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Adverse Events, Complications, and Secondary Surgical Intervention for Animal-Derived Resorbable Oral Barrier Membranes: A Report-Based Analysis of the Food and Drug Administration Manufacturer and User Facility Device Experience (FDA MAUDE) Database

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Abstract

Purpose

This study aimed to characterize the complications described in adverse event reports for animal-derived resorbable barrier membranes [Food and Drug Administration (FDA) product code NPL] and to determine whether reports of infection or wound dehiscence would describe secondary surgical intervention more often than reports without either complication.

Materials and Methods

Reports received by the FDA Manufacturer and User Facility Device Experience (MAUDE) database over a ten-year period were identified. Three reviewers independently analyzed each included report and coded anatomic site, main adverse event, individual complications, interventions, Clavien-Dindo severity grade, device attribution, and report informativeness. Inter-rater agreement was measured with Fleiss kappa. The primary outcome was any secondary surgical intervention (membrane, graft, or implant removal, surgical revision, repeat grafting, or tooth extraction). Groups were compared with the Fisher exact test.

Results

Graft loss, dehiscence, and infection or abscess were the most frequent complications. Most reports described secondary surgical intervention, and most were graded Clavien-Dindo 3a. Reports related to dehiscence or infection described reintervention more often than reports with neither complication. Agreement between reviewers was high for most complications and interventions.

Conclusions

In MAUDE reports for animal-derived resorbable membranes, the cases that led to further surgery were mostly failures of soft tissue healing: dehiscence, infection, and the graft loss that often came with them. These reports skew toward severe cases and cannot be used to estimate how often complications occur. Structured reporting of surgical site, timing, and basic risk factors would make the database more useful for these devices.

Categories: Dentistry
Keywords: adverse events, guided bone regeneration, maude database, medical device safety, resorbable collagen membrane

Introduction

Tooth loss triggers predictable remodeling of the alveolar ridge that can complicate endosseous dental implant placement. Ridge resorption after extraction is mostly horizontal; within six months, the ridge can lose up to 63 percent of its width but only 11 to 22 percent of its height [1]. When the deficiency is large enough, the remaining bone cannot support reliable implant positioning, so augmentation must occur before or concurrently with placement. Bone grafting has been reported in 29 to 50 percent of implant cases, in settings ranging from a national healthcare network to a single university hospital [2,3]. Guided bone regeneration supports this process with a barrier placed over the defect to hold the graft in place and keep gingival epithelium out of the space while osteoprogenitor cells populate the defect [4]. This process only works if the barrier stays intact for a defined interval, generally four to six weeks in periodontal regeneration

and 16 to 24 weeks in bone augmentation [4].

The first barrier membranes, most commonly made of expanded polytetrafluoroethylene, were non-resorbable and required surgical retrieval in a second procedure. Resorbable collagen membranes degrade enzymatically and have largely replaced them. Such barriers are now widely used in guided bone regeneration, though non-resorbable options are still chosen for large defects where space maintenance and rigidity matter more [5,6]. A meta-analysis of twenty-five randomized trials involving 684 patients found that resorbable membranes also carried fewer complications than non-resorbable ones, the latter of which showed membrane exposure in as many as 71 percent of cases [6]. Barrier membranes can also be derived from human tissue, such as amniotic membrane or acellular dermal matrix. These are not classified under product code NPL and are not represented in this analysis.

However, the advantage of resorbable membranes depends on uncomplicated healing. Wound dehiscence, membrane or graft exposure, and infection are the most frequently reported complications of oral bone regeneration, and a recent meta-analysis estimated a pooled complication rate of 26 percent for guided bone regeneration [7]. Exposure also reduces the amount of bone regenerated. Across eight studies, edentulous ridges that healed without membrane exposure gained roughly 74 percent more horizontal bone than exposed sites, and peri-implant dehiscence defects closed 27 percent more [8]. When exposure or infection cannot be managed conservatively, treatment escalates to debridement, removal of the membrane or the graft, or repeat augmentation. The patient then undergoes the second surgery that the resorbable membrane was intended to avoid.

Post-market surveillance data offer another view of these complications. The Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database collects reports of device-related adverse events and has been used to study dental devices for more than a decade. An analysis of reports received from 1996 to 2011 found that endosseous implants accounted for 53.5% of dental adverse event reports [9]. Later studies characterized reports for direct-to-consumer sequential aligners [10], mandibular repositioning appliances [11], and maxillary sinus-related events associated with endosseous dental implants (product code DZE) [12]. These studies described the types of events reported for each device, but bone graft materials and barrier membranes were not assessed, and the clinical consequences of complications, such as the need for further surgery, have not been examined in this data source. To our knowledge, no prior work has used public device reports to characterize complications and failures associated with intraoral resorbable barrier membranes (product code NPL).

In this study, we characterized the complications and interventions described in FDA MAUDE reports for animal-derived resorbable barrier membranes (product code NPL) received over the past ten years. We hypothesized that reports describing wound dehiscence or infection would describe secondary surgical intervention more often than reports describing neither. Because MAUDE is a collection of reports rather than a defined patient population, the study characterizes reported events and cannot estimate how often complications occur.

Materials And Methods

This study was a retrospective analysis of the United States FDA MAUDE database [13,14], which receives mandatory reports from manufacturers or user facilities and voluntary reports from clinicians or patients. Institutional review board approval was not required, as the database is publicly accessible and contains no identifiable patient information. The database was queried through the MAUDE online search using product code NPL, which denotes animal-derived intraoral resorbable barrier membranes indicated for guided bone regeneration. The search was performed on August 17, 2026, and all reports received between January 1, 2016, and May 22, 2026, were exported with full narrative text. Duplicate submissions were identified by report key.

Of the 171 reports identified, 21 were excluded. Fourteen were duplicate submissions, and seven could not be resolved to a single patient event: these described multiple patients or multiple surgical sites within one submission, or involved a device that was not used in a patient. The final analytic set included 150 reports.

For each report, reviewers coded the free-text event description into discrete variables. A single predominant adverse event was identified from a closed list. Anatomic location, including the jaw (maxilla, mandible, both, not stated), position (anterior, posterior, both, not stated), and tooth number, when available, was recorded. Complication and intervention variables were coded as separate binary (present/absent) fields, since reports often described more than one complication. Timing relative to membrane placement, prior and secondary procedures, Clavien-Dindo grade [15], the indication for membrane placement, associated biomaterial, device attribution, regenerative outcome, resolution status, and report informativeness were also coded from the free-text event description. Because reports rarely stated the type of anesthesia, any surgical reintervention was graded Clavien-Dindo 3a unless general anesthesia was explicitly reported (3b), since intraoral reinterventions are routinely performed under local anesthesia. An intervention counted toward the primary outcome only when the narrative tied it to the reported event at the same site. The complete variable list and coding definitions appear in Appendix 1.

Statistical analysis

All 150 reports were reviewed independently by three reviewers (KK, AK, SK). Main adverse event, indication, associated biomaterial, and regenerative outcome were grouped into broader categories before agreement and consensus were determined. Each reviewer coded every report independently, with no discussion between reviewers. Final category assignments for analysis were determined by majority agreement.

Inter-rater agreement was calculated using Fleiss kappa across all three reviewers. For the ordinal Clavien-Dindo grade, the mean of the pairwise quadratic weighted Cohen kappa values was also calculated. Kappa values were interpreted using conventional bands (slight, fair, moderate, substantial, almost perfect) [16]. Confidence intervals for Fleiss kappa were estimated by bootstrap resampling of reports (500 resamples). Categorical variables are reported as counts with percentages, and continuous variables as median with interquartile range (IQR).

For the primary comparison, reports with dehiscence or exposure, or infection or abscess, were compared with reports with neither complication using the Fisher exact test, with odds ratios (OR) and Woolf 95% confidence intervals (CI). Each complication present in at least ten reports was then compared separately in secondary, exploratory analyses. Analyses were conducted in R v4.4.5 (The R Core Team and The R Foundation for Statistical Computing, Vienna, Austria), and all tests were two-sided with significance set at $p < 0.05$.

Results

Report characteristics

One hundred fifty reports submitted between 2016 and 2026 were included, ranging from five reports (2020, 2023, and the partial year 2026) to 28 (2025) per calendar year. Three manufacturer groups accounted for most reports: Tutogen or RTI (72, 48.0%), Collagen Matrix (50, 33.3%), and Datum Dental (13, 8.7%). The manufacturer could not be determined in 10 reports (6.7%), and five reports (3.3%) involved other manufacturers. CopiOs Pericardium Membrane was involved in 66 reports (44.0%) (Table *1*).

Characteristic	n (%)
Manufacturer	
Tutogen or RTI	72 (48.0)
Collagen Matrix	50 (33.3)
Datum Dental	13 (8.7)
Other or not determined	15 (10.0)
Jaw	
Maxilla	33 (22.0)
Mandible	19 (12.7)
Both	4 (2.7)
Not stated	94 (62.7)
Region	
Posterior	37 (24.7)
Anterior	10 (6.7)
Both	2 (1.3)
Not stated	101 (67.3)
Indication for membrane placement	
Ridge or bone augmentation	63 (42.0)
Ridge preservation	14 (9.3)
Sinus augmentation	9 (6.0)
Soft tissue augmentation or recession	9 (6.0)

Other	2 (1.3)
Not stated	53 (35.3)
Concomitant biomaterial	
Allograft	45 (30.0)
Xenograft	14 (9.3)
Autograft	4 (2.7)
Synthetic	2 (1.3)
More than one graft type	4 (2.7)
Graft, type unspecified	24 (16.0)
Other or non-graft material	1 (0.7)
None or not stated	56 (37.3)
Main adverse event (grouped)	
Graft failure or premature resorption	49 (32.7)
Wound dehiscence	36 (24.0)
Infection	35 (23.3)
Pain, swelling, or hematoma	11 (7.3)
Hypersensitivity	7 (4.7)
Recession or other soft tissue	5 (3.3)
Neurosensory disturbance	3 (2.0)
Implant failure	2 (1.3)
Disease-transmission concern	2 (1.3)
Clavien-Dindo grade	
Grade 1	47 (31.3)
Grade 2	8 (5.3)
Grade 3a	93 (62.0)
Grade 3b	1 (0.7)
Grade 4b	1 (0.7)
Device attribution	
Probable	51 (34.0)
Possible	74 (49.3)
Unlikely	25 (16.7)
Status at last contact	
Ongoing or unresolved	111 (74.0)
Resolved	32 (21.3)
Not stated	7 (4.7)
Report informativeness	
Sufficient for analysis	113 (75.3)
Insufficient for analysis	37 (24.7)

TABLE 1: Characteristics of the 150 adverse event reports for product code NPL from FDA

MAUDE Database, Jan 2016-May 2026.

Percentages are of 150 reports. Manufacturer names were standardized before grouping; Tutogen or RTI includes RTI Surgical.

Many reports were missing basic context, including anatomic location, indication, and timing. The jaw was not specified in 94 reports (62.7%), and the anterior or posterior region was not specified in 101 reports (67.3%). Among reports that described anatomic location, the maxilla (33/56, 58.9%) and the posterior region (37/49, 75.5%) predominated. The indication for membrane placement was not stated in 53 reports (35.3%). Ridge or bone augmentation was the most common indication (63 of all 150 reports, 42.0%), followed by ridge or socket preservation (14, 9.3%), sinus augmentation (9, 6.0%), and soft tissue augmentation or gingival recession (9, 6.0%). An associated biomaterial was documented in 94 reports, most often allograft (45/94, 47.9%). The time from placement to the complication was described in only 43 reports (28.7%), with a median of 14 days (IQR 14-46). Reviewers judged the free-text event description as sufficient for characterization in 113 reports (75.3%).

Outcomes

The most common primary adverse event was graft or membrane failure, including premature resorption (49, 32.7%), followed by wound dehiscence (36, 24.0%) and infection (35, 23.3%). Reports described a median of 2 complications each (IQR 1-4; mean 2.8). As individual complications, graft loss was described in 67 reports (44.7%), dehiscence or exposure in 62 (41.3%), and infection or abscess in 49 (32.7%) (Table *2*).

Variable	n (%)	Fleiss kappa (95% confidence interval)
Complications		
Graft loss	67 (44.7)	0.80 (0.71-0.86)
Dehiscence	62 (41.3)	0.89 (0.83-0.94)
Infection or abscess	49 (32.7)	0.88 (0.81-0.94)
Inflammation	45 (30.0)	0.84 (0.75-0.91)
Implant failure	33 (22.0)	0.80 (0.69-0.90)
Swelling or edema	27 (18.0)	0.89 (0.81-0.95)
Pain	25 (16.7)	0.94 (0.87-0.99)
Premature resorption	24 (16.0)	0.80 (0.67-0.90)
Failure to resorb	23 (15.3)	0.87 (0.76-0.95)
Ridge or bone loss	19 (12.7)	0.66 (0.50-0.80)
Hypersensitivity	16 (10.7)	0.69 (0.51-0.82)
Insufficient bone	13 (8.7)	0.85 (0.68-0.95)
Sinus involvement	11 (7.3)	0.76 (0.60-0.93)
Neurosensory disturbance	4 (2.7)	0.83 (0.49-1.00)
Interventions		
Surgical revision	95 (63.3)	0.84 (0.77-0.91)
Membrane removal	46 (30.7)	0.75 (0.65-0.83)
Graft material removal	45 (30.0)	0.78 (0.68-0.85)
Observation only	36 (24.0)	0.69 (0.57-0.79)
Repeat grafting	28 (18.7)	0.90 (0.80-0.97)
Antibiotics	25 (16.7)	0.88 (0.79-0.96)
Other medication	16 (10.7)	0.71 (0.54-0.84)
Implant removal	14 (9.3)	0.70 (0.52-0.83)
Tooth extraction	4 (2.7)	1.00 (1.00-1.00)

TABLE 2: Complications and interventions described from 150 MAUDE adverse event reports (product code NPL), with inter-rater agreement via Fleiss kappa.

Counts from reviewer consensus; a report could describe multiple complications or interventions. Percentages are of 150 reports. Confidence intervals were estimated by bootstrapping with 500 resamples.

Surgical revision was the most common intervention (95 reports, 63.3%), and 36 reports (24.0%) described observation only. Severity was most often Clavien-Dindo grade 3a (93 reports, 62.0%), followed by grade 1 (47, 31.3%) and grade 2 (8, 5.3%). Attribution of complications to the device was “possible” in 74 reports (49.3%), “probable” in 51 (34.0%), and “unlikely” in 25 (16.7%). At last contact, the adverse event was ongoing in 111 reports (74.0%) and resolved in 32 (21.3%). The regenerative outcome was graft or bone loss in 62 reports (41.3%) and successful regeneration in 7 (4.7%).

Inter-rater agreement

Fleiss kappa ranged from 0.66 (ridge or bone loss) to 0.94 (pain) across the complication variables, and from 0.69 (observation only) to 1.00 (tooth extraction) across the intervention variables (Table *2*). Agreement was 0.89 for the primary adverse event and 0.85 for Clavien-Dindo grade (weighted kappa 0.91). Fleiss kappa for secondary surgical intervention was 0.85 (95% CI 0.78-0.91). Agreement was lowest for prior procedures

(0.49), followed by device attribution (0.55), report informativeness (0.63), resolution status (0.63), and regenerative outcome (0.65).

Secondary surgical reintervention

Secondary surgical intervention was described in 98 of 150 reports (65.3%). Surgical revision (95), membrane removal (46), and graft material removal (45) were the most frequent types, followed by repeat grafting (28), implant removal (14), and tooth extraction (4). Many reports described more than one type of surgical intervention.

Reports with dehiscence or exposure, or infection or abscess, described secondary surgical intervention more often than reports with neither complication (75.9% vs. 50.8%; OR 3.04; 95% CI 1.52-6.11; p = 0.002). Twenty-four reports described both dehiscence and infection and were counted once in the combined group. In separate comparisons, dehiscence (OR 2.61; 95% CI 1.26-5.41; p = 0.010) and infection (OR 3.96; 95% CI 1.68-9.29; p < 0.001) showed similar associations. Of all complications, graft loss had the strongest association with reintervention (OR 16.19; 95% CI 5.90-44.42; p < 0.001) (Table *3*).

Complication	Reports with secondary surgical intervention, n/N (%)		Odds ratio (95% confidence interval)	p-value
	Complication present	Complication absent		
Dehiscence or exposure, or infection or abscess	66/87 (75.9)	32/63 (50.8)	3.04 (1.52-6.11)	0.002
Dehiscence or exposure	48/62 (77.4)	50/88 (56.8)	2.61 (1.26-5.41)	0.010
Infection or abscess	41/49 (83.7)	57/101 (56.4)	3.96 (1.68-9.29)	<0.001
Inflammation	34/45 (75.6)	64/105 (61.0)	1.98 (0.90-4.34)	0.09
Graft loss	62/67 (92.5)	36/83 (43.4)	16.19 (5.90-44.42)	<0.001
Pain	23/25 (92.0)	75/125 (60.0)	7.67 (1.73-33.97)	0.002
Insufficient bone	12/13 (92.3)	86/137 (62.8)	7.12 (0.90-56.35)	0.03
Failure to resorb	19/23 (82.6)	79/127 (62.2)	2.89 (0.93-8.99)	0.09
Sinus involvement	9/11 (81.8)	89/139 (64.0)	2.53 (0.53-12.16)	0.33
Ridge or bone loss	15/19 (78.9)	83/131 (63.4)	2.17 (0.68-6.91)	0.21
Implant failure	25/33 (75.8)	73/117 (62.4)	1.88 (0.78-4.54)	0.21
Swelling or edema	20/27 (74.1)	78/123 (63.4)	1.65 (0.65-4.20)	0.37
Hypersensitivity	12/16 (75.0)	86/134 (64.2)	1.67 (0.51-5.48)	0.58
Premature resorption	14/24 (58.3)	84/126 (66.7)	0.70 (0.29-1.71)	0.49

TABLE 3: MAUDE reports (product code NPL) describing secondary surgical reintervention, by complication.

N = 150. For reports with (present) and without (absent) each complication, cells give the number of reports with secondary surgical intervention over the total number of reports in that group, with the percentage in parentheses. Fisher exact test was used for comparisons. Comparisons other than the first row were exploratory and not adjusted for multiple testing.

Discussion

In this analysis of 150 MAUDE reports for animal-derived resorbable barrier membranes, nearly two-thirds of reports described secondary surgical intervention, while only one-fourth described observation alone. Most reports were graded Clavien-Dindo 3a, meaning the event led to a surgical procedure without reported general anesthesia. Graft loss, dehiscence, and infection were the most frequent complications, and reports describing dehiscence or infection had higher odds of secondary surgical intervention than reports without those complications, supporting the hypothesis.

Comparisons with previous studies

The complication profile in these reports differs from those described for other dental devices in MAUDE. Reports for direct-to-consumer aligners frequently described bite problems, orofacial pain, and periodontal problems [10], and reports for mandibular repositioning appliances primarily involved allergic reactions or device breakage [11]. Sinus-related reports for endosseous implants were mostly descriptions of sinus membrane perforation [12]. In these studies, the events reported reflect how the device is used and how it can fail. Barrier membranes are placed within a healing surgical wound, and similarly, the reports in this study mainly described failures of healing: dehiscence, infection, and graft loss. An earlier review of dental device reports concluded that though MAUDE is one of the only available sources of adverse event information, it has substantial limitations as a safety surveillance tool [9]. The present study adds barrier membranes to the group of dental devices that have been examined in this way.

The proportions in these reports are much higher than complication rates from clinical studies. A meta-analysis of guided bone regeneration for ridge augmentation reported a 16.8% soft tissue complication rate, which included membrane exposure, dehiscence, and infection or abscess; these rates were comparable for resorbable (18.3%) and non-resorbable (17.6%) membranes [17]. In comparison, 41.3% of the reports analyzed in this study described dehiscence or exposure, 32.7% described infection or abscess, and 65.3% described reintervention. This difference is expected, as MAUDE cannot feasibly capture every adverse event related to a device, and reports are made when someone considers the event worth reporting [14]. Events that resolve without further treatment are less likely to be reported, so the dataset is weighted toward the severe end of the complication spectrum. The same pattern appears in Clavien-Dindo severity grading. In a previous cohort of 1,171 dental implants, 54.8% of complications were grade 1 and 28.5% were grade 3a [18], but most of the present reports were grade 3a (62.0%). These figures are offered as context only; differences in definitions, follow-up, and the absence of a denominator mean they cannot be compared quantitatively.

Resorbable collagen membranes are consistently described as safer than non-resorbable membranes. A 2025 meta-analysis of 11 studies with 1,003 patients found that absorbable membranes had a higher success rate, greater graft thickness, and fewer adverse reactions than non-absorbable membranes [19]. However, resorbability does not necessarily eliminate the risk of infection when a membrane is placed in the oral cavity. A 2023 review found that exposed membranes were colonized by bacteria across material types, including collagen, and that colonization reduced integration and bone gain in every case [20]. Additionally, the effect of exposure on regeneration has been well-described in the literature, including a meta-analysis that found six times greater bone formation when a membrane did not become exposed [21].

In this dataset, graft loss, dehiscence, and infection tended to appear together in the same reports. Each complication was also associated with secondary surgical intervention when compared individually. One possible explanation for this clustering is that an exposed membrane becomes colonized and then fails to protect the graft beneath it. Reports describing dehiscence or infection were more likely to include secondary surgical intervention (75.9% vs. 50.8%; OR 3.04), and the association held when each was considered separately, with overlapping confidence intervals (OR 2.61 for dehiscence, 3.96 for infection). The reports cannot test the proposed sequence, since timing was missing from most of them and each report is a single narrative written after the fact. The graft-loss association needs particular caution. Graft loss showed the strongest association of any complication (OR 16.19), and 45 of the 67 graft-loss reports also described dehiscence or infection, but graft loss is often discovered during removal or repeat grafting, which are themselves counted as reintervention. The odds ratio likely reflects how the two are documented as much as any predictive relationship. The proposed sequence also parallels how exposure is managed clinically. Prior work describes management ranging from topical antiseptics to removal of the membrane or graft [22], and treatment that may include medication or surgical re-entry to remove exposed membranes or contaminated grafts [23]. The reports in this study appear to represent cases at the surgical end of that range.

Properties of the membrane itself may also contribute to these reports. Premature resorption was described in 24 reports (16.0%) and failure to resorb in 23 (15.3%). Collagen membranes can differ in tissue source and cross-linking, which affect their usable lifetime [4]. Cross-linking slows degradation, but in a randomized study of 52 patients, cross-linked membranes were exposed more often than non-cross-linked membranes (50% vs. 23.1%), and neither type resisted degradation in the oral cavity [24]. In a multicenter randomized trial, premature exposure of a cross-linked membrane was associated with inflammation of the adjacent soft tissue, and the authors suggested that cross-linking may impair soft tissue healing after exposure [25]. A systematic review reported an exposure rate approximately 30% higher with cross-linked than with non-cross-linked membranes [26]. The product named most often in the present reports (CopiOs, 44.0% of reports) is a bovine-derived pericardium membrane. Its share of reports likely reflects how widely it is used and how its manufacturer reports, and says nothing about its safety relative to other products. In a canine model, it showed no adverse immune response and bone regeneration similar to a porcine-derived membrane after 16 weeks [27]. Unfortunately, MAUDE reports rarely describe a membrane's cross-linking status and do not provide the total number of membranes used, so comparisons of complication rates between products are less fruitful.

The animal origin of these membranes raises a separate concern. Two reports in this dataset raised concern about disease transmission from the membrane. A systematic review of bovine-derived bone substitutes concluded that these materials may carry a risk of prion transmission and found no studies evaluating whether the manufacturing processes used for bovine bone inactivate prions [28]. Two reports cannot

establish any risk, but they are consistent with existing concerns in the dental literature.

The missing information within the reports is indicative of the quality of adverse event reporting systems. The jaw affected was not stated in 63% of reports, the indication for placement in 35%, and the timing of the event in 71%. Reviewers agreed closely on concrete information, such as whether the membrane was exposed or removed, and agreed less well on variables requiring more interpretation, such as device attribution, resolution status, regenerative outcome, and report informativeness. Device attribution (Fleiss kappa 0.55) and prior procedures (0.49) were among the least reliable fields. Reporting volume in MAUDE has also changed with regulatory updates, including electronic reporting in 2015 and summary malfunction reporting in 2018 [29], which could explain some of the year-to-year variation, though we did not test this. MAUDE event descriptions are not structured to capture patient or surgical risk factors, even though these are crucial to interpreting complication risk. Smoking and immediate implant placement are risk factors for dehiscence [18,22]. Structured fields capturing the surgical site, the time since placement, the intervention performed, and basic risk factors such as smoking status would make future reports considerably more useful.

Clinical implications

Overall, two clinical observations follow from the patterns identified in this study. First, these reports are consistent with what failed conservative management can look like in practice: dehiscence, infection, and graft loss tend to occur together, and together they are associated with further surgical intervention. Second, the principles commonly cited for effective bone regeneration, including primary wound closure [30], directly address wound dehiscence. This is consistent with the perspective that soft tissue management is central to preventing these complications [17]. The reports cannot establish when exactly escalation from conservative care should occur, and prospective data on exposed resorbable membranes would be needed to answer that question more definitively.

Limitations

This study has several limitations, some of which are inherent to MAUDE. Reporting is voluntary for clinicians and patients, and reports are not independently verified. The total number of membranes used is unknown, so the incidence of complications or interventions cannot be estimated. This limitation applies to every MAUDE-based study [9,14]. Product code NPL covers animal-derived membranes only, so these findings cannot be compared directly with synthetic or non-resorbable membranes. Event descriptions were often brief, and several variables, including the primary adverse event, the indication, and the associated biomaterial, were grouped into categories after coding was completed. Secondary comparisons were exploratory and were not corrected for multiple testing. Finally, reports were unevenly distributed across manufacturers, with Tutogen or RTI and Collagen Matrix together accounting for 122 of 150 reports. Comparisons were not adjusted by manufacturer, and differences in how manufacturers report events could affect the analysis. Reports may not be fully independent; more than one report could concern the same facility or manufacturer, which would make confidence intervals narrower than they should be. High inter-rater agreement shows the coding was reproducible, but not that the coded categories accurately capture what happened clinically. MAUDE provides no comparison group and no follow-up, and patient and surgical risk factors such as smoking were rarely reported, so the associations could not be adjusted for them. Source species is largely confounded with manufacturer, so differences between bovine and porcine membranes cannot be separated from differences in manufacturer reporting.

Conclusions

Adverse event reports for animal-derived resorbable membranes in MAUDE most often describe graft loss, dehiscence, and infection, and close to two-thirds describe a second surgery. Reports mentioning dehiscence or infection describe reintervention more often than reports without either. These are selected, unverified reports with no denominator, so they show the severe events represented in the database rather than how often complications happen in practice. Within that limit, exposure, infection, and graft loss tend to show up together in the reports that end in reoperation.

Appendices

Appendix 1

Variable	Definition
Anatomic site	Jaw: maxilla, mandible, both, or not stated
	Region: anterior, posterior, both, or not stated
	Tooth numbers were used to derive jaw/region when reported
Main adverse event	Primary adverse event per report
	Closed list of categories for grouping: wound dehiscence, infection, graft failure or premature resorption, implant failure, hypersensitivity, pain/swelling/hematoma, neurosensory disturbance, disease-transmission concern, soft-tissue/recession
Complications	Independent variables, coded present/absent
	Dehiscence; infection; inflammation; premature resorption; failure to resorb; graft loss; insufficient bone; ridge loss; implant failure; hypersensitivity; pain; swelling or edema; neurosensory disturbance; sinus involvement
Interventions	Independent variables, coded present/absent
	Observation only; antibiotics; other medication; membrane removal; graft material removal; implant removal; surgical revision; repeat grafting; tooth extraction
Timing	Time of the event relative to membrane placement, in days
Prior procedures	Prior procedures at the site
Secondary procedures	Secondary procedures defined as re-grafting or re-treatment of the same site
Indication	Reason the membrane was placed
Concomitant biomaterial	Associated biomaterial present in the surgical site
Device attribution	Probable, possible, or unlikely
	Based on whether a device mechanism was described, an alternative cause was documented, or other biomaterials were present in the site
Regenerative outcome	Outcome of the regenerative procedure
Resolution status	Whether the event was resolved at last contact
Report informativeness	Whether the event description held enough clinical detail for analysis
Severity	Clavien-Dindo grade [15]
	1: any deviation from the normal postoperative course without antibiotics or surgical treatment
	2: deviation requiring antibiotics
	3: requiring surgical, endoscopic, or radiological intervention (3a, not under general anesthesia; 3b, under general anesthesia)
	4: life-threatening complication requiring intensive care (4a, single organ dysfunction; 4b, multiorgan dysfunction)
	5: death
Primary outcome	Secondary surgical reintervention
	Membrane removal, graft material removal, implant removal, surgical revision, repeat grafting, or tooth extraction

TABLE 4: Variables and coding definitions.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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