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A Retrospective, Multicenter, Observational Real World Post Market Clinical Follow Up Study to Evaluate Acute Safety and Device Procedural Success of ADVAPD (Polydioxanone) Surgical Suture. (ADVAPD PMCF Study)

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Abstract
In this real-world experience Post-marketing Clinical Follow-up study conducted in accordance with EU MDR 2017/745 in 70 subjects from >55 surgical centers across various surgical specialties, ADVAPD (Polydioxanone) monofilament, synthetic absorbable sterile surgical sutures demonstrated excellent suture, needle, and overall performance. No wound complications or adverse events were reported in this study during the follow-up period of 3 months, and there were no reports of prolonged or repeat hospitalization. ADVAPD (Polydioxanone) sutures are a safe and effective option for a very wide variety of surgical procedures in a diverse population.

Keywords: Polydioxanone, Monofilament, Synthetic absorbable suture, Paediatric surgery.

INTRODUCTION

Sutures are sterile surgical threads used to approximate and/or ligate tissues. They are essential for wound closure in a variety of surgical procedures, including general surgery, gynecology, ophthalmology, and cardiovascular surgery. Sutures are available in a wide range of materials, including natural (e.g., catgut, silk) and synthetic (e.g., nylon, polyester, polyglactin 910). [1]

Advanced MedTech Solutions (AMS) (https://www.amsltd.com/products/ADVAPD) ADVAPD suture is a synthetic absorbable sterile surgical suture composed of a copolymer made from Polyester and Polydioxanone. ADVAPD suture is available in both dyed and undyed form. ADVAPD suture is dyed with D and C Violet No. 2. ADVAPD suture complies with United States Pharmacopeia requirement for "Absorbable Surgical Suture" and the European Pharmacopoeia for "Sterile Synthetic Absorbable Monofilament Sutures".

ADVAPD suture is indicated for use in general soft tissue approximation, including use in ophthalmic surgery and Paediatric cardiovascular tissue where growth is expected to occur. ADVAPD suture is not

indicated in adult cardiovascular tissues, peripheral nerve anastomosis & microsurgery. These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable.

ADVAPD suture being an absorbable suture, should not be used where extended approximation of tissue under stress is required. The use of this suture is also contraindicated in patients with known sensitivities or allergies to Polydioxanone.

The absorption process begins at the suture surface and progresses inward. The progressive loss of tensile strength and eventual absorption of ADVAPD occurs by means of hydrolysis. Absorption begins as a loss of tensile strength followed by a loss of mass. The suture is designed to maintain 80% of its tensile strength for 14 days, 70% for 28 days. The rate of absorption depends on several factors, including the suture diameter, the type of tissue, and the patient's individual metabolism. ADVAPD (Polydioxanone) sutures are completely absorbed within 180 to 238 days.

Suture construction	Suture Color	Tensile strength Retention (%)		Mass Absorption* (days)
Monofilament	Undyed / Violet	14 days	80%	Between 180 to 238 days
		28 days	70%	
		42 days	45%	

*Mass Absorption: Time in days required for suture to be totally absorbed in the body.

ADVAPD suture is designed to offer the following advantages.

Features	Benefits
Monofilament Construction	Smooth passage through the tissue with minimal tissue drag and minimal trauma
Reduced surface area and lack of interstitial spaces in monofilament	Minimal risk of bacteria to harbour
Acapillarity	Lesser chance of bacterial transmission, lesser chance of infection
Retention strength upto 6 weeks	Enduring support to even slow healing tissue like fascia.
Robust manufacturing process & superior premium aluminium packaging	Least moisture content in the suture foil ensures strength & long- term sterility throughout shelf life

The current level of evidence for synthetic absorbable sterile surgical sutures composed of a copolymer made from polyester and polydioxanone is supported by several studies that evaluate their mechanical properties, handling characteristics, and clinical performance.

Polydioxanone (PDS) sutures are well-documented for their high tensile strength and elongation properties. Studies have shown that PDS sutures maintain significant tensile strength over time, with initial tensile strength comparable to other absorbable sutures like polyglyconate (Maxon) and self-reinforced poly L-lactide (SR-PLLA).[1] PDS sutures typically retain their tensile strength for up to 20 weeks, which is longer than many other absorbable sutures.[2]

In terms of handling and knot performance, PDS sutures have been shown to have intermediate knot performance compared to other monofilament sutures, with some studies indicating that newer generations like PDS-2 do not significantly improve upon the original PDS in terms of knot security.[3] However, PDS sutures are noted for their high elongation before breakage, which can be advantageous in certain surgical applications.[4]

Clinical studies have also highlighted the benefits of PDS sutures in terms of reduced tissue reaction and lower bacterial colonization compared to multifilament sutures, which can be critical in minimizing infection risk and promoting wound healing.[5] Additionally, PDS sutures have demonstrated superior performance in maintaining tensile strength and stability over time, making them suitable for applications requiring prolonged support.[6]

Overall, the evidence supports the use of synthetic absorbable sutures composed of polyester and polydioxanone for their favorable mechanical properties, handling characteristics, and clinical outcomes.

Synthetic absorbable sterile surgical sutures composed of a copolymer made from polyester and polydioxanone (PDS) are particularly beneficial for specific patient populations due to their unique properties. These sutures are known for their high tensile strength, prolonged strength retention, and minimal tissue reactivity, making them suitable for various clinical scenarios.

1. **Patients with High Infection Risk:** PDS sutures are monofilament, which reduces bacterial colonization compared to multifilament sutures. This property is advantageous in patients at high risk of infection, such as those undergoing dentoalveolar surgery, where monofilament sutures like PDS have shown superior wound healing and lower microbial colonization.[5,7]
2. **Patients Requiring Prolonged Wound Support:** PDS sutures maintain tensile strength for up to 20 weeks, making them ideal for patients requiring prolonged wound support. This includes patients with wounds that heal slowly or those undergoing procedures where tissue support is critical over an extended period, such as in orthopedic or abdominal surgeries.[8]
3. **Patients with High Tissue Reactivity:** The minimal tissue reaction associated with PDS sutures makes them suitable for patients with a history of significant tissue reactivity or those undergoing surgeries where minimizing inflammation is crucial. This can be particularly relevant in surgeries involving delicate tissues or in patients with a predisposition to hypertrophic scarring.[9]
4. **Pediatric and Geriatric Patients:** These populations often benefit from the reduced need for suture removal and the associated discomfort. The absorbable nature of PDS sutures eliminates the need for suture removal, which can be particularly advantageous in pediatric and geriatric patients who may have difficulty with follow-up procedures.

In summary, PDS sutures are beneficial for patients at high risk of infection, those requiring prolonged wound support, individuals with high tissue reactivity, and pediatric or geriatric patients. These properties make PDS sutures a versatile and valuable option in various surgical contexts.

Common complications associated with synthetic absorbable sterile surgical sutures composed of a copolymer made from polyester and polydioxanone (PDS) include:

1. **Inflammatory Response:** PDS sutures can induce a mild inflammatory response, characterized by the presence of a few inflammatory cells and scar fibrosis. This reaction is generally less severe compared to other absorbable sutures like polyglactin 910.[10]
2. **Surface Cracking:** Over time, PDS sutures may develop triangular cracks on their surface, which can potentially affect their mechanical integrity.[10]

3. **Suture Sinus Formation:** Although less common than with non-absorbable sutures like braided silk, PDS sutures can still lead to late suture sinus formation. This complication is generally less severe and resolves more quickly with percutaneous drainage compared to non-absorbable sutures.[11]
4. **Wound Dehiscence and Infection:** While the rates of wound dehiscence and early wound infection are not significantly different from those observed with non-absorbable sutures, these complications can still occur. PDS sutures are associated with a lower incidence of late suture sinus formation compared to non-absorbable sutures.[11]
5. **Tissue Reaction and Healing:** PDS sutures exhibit less bacterial colonization and postoperative slack compared to other suture materials, which can positively influence wound healing. However, the tissue reaction to absorbable sutures like PDS may still adversely affect wound healing in some cases.[5]

In summary, while PDS sutures are generally well-tolerated and associated with fewer complications compared to some other suture materials, they are not without potential issues, including mild inflammatory responses, surface cracking, and occasional suture sinus formation.

ADVAPD sutures have been used widely in various types of surgical procedures. We are not aware of any systematic study done till date in an Indian population to determine safety and performance of the Polydioxanone suture in real world scenario.

MATERIALS AND METHODS

Study Design and Conduct

A real-world experience study was designed as 'A Multicenter, Real World Retrospective Post Market Clinical Follow-up Study to Evaluate Acute Safety and Device Procedural Success of Polydioxanone (ADVAPD) Surgical Suture.' (ADVAPD PMCF STUDY)

A combination of heterogeneous data from different centers was collected to reinforce analyses and strengthen clinical outcomes.

ETHICS COMMITTEE APPROVAL

Institutional Ethics Committee approval was obtained from the ACEAS Independent Ethics Committee, Ahmedabad -380015 after submitting the clinical study documents (Product Information, PMCF protocol (AMS/ADVAPD/2021 Ver. 02), CRF, etc.). The informed consent was waived on account of this being a retrospective study. Since ADVAPD is a CE-certified device, the study was conducted as per the regulatory guidelines of EU MDR 2017/745. The study done as per the ICH – GCP, ICMR guidelines and New Drugs & Clinical Trials Rules 2019 (India).

ELIGIBILITY AND INCLUSION

The study was planned to include 156 subjects, we could not reach these numbers due to various reasons like less than expected sales, instability in our organization, etc. PMCF data of 70 Subjects was collected from January 2023 to December 2023 for which analysis has been done.

All the subjects enrolled met the inclusion criteria in the study were included in this retrospective study:

Inclusion criteria

- Patients who have been treated with ADVAPD (Polydioxanone) suture.

Exclusion criteria

- As this is retrospective review of the data, there are no formal exclusion criteria for the study.

Outcome measures/ endpoints

Primary Endpoint

- Number of Subjects presenting with wound complications [Time Frame: 03 months].
- Any wound disruption, wound dehiscence, fluid accumulation, and separation (Surgical Site Infection (SSI), Hematoma, Separation, Seroma, etc).

Secondary Endpoint

- Mean Operation Time in minutes [Time Frame: Intraoperative]
- Total procedure time [Time Frame: Intraoperative]
- Any Device Malfunction or Device Failure [Time Frame: Intra and Postoperative]
- Any Device Malfunction or Device Failure related to the use of ADVAPD (based on the Investigator's Investigation for events not limited to Failure to perform or any other Malfunction when used in compliance with the Instructions for Use.)
- Length of Hospital Stay in days [Time Frame: From Postoperative through 03 month]
- Number of patients requiring Reoperation or Additional Surgical procedure [Time Frame: From Postoperative through 03 months]
- Number of patients presenting with Adverse Events related to the use of ADVAPD surgical suture [Time Frame: From Postoperative through 03 months] (Any Adverse Events related to the use of ADVAPD were based on the Investigator's Investigation.)
- Number of patients requiring Additional Surgical procedure resulting from Device malfunction, Device failure or any Adverse events [Time Frame: From Postoperative through 03 months]

All comer Subjects with ADVAPD of any size or length were included in study and follow up for 3 months as per PMCF plan.

RESULTS AND DISCUSSION

Study Report

Data of 70 subjects was collected and analysed from different Surgeons and Hospitals from January 2023 till December 2023.

STUDY POPULATION: AGE, GENDER, MEDICAL AND TREATMENT HISTORY BASELINE CHARCTERISTICS

For Baseline Characteristics, the following attributes were studied.

1. Subjects' Age
2. Subjects' Gender
3. Medical History

Mean Age of the Study population age was 45.88 years with lowest age of 3 and highest age of 69, describe categories with 74 % of males and 26% of Females. One subject had medical history of diabetes mellitus.

Table 1: Gender distribution of the subjects

Gender	70 subjects
Female	74%
Male	26%

Figure 1: Gender distribution of the subjects

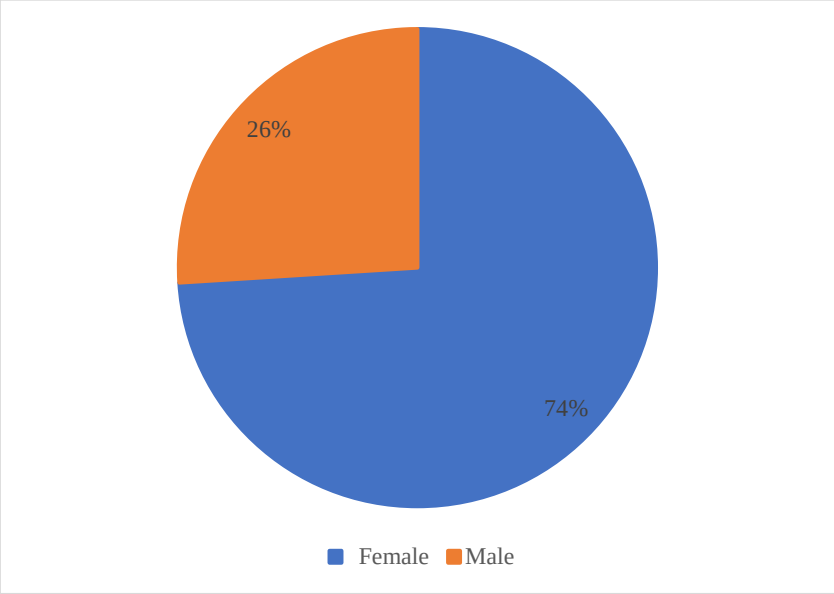


Table 2: Age categories

Age categories	70 Subjects
≤ 18 years	1%
Between 18 and 65 years	93%
≥ 65 years	6%

Figure 2: Age Categories

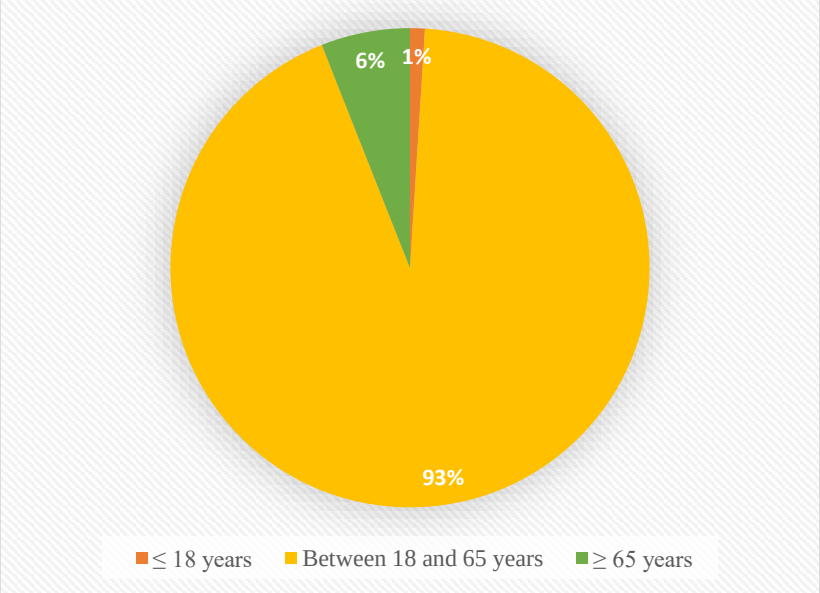
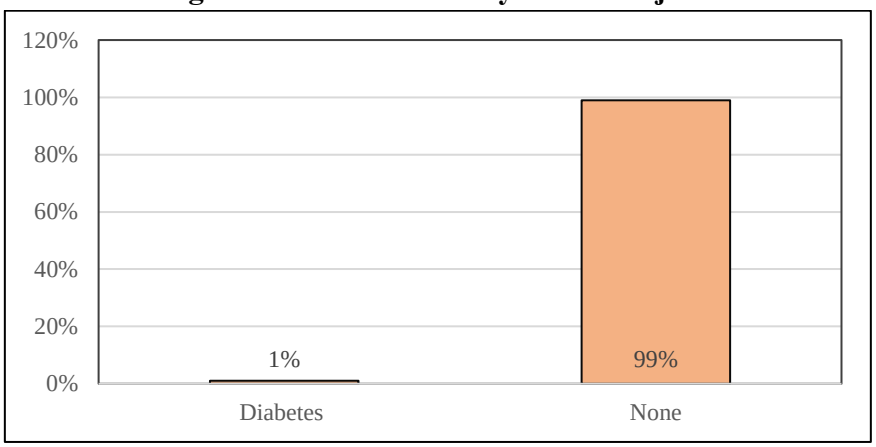


Table 3: Medical history of the subjects

Medical history	70 Subjects	Percentage
Diabetes	1	1%
None	69	99%

Figure 3: Medical History of the subjects



OPERATIVE DATA ANALYSIS

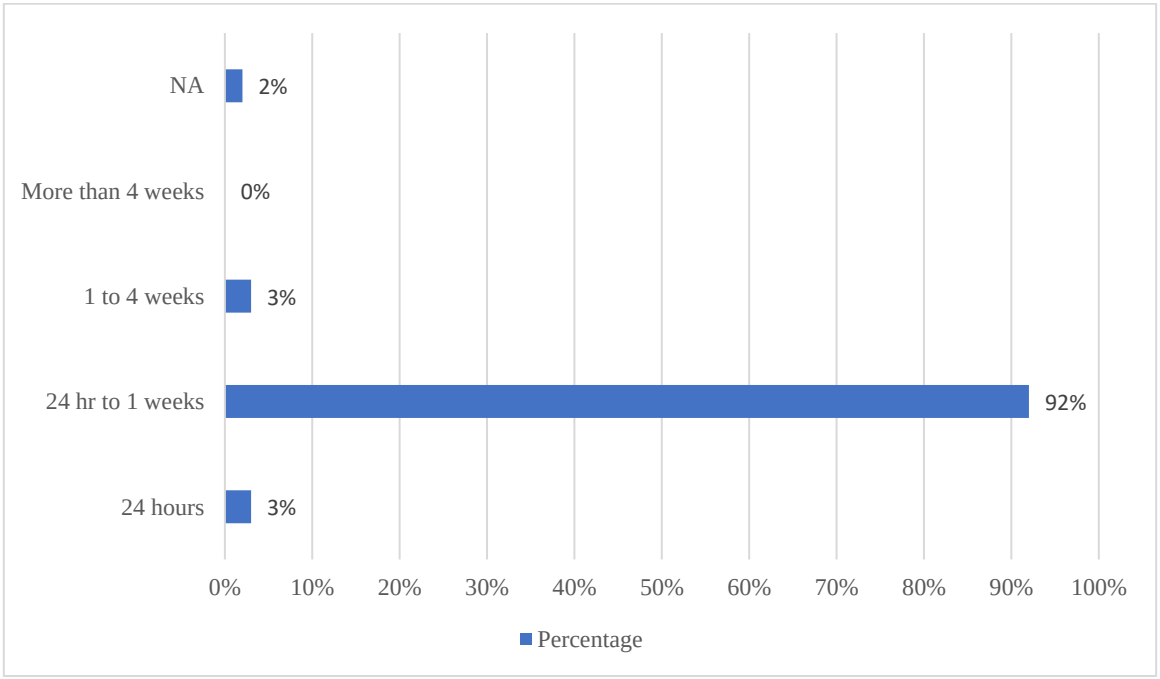
LENGTH OF HOSPITAL STAY

In total, the length of hospital stays of 92% of the subjects was 1-4 weeks, 3% of 24 hours to 1 week, 3% of more than 4 weeks, however 2% data was not available.

Table 4: Length of hospital stay.

Length of Hospital Stay	70 Subjects	Percentage
24 hours to 1 week	2	3%
1 to 4 weeks	55	92%
More than 4 weeks	2	3%
24 hours	0	0%
NA	1	2%

Figure 4: Length of hospital stay



PATIENT BASELINE INFORMATION

CLINICAL PRESENTATION ON THE DAY 0

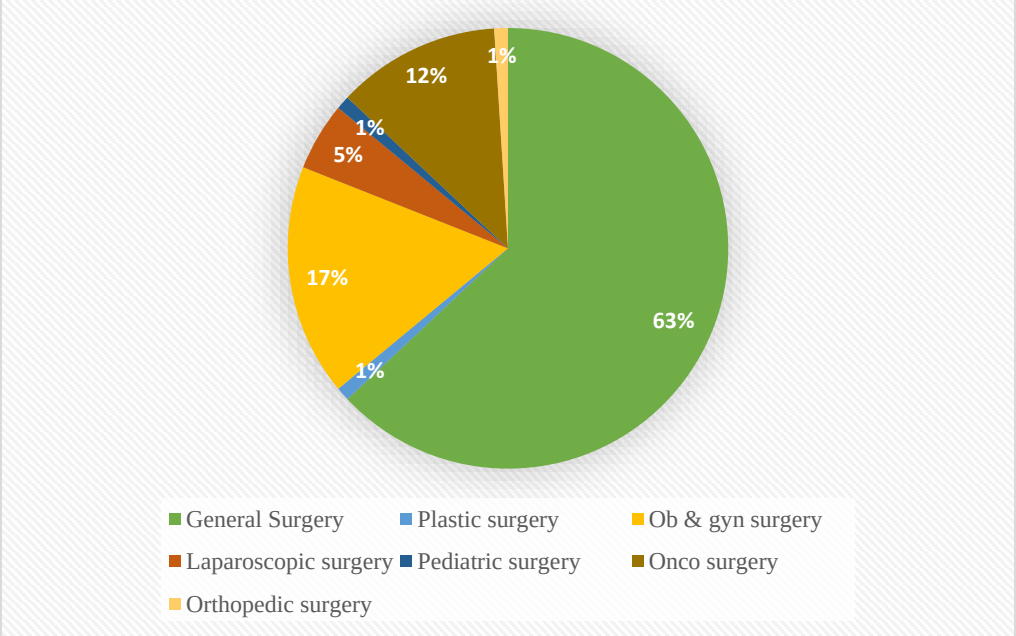
Of the 70 subjects, 63% of the Subjects underwent procedures in General Surgery, 17% in Ob and Gyn Surgery, 5% in laparoscopic surgery and 12% in Onco surgery, 1% in Orthopaedic Surgery, 1% in Paediatric surgery and 1% in Plastic surgery.

STATICAL ANALYSIS: SURGERY

Table 5: List of surgical procedure where ADVAPD was used.

Surgery name	Number of subjects (70 subjects)	Percentage
General surgery	44	63%
Obstetrics & gynaecology surgery	12	17%
Laparoscopic surgery	3	5%
Onco surgery	8	12%
Orthopaedic surgery	1	1%
Paediatric surgery	1	1%
Plastic surgery	1	1%

Figure 5: Percentage of procedures in various Surgical Categories



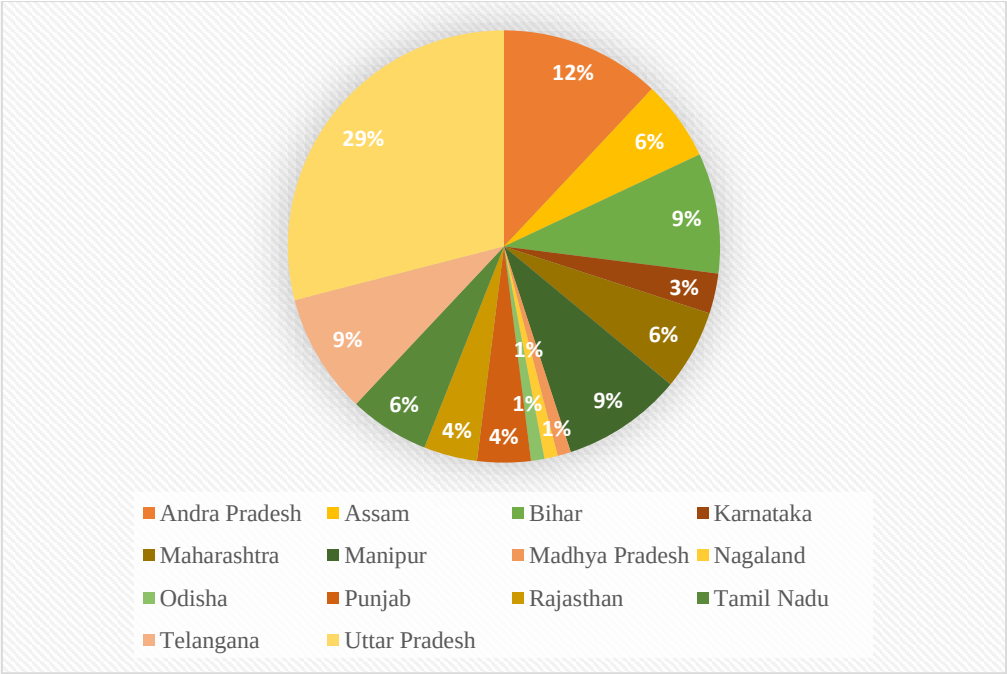
STATISTICAL ANALYSIS: STATE

In total, 29% of the Subjects from Uttar Pradesh, 12% from Andra Pradesh, 9% from Manipur, 9% from Telangana, 9% from Bihar, 6% from Tamil Nadu, 6% from Assam, 4% from Punjab, 4% from Rajasthan, 3% from Karnataka, 2% from Jharkhand, 1% from Madhya Pradesh, 1% from Nagaland, and 1% from Odisha.

Table 6: Number of subjects from different states

State	Number of Subjects (70 Subjects)	Percentage
Andra Pradesh	8	12%
Assam	4	6%
Bihar	6	9%
Karnataka	2	3%
Maharashtra	4	6%
Manipur	6	9%
Madhya Pradesh	1	1%
Nagaland	1	1%
Odisha	1	1%
Punjab	3	4%
Rajasthan	3	4%
Tamil Nadu	4	6%
Telangana	6	9%
Uttar Pradesh	20	29%

Figure 6: Number of Subjects from different states



ADVAPD HANDLING CHARACTERISTICS

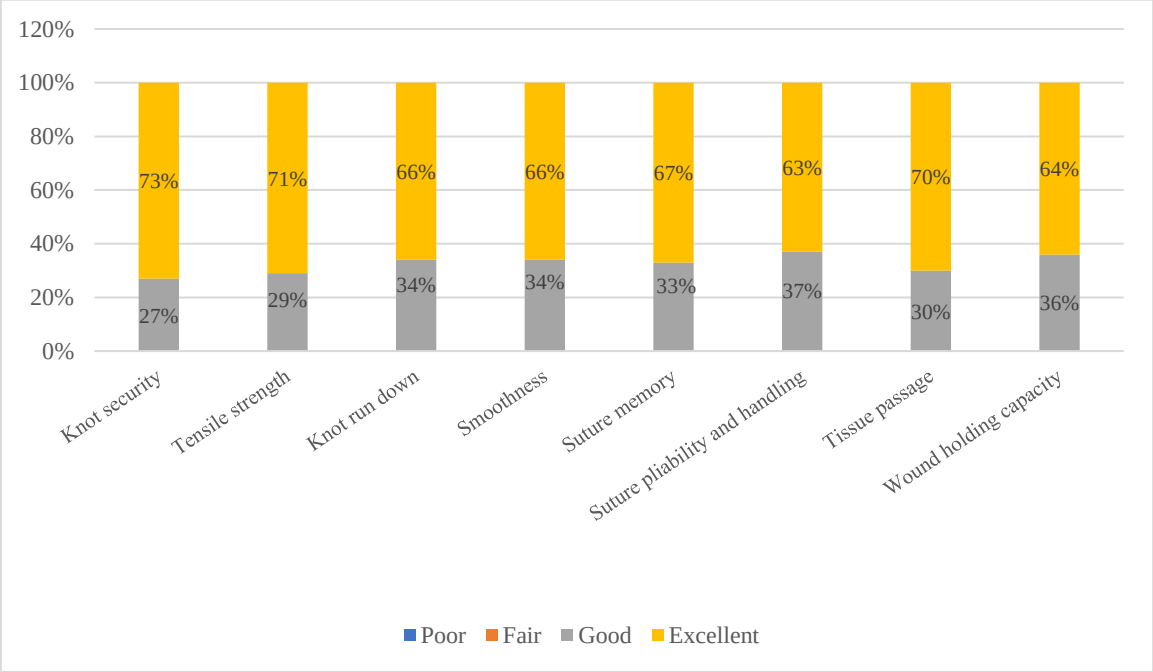
SUTURE PERFORMANCE

For Suture Performance, Knot Security, Tensile Strength, Knot Run Down, Smoothness, Suture Memory, Suture Pliability and Handling, Tissue Passage, and Wound Holding Capacity attributes were studied.

Table 7: Rating of Suture Performance attributes

70 Number of Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Knot security	0%	0%	27%	73%
Tensile strength	0%	0%	29%	71%
Knot run down	0%	0%	34%	66%
Smoothness	0%	0%	34%	66%
Suture memory	0%	0%	33%	67%
Suture pliability and handling	0%	0%	37%	63%
Tissue passage	0%	0%	30%	70%
Wound holding capacity	0%	0%	36%	64%

Figure 7:Suture Performance attributes



NEEDLE PERFORMANCE

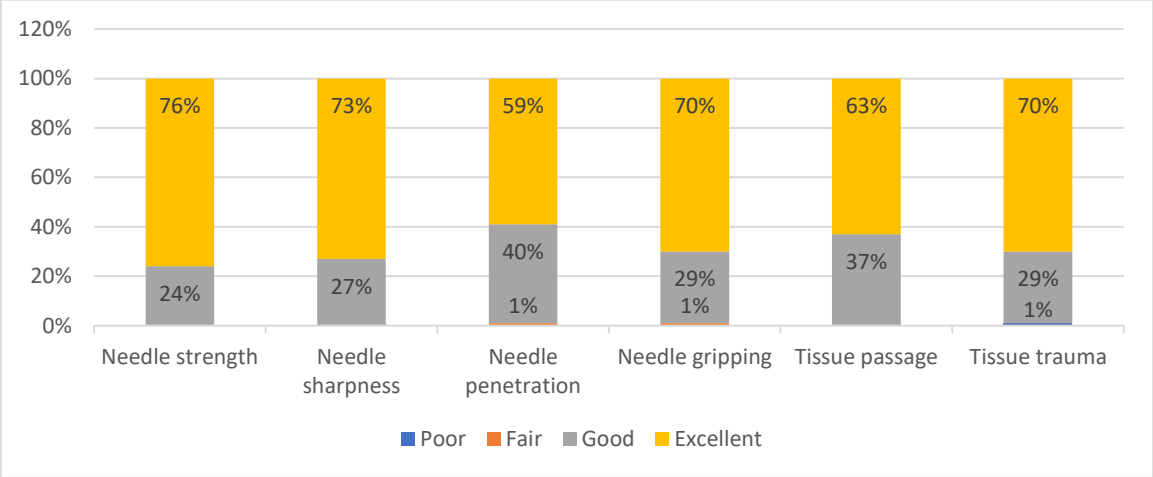
For needle performance like Needle strength, Needle sharpness, Needle penetration, Needle gripping, Tissue passage, and Tissue trauma were studied.

Table 8: Rating of Needle Performance attributes

70 Number of Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Needle strength	0%	0%	24%	76%
Needle sharpness	0%	0%	27%	73%
Needle penetration	0%	1%	40%	59%
Needle gripping	0%	1%	29%	70%
Tissue passage	0%	0%	37%	63%

Tissue trauma	1%	0%	29%	70%

Figure 8: Needle performance attributes



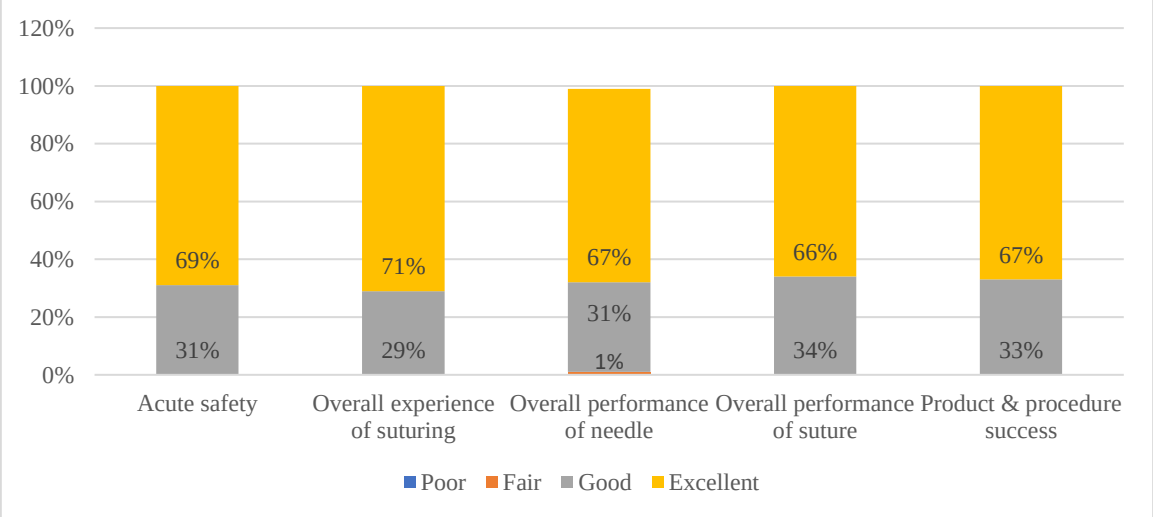
OVERALL PERFORMANCE

For Overall Performance of The Product, Acute Safety, Overall Experience of Suturing, Overall Performance of Needle, Overall Performance of Suture, Product & Procedure Success attributes were studied.

Table 9: Rating of Overall performance of the product

70 Number of Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Acute safety	0%	0%	31%	69%
Overall experience of suturing	0%	0%	29%	71%
Overall performance of needle	0%	1%	31%	67%
Overall performance of suture	0%	0%	34%	66%
Product & procedure success	0%	0%	33%	67%

Figure 9: Overall performance



CLINICAL PRESENTATION FOR THREE MONTHS FOLLOW UP DATA

At 3 months follow up, the following attributes were studied.

1. Tissue approximation
2. Wound complications like wound disruption, wound dehiscence, fluid accumulation, separation.
3. Suture Absorption time
4. Details of adverse events/ serious adverse events

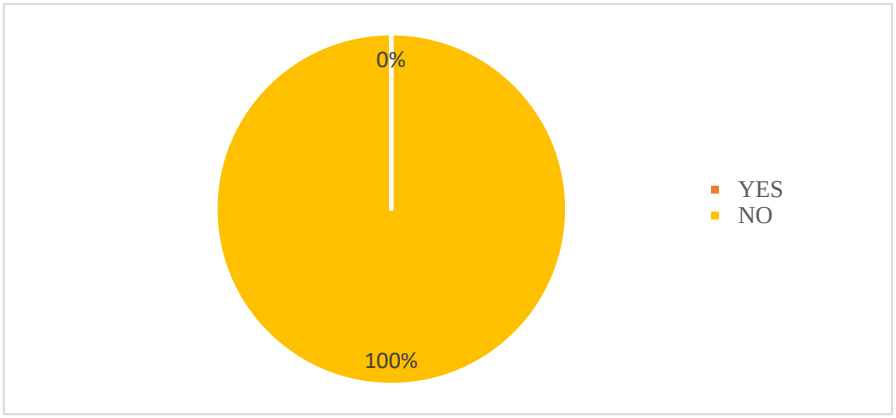
WOUND COMPLICATION

No wound complication was seen in any of the subjects at the end of 3 months follow up.

Table 10: Wound complication

Wound complication	70 Subjects
Yes	0%
No	100%

Figure 10: Wound Complication



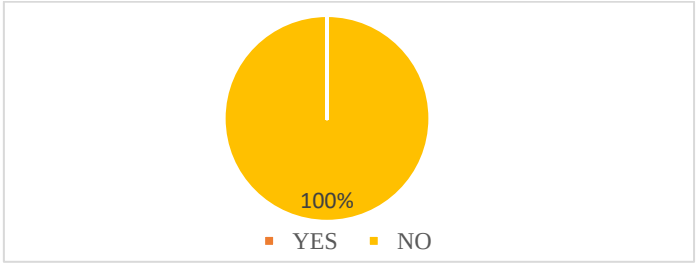
ADVERSE EVENTS (AE) OR SEVERE ADVERSE EVENTS (SAE):

In all the cases of clinical application in different surgical sites, there were no adverse events or severe adverse events reported on the day of operation or surgery and at 3 months follow up.

Table 11: Adverse reaction

Adverse reaction	70 Subjects
Yes	0%
No	100%

Figure 11:Adverse reaction



Absorption of ADVAPD is essentially complete up to 180 to 238 days.

LIMITATIONS

PMCF studies can suffer from limitations like limited data and subject selection bias. Best efforts to overcome these limitations were made by collecting sufficient data from an extremely high number of surgical centres across a wide geography and surgical specialties, by maintaining a high rate of follow-up data collection and analysing data with a very high standard of accuracy.

CONCLUSION

- In this real-world experience study in 70 subjects, ADVAPD (Polydioxanone) monofilament, synthetic absorbable sterile surgical sutures are used in a variety of surgical procedures. Follow-up data was obtained with a high rate of completion and high degree of accuracy.
- The study included subjects' data from >55 surgical centers across 13 different states of India, and included usage across 7 different surgical specialties, which demonstrates the wide diversity of clinical use of ADVAPD (Polydioxanone) sutures.
- The study successfully achieved its primary and secondary safety and performance objectives, over a significantly long 3-month follow-up period.
- ADVAPD demonstrated excellent suture, needle and overall performance and were consistently rated excellent in surgeon's feedback across surgical specialties.
- No wound complications or adverse events were reported in this study during the follow-up period of 3 months, and there were no reports of prolonged or repeat hospitalization.
- ADVAPD (Polydioxanone) sutures are a safe and effective option for a very wide variety of surgical procedures in a diverse population.

Acknowledgements

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Financial Disclosure statement

The study was sponsored by Advanced MedTech Solutions Pvt Ltd., Gujarat, India. No Financial remuneration or other benefits were paid to the hospitals or doctors contributing the subjects' data. The authors are full-time employees of Advanced MedTech Solutions Pvt. Ltd.

Conflict of Interest

No conflict of interest of any of the parties. Source documents can be made available on request.

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