, Embase, Scopus and other databases. Safety and performance of PDO implants in patients were assessed and compared to the implantation of non-PDO devices, when possible, based on scoring systems developed by the authors that analyse surgical site infection (SSI) rates, inflammatory reaction rates, foreign body response, postoperative pain and fever.

RESULTS: FDA databases search revealed that 48 implants have been approved since 1981, with 1294 adverse reactions or product malfunction in the last decade and 16 recalls. A total of 49 clinical trials and 104 scientific publications were found. PDO sutures and meshes/plates had low rates of SSI, inflammatory reaction, foreign body response and postoperative fever. PDO clips/staples reported high rates of SSI, postoperative fever and pain, with sub-optimal clinical performance and poor safety rates. The remaining implants identified showed high levels of safety and performance. Safety scores of PDO implants and non-PDO alternatives are similar. PDO monofilament sutures perform better than non-PDO alternatives but performance did not differ with remaining PDO implant types.

CONCLUSIONS: Although PDO clips/staples should be implanted with caution and monitored carefully, in general, safety and performance scores of other PDO implants did not differ from non-PDO alternatives. This review will be a useful reference for researchers and industries developing new PDO medical devices.

Keywords: Clinical outcomes, synthetic polymer, medical devices, implants, polydioxanone, safety, performance.

1. Introduction

Medical devices can be used for diagnosis, treatment, cure or prevention of disease in humans and animals.¹ A variety of materials can be used in the manufacture of medical devices with consideration to their medical application and material properties, such as strength, stability and degradation profile. Ideal medical implants are affordable and easily available but should also provide good biocompatibility, avoiding any foreign body reaction.² Medical device implants can take the form of degradable and non-degradable materials, and the former should degrade to nontoxic products after their function has been achieved.³ A key advantage of a biodegradable device over a non-degradable device, is that it does not require a second surgery for implant removal which reduces the number of hospital visits by the patient, healing time and hospital costs, while also avoiding a potential long term immune response.⁴

Commonly, degradable medical devices are made from polymers which are chains of repeated monomers and can be natural or synthetic. These types of materials are attractive for medical applications due to their ability to tailor mechanical properties and degradation profiles, and the possibility to have designed functional groups for different medical purposes.^{3,5} The small variability between batches and typically reduced chronic foreign body reactions are also an advantage of synthetic polymers when compared to natural polymers^{6,7}, such as silk, cellulose and chitosan. Different polymers are already in use in different clinical applications, including vascular stents, bone cements and wound dressings.⁵

Polyesters are a class of polymers in which their degradation is caused by the hydrolysis of ester linkages and the degradation products of these type of polymers are resorbed through metabolic pathways.³ Some of the most common biodegradable synthetic polyesters used for medical applications include poly(glycolic acid), poly(lactic acid) and poly(caprolactone) which are the main components of common sutures and suture anchors including Safil® sutures, VICRYL® sutures and MONOCRYL® sutures, respectively.^{3,5}

Polydioxanone (PDO) is another polyester commonly used for the manufacturing of biodegradable medical devices. Also known as PDS, poly-p-dioxanone, PDX or PDDX, it is a synthetic and absorbable colourless polyester that was first manufactured in the early 1980s.⁸ PDO is commonly synthesised by ring-opening polymerisation of p-dioxanone in the presence of an organometallic catalyst and heat (Figure 1).^{9,10} According to literature provided with existing PDO products, this polymer is considered nonantigenic and nonpyrogenic and is found to induce minimal tissue reaction during absorption after implantation. PDO is degraded by hydrolysis and is completely metabolised in the body.⁹ Due to its relatively prolonged absorption duration (182-238 days) and synthetic nature, PDO is widely used in dyed or undyed medical devices to be implanted where a long lasting absorbable material is desirable.¹¹ PDO is a semi-crystalline polymer (approximately 55% crystalline) with a glass transition temperature ranging between -10°C and 0°C and a melting temperature of 110-115°C.^{6,9,10} These characteristics allow PDO sutures to be manufactured via an extrusion process at the lowest possible temperature, preventing spontaneous depolymerisation.⁹

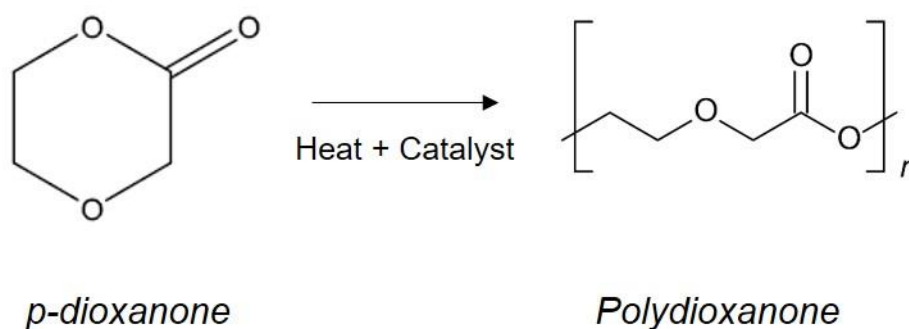


Figure 1. Chemical structure of monomer *p*-dioxanone and polymer polydioxanone.

In the medical field, PDO has been implanted in different shapes and sizes and several PDO medical devices are already used as standard practice in surgeries namely PDS™ II sutures (Ethicon) and OrthoSorb® orthopaedic pins (Johnson & Johnson International). PDO sutures are generally highly flexible due to the presence of an ether oxygen group within the polymer backbone.⁹ However, even though PDO devices are widely used, there has been concern regarding the acidic degradation products released in the body.⁴

To the authors' knowledge, no publication has provided an overview of the clinical safety and performance of PDO implants to date. In order to aid the development of future PDO medical implants, we review the safety and performance outcomes of CE marked and/or FDA approved PDO implantable medical devices and their use in clinical trials or other medical applications.

2. Methods

2.1. List of PDO medical implants approved by FDA

We performed a search through the FDA 510(k) and Premarket Approval (PMA) databases in March 2019 using the search terms 'polydioxanone', 'PDO', 'PDS', 'PDX', 'PDDX' and 'poly-p-dioxanone' to find all approved PDO medical devices that are implantable. Inclusion criteria are: implantable medical devices made of PDO with or without antibacterial coating. Exclusion criteria are: non-medical devices, devices not made of PDO, devices made non-exclusively of PDO (excluding antibacterial coating), devices that are not implantable in the human body, and devices made of unspecified material. It should be noted that, as discussed in section 4.1, clinical data is not mandatory for a premarket notification 510(k) submission. Clearance by FDA to market a medical device using this process is by substantiation of equivalence to other marketed predicate devices; therefore, the FDA 510(k) database may contain medical devices which have not yet been commercialised or used clinically.

After analysis and selection of obtained results, a predicate tree was designed based on a relationship of substantial equivalence provided in each 510(k) submission, when available.

2.2. Manufacturer and User Facility Device Experience Adverse Event Reports

The FDA's Manufacturer and User Facility Device Experience (MAUDE) Adverse Event Report database was searched for the search terms listed in 2.1 by year, from 2008 to 2018.

The same inclusion and exclusion criteria apply. Results were also excluded if they were neither adverse event reports nor product problem reports. This database was searched in May 2018 and the number of results was counted by event type and year.

2.3. Medical Device Recalls

The FDA Medical Device Recalls database was searched in May 2018 using the same search terms listed in 2.1 and by analysing the information provided with each 510(k) submission. The same inclusion and exclusion criteria apply.

2.4. Clinical studies search strategy and criteria

A review was performed to systematically analyse the clinical safety of PDO medical implants. We performed a search through the Clinical Trials.gov and the International Clinical Trial Platform (ICTRP) websites using the search terms listed in 2.1 and adding the brand name of PDO devices found in the FDA search as extra search terms. Four research databases (MEDLINE, Embase, Scopus and Web of Science) were also used. In these research databases, the search terms listed in 2.1 were used together with 'clinical trial', 'patient', 'human' and 'clinical'. In addition, bibliographical references of identified articles were reviewed. Inclusion criteria applied were: clinical trials or studies performed in patients or case reports where PDO medical implants represented at least one of independent variables. Exclusion criteria applied to studies were: ongoing clinical trials with no public results, non-English language publications, studies not performed with human patients, reviews, and abstract only publications. These searches were performed in March 2019. Relevant clinical trials and scientific publications that evaluated and compared PDO devices with non PDO devices were analysed and scored separately based on surgical outcomes (Appendix 1). A second scoring system was created (Appendix 2) to analyse all publications that meet the inclusion/exclusion criteria. This second scoring system looked at the percentage of unfavourable outcomes and percentage of successful implants to evaluate safety and performance, respectively. Outcomes were only scored when they were explicitly reported and related to the device. Five major factors were analysed in both scoring systems with regards to material safety: surgical site infection rate, presence of inflammatory reaction, presence of foreign body response, presence of postoperative fever, and presence of postoperative pain. Performance levels were evaluated separately based on the success of implants.

3. Results

3.1. PDO devices with regulatory approval

A number of 81 submissions were reported from the 510(k) database, with only 47 being admissible and relevant to this study. The remaining 34 submissions referred to medical devices that either had other polymers in their composition, were not implanted in the body or insufficient information was provided to meet requirements. A list of admissible devices can be found in Appendix 3.

The only PDO device found in the PMA database was PDS suture from Ethicon (PMA number N18331) with supplements from S001 to S027. These PMA supplements are based

on changes to the original device and can include changes in the device itself, its packaging or labelling or its manufacturing process. The name of this suture was changed to PDS II with supplement S022 dated from 1990.

Based on the search results described, PDO medical implants can be distributed into four main categories: sutures, plates/meshes, clips/staples, and screws/pins (Appendix 3). Based on this data, an evolution of the approved PDO medical implants can be seen in Figure 2. The higher number of approvals over time shows there is an ongoing and an increased interest in PDO implants and their use in patients since PDO was first introduced in 1981.⁸

Based on the available information on admissible 510(k) submissions, a predicate tree was designed (Appendix 4). Each device is linked to its predicates and to the devices they are predicates to, on the basis of substantial equivalence. Due to limited information provided by the 510(k) database, predicates are unidentified for 9 submissions. The majority of FDA approved PDO devices are sutures and are linked directly or indirectly to PDS™ II which was approved via PMA route. Based on the information available, at least 6 submissions involve sutures that differ from their predicate based on minor modifications (for instance, additional suture size). Moreover, 10 implants are considered substantially equivalent to non-PDO devices in a direct way, with 6 of them also being considered substantially equivalent to other PDO devices.

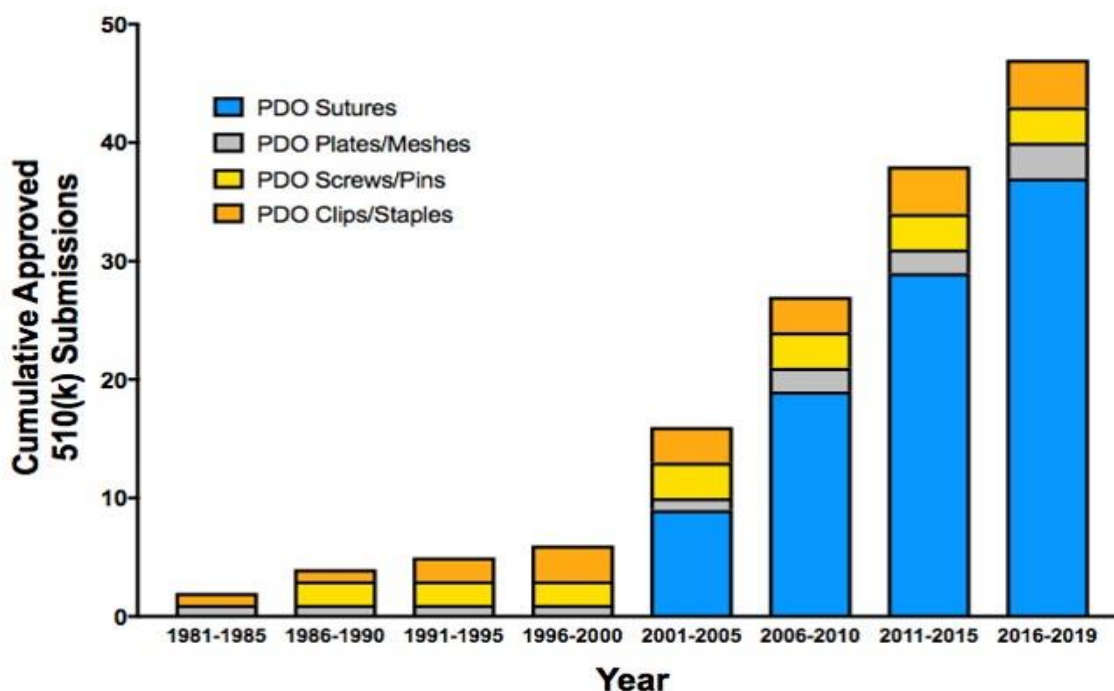






Figure 2. Cumulative number of 510(k) submissions of different types of PDO medical devices.

Shape, surface area and weight of an implant can affect how the body reacts to it, even if the core material is the same.¹² For that reason, these factors should be assessed when analysing different types of medical devices. In Table 1 it is possible to see the differences in dimensions and weight of common PDO devices. We calculated the estimated weight of each

based on an estimated PDO density of 1,318 g/cm³.¹³ It should be noted that the estimated weight is per device and does not necessarily correspond to the weight of PDO that is implanted in the body during surgery, dependent upon device application.

Table 1. Dimensions of different types of PDO devices, their estimated weight and representative figure. Basic information regarding the characteristics of the different implant types can be found in Appendix 5.

PDO Device	Type of device	Product Code	Dimensions	Estimated Weight	Representative Figure
PDS™ II	Monofilament suture	Z997G	USP 2-0 70 cm length ¹¹	0.2 g	
PDS™ Flexible Plate	Unperforated Plate	ZX5	0.25 x 40 x 50 mm ¹⁴	0.7 g	
OrthoSorb®	Straight Pin	84-2052	∅ 2 mm length 40 mm ^{15,16}	0.2 g	
Lapra-Ty®	Clip	XC200	0.3 cm beam length 0.3 cm width ¹⁷	0.1 g	 Open Closed

3.2. MAUDE Averse Event Reports

The MAUDE database revealed 6859 results. After applying the inclusion and exclusion criteria, 1377 results were admissible. After removing duplicates, the search totalled 1278 results identifying adverse event reports and product problem reports. Figure 3 represents the number of adverse event reports and product problem reports related to PDO devices from 2008 to April 2018 (included). As it can be seen, the main reason for adverse events and product problems is injury and malfunction. No deaths were reported as being caused by PDO implants.

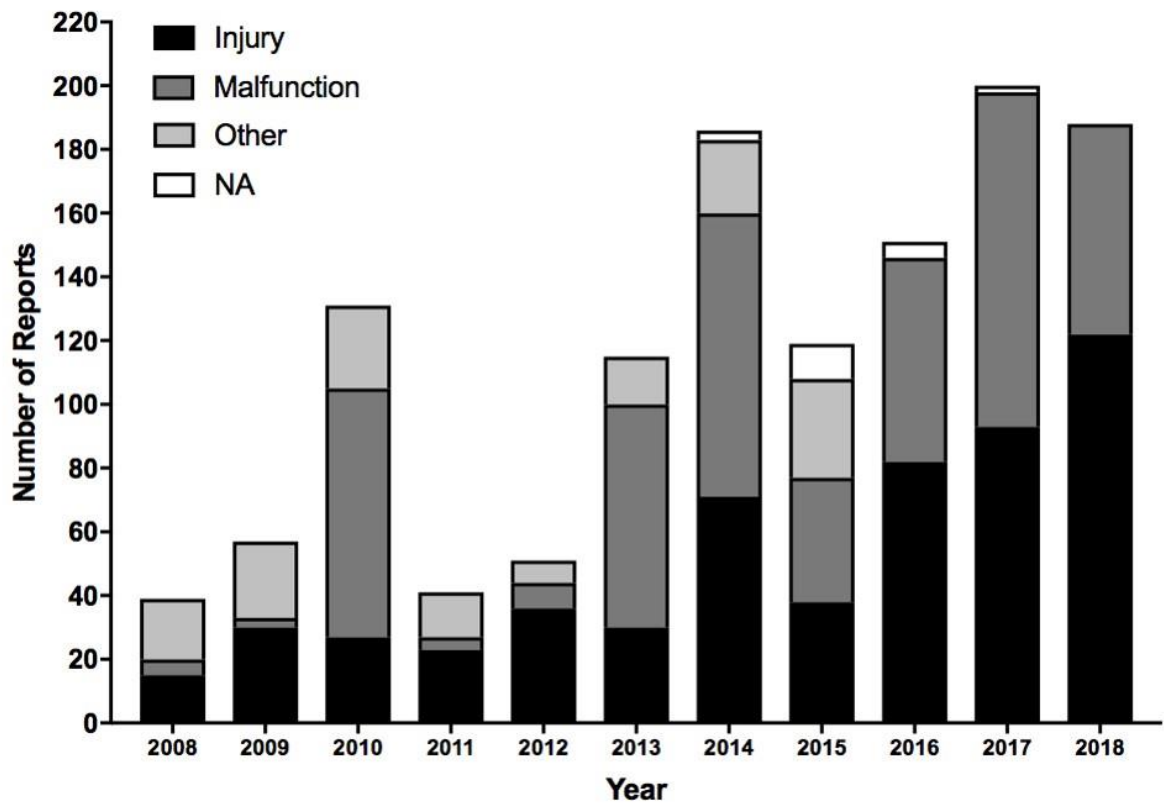


Figure 3. Manufacturer and User Facility Device Experience results by year reporting adverse events and product problems reports involving PDO implants. NA = not available.

3.3. Medical Devices Recalls

The FDA Medical Device Recalls database provided 24 results. After applying the inclusion/exclusion criteria and removing duplicates, 16 recalls involving PDO devices were deemed admissible. These are presented in Table 2.

Table 2. PDO medical device recalls.

Trade Name	PMA / 510(k) Number	FDA Recall Posting Date	Recall Number	Recall Class	Reason for Recall
Absolok	K812323	2005	Z-0654-05	2	Possible sterility issue.
		2005	Z-0655-05	2	Possible sterility issue.
		2005	Z-0656-05	2	Possible sterility issue.
		2005	Z-0657-05	2	Possible sterility issue.
		2007	Z-1016-2007	2	Possible sterility issue.
Monodek	K030212	2014	Z-1509-2014	2	The product did not meet minimum knot tensile strength requirements.
		2014	Z-1534-2014	2	The product did not meet minimum and/or average minimum resorption strength requirements.
Mono-Dox	K013274	2007	Z-0809-2007	2	Possible sterility issue.

		2008	Z-2582-2010	2	Possible compromise of seal integrity of the inner product pouch.
		2009	Z-0259-2012	2	Possible compromise of seal integrity of the outer product pouch.
PDS™ II	N18331	2009	Z-1313-2009	2	Possible sterility issue.
		2009	Z-1314-2009	2	Possible sterility issue.
		2018	Z-1338-2018	2	Incorrect expiry date on the label.
PDS™ Plus	K061037	2018	Z-1339-2018	2	Incorrect expiry date on the label.
		2018	Z-1340-2018	2	Incorrect expiry date on the label.
PDS™ Barbed Suture	K113004	2013	Z-0458-2014	2	The product has a small number of tab failures and fascial dehiscences in lower abdominal incisions.

PDS™ Barbed suture (K113004) was recalled in 2013 due to a small number of tab failures and fascial dehiscences in lower abdominal incisions while the others were recalled due to packaging and sterility issues or by not meeting the product specifications. It is evident from the data that none of these devices were recalled due to problems with device material.

3.4. Clinical trials and clinical studies

After removal of duplicates and application of the inclusion/exclusion criteria, 153 publications involving clinical studies were deemed acceptable and analysed. Of the admissible publications, 49 were clinical trials with published results and 104 were scientific publications. Scientific publications include retrospective studies and case reports. Publications show there is a high report of PDO implants in Trauma and Orthopaedic Surgery, Otolaryngology and General Surgery.

Scientific publications and clinical trials were scored according to Appendix 1 and Appendix 2. While using the scoring system, 11 publications and clinical trials did not comment on any of the assessed five unfavourable outcomes and performance and as such were removed from analysis. When comparing the different types of PDO implants (Figure 4), the highest percentage of unfavourable outcomes was reported for clips and staples, resulting in lower safety scores. Figure 5 shows that PDO devices have over 90% safety and over 65% performance efficacy, with the exception of PDO clips and staples.

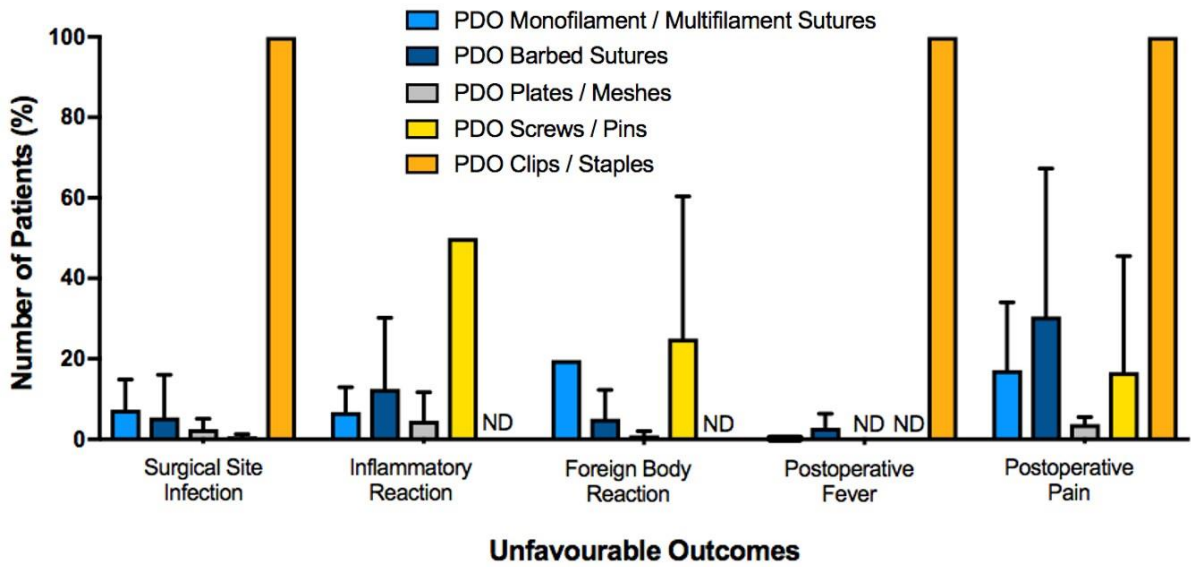


Figure 4. Percentage of unfavourable outcomes of PDO implants according to type of implant. ND = No data.

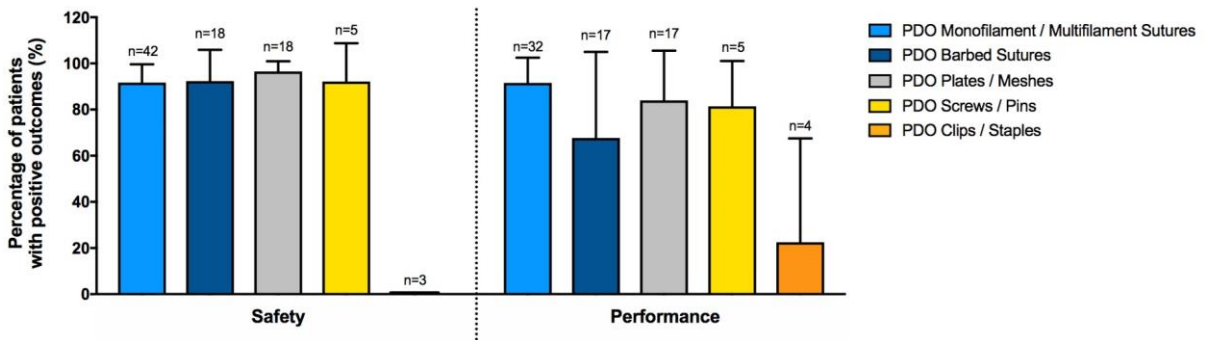


Figure 5. Safety and performance efficacy of PDO implants. n = number of publications.

Figure 6 compares safety and performance of PDO implants with non-PDO implants according to Appendix 1. With regards to safety, PDO implants generally have higher safety scores than non-PDO repairs. With regards to performance, in general it did not differ when comparing to non-PDO devices.

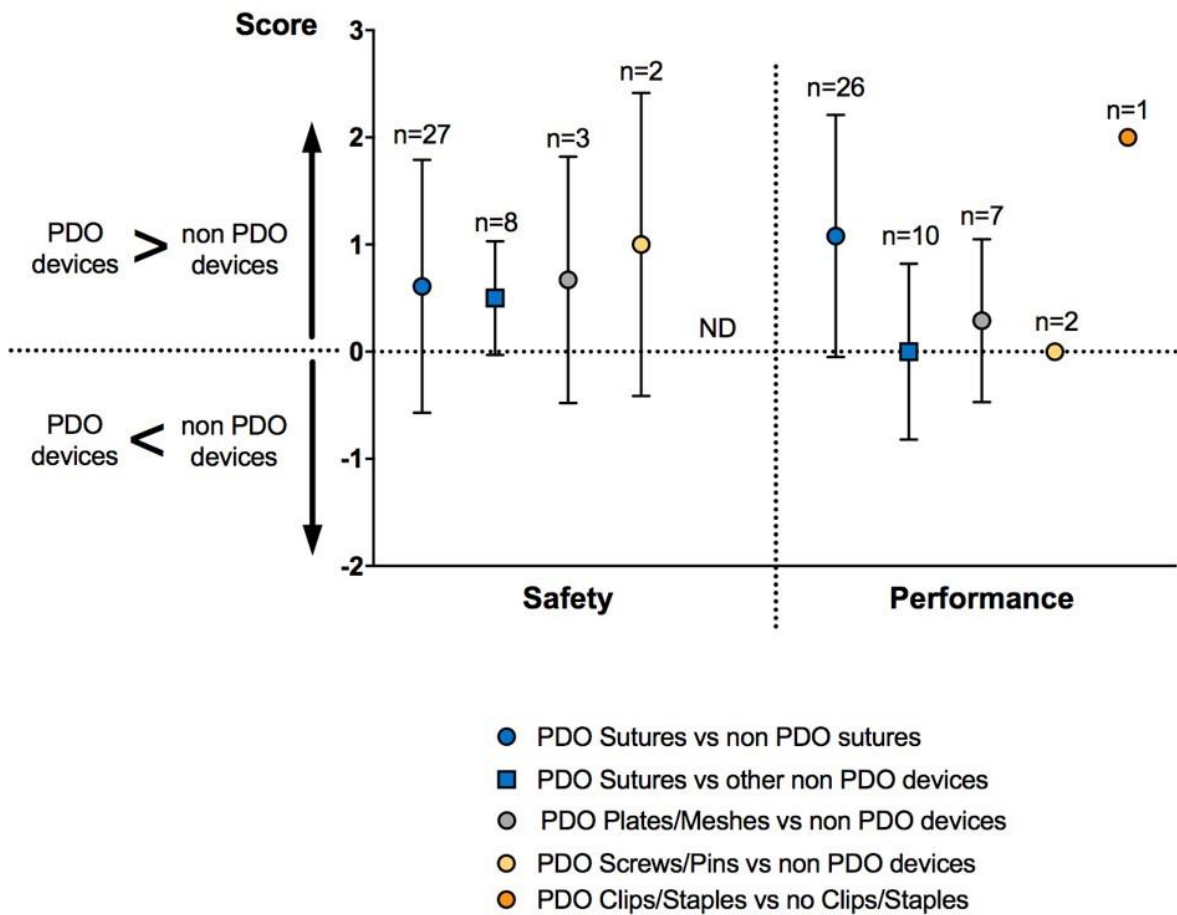


Figure 6. Comparison of PDO implants with non PDO implants regarding safety and performance efficacy. n = number of publications, ND = No data.

4. Discussion

4.1. Marketed medical implants and their classification

The U.S. Food and Drug Administration (FDA) regulates all medical devices marketed in the United States since 1976. The FDA process aims to ensure all devices are safe and effective, from development to distribution and use.¹⁸ The 1976 Medical Device Amendments separated medical devices into regulatory classes based on their degree of risk: Class I, Class II and Class III, where the latter include the most complex and highest risk devices. This classification process is similar to the one that the European Commission has in place in Europe, as defined by the 2017/745 Medical Device Regulation. Most Class II devices are required to submit a premarket notification (510(k)) while most of Class III devices require PMA before they are marketed. While Class III devices have the most stringent level of regulation, they may be marketed through the 510(k) route if they are substantially equivalent to any other devices marketed before May 28 1976, unless the FDA requires PMA data.¹⁸ With the 510(k) premarket notification route, manufacturers have the opportunity to obtain a faster market approval as long as they can prove their device is substantially equivalent to a device that is already legally marketed. This marketed device is called the predicate if equivalence claims are substantiated. This substantial equivalence is based on

intended use, technological characteristics, and safety and efficacy. In order to demonstrate equivalence, animal data or human clinical trials results may be included as part of the 510(k) submission. However, it should be noted that approval to market via the 510(k) route does not necessarily mean there is clinical data available or that the device was used previously in other markets, such as in Europe. On the other hand, PMA requires more detailed information namely clinical protocols, adverse reactions and complications, patient complaints, technical data, and non-clinical data (e.g. toxicology, tensile strength, and shelf-life).¹⁸ Additions to the 1976 Medical Device Amendments were later introduced in the 1990's, including the Medical Device Reporting, which made possible for the FDA to receive information about significant medical device adverse events. In addition, the FDA has to make publicly available the FDA 510(k) premarket reviews following the Safe Medical Devices Act of 1990.¹⁸

As presented earlier, 47 PDO implants were approved via 510(k) route and only one implant was approved via the PMA process (Appendix 4). This PMA approved device (PDS™ suture, approved for commercialisation in 1982) was considered, directly or indirectly, as a predicate to the majority of PDO sutures subsequently approved via 510(k). Thus, over 97% of PDO sutures' submissions (all approved on the basis of substantial equivalence) were not necessarily required to detail comprehensive information about the product, such as non-clinical data and/or animal/clinical data, unless specified by the FDA. This kind of approach may cause a problem if the predicate causes adverse reactions in clinical use post market approval that can lead to product recall. However, this does not necessarily mean medical devices that reference the recalled product as predicate would also be under investigation. Additionally, 10 PDO implants were found to have non-PDO devices as predicates directly, namely on the basis of similar function or shape. Suppliers of these implants might not be considering the combined impact of material and shape for the desired function in these submissions, and their influence on the degradation process and host tissue reaction after implantation. Since animal and/or clinical data may not be required for 510(k) submission, host tissue reaction and possible adverse reactions would not be assessed until the device is implanted in patients after market approval. Finally, since 9 PDO medical implants have no publicly available data regarding their predicates, it is not possible for authors to assess predicate suitability.

As explained in sections 4.4 and 4.5.2, implant mass can greatly impact biocompatibility. Table 1 showed that a PDS Plate weighs more than comparative PDO implants and that Lapra-Ty® had the lowest weight and dimensions. Shape, dimensions, surface characteristics, weight of the device and mechanical integrity can influence how the host tissue reacts with the different implants, even though they are manufactured from the same material.¹² For that reason, these parameters need to be taken into account when designing an implant.

The effect of approved PDO implants in patient safety and efficacy is further discussed in section 4.5.

4.2. MAUDE Averse Event Reports

MAUDE database is limited to adverse event reports within the past ten years. This database consists of all voluntary, user facility, distributor and manufacturer reports since

early 1990's. It is the manufacturers and importers' responsibility to submit reports when they become aware of information that reasonably suggests that one of their medical devices contributed to a death or serious injury or has malfunctioned.

When examining Figure 3, there is a high number of malfunction and injury reports (1278 reports) for the different types of PDO implants but this is a small percentage when considering the number of patients that have PDO devices implanted each year (in comparison, in the same time period, over 4000 reports were found for VICRYL® sutures - made of polyglactin 910 - alone). In addition, it is not possible to say that these reported incidents were caused by the medical device material or shape rather than as result of the surgical procedure or technique used. This is due to the fact that, in the majority of cases, it was not possible to recover the medical device for investigation, or further information was not available or provided by FDA. None of these adverse events and product problem reports claimed that PDO devices were related to any patient death.

4.3. Medical Device Recalls

Medical Device recalls occur when a device is defective and/or presents a risk to health. Sometimes this means the device just needs to be checked, adjusted or fixed and does not mean a product is discontinued or withdrawn from the market. Recalls can be categorised into three different categories: Class I (there is a reasonable chance that a product will cause serious health problems or death), Class II (product may cause a temporary or reversible health problem or there is a slight chance it will cause serious health problems or death) and Class III (product is not likely to cause any health problem or injury). The FDA Medical Device Recalls database contains recall reports dating back to November 2002.

As it is possible to see from Table 2, none of these devices were recalled due to device material, as the chemistry of the device could not have influenced the seal or packaging integrity nor the meeting of final specifications, as this is part of the quality control process of each product during manufacturing. Regarding PDS™ Barbed Suture's recall, fascial dehiscence may have been caused by the barbs on the suture, rupturing the fascia along the surgical incision. There is no information if this product is still on the market and the product cannot be found in an online search.

4.4. PDO degradation process

It is important to understand the biodegradation process of PDO when looking at biocompatibility and the use of PDO implants. The degradation process of a biodegradable implant should ideally match the healing rate of the tissue where it is implanted, thus maintaining the device's mechanical properties while they are required.⁷ The degradation process can occur after implantation but also start during manufacturing while PDO is being melted and/or extruded into the desired shape. This initial degradation can lead to a decrease of molecular weight and as such moisture and high temperature should be minimised during manufacturing to prevent changes in the polymer's properties and further impact product shelf life.

Hygroscopic polymers like PDO can be hydrolysed, resulting in degradation by-products such as glycoylate that can be excreted in urine, or be metabolized via citric acid cycle to form carbon dioxide and water.^{9,19} Several authors also reported oxalic acid, propylene glycol, 2-hydroxyacetic acid and glyoxylic acid as degradation products.²⁰ The release of glyoxylic acid can contribute to a chronic inflammatory response due to a local decrease in pH.^{21,22} Additionally, this acidic environment can be caused by a sudden and rapid release of degradation products or by a large amount of material present or large surface area.⁴ When compared on a weight basis to other polymers such as PLA and PGA, PDO degradation products are less acidic, which could cause less inflammatory reaction.²¹

Biomaterial degradation is affected by the surrounding area and tissue namely by the mechanical forces involved, disease or healthy state and vascularisation.²³ Microstructural cracks created by a high stress environment can lead to an enhanced exposed surface area and to a loss of mechanical strength in addition to any chemical reactions that may occur simultaneously.¹⁹ During the early stages of degradation, the water penetrates the bulk of the implant, breaking the chemical bonds in the amorphous phase.^{6,7} This step cuts down long polymer chains, reducing the average molecular weight and increasing polydispersity. At this point, the implant's gross material properties are still maintained as they are defined by the crystalline regions, which are unaffected.⁶ Decrease of average molecular weight usually occurs before any material loss is observed.²⁴ At the last stage of degradation, the water hydrolyses the small water-soluble fragments which leads to loss of polymer mass, molecular weight and physical properties.^{6,25-27} The resulting degradation products are then quickly removed from the surface in the surrounding fluid. However, in the interior of the device, the inability to diffuse degradation products creates an acidic environment that will then lead to an accelerated hydrolysis of the ester bonds. This process explains why a low porosity implant may degrade faster than a high porosity implant, having a lower functional lifespan.^{4,6,19,25,26,28}

Biomaterial degradation is also dependent on basal metabolic rates of the test subjects, with degradation rates in human being slower than in laboratory animals.^{15,29} *In vitro* studies using PDO sutures showed that after 10 weeks in a buffer solution, sutures still retained over 96% of their weight.²⁶ While testing PDS™ II sutures *in vitro*, Ooi and Cameron²⁷ also observed that there is an initial hydration of the material during the first two days, followed by a dormant stage up to 20 days when scission of the tie chain initiates. An active stage then follows, in up to 60 days, when there is a decrease in tensile breaking strength and strain, and an increase in water uptake. Lin et al. reported a loss of around 67% tensile strength in 14-28 days of hydrolysis using PDS™ sutures in PBS buffer, with low loss of tensile strength in 42-60 days.⁷ However, with regards to mass absorption, only 1.5% of mass was absorbed at 60 days, while 90% of tensile strength was already gone. In some cases, this material left after the suture has achieved its purpose may cause foreign body reaction and granuloma formation⁷ but this outcome will disappear once the material is fully degraded. Complete absorption of PDS™ sutures has been reported from 117 to 240 days, with 67% loss of tensile strength at 14-28 days postimplantation.⁷ PDO clips can take more than 180 days to fully degrade.²⁰ PDO pins have also been reported as 80% being visible at 3 and 6 months post implantation in an animal model, with total resorption by 24 months.¹⁵ In addition, *in vitro* toxicity of

degradation products may not match *in vivo* biocompatibility. In an *in vivo* study, 93% of PDS™ sutures' degradation products were removed in urine.⁸ Other studies have also indicated that PDO has good biocompatibility and a positive biological safety in rabbits.³⁰

4.5. Safety scoring system – measured outcomes

Surgical site infections (SSI), foreign body reaction (FBR), inflammatory reaction, postoperative pain and fever have been analysed in clinical trials results and scientific papers that reported the use of PDO implants, based on the shape and type of the device. There is no uniform assessment across the different papers since authors evaluated different outcomes. For that reason, postoperative fever and pain were considered as separate outcomes from SSI and FBR because authors may not explicitly define SSI and FBR as the cause for postoperative fever and pain. Based on these outcomes we developed two scoring systems: one for the evaluation of PDO implants based on the percentage of patients with adverse reactions reported (Appendix 2) and another scoring system comparing PDO with non PDO implants (Appendix 1). In this section, we explain how the five mentioned outcomes can be influenced by implant material.

4.5.1. Surgical Site Infections

According to Gabriel et al., in the U.S. around two million people are infected each year due to hospital stays, causing 90 000 yearly deaths.³¹ SSI rates can be affected by different factors including general condition of the patient (such as age, fitness, and comorbidities), the presence of pathogenic bacteria, lack of pre-operative skin disinfection, contaminated surgical instruments and nosocomial infections acquired secondary to prolonged hospital stays.³²

Implantable medical devices can also be a cause of SSI (known as implant-related infection) due to bacterial colonisation and a high and continuous implantation time. This bacterial colonisation could lead to the formation of a multilayer biofilm which could result in failure of the implanted device and its consequential removal. This biofilm could also lead to high resistance to host defence mechanisms and antibiotic treatment.³² The material surface characteristics are very important in bacterial adhesion, namely the surface chemical composition, surface roughness, surface configuration and exposed area, when interacting with the bacterial properties (bacterial hydrophobicity and bacterial surface charge).³² Medical devices, particularly sutures, have evolved to try to prevent high infection rates through the addition of antimicrobial coatings, however conflicting information has been found regarding their efficiency.^{33–35} Medical device roughness and configuration play a major role in bacterial adhesion as several studies showed that bacterial adhesion is promoted by surface irregularities.^{36,37} This suggests that multifilament sutures may be more prone to causing implant-related infection due to their higher surface area when compared to monofilament sutures.^{38,39} However, chemical composition can also affect bacterial adhesion: *in vitro* and animal experiments showed that implants made of PMMA have been found to be more prone to cause infection, as opposed to titanium and cobalt-chromium

implants^{37,40,41}, which can be related to material properties such as surface charge and hydrophobicity, as discussed previously.

Figure 4 shows that PDO sutures, meshes/plates and screws/pins had low SSI rates (below 10%) possibly due to low porosity and smooth exposed area. With regards to PDO clips/staples, SSI was reported in 2 case reports. Brusky and Tran⁴² reported that a patient showed urinary tract infection five weeks after an uneventful right laparoscopic transperitoneal Anderson-Hynes dismembered pyeloplasty when Lapra-Ty® clips were used to anchor polyglactin sutures. Further study confirmed that Lapra-Ty® clips had migrated into the ureter, possibly being the cause of the urinary infection described. Finley et al.⁴³ also reported Lapra-Ty® clip migration in one patient, which could also have caused the reported infection.

4.5.2. Foreign Body Reaction and Inflammatory Reaction

Inflammatory response and FBR are expected tissue reactions following implantation of biomaterials.⁴⁴ An inflammatory reaction is defined as the reaction of vascularized living tissue to local injury and can still be initiated even if the implanted material is nontoxic, nonimmunogenic and chemically inert.^{45,46} An inflammatory response can be divided into two stages: acute and chronic inflammation. Each stage is characterised by specific cell types, duration, and overall biological importance.⁴⁷ This process has been extensively studied and reviewed.^{45,48,49} Acute inflammation can be caused by tissue damage elicited when a medical device is implanted, and is part of the normal wound-healing process. During this stage, blood proteins (such as albumin, antibodies, and fibrinogen) are adsorbed onto the medical device surface.^{46,47} Chemical and physical properties (such as surface chemistry and hydrophobicity) of the device will greatly influence the composition of the adsorbed protein layer. It is the presentation of the various plasma proteins on the material's surface that creates a high affinity matrix for the subsequent attachment and activation of a range of inflammatory cells, and not the material itself.^{47,48} In addition, material charge may directly affect macrophage and polymorphonuclear neutrophils adhesion.^{48,50}

With long term or permanent non-degradable implants, the inflammatory response generally evolves into a chronic reaction,⁵¹ thus changing the cellular population surrounding the implant. At this stage, monocyte derived macrophages are the dominant cell type and will try to break down, encapsulate and remove the implanted material, while remodelling the surrounding extracellular matrix.⁴⁷ With biodegradable implants, chronic inflammation is a possibility in some cases and it can accelerate degradation due to the release of hydrolytic enzymes and reactive oxygen and nitrogen species, which reduces the polymer molecular weight.⁴⁷ This way, chronic inflammation could negatively affect the efficacy of implanted devices in permanent or long term applications. It is worth noting that this reaction will be limited in time and affected area when using biodegradable materials. While the implant is being resorbed, inflammation and FBR will gradually decrease until it disappears.^{44,51,52} Several approaches have been developed to target the issues of inflammation and medical devices including the use of bioinert surfaces and bioactive strategies.^{47,53}

The implantation of medical devices can also induce a primary reaction of the nonspecific immune system to foreign materials known as FBR. Usually the FBR is the end-stage response of the inflammatory and wound healing responses but they can happen simultaneously.⁴⁴ The FBR consists of material-dependent and material-independent processes, and can be induced when local tissues are not able to clear polymeric hydrolytic debris.^{23,44} Usually, synthetic materials do not elicit a specific biological reaction.⁴⁵ The FBR to biomaterials involves foreign body giant cells and components of granulation tissue. Surface properties, shape of the implant and the relationship between surface area and volume of the implant affect the composition of the FBR. For instance, high surface area-to-volume ratio implants and porous materials such as plates and meshes will have an increased number of macrophages and foreign body giant cells at the implant site. On the other hand, smooth surface implants like monofilament sutures will result in more fibrotic tissue at the implant site. During the early stages of inflammation and wound healing, macrophages are activated upon adherence to the implant surface due to the device's non-native chemical and physical properties.⁴⁵ Adherent macrophages and foreign body giant cells can then lead to the degradation of biomaterials and possible device failure.⁴⁴ FBR can also lead to suture extrusion and rejection and stitch abscesses if a bulky material is present. This transepidermal elimination is aided by superficial suture placement and increased mass of suture materials.^{27,54} FBR may persist at the tissue-device interface for the lifetime of the implant, but after resorption only connective tissue remains.⁴⁵

Figure 4 shows that inflammatory reaction and FBR rates were below 20% for barbed and monofilament/multifilament sutures and below 5% for PDO plates/meshes. Even though PDO plates are the bulkiest device, they reportedly caused FBR in a smaller percentage of patients than other devices, which was not anticipated since porous and bulkier devices are expected to have a higher number of associated macrophages and foreign body giant cells. This difference could be related to the high vascularity and low mobility of the host tissue where these devices were implanted, for instance, during nasal reconstruction.^{14,55-57} Regarding PDO screws/pins, Kalla and Janzen²³ described a FBR and inflammation in one patient caused by Orthosorb[®]. This type of PDO pin had been implanted in both feet during separate surgeries for bunionectomy. FBR and inflammation was only observed on the right foot after the second surgery. Kalla and Janzen²³ suggested that the observed FBR could have been caused by low vascularity and temperature at the implantation site, and also due to a possible immunological sensitisation to Orthosorb[®] after the first surgery. However, it is worth noting that this was the only reported case of FBR in the available publications. No paper reported the rate of inflammatory reaction or FBR after the implantation of PDO clips/staples. It is also worth noting that only 0.2% patients reportedly had FBR in the 142 clinical studies analysed.

4.5.3. Postoperative fever

The reported incidence of postoperative fever varies, but can be expected in 13-14% of patients.^{58,59} Figure 4 shows that postoperative fever was below 4% in monofilament/multifilament and barbed sutures, which is better than reported rates. PDO clips had a high postoperative fever caused by clip migration as discussed previously.

Postoperative fever assessments following the implantation of PDO plates/meshes and screws/pins were not reported in any of the publications reviewed. It is worth noting that, when analysing clinical trial results and scientific publications, there is no distinction in data analysis between a fever that develops within the first 48h after surgery (which is usually benign and self-limiting and may be procedure-related) and fever that develops later on (which is more likely to have an infectious cause).⁵⁸⁻⁶⁰ The interruption of the normal host defence mechanisms, such as medical device implantation, is a risk factor for development of other comorbidities that can lead to fever.⁶⁰

4.5.4. Postoperative pain

Postoperative pain was reported in less than 4% patients implanted with PDO plates/meshes, which is expected since this type of implant reported low levels of SSI, inflammatory reaction and FBR. However, pain levels were higher for monofilament/multifilament sutures (17%), barbed sutures (31%) and screws/pins (17%). Barbed sutures could be causing more local pain than monofilament sutures due to their barbs that attach to the surrounding tissue to keep the suture in place.

4.6. Surgical outcomes from clinical trials and scientific publications

When analysing the percentage of unfavourable outcomes (Figure 4), clinical studies revealed a low percentage of SSI and postoperative fever for PDO sutures, plates/meshes and screws/pins. FBR percentage was higher for PDO screws/pins, followed by monofilament/multifilament sutures and then barbed sutures. Figure 4 also shows that PDO clips/staples have a high rate of SSI, postoperative fever and postoperative pain. These safety results were solely based on three publications of case reports of Lapra-Ty[®] suture clips, totalling 3 patients that had history of pyelonephritis (inflammation of the kidney). In these three case reports, clip migration was observed, causing the pain and fever reported. As suggested by other work⁶¹, case reports analysed in this review may not be representative of the use of these suture clips. This also implies that it was not the fact that these devices are made of PDO that caused this biological reaction, but a failure in device function. However, this needs to be investigated further. Only one study⁶² was found which reported good performance with Lapra-Ty[®] clips.

Overall, PDO implants are safe in over 90% of cases and perform as expected in over 80% of cases for sutures, plates/meshes and screws/pins. PDO barbed sutures have a lower performance efficacy rate (67%) and when analysing clinical studies reporting the use of this type of PDO sutures, two case reports^{63,64} described failure of performance due to barb attachment to adjacent tissue and surgical approach and confounding comorbidities, making it clear that in these cases, the performance of the barbed suture was not influenced by the material used.

Figure 6 compares safety and performance of PDO implants with non-PDO devices. Results show that PDO implants show a trend of better safety levels than non-PDO devices. In some

cases, PDO devices are compared to non-degradable implants, which can cause long term FBR, decreasing their safety rates. No publication was found reporting safety outcomes involving PDO clips/staples. Regarding performance, PDO sutures perform better than non-PDO sutures but perform just as well when compared to meshes or surgical glues. It is worth noting that from the 25 papers that assessed suture performance, 7 of them compared PDO barbed sutures with non-PDO monofilament sutures. With barbed sutures, the barbs attach to the tissue, locking the suture in place and preventing the incision from opening, which generally increased the performance values of PDO sutures compared to non-PDO smooth monofilament sutures. PDO plates/meshes also show a trend of increased performance levels when compared to non-PDO repair.

PDO screws/pins present similar performance when compared to the non-PDO alternatives but should be noted that only a small number of clinical studies reported performance for these types of devices. Only one publication was found comparing PDO clips/staples (Lapra-Ty® clips) to non-PDO repair, resulting in a score of 2 for performance. From this low number of publications, it is not possible to infer the general performance of these type of devices, since that will also depend on the application of the device and the way it is used by surgeons.

4.7. Future of medical implants

PDO implants have been traditionally manufactured through extrusion, but different techniques can be used while considering the different aspects of designing implants mentioned previously. The manufacturing process should also be taken into account to minimise changes in mechanical properties (unless these are desired for intended use), in particular if the main component is a hydrolytic material. PDO implants should be manufactured with the aim to reduce humidity whenever possible in order to not accelerate degradation.⁶ Excessive high temperatures during manufacturing can also change the mechanical properties of PDO.⁶⁵ For these reasons, manufacturers should not sterilise PDO medical devices by autoclaving or dry heat, but should consider ethylene oxide since this polymer is also sensitive to gamma radiation. Additives can be used during manufacturing to scale up the process or to reduce degradation but care must be taken regarding the potential impact to biological safety.⁶ This review assumes that no additives were left in PDO implants.

4.8. Limitations to this study

It is worth noting that FDA claims that Medical Device Reports data alone cannot be used to conclude about the existence, severity or frequency of problems associated with a device and that establishing relationships between devices and adverse events is especially difficult if circumstances surrounding the event have not been verified or if the device has not been directly evaluated. Clinical studies were analysed in this paper to provide more information regarding safety of this type of implants. We assessed all relevant publications, but we are aware that the number of patients in each clinical publication may not be representative of the general population with implanted PDO devices. Furthermore, when comparing

implanted devices made with different materials, the different degradation rate (if applicable) and implantation site may affect the observed results.

In addition, despite a medical device being approved by the FDA, it does not mean it is currently being sold in the market. Moreover, medical device technical information, such as degradation profile, molecular weight, animal tests performed, is not available due to confidentiality. This lack of transparency makes it harder to assess the medical device as a whole during its application in the human body.

5. Conclusion

PDO medical implants are widely used in a number of different surgical specialties with varying shapes, sizes and configurations. The results of this review show that no product has been recalled due to the material used and that no PDO implant caused a patient death. In addition, the low percentage of adverse reactions from the use of PDO implants in patients show that PDO sutures, plates/meshes and screws/pins are safe to use and perform as expected. Care must be taken when using PDO clips/staples so that they are applied correctly since failure in function can cause PDO clips to migrate and cause adverse reactions. When compared to non-PDO repair, PDO implants are generally safe and perform at least as well as alternatives.

This review suggests that, as a biodegradable polymer and while considering the biological properties of the host tissue and the shape and dimensions of the device, PDO is a safe material to use in the development of further and innovative biodegradable medical implants.

Declaration of conflicting interests

The Authors declare that there is no conflict of interest.

Acknowledgements

This research was funded by the National Institute for Health Research (NIHR) Invention for Innovation (i4i) [II-LB-0715-20001], the Wellcome Trust [106946] and by the NIHR Oxford Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The authors also would like to thank Dr Jo Proffitt for her support in the medical device regulatory field.

References

1. U.S. Food & Drug Administration. Classify Your Medical Device - Is The Product A Medical Device?, <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm> (2018, accessed 4 May 2018).
2. Romo T, McLaughlin LA, Levine JM, et al. Nasal implants: autogenous, semisynthetic, and synthetic. *Facial Plast Surg Clin North Am* 2002; 10: 155–166.
3. Gunatillake PA, Adhikari R. Biodegradable Synthetic Polymers for Tissue Engineering. *Eur Cells Mater* 2003; 5: 1–16.
4. Slivka MA, Chu CC, Zhang YL. Laser confocal microscopic study of pH profiles of synthetic absorbable fibers upon in vitro hydrolytic degradation. *J Mater Sci Mater Med* 2001; 12: 241–247.
5. Maitz MF. Applications of synthetic polymers in clinical medicine. *Biosurface and Biotribology* 2015; 1: 161–176.
6. Middleton JC, Tipton AJ. Synthetic biodegradable polymers as orthopedic devices. *Biomaterials* 2000; 21: 2335–2346.
7. Lin HL, Chu CC, Grubb D. Hydrolytic degradation and morphologic study of poly-p-dioxanone. *J Biomed Mater Res* 1993; 27: 153–166.
8. Ray J, Doddi N, Regula D, et al. Polydioxanone (PDS), a novel monofilament synthetic absorbable suture. *Surg Gynecol Obstet* 1981; 153: 497–507.
9. Bose S, Bandyopadhyay A. *Materials and Devices for Bone Disorders*. 1st ed. Academic Press, 2016.
10. Boland ED, Coleman BD, Barnes CP, et al. Electrospinning polydioxanone for biomedical applications. *Acta Biomater* 2005; 1: 115–123.
11. Ethicon. Z997G, <https://www.ethicon.com/na/epc/code/z997g> (2017, accessed 6 July 2018).
12. Matlaga BF, Yassenchak LP, Salthouse TN. Tissue response to implanted polymers: The significance of sample shape. *J Biomed Mater Res* 1976; 10: 391–397.
13. Zhang X. *Science and Principles of Biodegradable and Bioresorbable Medical Polymers: Materials and Properties*. 1st ed. Woodhead Publishing, 2016.
14. Tweedie DJ, Lo S, Rowe-Jones JM. Reconstruction of the nasal septum using perforated and unperforated polydioxanone foil. *Arch Facial Plast Surg* 2010; 12: 106–113.
15. Sirlin CB, Boutin RD, Brossmann J, et al. Polydioxanone Biodegradable Pins in the Knee. *Am J Roentgenol* 2001; 176: 83–90.
16. ESutures. 84-2052: DePuy Orthosorb Resorbable Pin Kit, <https://www.esutures.com/product/0-in-date/36-depuy-mitek/461-orthosorb/46254934-depuy-orthosorb-resorbable-pin-kit-84-2052/> (accessed 6 July 2018).
17. ESutures. XC200-SD: Ethicon Lapra-Ty Absorbable Suture Clips, <https://www.esutures.com/product/0-in-date/28-ethicon-endo-surgery/218-suture-clips/46207720-ethicon-lapra-ty-absorbable-suture-clips-6-clips-per-cartridge-.118->

- beam-width-.12-width-short-dated-XC200/ (accessed 6 July 2018).
18. Pietzsch JB, Aquino LM, Yock PG, et al. Review of U.S. Medical Device Regulation. *J Med Device* 2007; 1: 283.
 19. Maurus PB, Kaeding CC. Bioabsorbable Implant Material Review. *Oper Tech Sports Med* 2004; 12: 158–160.
 20. Holland SJ, Tighe BJ, Gould PL. Polymers for biodegradable medical devices. 1. The potential of polyesters as controlled macromolecular release systems. *J Control Release* 1986; 4: 155–180.
 21. Lanza R, Langer R, Vacanti JP. *Principles of tissue engineering*. 4th ed. Academic Press, 1985.
 22. Modjarrad K, Ebnesajjad S. *Handbook of Polymer Applications in Medicine and Medical Devices*. 1st ed. William Andrew, 2014.
 23. Kalla TP, Janzen DL. Orthosorb: A case of foreign-body reaction. *J Foot Ankle Surg* 1995; 34: 366–370.
 24. Pitt GG, Gratzl MM, Kimmel GL, et al. Aliphatic polyesters II. The degradation of poly (DL-lactide), poly (ϵ -caprolactone), and their copolymers in vivo. *Biomaterials* 1981; 2: 215–220.
 25. Sabino MA, Albuerne J, Müller A, et al. Influence of in vitro hydrolytic degradation on the morphology and crystallization behavior of poly(p-dioxanone). *Biomacromolecules* 2004; 5: 358–370.
 26. Sabino MA, González S, Márquez L, et al. Study of the hydrolytic degradation of polydioxanone PPDx. *Polym Degrad Stab* 2000; 69: 209–216.
 27. Ooi CP, Cameron RE. The hydrolytic degradation of polydioxanone (PDSII) sutures. Part I: Morphological aspects. *J Biomed Mater Res* 2002; 63: 280–290.
 28. Athanasiou KA, Schmitz JP, Agrawal CM. The Effects of Porosity on in Vitro Degradation of Polylactic Acid–Polyglycolic Acid Implants Used in Repair of Articular Cartilage. *Tissue Eng* 1998; 4: 53–63.
 29. Böstman OM. Osteolytic changes accompanying degradation of absorbable fracture fixation implants. *J Bone Joint Surg Br* 1991; 73: 679–82.
 30. Gong Z, Xu Z, Qin X. [Research on biocompatibility and in vivo degradation of biodegradable chest wall prosthesis materials in experimental animals]. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2007; 21: 867–871.
 31. Gabriel GJ, Som A, Madkour AE, et al. Infectious disease: Connecting innate immunity to biocidal polymers. *Mater Sci Eng R Reports* 2007; 57: 28–64.
 32. Armentano I, Arciola CR, Fortunati E, et al. The interaction of bacteria with engineered nanostructured polymeric materials: A review. *Sci World J*; 2014.
 33. Diener MK, Knebel P, Kieser M, et al. Effectiveness of triclosan-coated PDS Plus versus uncoated PDS II sutures for prevention of surgical site infection after abdominal wall closure: The randomised controlled PROUD trial. *Lancet* 2014; 384: 142–152.
 34. Mingmalairak C, Ungbhakorn P, Paocharoen V. Efficacy of antimicrobial coating suture coated polyglactin 910 with triclosan (Vicryl plus) compared with polyglactin 910 (Vicryl) in reduced surgical site infection of appendicitis, double blind randomized

- control trial, preliminary safety report. *J Med Assoc Thai* 2009; 92: 770–5.
35. Baracs J, Huszár O, Sajjadi SG, et al. Surgical Site Infections after Abdominal Closure in Colorectal Surgery Using Triclosan-Coated Absorbable Suture (PDS Plus) vs. Uncoated Sutures (PDS II): A Randomized Multicenter Study. *Surg Infect (Larchmt)* 2011; 12: 483–489.
 36. McAllister EW, Carey LC, Brady PG, et al. The role of polymeric surface smoothness of biliary stents in bacterial adherence. *Gastrointest Endosc* 1993; 39: 422–5.
 37. Cordero J, Munuera L. The influence of the chemical composition and surface of the implant on infection. *Injury* 1996; 27: SC34-37.
 38. King MW, Gupta BS, Guidoin R. *Biotextiles as medical implants*. 1st ed. Woodhead Publishing, 2013.
 39. Sharp W V, Belden TA, King PH, et al. Suture resistance to infection. *Surgery* 1982; 91: 61–3.
 40. Chang CC, Merritt K. Infection at the Site of Implanted Materials with and without Preadhered Bacteria. *J Orthop Res J Bone Jt Surg* 1994; 12: 526–531.
 41. Cordero J, Munuera L, Folgueira MD. Influence of bacterial strains on bone infection. *J Orthop Res* 1996; 14: 663–667.
 42. Brusky JP, Tran VQ. Resorbable Clip Migration Resulting in Ureteral Obstruction and Sepsis After Laparoscopic Pyeloplasty. *J Endourol* 2010; 24: 1563–1564.
 43. Finley DS, Perer E, Eichel L, et al. Ureteral pseudodiverticulum associated with absorbable suture clips after laparoscopic pyeloplasty: case report. *J Endourol* 2005; 19: 726–729.
 44. Anderson JM, Rodriguez A, Chang DT. Foreign Body Reaction to Biomaterials. *Semin Immunol* 2008; 20: 86–100.
 45. Anderson JM, Cook G, Costerton B, et al. Host Reactions to Biomaterials and Their Evaluation. In: *Biomaterials Science - An Introduction to Materials in Medicine*. 1996, pp. 293–296.
 46. Tang L, Eaton JW. Fibrin(ogen) Mediates Acute Inflammatory Responses to Biomaterials. *J Exp Med* 1993; 178: 2147–2156.
 47. Slee JB, Christian AJ, Levy RJ, et al. Addressing the Inflammatory Response to Clinically Relevant Polymers by Manipulating the Host Response Using ITIM Domain-Containing Receptors. *Polym* 2015; 6: 2526–2551.
 48. Luttikhuisen DT, Harmsen MC, Van Luyn MJA. Cellular and Molecular Dynamics in the Foreign Body Reaction. *Tissue Eng* 2006; 12: 1955–1970.
 49. Love RJ, Jones KS. The recognition of biomaterials: Pattern recognition of medical polymers and their adsorbed biomolecules. *J Biomed Mater Res Part A* 2013; 101A: 2740–2752.
 50. Hunt JA, Flanagan BF, McLaughlin PJ, et al. Effect of biomaterial surface charge on the inflammatory response: Evaluation of cellular infiltration and TNF α production. *J Biomed Mater Res* 1996; 31: 139–144.
 51. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. *J Long Term Eff Med Implants* 2011; 21: 93–122.

52. Hjort H, Mathisen T, Alves A, et al. Three-year results from a preclinical implantation study of a long-term resorbable surgical mesh with time-dependent mechanical characteristics. *Hernia* 2012; 16: 191–197.
53. Bridges AW, García AJ. Anti-Inflammatory Polymeric Coatings for Implantable Biomaterials and Devices Inflammation and Device Performance. *J Diabetes Sci Technol*; 2.
54. Murtha AP, Kaplan AL, Paglia MJ, et al. Evaluation of a Novel Technique for Wound Closure Using a Barbed Suture. *Plast Reconstr Surg* 2006; 117: 1769–1780.
55. Petropoulos I, Nolst Trenite G, Boenisch M, et al. External septal reconstruction with the use of polydioxanone foil: Our experience. *Eur Arch Oto-Rhino-Laryngology* 2006; 263: 1105–1108.
56. Boenisch M, Trenité GJN. Reconstructive septal surgery. *Facial Plast Surg* 2006; 22: 249–254.
57. James SE, Kelly MH. Cartilage recycling in rhinoplasty: polydioxanone foil as an absorbable biomechanical scaffold. *Plast Reconstr Surg* 2008; 122: 254–60.
58. House J, Alexandraki I. Evaluation of postoperative fever. *BMJ Best Practice*, <https://bestpractice.bmj.com/topics/en-us/898#referencePop3> (accessed 15 June 2018).
59. Burke L. Postoperative fever: A normal inflammatory response or cause for concern. *J Am Acad Nurse Pract* 2010; 22: 192–7.
60. Gross K. Postoperative Fever. In: Myers JA, Millikan KW, Saclarides TJ (eds) *Common Surgical Diseases: An Algorithmic Approach to Problem Solving*. Springer New York, 2015, pp. 341–342.
61. Shalhav AL, Orvieto MA, Chien GW, et al. Minimizing knot tying during reconstructive laparoscopic urology. *Urology* 2006; 68: 508–513.
62. Yasui T, Itoh Y, Maruyama T, et al. The single-knot method with Lapra-Ty clips is useful for training surgeons in vesicourethral anastomosis during laparoscopic radical prostatectomy. *Int Urol Nephrol* 2009; 41: 281–285.
63. Wright RC, Gillis CT, Yacoubian S V., et al. Extensor mechanism repair failure with use of bidirectional barbed suture in total knee arthroplasty. *J Arthroplasty* 2012; 27: 1–4.
64. Donnellan NM, Mansuria SM. Small Bowel Obstruction Resulting from Laparoscopic Vaginal Cuff Closure with a Barbed Suture. *J Minim Invasive Gynecol* 2011; 18: 528–530.
65. Abhari RE, Mouthuy PA, Zargar N, et al. Effect of annealing on the mechanical properties and the degradation of electrospun polydioxanone filaments. *J Mech Behav Biomed Mater* 2017; 67: 127–134.
66. Moya AP. Barbed Sutures in Body Surgery. *Aesthetic Surg J* 2013; 33: 57S–71S.
67. Klinge U, Park J-K, Klosterhalfen B. The ideal mesh? *Pathobiology* 2013; 80: 169–75.
68. Hehl G, Strecker W, Richter M, et al. Clinical experience with PDS II augmentation for operative treatment of acute proximal ACL ruptures - 2-year follow-up. *Knee Surg Sports Traumatol Arthrosc* 1999; 7: 102–106.
69. Justinger C, Slotta JE, Ningel S, et al. Surgical-site infection after abdominal wall

- closure with triclosan-impregnated polydioxanone sutures: Results of a randomized clinical pathway facilitated trial (NCT00998907). *Surg (United States)* 2013; 154: 589–595.
70. Tan-Kim J, Nager CW, Grimes CL, et al. A randomized trial of vaginal mesh attachment techniques for minimally invasive sacrocolpopexy. *Int Urogynecol J Pelvic Floor Dysfunct* 2015; 26: 649–656.
 71. Brodin RE. Prospective, randomized evaluation of midline fascial closure in gastric bariatric operations. *Am J Surg* 1996; 172: 328–331.
 72. Ulman I, Erikçi V, Avanoğlu A, et al. The effect of suturing technique and material on complication rate following hypospadias repair. *Eur J Pediatr Surg* 1997; 7: 156–7.
 73. Seiler CM, Bruckner T, Diener MK, et al. Interrupted or Continuous Slowly Absorbable Sutures For Closure of Primary Elective Midline Abdominal Incisions. *Ann Surg* 2009; 249: 576–582.
 74. Bloemen A, Van Dooren P, Huizinga BF, et al. Randomized clinical trial comparing polypropylene or polydioxanone for midline abdominal wall closure. *Br J Surg* 2011; 98: 633–639.
 75. Albertsmeier M, Seiler CM, Fischer L, et al. Evaluation of the safety and efficacy of MonoMax® suture material for abdominal wall closure after primary midline laparotomy - A controlled prospective multicentre trial: ISSAAC [NCT005725079]. *Langenbeck's Arch Surg* 2012; 397: 363–371.
 76. Bassi A, Tulandi T. Evaluation of Total Laparoscopic Hysterectomy With and Without the Use of Barbed Suture. *J Obstet Gynaecol Canada* 2013; 35: 718–722.
 77. Timmermans L, Eker HH, Steyerberg ES, et al. Short-term results of a randomized controlled trial comparing primary suture with primary glued mesh augmentation to prevent incisional hernia. *Ann Surg* 2015; 261: 276–281.
 78. Kim-Fuchs C, Angst E, Vorburger S, et al. Prospective randomized trial comparing sutured with sutureless mesh fixation for Lichtenstein hernia repair: long-term results. *Hernia* 2012; 16: 21–27.
 79. Allahdin S, Glazener C, Bain C. A randomised controlled trial evaluating the use of polyglactin mesh, polydioxanone and polyglactin sutures for pelvic organ prolapse surgery. *J Obstet Gynaecol (Lahore)* 2008; 28: 427–431.
 80. Bayraktar B, Özemir IA, Saıırođlu J, et al. A retrospective analysis of early and late term complications in patients who underwent application of retention sutures for gastrointestinal tract malignancies. *Turkish J Surg* 2015; 31: 15–19.
 81. Breuninger H. Intracutaneous butterfly suture - A horizontal buried interrupted suture for high tension. *Eur J Plast Surg* 1998; 21: 415–419.
 82. Cameron AEP, Parker CJ, Field ES, et al. A randomised comparison of polydioxanone (PDS®) and polypropylene (Prolene®) for abdominal wound closure. *Ann R Coll Surg Engl* 1987; 69: 113–115.
 83. Cassie AB, Chatterjee AK, Mehta S, et al. Pain quantum and wound healing: A comparison of interrupted inversion PDS and standard nylon sutures in abdominal skin closure. *Ann R Coll Surg Engl* 1988; 70: 339–342.
 84. Chusak RB, Dibbell DG. Clinical Experience with Polydioxanone Monofilament

- Absorbable Sutures in Plastic Surgery. *Plast Reconstr Surg* 1983; 72: 217–220.
85. Constantine FC, Ahmad J, Geissler P, et al. Simplifying the management of caudal septal deviation in rhinoplasty. *Plast Reconstr Surg* 2014; 134: 379e–388e.
 86. Coras B, Hohenleutner U, Landthaler M, et al. Comparison of two absorbable monofilament polydioxanone threads in intradermal buried sutures. *Dermatologic Surg* 2005; 31: 331–333.
 87. Deerenberg EB, Harlaar JJ, Steyerberg EW, et al. Small bites versus large bites for closure of abdominal midline incisions (STITCH): A double-blind, multicentre, randomised controlled trial. *Lancet* 2015; 386: 1254–1260.
 88. Fearon JA. Rigid fixation of the calvaria in craniosynostosis without using ‘rigid’ fixation. *Plastic and Reconstructive Surgery* 2003; 111: 27–38.
 89. Gillatt DA, Corfield AP, May RE, et al. Polydioxanone suture in the gastrointestinal tract. *Ann R Coll Surg Engl* 1987; 69: 54–56.
 90. Varshney S, Manek P, Johnson C. Six-fold suture: wound length ratio for abdominal closure. *Ann R Coll Surg Engl* 1999; 81: 333–336.
 91. Guyuron B, Vaughn C. Comparison of Polydioxanone and Polyglactin 910 in Intradermal Repair. *Plast Reconstr Surg* 1986; 98: 817–820.
 92. Helbling C, Schlumpf R. Sutureless Lichtenstein: First results of a prospective randomised clinical trial. *Hernia* 2003; 7: 80–84.
 93. Hohenleutner U, Egner N, Hohenleutner S, et al. Intradermal buried vertical mattress suture as sole skin closure: Evaluation of 149 cases. *Acta Derm Venereol* 2000; 80: 344–347.
 94. Hoile RW. The use of a new suture material (polydioxanone) in the biliary tract. *Ann R Coll Surg Engl* 1983; 65: 168–171.
 95. Iwase K, Higaki J, Tanaka Y, et al. Running closure of clean and contaminated abdominal wounds using a synthetic monofilament absorbable looped suture. *Surg Today* 1999; 29: 874–879.
 96. Justinger C, Moussavian MR, Schlueter C, et al. Antibiotic coating of abdominal closure sutures and wound infection. *Surgery* 2009; 145: 330–334.
 97. Justinger C, Schuld J, Sperling J, et al. Triclosan-coated sutures reduce wound infections after hepatobiliary surgery—a prospective non-randomized clinical pathway driven study. *Langenbeck’s Arch Surg* 2011; 396: 845–850.
 98. Kasturi S, Bentley-Taylor M, Woodman PJ, et al. High uterosacral ligament vaginal vault suspension: Comparison of absorbable vs. permanent suture for apical fixation. *Int Urogynecol J* 2012; 23: 941–945.
 99. Abbas Khan MA, Bhutto AM, Farid M, et al. Aesthetic sculpting for the natal cleft and buttock lift using an innovative periosteal-dermal suture suspension technique. *J Craniofac Surg* 2012; 23: 172–174.
 100. Kohler A, Lavanchy JL, Lenoir U, et al. Effectiveness of Prophylactic Intraperitoneal Mesh Implantation for Prevention of Incisional Hernia in Patients Undergoing Open Abdominal Surgery: A Randomized Clinical Trial. *JAMA Surg* 2019; 154: 150–158.
 101. Kreitmann B, Riberi A, Metras D. Evaluation of an Absorbable Suture for Sternal

- Closure in Pediatric Cardiac Surgery. *J Card Surg* 1992; 7: 254–256.
102. Leaper DJ, Allan A, May RE, et al. Abdominal wound closure: A controlled trial of polyamide (Nylon) and polydioxanone suture (PDS). *Ann R Coll Surg Engl* 1985; 67: 273–275.
 103. Williams ZF, Tenzel P, Hooks WB, et al. Suture to wound length ratio in abdominal wall closure: how well are we doing? *Hernia* 2017; 21: 869–872.
 104. Luciani N, Anselmi A, Gandolfo F, et al. Polydioxanone sternal sutures for prevention of sternal dehiscence. *J Card Surg* 2006; 21: 580–584.
 105. Millbourn D, MD; Cengiz Y, MD, PhD; Israelsson L A., MD P. Effect of Stitch Length on Wound Complications After Closure of Midline Incisions. *Arch Surg* 2009; 144: 1056–1059.
 106. Muysoms FE, Detry O, Vierendeels T, et al. Prevention of Incisional Hernias by Prophylactic Mesh-augmented Reinforcement of Midline Laparotomies for Abdominal Aortic Aneurysm Treatment. *Ann Surg* 2016; 263: 638–645.
 107. Nahas FX, Augusto SM, Ghelfond C. Nylon Versus Polydioxanone in the Correction of Rectus Diastasis.pdf. *Plast Reconstr Surg* 2001; 107: 700–706.
 108. Nahas FX, Ferreira LM, Ely PB, et al. Rectus diastasis corrected with absorbable suture: A long-term evaluation. *Aesthetic Plast Surg* 2011; 35: 43–48.
 109. Ohira G, Kawahira H, Miyauchi H, et al. Synthetic polyglycomer short-term absorbable sutures vs. polydioxanone long-term absorbable sutures for preventing incisional hernia and wound dehiscence after abdominal wall closure: a comparative randomized study of patients treated for gastric or colon. *Surg Today* 2015; 45: 841–845.
 110. Okano K, Kakinoki K, Yachida S, et al. A simple and safe pancreas transection using a stapling device for a distal pancreatectomy. *J Hepatobiliary Pancreat Surg* 2008; 15: 353–358.
 111. Parara SM, Manios A, De Bree E, et al. Significant differences in skin irritation by common suture materials assessed by a comparative computerized objective method. *Plast Reconstr Surg* 2011; 127: 1191–1198.
 112. Ruiz-Tovar J, Alonso N, Ochagavía A, et al. Effect of the Abdominal Fascial Closure with Triclosan-Coated Sutures in Fecal Peritonitis, on Surgical Site Infection, and Evisceration: A Retrospective Multi-Center Study. *Surg Infect (Larchmt)* 2018; 19: 61–64.
 113. Schenk S, Landsiedl F, Enenkel M. Arthroscopic single-stranded semitendinosus tendon- versus PDS-augmentation of reinserted acute femoral anterior cruciate ligament tears: 7 year follow-up study. *Knee Surgery, Sport Traumatol Arthrosc* 2006; 14: 318–324.
 114. Spencker S, Coban N, Koch L, et al. Comparison of skin adhesive and absorbable intracutaneous suture for the implantation of cardiac rhythm devices. *Europace* 2011; 13: 416–420.
 115. Tan EK, Kannan RY, Page RE. The use of Vicryl™ in extensor tendon repairs. *Eur J Plast Surg* 2009; 32: 19–22.
 116. Yamaoka Y, Ikeda M, Ikenaga M, et al. Efficacy of skin closure with subcuticular

- sutures for preventing wound infection after resection of colorectal cancer: a propensity score–matched analysis. *Langenbeck's Arch Surg* 2015; 400: 961–966.
117. Zhang J, Zhang HK, Zhu HY, et al. Mass Continuous Suture versus Layered Interrupted Suture in Transverse Abdominal Incision Closure after Liver Resection. *World J Surg* 2016; 40: 2237–2244.
 118. Warner JP, Gutowski KA. Abdominoplasty With Progressive Tension Closure Using A Barbed Suture Technique. *Aesthetic Surg J* 2009; 29: 221–225.
 119. Murphey AW, Nguyen SA, Fuller C, et al. TranQuill sling snoreplasty for snoring: A single-arm pilot study for safety and effectiveness. *Laryngoscope* 2016; 126: 243–248.
 120. Yeo SH, Lee YB, Han DG, et al. Early Complications from Absorbable Anchoring Suture Following Thread-Lift for Facial Rejuvenation. *Arch Aesthetic Plast Surg* 2017; 23: 11–16.
 121. Kelley BP, Heller L. A novel approach to repair of wound dehiscence in the complicated patient. *Hernia* 2012; 16: 369–372.
 122. Liatsikos E, Knoll T, Kyriazis I, et al. Unfavorable outcomes of laparoscopic pyeloplasty using barbed sutures: A multi-center experience. *World J Urol* 2013; 31: 1441–1444.
 123. Emanuelsson P, Gunnarsson U, Strigård K, et al. Early complications, pain, and quality of life after reconstructive surgery for abdominal rectus muscle diastasis: A 3-month follow-up. *J Plast Reconstr Aesthetic Surg* 2014; 67: 1082–1088.
 124. Bogliolo S, Nadalini C, Iacobone AD, et al. Vaginal cuff closure with absorbable bidirectional barbed suture during total laparoscopic hysterectomy. *Eur J Obstet Gynecol Reprod Biol* 2013; 170: 219–221.
 125. Giampaolino P, De Rosa N, Tommaselli GA, et al. Comparison of bidirectional barbed suture Stratafix and conventional suture with intracorporeal knots in laparoscopic myomectomy by office transvaginal hydrolaparoscopic follow-up: A preliminary report. *Eur J Obstet Gynecol Reprod Biol* 2015; 195: 146–150.
 126. Chan VWK, Chan P-K, Chiu K-Y, et al. Does Barbed Suture Lower Cost and Improve Outcome in Total Knee Arthroplasty? A Randomized Controlled Trial. *J Arthroplasty* 2017; 32: 1474–1477.
 127. Gililland JM, Anderson LA, Sun G, et al. Perioperative closure-related complication rates and cost analysis of barbed suture for closure in TKA. *Clin Orthop Relat Res* 2012; 470: 125–129.
 128. Blanc P, Lointier P, Breton C, et al. The Hand-sewn Anastomosis with an Absorbable Bidirectional Monofilament Barbed Suture Stratafix® During Laparoscopic One Anastomosis Loop Gastric Bypass. Retrospective Study in 50 Patients. *Obes Surg* 2015; 25: 2457–2460.
 129. Gys B, Gys T, Lafullarde T. The Use of Unidirectional Knotless Barbed Suture for Enterotomy Closure in Roux-en-Y Gastric Bypass: a Randomized Comparative Study. *Obes Surg* 2017; 27: 2159–2163.
 130. Kang SH, Moon SH, Rho B II, et al. Wedge-shaped polydioxanone threads in a folded configuration (“Solid fillers”): A treatment option for deep static wrinkles on the upper face. *J Cosmet Dermatol* 2019; 18: 65–70.
 131. Lee H, Yoon K, Lee M. Outcome of facial rejuvenation with polydioxanone thread for

- Asians. *J Cosmet Laser Ther* 2018; 20: 189–192.
132. Peleg D, Ahmad RS, Warsof SL, et al. A randomized clinical trial of knotless barbed suture vs conventional suture for closure of the uterine incision at cesarean delivery. *Am J Obstet Gynecol* 2018; 218: 343.e1-343.e7.
 133. Shermak MA, Mallalieu J, Chang D. Barbed suture impact on wound closure in body contouring surgery. *Plast Reconstr Surg* 2010; 126: 1735–1741.
 134. Ting NT, Moric MM, Della Valle CJ, et al. Use of Knotless Suture for Closure of Total Hip and Knee Arthroplasties. A Prospective, Randomized Clinical Trial. *J Arthroplasty* 2012; 27: 1783–1788.
 135. Yanazume S, Togami S, Fukuda M, et al. New Continuous Barbed Suture Device with Stratafix for the Vaginal Stump in Laparoscopic Hysterectomy. *Gynecol Minim Invasive Ther* 2018; 7: 167–171.
 136. Zayed MA, Fouda UM, Elsetohy KA, et al. Barbed sutures versus conventional sutures for uterine closure at cesarean section; a randomized controlled trial. *J Matern Neonatal Med* 2019; 32: 710–717.
 137. Baumann A, Burggasser G, Gauss N, et al. Orbital floor reconstruction with an alloplastic resorbable polydioxanone sheet. *Int J Oral Maxillofac Surg* 2002; 31: 367–373.
 138. Rimmer J, Ferguson LM, Saleh HA. Versatile applications of the polydioxanone plate in rhinoplasty and septal surgery. *Arch Facial Plast Surg* 2013; 14: 323–30.
 139. Fuller JC, Levesque PA, Lindsay RW. Polydioxanone plates are safe and effective for L-strut support in functional septorhinoplasty. *Laryngoscope* 2017; 00: 8–10.
 140. Huang K, Ding X, Lv B, et al. Reconstruction of large-size abdominal wall defect using biodegradable poly-p-dioxanone mesh: An experimental canine study. *World J Surg Oncol* 2014; 12: 1–8.
 141. Dayan SH, Ashourian N. Polydioxanone Absorbable Plate for Cartilaginous Grafting in Endonasal Rhinoplasty. *JAMA Facial Plast Surg* 2016; 18: 47–53.
 142. Becker ST, Terheyden H, Fabel M, et al. Comparison of collagen membranes and polydioxanone for reconstruction of the orbital floor after fractures. *J Craniofac Surg* 2010; 21: 1066–1068.
 143. Daley M, Brizard CP, Konstantinov IE, et al. Absorbable pulmonary artery banding: A strategy for reducing reoperations. *Eur J Cardio-thoracic Surg* 2017; 51: 735–739.
 144. Dörfer CE, Kim TS, Steinbrenner H, et al. Regenerative periodontal surgery in interproximal intrabony defects with biodegradable barriers. *J Clin Periodontol* 2000; 27: 162–168.
 145. Eickholz P, Kim T-S, Steinbrenner H, et al. Guided Tissue Regeneration With Bioabsorbable Barriers: Intrabony Defects and Class II Furcations. *J Periodontol* 2005; 71: 999–1008.
 146. Eickholz P, Krigar D-M, Pretzl B, et al. Guided Tissue Regeneration With Bioabsorbable Barriers. II. Long-Term Results in Infrabony Defects. *J Periodontol* 2005; 75: 957–965.
 147. Epprecht L, Schlegel C, Holzmann D, et al. Closure of nasal septal perforations with a polydioxanone plate and temporoparietal fascia in a closed approach. *Am J Rhinol*

- Allergy* 2017; 31: 190–195.
148. Gierloff M, Karl Seeck NG, Springer I, et al. Orbital floor reconstruction with resorbable polydioxanone implants. *J Craniofac Surg* 2012; 23: 161–164.
 149. Iizuka T, Mikkonen P, Paukku P, et al. Reconstruction of orbital floor with polydioxanone plate. *Int J Oral Maxillofac Surg* 1991; 20: 83–87.
 150. Kontio R, Suuronen R, Salonen O, et al. Effectiveness of operative treatment of internal orbital wall fracture with polydioxanone implant. *Int J Oral Maxillofac Surg* 2001; 30: 278–285.
 151. Krokidis M, Burke C, Spiliopoulos S, et al. The use of biodegradable stents in malignant oesophageal strictures for the treatment of dysphagia before neoadjuvant treatment or radical radiotherapy: A feasibility study. *Cardiovasc Intervent Radiol* 2013; 36: 1047–1054.
 152. Moina DG, Moina G, Rancati A. A Technique to Correct Severe Lateral Crural Concavity: Adjunctive Use of a Polydioxanone Plate During Lateral Crural Reverse Plasty. *Aesthetic Plast Surg* 2014; 38: 1094–1100.
 153. Pau M, Reinbacher K, Feichtinger M, et al. Perforating the polydioxanone sheet: Avoiding intraorbital hematoma after open treatment of orbital floor fractures. *J Craniofac Surg* 2012; 23: 1129–1130.
 154. Repici A, Pagano N, Rando G, et al. A retrospective analysis of early and late outcome of biodegradable stent placement in the management of refractory anastomotic colorectal strictures. *Surg Endosc* 2013; 27: 2487–2491.
 155. Sand JP, Desai SC, Branham GH. Septal Perforation Repair Using Polydioxanone Plates. *Plast Reconstr Surg* 2015; 136: 700–703.
 156. Small HN, Braly WG, Tullos HS. Fixation of the Chevron osteotomy utilizing absorbable polydioxanone pins. *Foot Ankle Int* 1995; 16: 346–350.
 157. Chandran P, Kamath RP, Nihal A. Osteochondral fracture of talus treated with bioabsorbable pins. *Foot* 2008; 18: 56–58.
 158. Prior TD, Grace DL, MacLean JB, et al. Correction of hallux abductus valgus by Mitchell's metatarsal osteotomy: Comparing standard fixation methods with absorbable polydioxanone pins. *Foot* 1997; 7: 121–125.
 159. Gill LH, Martin DF, Coumas JM, et al. Fixation with bioabsorbable pins in chevron bunionectomy. *J Bone Jt Surg - Ser A* 1997; 79: 1510–1518.
 160. McManners J, Moos KF, El-Attar A. The use of biodegradable fixation in sagittal split and vertical subsigmoid osteotomy of the mandible: A preliminary report. *Br J Oral Maxillofac Surg* 1997; 35: 401–405.
 161. Miller M, Anderson JK, Pearle MS, et al. Resorbable clip migration in the collecting system after laparoscopic partial nephrectomy. *Urology* 2006; 67: 2005–2006.
 162. Neubauer NL, Schink PJ, Pant A, et al. A comparison of 2 methods of vaginal cuff closure during robotic hysterectomy. *Int J Gynecol Obstet* 2013; 120: 99–101.
 163. Kasi Ganesh S, Panneerselvam E, Sharma AK, et al. Knotless Suture for Wound Closure in Intraoral Surgery—A Report of 2 Cases. *J Oral Maxillofac Surg* 2018; 76: 1954.e1-1954.e4.

164. Gupta D, Sharma U, Chauhan S, et al. Improved outcomes of scar revision with the use of polydioxanone suture in comparison to polyglactin 910: A randomized controlled trial. *J Plast Reconstr Aesthetic Surg* 2018; 71: 1159–1163.
165. Gys B, Gys T, Ruysers M, et al. Laparoscopic Linear Stapled Running Enterotomy Closure in Roux-en-Y Gastric Bypass Using Absorbable Unidirectional Barbed Suture (Stratafix® 2/0). *Obes Surg* 2017; 27: 2740–2741.
166. Obwegeser JA. Osteosynthesis using biodegradable poly-p-dioxanon (PDS II) in Le Fort I-osteotomy without postoperative intermaxillary fixation. *J Cranio-Maxillofacial Surg* 1994; 22: 129–137.
167. Christgau M, Bader N, Felden A, et al. Guided tissue regeneration in intrabony defects using an experimental bioresorbable polydioxanon (PDS) membrane: A 24-month split-mouth study. *J Clin Periodontol* 2002; 29: 710–723.
168. Pretzl B, Kim TS, Steinbrenner H, et al. Guided tissue regeneration with bioabsorbable barriers III 10-year results in infrabony defects. *J Clin Periodontol* 2009; 36: 349–356.