Received May 5, 2023, accepted October 3, 2023, date of publication November 28, 2023

An Analysis of Adverse Event Reports in FDA's MAUDE Database

By Spilios Zisimopoulos, Nicolas Pallikarakis

Institute of Biomedical Technology (INBIT), Greece

ABSTRACT

Background and Objectives: Medical devices (MDs) are pivotal in the modern healthcare environment. Adverse events are an expected part of an MD's lifecycle. Various vigilance systems have been established worldwide to prevent such events' recurrence. The Manufacturer and User facility Device Experience (MAUDE) database of the US Food and Drug Administration (FDA) is a publicly accessible database that contains data on medical device reports (MDRs) submitted to FDA since 1991. This study aims to examine the evolution of MD adverse event reports and analyze several characteristic parameters as they evolved during the last three decades.

Material and Methods: An analysis of MAUDE data was performed to examine the outcomes and device characteristics of adverse event reports from 1991 up to 11/2022. These outcomes included the event type, remedial action, report source, reporter occupation and device evaluation by manufacturer. Specific MD groups were analyzed separately to examine their effect on the event outcomes. Segregated files of the database that contain different types of information on adverse event reports were combined to investigate the various aspects of these reports.

Results: Event outcomes are presented as annual histograms. An overall of about 15 million reports have been submitted to MAUDE during the 30 years examined with more than 2.5 million of them during the first 10 months of 2022. This number is growing at an increasing rate. Most of the events (63.5%) have resulted in simple device malfunctions without serious implications to the patient. Depending on the device type, however, the health risks may be higher (98.4% injuries from specific dental implants and 3.2% deaths from implantable defibrillators). About 20% of the reports have led to recalls or corrective actions. Most of the reports (96%) are submitted by manufacturers, and over 70% of the devices returned to them are evaluated, following the requirements of FDA 21 CFR, 803. Finally, the average device age was found to be 5.4 years, with an increasing tendency observed over the years, while 43% of the events that occur are associated with devices during their first year of operation.

Conclusion: A medical device adverse event reporting system is a critical component of safety in the use of medical technology in modern healthcare. The information available in MAUDE and its use continues to grow at an accelerated rate and allows critical improvements of MDs, especially in terms of risk prevention, as it gives perception about their safety issues. FDA has taken various steps to encourage and facilitate adverse event reporting and make the data available to the public.

Keywords – *MAUDE, FDA, Adverse Events Reports, Medical Devices, Vigilance.*

INTRODUCTION

In today's world, medical devices (MDs) have become a fundamental component of modern healthcare systems. MDs range from simple face masks and syringes to complex implantable devices and medical imaging systems and are used to diagnose, treat, and manage various medical conditions. However, like any other medical procedure, MDs are not without risks. Adverse events can occur due to various factors like device malfunction or misuse, resulting in serious patient harm. To prevent and mitigate these risks, it is essential to have a robust MD vigilance system involving Health Competent Authorities[1] and MD manufacturers that investigate and eventually perform necessary remedial actions following adverse events with MDs. In most developed countries MD vigilance systems have been implemented for more than 30 years, aiming to reduce the likelihood of similar adverse events happening again in another place and time. The cornerstone of the MD vigilance systems is adverse event reporting.

A medical device adverse event reporting system is a mechanism that enables healthcare facilities, patients, and manufacturers to report incidents associated with MDs. These systems provide standardized processes for reporting such events and allow the collecting and analysis of information related to MD safety. Such a system is of the utmost importance, as it is critical in ensuring patient safety and improving healthcare quality.

One of the primary benefits of an MD adverse event reporting system is that it enables healthcare providers and manufacturers to identify and address safety concerns related to medical devices. The report of adverse events by healthcare facilities helps manufacturers gain insight into the performance and safety of their devices. The information provided can then be used to identify design flaws, manufacturing defects, software problems, or other issues that may contribute to adverse events and take appropriate action to address these issues, such as modifying the device design or implementing new quality control processes. On the other hand, when information about the risks associated with specific devices is publically available, healthcare providers can investigate whether an event they faced has also been manifested in a different facility, and, in that case, follow the instructions that the manufacturer has proposed.

A medical device adverse event reporting system also enables better communication between healthcare providers, regulatory agencies, and competent authorities. When adverse events are reported, the authorities can use this information to take appropriate action when necessary. For example, if a particular device is associated with a high rate of adverse events, regulatory agencies may require additional testing or labeling changes from the manufacturer to improve safety.

Finally, a medical device adverse event reporting system can promote transparency and accountability in the healthcare industry.[(a)] By publicly making information about adverse events, the system can help hold manufacturers, distributors, and healthcare providers accountable for their actions. This can help with the trust-building process between patients and healthcare providers and ensure that the healthcare industry is held to the highest safety and quality standards.

The aim of this study is to examine the evolution of medical device adverse event reports, available at the Manufacturer and User facility Device Experience (MAUDE) database of the US Food and Drug Administration (FDA) and analyze several characteristic parameters of these reports as they evolved during the last three decades.

Adverse events reporting systems

There are several MDs adverse event reporting systems worldwide, aiming to address safety issues that arise from the use of medical devices. The reports can be generally made by manufacturers, healthcare professionals and volunteers.

FDA's MAUDE database, designed to collect reports of adverse events associated with MDs is the most well known, it is available to the public and can be accessed online, allowing the analysis of the available data.[2] MAUDE contains the reports submitted through the Medical Device Reporting (MDR) system, which are used by manufacturers,

[a] The Competent Authorities for Medical Devices (CAMD) facilitate implementing and enforcing the Regulations on medical devices and on In Vitro Diagnostic medical devices in the EU. https://health.ec.europa.eu/medical-devices-dialogue-between-interested-parties/overview_en#competent-authorities-for-medical-devices---camd

importers and users of MDs. The MDR system is a mandatory reporting system, and manufacturers must report any adverse event that involves their device.[3]

The European Databank on Medical Devices (EUDAMED) is maintained by the European Union (EU) and is designed to provide a living picture of the lifecycle of MDs, including modules related to device registration, notified bodied and certificates among others. The database has been established in the 2000s according to the MDs Directives: 90/385/EEC for the Active Implantable Medical Devices (AIMD), 93/42/EEC (MD) for the Medical Devices and 98/79/EC for the In Vitro Diagnostics. The EU vigilance system is based on the MEDDEV 2.12/1 rev.8 series of guidelines of 2012[(b)] on Post-Market surveillance and Vigilance System adopted in 2019.[(c)] The EU's new 2017/745 and 2017/746 MDRs, reshaped the structure and use of EUDAMED to improve the safety and performance requirements of medical devices bearing a CE Mark.[4] However, access to EUDAMED is restricted only to Competent Authorities and partially to Notified Bodies for devices that are involved, and the information on MDs related incident reports is not yet available to other parties, despite the explicit reference in the regulations.

Various other adverse event reporting systems are being used at the national level. Some well known examples are the Australian Therapeutic Goods Administration (TGA) Adverse Event Reporting System,[5] Health Canada's Medical Device Adverse Event Reporting (MDAERS)[,6] UK's Medicines and Healthcare products Regulatory Agency (MHRA)[7] and Germany's Federal Institute for Drugs and Medical Devices (BfArM).[8] These systems are used to report or access adverse events associated with MDs and are open to healthcare professionals, patients and manufacturers, while they can also be accessed online. Many other countries have also similar systems in place, and many manufacturers have their own reporting systems for post-market surveillance purposes.

Relevant work using MAUDE

A search was performed in the PubMed database on papers published from 2000 to date, with the term *"MAUDE database"* included in the title or abstract of the paper (MAUDE database [Title/Abstract]). This was done to include only papers whose content was focused on the analysis of MAUDE's data, and the search yielded 303 results. Next, another query was performed, adding the terms "*MAUDE*" and "*FDA*" in the title or abstract of the journal papers (MAUDE database [Title/Abstract] OR (MAUDE[Title/Abstract] AND FDA [Title/Abstract])). The latter broader search was performed to find articles that may have been eluded from the initial query, while keeping their content mainly based on data from MAUDE and excluding ones with simple references and various irrelevant synonyms. The final search yielded 308 results up to 2022 (Figure 1), with 31 additional articles been published during the first quarter of 2023. Most of these studies analyze adverse events for specific medical device groups.[9] Recent years examples involve MDs like Injectable Fillers, Deep Brain Stimulators, middle ear prostheses, ossicular prostheses and catheters.[10–14] During the last years, a couple of studies analyzed MAUDE data taking into consideration the full spectrum of medical device groups.[15–17] However, they were focused on limited aspects of the available data, like reporting source and reporter occupation, and they were published before the boom of reports submitted to MAUDE after 2019 (Figure 2).

The number of studies mining the information used from MAUDE are constantly increasing during the last ten years and provide very valuable insights on safety

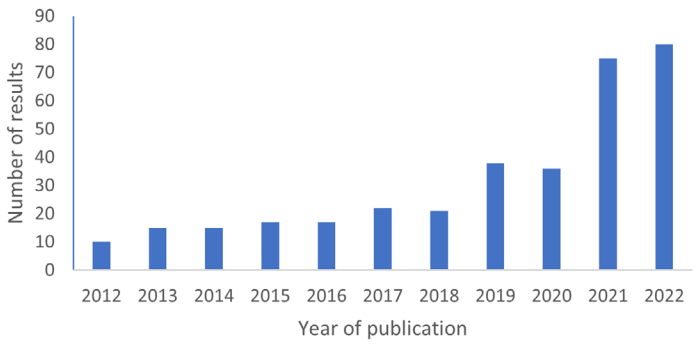

FIGURE 1. PubMed articles with relevant MAUDE terms in title/abstract.

[b] https://ec.europa.eu/docsroom/documents/32305
[c] ttps://ec.europa.eu/docsroom/documents/32305

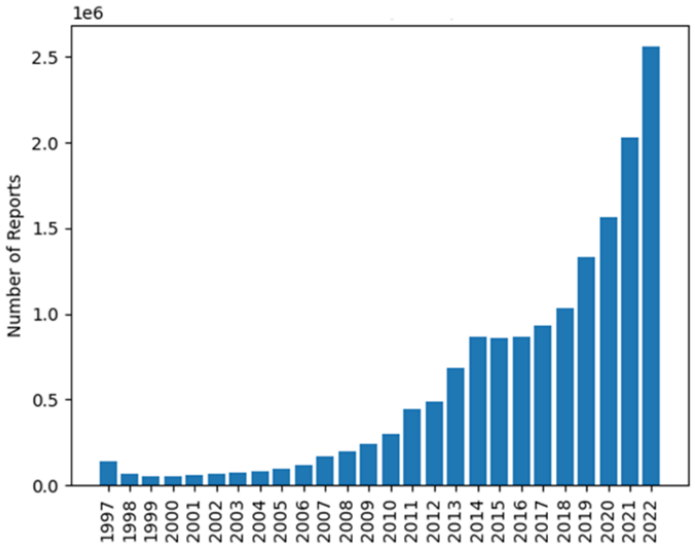

FIGURE 2. Annual MAUDE adverse event reports. Data until 4/11/2022

issues concerning MDs. This trend was reported in a study by P. Malataras and N. Pallikarakis, regarding the use of MAUDE's data in research between the years 2005 and 2014,[9] where a linear increase of papers published each year was showcased. To add into that, a sharp increase of publications has been observed in the last couple of years, highlighting the developing interest in utilizing FDA's MAUDE data as shown in Figure 2.

MATERIALS & METHODS

The MAUDE database was used for the analysis performed in this study. Of all the afore-mentioned adverse event report databases, MAUDE is the best structured and most complete, with data ranging from 1991 to date. Furthermore, it can be easily accessed and has been used in other studies in the past. Data processing and analysis was performed using the Jupyter Notebook web application, along with the Python Data Analysis (pandas) and Numerical Python (NumPy) Libraries.

Data acquisition and pre-processing

All data used in this study are publicly available on FDA's MAUDE page.[2] Data available in MAUDE span from 1991 up to 2022 (user facility reports since 1991, distributor and voluntary reports since 1993 and manufacturer reports since 1996). For the remainder of this work, data referring to the year 1997 will consist of events reported between 1991 up to 1997, according to MAUDE's "*foidevthru1997*" file. Data regarding 2022 contains reports that were available on MAUDE until 4/11/2022, due to the time of research. For the remainder of the work, data up to 4/11/2022 will be referred to as data for the year 2022. Device information associated with an event was taken from the available "*foidevxxxx*" and "*devicexxxx*" files, were xxxx annotates the year. Information about the adverse event was found in the files named "mdrfoithru2021", which contains data from inception up to 2021 and "*mdrfoi*", which contains data of the present year (i.e., 2022). The device and mdrfoi files were joined together using the "*MDR_REPORT_KEY*" field as primary key.

Data pre-processing

A total mdrfoi dataframe was created by merging the "mdrfoithru2021" and "mdrfoi" files. After data cleaning by deleting rows with wrong field format, wrong delimiter, unreadable characters, duplicate key values etc. 15,387,348 lines of data remained. The same process was carried out for all "devicexxxx" files, and a total device dataframe was created containing 15,386,069 lines of data. After merging these mdrfoi and device dataframes, using the MDR report key value as primary key, a final dataframe with 15,343,314 lines of data was created, upon which the analysis of adverse event reports was carried out.

Event Outcomes

All adverse event reports available on MAUDE were analyzed under the scope of various event outcomes. Using the various outcome codes presented below as queries, the data are organized and presented as histograms of number of reports for each year until 2022. Outcomes included whether the device was evaluated by the manufacturer, event type, remedial action, problem code, and device age (year of report minus year of manufacture).

Event Type

The Event Type (H1 field on the 3500A form) is used to describe the impact of adverse events. It is only considered relevant by the FDA when the reporter of the event is a manufacturer and makes use of the following codes:

D = Death, {IN, IL, IJ} = Injury, M = Malfunction, O = Other, {Blank}= No answer provided. Only one code may be used for each event. A malfunction refers to an adverse event where the device demonstrated an unexpected behavior, without any further implications to the patient or the user. One should keep in mind that the submission of an MDR itself is not evidence that the device caused or contributed to the adverse outcome or event. Moreover, the Event Type field is not available on the form for voluntary reporting of adverse events.

Remedial Actions

A Remedial Action (H7 field on the 3500A form) corresponds to any actions outside the scope of routine maintenance of a device, when necessary to prevent an adverse event from recurring that could pose safety issues. The following codes and their interpretations are being used by the MAUDE database at this point: RC = Recall, RP = Repair, RL = Replace, RB = Relabeling, OT = Other, NO = Notification, IN = Inspection, PM = Patient Monitoring, MA = Modification/Adjustment, {Blank}= Invalid Data/ NaN. According to 21 CFR Part 7, recall means a firm's removal or correction of a marketed product that the FDA considers to be in violation of the laws it administers and against which the agency would initiate legal action, e.g., seizure.[(d)] A recall can be initiated by the manufacturer, the FDA, or both, and may be required when a device poses a significant risk of harm to patients or users. Replacement, on the other hand, is the process of providing a new, corrected or modified device to replace a defective or unsafe device that has already been distributed to patients or healthcare facilities. A replacement may be initiated by the manufacturer as a proactive measure to address a safety issue or may be required by the FDA as part of a recall. In some cases, the manufacturer may offer a replacement device to patients as a voluntary corrective action, even if the device has not been recalled by the FDA.

Apart from the removal of the unsafe device from the market and the notification, healthcare providers and patients may be requested to return the device for corrective action to address the safety issue. Correction means repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product without its physical removal to some other location. As a result, an adverse event report may be associated with one or more remedial action codes, for example RC, RP.

Report Source

The Reporting Source refers to the official submitter of the report to FDA. The available codes are P= Voluntary report, U = User Facility report, D = Distributor report and M = Manufacturer report. The initial reporter of the event can be any person. For example, an affected patient may choose to submit the report himself (using the 3500 form), which will then be classified as voluntary report, or send it to the manufacturer who is obligated to submit it (using the 3500A form). In the latter case, the code M will be used. Track is also kept of the initial reporter.

Initial Reporter Occupation

Regardless of the formal submitter of an event to FDA (i.e., a user or a manufacturer), the occupation of the initial reporter is recorded separately (E3 field on the 3500A form). The classification codes for the initial reporter occupation consist of three digits and can be found on the MAUDE database site.[(e)] The available occupations range from physician and patient to biomedical engineer or attorney.

Device Evaluated by Manufacturer

According to CFR 21, 803, §50, manufacturers are responsible for conducting an investigation of each event and evaluating the cause of the event. In case the device was returned to them and information in a report is not complete, they must provide an explanation on why, as well as the steps taken to obtain it. To this end, the *"Device Evaluated By Manufacturer"* (H3 field on the 3500A form) is being used. The acceptable values are: Y = Yes, N = No, R = Device not returned to manufacturer and {BLANK}= No answer provided. These values are mutually exclusive.

[d] https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-7

[e] https://www.fda.gov/medical-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities/about-manufacturer-and-user-facility-device-experience-maude

Device Age

The associated device age for the adverse events was calculated by subtracting the year of the device manufacture date (H4 field on the 3500A form), as filled in by the manufacturer of the device, from the year in which the report was submitted to the FDA.

Device Groups

Event outcomes such as Event Type and Remedial Action were analyzed separately for various device groups. This was done to investigate the differences an adverse event may have regarding the involved device. The MD groups chosen were ones with a notable percentage of each year's total reports and are presented in Table 1.

TABLE 1. Medical Device Groups with Frequently Presented Adverse Events

FDA Group Code	Group Name
CFR	HEXOKINASE, GLUCOSE
LFR	GLUCOSE DEHYDROGENASE, GLUCOSE
NBW	SYSTEM, TEST, BLOOD GLUCOSE, OVER THE COUNTER
MDS	SENSOR, GLUCOSE, INVASIVE
OYC	PUMP, INFUSION, INSULIN, TO BE USED WITH INVASIVE GLUCOSE SENSOR
PQF	SENSOR, GLUCOSE, INVASIVE, NON-ADJUNCTIVE
LWS	IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (NON-CRT)
DZE	IMPLANT, ENDOSSEOUS, ROOT-FORM
FRN	PUMP, INFUSION
KWA	PROSTHESIS, HIP, SEMI-CONSTRAINED (METAL UNCEMENTED ACETABULAR COMPONENT)

RESULTS

Number of Reports

The histogram of the annual number of submitted reports to FDA from 1997 to 2022 is presented in Figure 1. About 15 million reports have been submitted to MAUDE until the end of 2022 and over 2.5 million of them occurred during the last year. A big increase in the number of reports can be observed over the last few years.

Event Types

Table 2 presents the distribution of event types for 6 different examples of prominent MD groups, as well as all the average values for all available FDA Device groups that exist in MAUDE. From the grand total of the reports in Table 2, we can see that most of the events result in simple device malfunction, without further implications to the patient (63.5%). About 1% of the total reported events is associated with patient death.

TABLE 2. Event Type Distribution for Various MD Groups

	Event type			
	Malfunction	**Injury**	**Death**	**Other - n/a**
Glucose monitors ['MDS', 'OYC', 'PQF']	89.1	10.7	0.2	≈ 0.0
Glucose test ['CFR', 'LFR', 'NBW']	90.2	9.0	≈ 0.0	0.8
Pump, Infusion	98.3	1.4	≈ 0.1	≈ 0.2
Implantable Cardioverter Defibrillator (Non-CRT)	36.3	60.0	3.2	≈ 0.5
Prosthesis, Hip, Semi-Constrained (Metal Uncemented Acetabular Component)	2.7	95.0	0.3	≈ 0.0
Implant, Endosseous, Root-Form	1.6	98.4	≈ 0.0	≈ 0.0
Average for all Device Groups	**63.5**	**34.3**	**1.2**	**1.0**

The average numbers derived from all the available device types can vary significantly across different device groups. As observed in the trend (Figure 3), there is a steady decline in the ratio of adverse events that result in deaths, from 2.5% up until 1997 to 0.3% in 2022 (R^2 = 0.66). Similarly, events with outcome categorized as "Other" or without applicable information (n/a) decreased from 7.5% in 1997 to almost 0% in 2022 (R^2 = 0.85), showing

the increased completeness of the information provided to the FDA over the years. Subsequently, more incidents are manifested as device malfunctions, with 73% reported as such in 2022, compared to only 40% up to 1997 (R^2 = 38%). Although injury reports dropped from 49.2% in the period 1991 - 1997 to 26.6% in 2022, their fluctuations seem to be independent of the time ($R^2 \approx 0$).

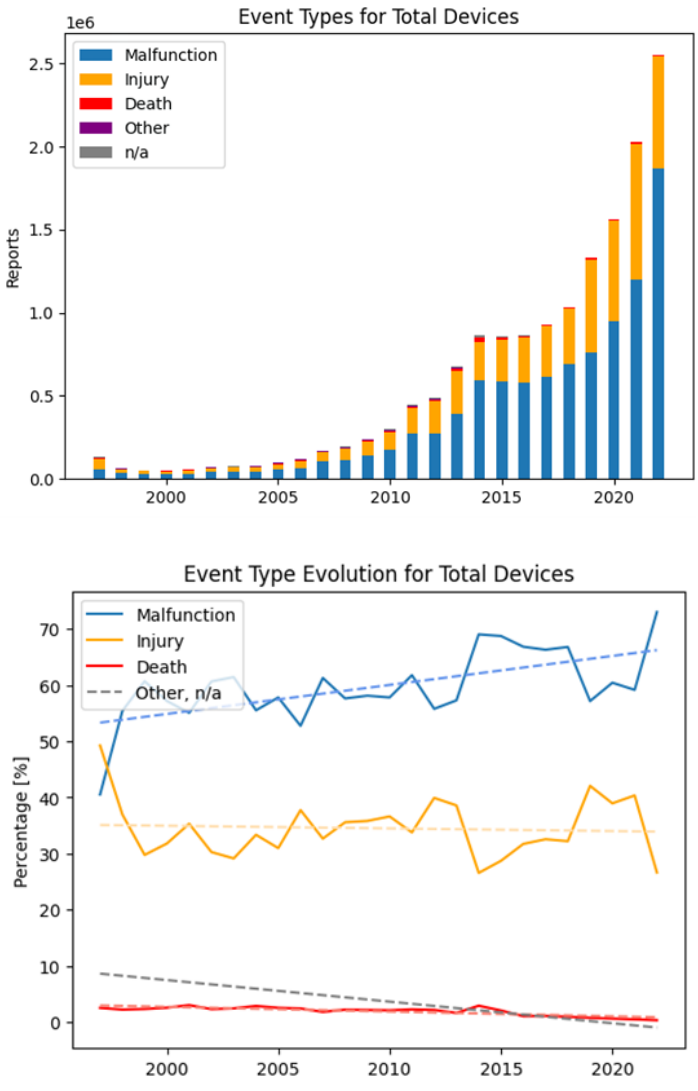

FIGURE 3. Adverse Event Types. Number of reports(top) and percentage evolution(bottom).

According to Table 2, more than 90% of events related to glucose test groups have been about device malfunctions, with the rest (about 10%) being associated with injuries. In contrast, about 95% of the reported incidents of Metal Uncemented Acetabular Component hip prostheses (KWA) resulted in patient injury. Similarly with implantable defibrillators, the majority of dental implant event types were categorized as injuries (98.4%). Implantable defibrillators adverse events have the highest probability of death (3.2%) compared to the rest of the examined device groups, due to their crucial role in physiological heart function. Finally, most of the reports regarding infusion pumps (over 98%) were about simple device malfunctions.

Figure 4 shows that most reports have no remedial action connected with them (80%). Nevertheless, for the remaining 20%, where information is available, the most common action happens to be a recall, which is associated with three-quarters of adverse events (Table 3). Repair of the affected devices was a common action during 2011, 2013 and 2014 and may depend on the types of affected devices. Actions categorized as "Other" were more common until the mid '10s, while being the most common remedial action during the older years. Recently, the "Other" category stopped being used so frequently (7% of total reports).

Remedial Actions

Different MD groups are associated with different remedial actions (Table 3). For example, reports involving continuous glucose monitoring devices and infusion pumps resulted in a recall action by the manufacturer or FDA 9 out of 10 times. On the other hand, dental implants resulted in almost no recalls, and the main action taken by the manufacturers was either an inspection (69.7%) or replacement of the implant (26.0%). Finally, about 1 out of 10 reports about glucose test device groups led to a recall, as devices like test strips are not so crucial to patient safety compared to previously referred devices. Replacement (38.0%), Notification (28.6%) and Other (23.3%) were the most frequent remedial actions for dealing with issues such as incorrect measurements.

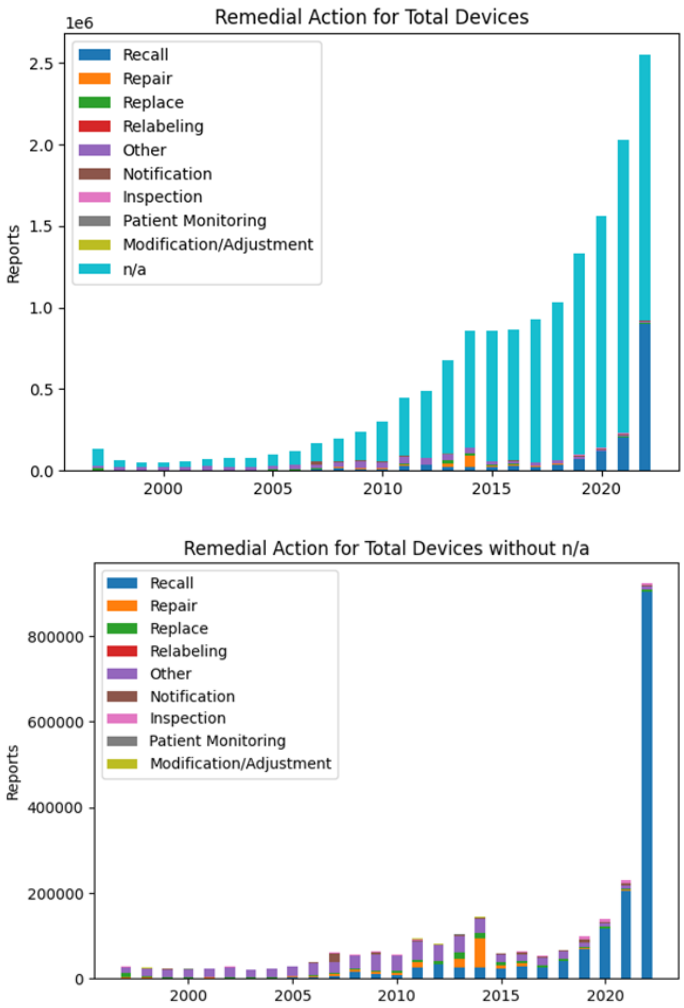

FIGURE 4. Adverse event remedial actions.

Report Source

The majority of the total reports (96%) were filed by the device manufacturers, as shown in Figure 5. This concerns the stricter requirements about adverse event reporting imposed on manufacturers. In the last 4 years there has been an increase in distributor reports. During these years, dental implants and implantable defibrillators were the main types of devices reported.

Initial Reporter Occupation

Figure 6 presents the occupation of the initial adverse event reporter. The initial reporter may be different than the one that submits the final report to FDA, like in the case when a user of a medical device notifies an event to its manufacturer, who is then obligated to file an official report to the FDA. Physicians and other health care professionals have a constant rate of reporting adverse events. In the years 2012 and 2013, a considerable number of events were reported by attorneys. This was the period of lawsuits filed against metal-on-metal hip prosthetics manufacturers.[18,19]

Between 2013 and 2018 about 15% of reports (peaking at 21% in 2016) were made by the patients themselves. During this period, insulin pumps and glucose sensor events were predominant, so it makes sense that home users initially made a lot of the reports. An increase in the percentage of reports initially submitted by dentists can be observed after 2019. Deeper analysis showed

TABLE 3. Adverse Event Remedial Action Distribution for Various MD Groupss

	Remedial Action (%)								
	Recall	**Repair**	**Replace**	**Relabeling**	**Other**	**Notification**	**Inspection**	**Patient Monitoring**	**Modification/ Adjustment**
Glucose monitoring ['MDS', 'OYC', 'PQF']	93.58	0.01	4.27	0.01	0.12	1.99	0.01	0.01	≈ 0.0
Glucose test ['CFR', 'LFR', 'NBW']	9.55	0.10	38.03	0.02	23.27	28.60	0.02	≈ 0.0	0.40
Pump, Infusion	89.86	9.53	0.05	≈ 0.0	0.42	0.10	0.02	≈ 0.0	0.03
Implant, Endosseous, Root-Form	0.36	0.03	26.04	0.02	3.76	0.06	69.66	0.06	0.01
Average for all Device Groups	**74.0**	**7.0**	**5.5**	**≈0.1**	**7.0**	**3.6**	**2.1**	**0.2**	**0.5**

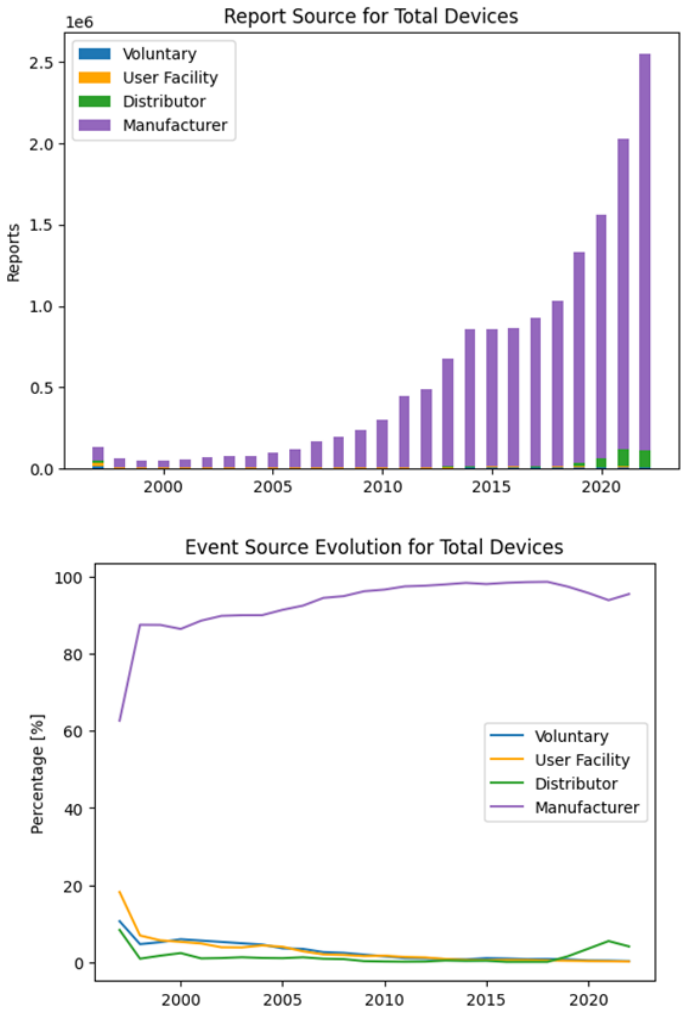

FIGURE 5. Adverse events report source.

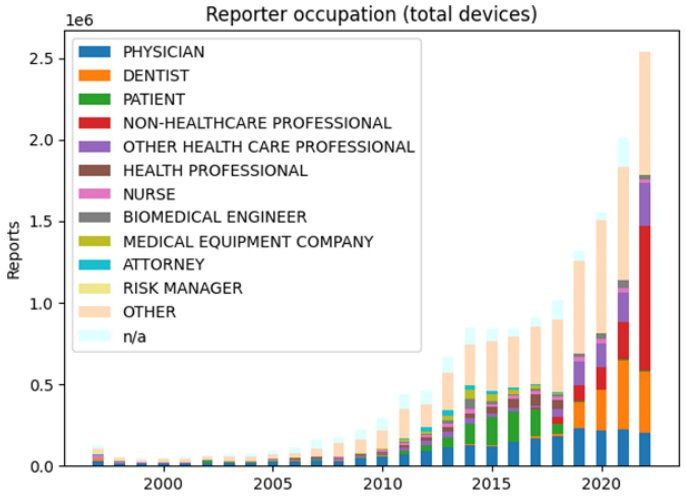

FIGURE 6. Adverse event initial reporter occupation.

that many of the events were caused by dental implants (peaking at 24% of the total reports in 2021) during the last 4 years. Finally, more events have been reported in the previous five years, especially in 2022 (35%), by other non-healthcare professionals than in the past.

Device Evaluated by Manufacturer

Figure 7 shows the status of reports as far as the device evaluation by the manufacturer is concerned. More than half of the devices reported (52.3%) are sent to the manufacturer, and most of them are evaluated (70.8% of sent devices). 2022 was an exception, with 55% of the devices sent to the manufacturer not being evaluated.

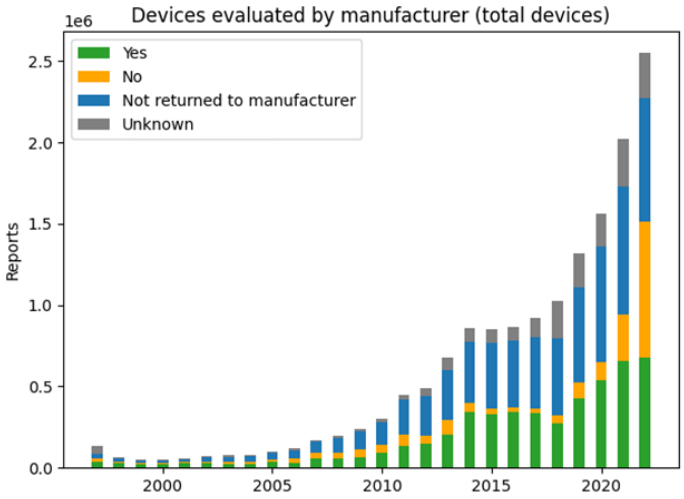

FIGURE 7. Device evaluation by manufacturers.

Device Age

The mean age of the devices involved in all adverse events of the MAUDE database is 5.4 years. However, this result is strongly influenced by the impact of the last couple of years' reports, as shown in Figure 8. Up until 2019, the average device age was 2.8 years. The seeming rise in the device's age might be related to the reported devices' types. Most of the events (43%) are associated with devices during their first year of operation.

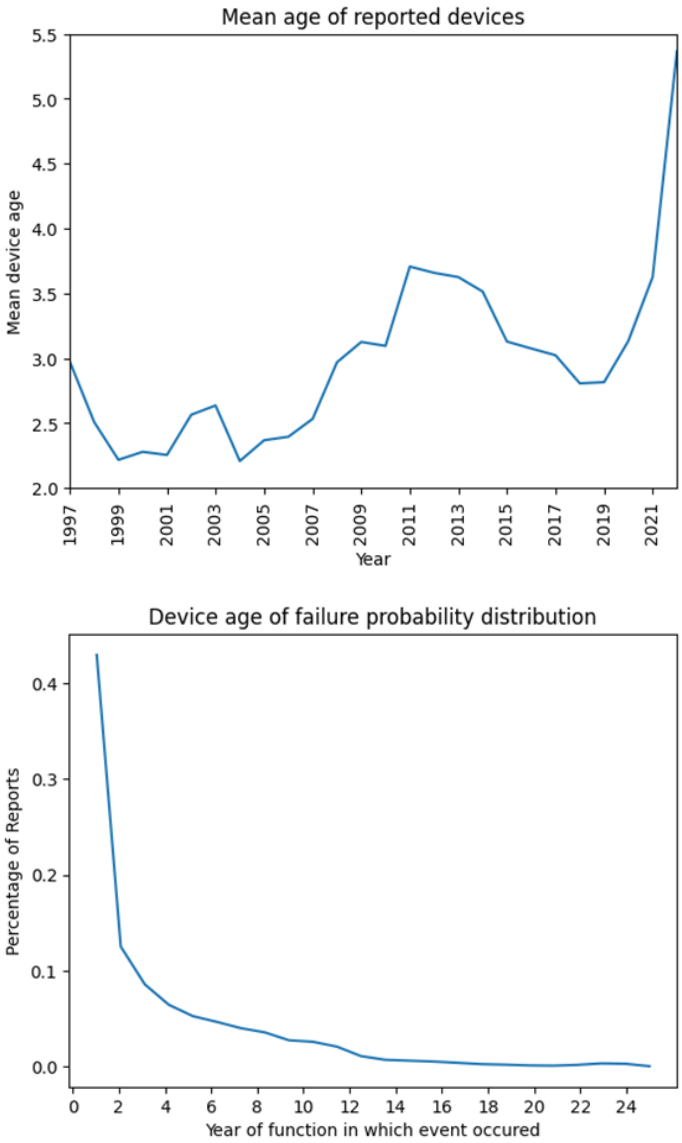

FIGURE 8. Device age distribution. Annual mean age of reported devices (top) and Total device age histogram (bottom).

DISCUSSION

There has been an obvious increase in the number of reports over the last years (see Figure 1), which can be attributed to several factors. One reason is the increased awareness and reporting of adverse events by healthcare professionals and patients due to improved access to information and reporting systems. Another reason is the growing number and complexity of MDs, which increases the likelihood of adverse events. In addition, the FDA has expanded the types of adverse events that must be reported by manufacturers and healthcare facilities, which has led to an increase in the number of reports submitted to MAUDE. Other changes included updated reporting requirements for specific devices and improved clarity on using the FDA Forms 3500/ 3500A for reporting. These requirements are outlined in the Code of Federal Regulations (CFR) Title 21, Part 803,(f) which establishes the mandatory medical device reporting criteria. This Rule was published in 2014 and implemented in 2015. Under its requirements, manufacturers and importers of MDs are required to report to the FDA any serious injuries or deaths associated with their devices within 30 calendar days of becoming aware of the incident. Additionally, manufacturers must report any malfunctions that could result in a serious injury or death within 5 workdays of becoming aware of the issue. Moreover, healthcare facilities, such as hospitals, nursing homes, and outpatient clinics, must report certain adverse events related to MDs to the FDA within 10 days. These events include incidents that result in serious injury or death or require intervention to prevent serious injury or death. Finally, in 2014, the FDA published a final rule on Electronic Medical Device Reporting (eMDR), effective from 2015, that requires manufacturers and importers to submit MDRs to the FDA in an electronic format that the FDA can process, review, and archive(20). Last but not least, in the previous two decades, there has been observed an increasing number of MDs that have received a 510(k) clearance compared to a premarket approval (PMA). Safety issues are raised as the clearance provision pathway does not require clinical trials and is less rigorous than the PMA process (21,22).

Considering the number of total reports in MAUDE and the death event type percentage of these reports presented in Table 2, it means that more than 180,000 adverse events are historically related to patient death. However, this number can be used only as an approximation due to the limitations of the database (i.e., multiple reports on the same incident, underreporting, incomplete

[f] https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803. Medical Device Reporting: Electronic Submission Requirements. A Rule by the Health and Human Services Department, and the Food and Drug Administration. Published 2014. Effective after 2015.

information, etc.). Although the decrease in deaths and increase in malfunctions reported in Figure 3, although possible, does not explicitly indicate an increase in device safety, as it could also mean the intensified reporting of less severe adverse events compared to the past years.

Some intuition can be gained about the event types for each examined device group. Glucose testing devices, such as test strips, are associated mainly with a less serious malfunction (see Table 2). An example of such a malfunction could be wrong glucose test results. Although not crucial as an adverse event itself, such a malfunction could pose more serious consequences for the patient in the long term. This may be why these devices have a very high rate of recalls (Table 3). In contrast to glucose testing devices, most of the reported incidents of hip prostheses (KWA) resulted in serious patient injury, with a probability of patients having to undergo revision surgery. Patient injury was almost universal (98.4%) for dental implant adverse events. A factor that may be of importance is the absence of implant dentistry from the recognized dental specialties of the American Dental Association.(g) Although the FDA monitors and regulates MDs, it does not act toward healthcare practice regulations. The fact that implantable defibrillators adverse events showcase the highest probability of death (3.2%) compared to the rest of the examined device groups is expected, due to their crucial role in physiological heart function. Finally, the fact that almost all the reports regarding infusion pumps were about simple device malfunctions, without further serious implications to the patients, may indicate an increased awareness regarding adverse event reporting of crucial devices. However, it should be noted that infusion pumps malfunctions have a high potential for patient injury and must be treated as near-miss adverse events. These events are incidents that can potentially cause harm to a patient but are caught or mitigated before any actual harm occurs. Examples of reported infusion pump problems that could lead to such incidents include lack of warning when inappropriate data is entered or failure to generate audible alarms for critical problems such as an occlusion in the tubing.23 and adverse events are often avoided due to luck or vigilant healthcare professionals.

Remedial action codes were found to be often omitted from the adverse event reports. It is unclear whether this is because the event resulted in no action to be taken by the manufacturer or the information was not correctly updated in the database. As a silver lining, the rate of existing remedial actions has risen in the last year. Moreover, the "Other" category is used less frequently, which may indicate that the report form became more user friendly and awareness toward adverse event reporting has risen.

The fact that the device manufacturers have filed 96% of the reports, while the trend is continuously rising (Figure 5), is related to the stricter requirements imposed on manufacturers by CFR 21, 803. This is also the reason behind the high device evaluation percentage by the manufacturers (Figure 7). Adding to this, many users from facilities or homecare prefer to file a report to the manufacturer, who then submits it to FDA. This is the reason why the initial reporter occupation is analyzed separately. Data for 1997 consists of all data available from 1991 to that year. According to MAUDE, user facility reports have been submitted since 1991, distributor and voluntary reports since 1993 and manufacturer reports since 1996. For this reason, the report rates by manufacturers are quite low until 1996, compared to the next years.

According to CFR 21, 803, §50, manufacturers are responsible for conducting an investigation on each event and evaluating the cause of the event. If the device was returned to them and information in a report is incomplete, they must explain why and the steps taken to obtain it. This is why most devices returned to the manufacturer by the user facility or the distributors are evaluated (70.8% on average). The last year was an exception, and the reason could be further investigated.

Regarding the MAUDE database, several issues were discovered. First, there are some instances of unintuitive or straight up incorrect information on the use or description of the files. As an example, the "*deviceproblemcodes*" file should contain the MDR report keys with the corresponding device problem code, while the "*foidevproblem*" file should contain a list of device problem codes with their matching code description, according to the site's

g https://ncrdscb.ada.org/recognized-dental-specialties

description. However, the data contained in these files are interchanged. Additionally, "*mdrfoi*" file's description was not updated for the current year, at the time of this work. Though it contained data from 2023, it read "*MAUDE Base records received for 2022*". The mdrfoithruxxxx file also contains a vast amount of information of 5 GB, making it difficult for casual users to access it. Splitting it as is the case with device files would facilitate further database usage.

Other shortcomings of MAUDE derive from adverse event reporting system issues. A common problem for all vigilance systems worldwide is underreporting adverse events. Though events seem to be reported more frequently during the last years, it is still plausible that more adverse events occur than those finally reported to the FDA. The rate of medical device adverse events underreporting is difficult to determine, as the number of incidents is unknown accurately. Non-reporting can be attributed to many factors, such as fear of blame, lack of time, complexity of the reporting system, or even perceived ineffectiveness. Adding to this, in cases of human error, underreporting is expected to be even more prevalent.24,25

Other issues may be the symptoms of underutilizing the MDR system's potential. For example, although more than one remedial action code can be assigned to an adverse event, in practice reports in MAUDE, use a single code. As a result, when an event is marked with a corrective action (i.e. replacement of the device), the recall code is omitted and vice versa. Therefore, it becomes unclear whether the corrective action was part of a recall, or a voluntary preventive manufacturer action.

Finally, it is important to note that an increase in adverse event reports does not necessarily mean that the number of adverse events has increased, but rather that reporting systems have become more effective in capturing and documenting these events.

CONCLUSIONS

It is obvious that the FDA encourages reporting adverse events and MAUDE plays an essential role in identifying potential safety issues and facilitating corrective actions that protect public health. It also provides an essential source of data for review studies in this area, as demonstrated by the increasing number of related publications mentioned in the introduction.

In Europe, despite the explicit reference in the MD regulations on the availability of the vigilance data in the EUDAMED, this part of the database is still not accessible. This fact restricts the utilization of this critical data for advancing safety in medical technology in Europe and worldwide.

In conclusion, using an adverse event reporting system efficiently facilitates communication between regulatory agencies and healthcare providers and promotes transparency and accountability in the healthcare industry. Ensuring that MDs are safe and effective will improve patient outcomes, with clear benefits for the healthcare sector that remains a cornerstone of our society.

REFERENCES

1. Wiig S, Aase K, Bourrier M, Roise O.Transparency in Health Care: Disclosing Adverse Events to the Public | SpringerLink [Internet]. [cited 2023 May 5]. Available from: https://link.springer.com/chapter/10.1007/978-3-319-74098-0_8
2. FDA. About Manufacturer and User Facility Device Experience (MAUDE) [Internet]. FDA; 2023 [cited 2023 Apr 11]. Available from: https://www.fda.gov/medical-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities/about-manufacturer-and-user-facility-device-experience-maude
3. FDA. 2023 Medical Device Reporting (MDR): How to Report Medical Device Problems. [cited 2023 Apr 11]. Available from: https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems
4. EUDAMED database - EUDAMED [Internet]. [cited 2023 Apr 11]. Available from: https://ec.europa.eu/tools/eudamed/#/screen/home
5. Government of Australia Department of Health and Aged Care. Therapeutic Goods Administration (TGA). Safety monitoring: Medical devices [Internet]. 2022 [cited 2023 Apr 11]. Available from: https://www.tga.gov.au/safety/safety/safety-monitoring-medical-devices

6. Government of Canada - Health Canada. Find recalls, advisories and safety alerts – Canada.ca [Internet]. 2021 [cited 2023 Apr 11]. Available from: https://recalls-rappels.canada.ca/en
7. MHRA.GOV.UK. 2023 [cited 2023 Apr 11]. Alerts, recalls and safety information: drugs and medical devices. Available from: https://www.gov.uk/drug-device-alerts
8. Federal Institute for Drug and Medical Devices. Field corrective actions [Internet]. [cited 2023 Apr 11]. Available from: https://www.bfarm.de/EN/Medical-devices/Tasks/Risk-assessment-and-research/Field-corrective-actions/_node.html
9. Malataras P, Pallikarakis N. Spin-off use of adverse events data: why and how. The case of FDA's MAUDE. Global CE J. 2018;1(1):9–23.
10. Rayess HM, Svider PF, Hanba C, Patel VS, DeJoseph LM, Carron M, et al. A Cross-sectional Analysis of Adverse Events and Litigation for Injectable Fillers. JAMA Facial Plast Surg. 2018 May 1;20(3):207–14.
11. Rahimpour S, Kiyani M, Hodges SE, Turner DA. Deep brain stimulation and electromagnetic interference. Clin Neurol Neurosurg. 2021 Apr;203:106577.
12. Carey J, Gabbireddy S, Mammen L, Rosamilia G, Patel V, Foyt D, et al. FDA MAUDE database analysis of titanium middle ear prosthesis. J Otol. 2022 Jan;17(1):18–24.
13. Tong JY, Pasick LJ, Benito DA, Monfared A, Sataloff RT. Adverse Events Associated With Ossicular Prostheses: Utility of a Federal Database. Otol Neurotol. 2022 Feb 1;43(2):e229–34.
14. Alhusain R, Dayco J, Awadelkarim A, Almas T, Halboni A, Ahmed AK, et al. Turnpike Catheter failure, causes and mechanisms: Insights from the MAUDE database. Ann Med Surg (Lond). 2022 Jun;78:103923.
15. Ensign LG, Cohen KB. A Primer to the Structure, Content and Linkage of the FDA's Manufacturer and User Facility Device Experience (MAUDE) Files. EGEMS (Wash DC). 5(1):12.
16. Kavanagh KT, Brown RE, Kraman SS, Calderon LE, Kavanagh SP. Reporter's occupation and source of adverse device event reports contained in the FDA's MAUDE database. Patient Relat Outcome Meas. 2019 Jul 2;10:205–8.
17. Connor MJ, Tringale K, Moiseenko V, Marshall DC, Moore K, Cervino L, et al. Medical Device Recalls in Radiation Oncology: Analysis of U.S. Food and Drug Administration Data, 2002–2015. Int J Radiat Oncol Biol Phys. 2017 Jun 1;98(2):438–46.
18. Bitar C, Krupic F, Felländer-Tsai L, Crnalic S, Wretenberg P. Living with a recalled implant: a qualitative study of patients' experiences with ASR hip resurfacing arthroplasty. Patient Safety in Surgery. 2021 Jan 6;15(1):2.
19. Drugwatch. Drugwatch.com. [cited 2023 Apr 25]. Hip Replacement Recall | Causes and FDA Information. Available from: https://www.drugwatch.com/hip-replacement/recalls/
20. FDA. Federal Register. 2014 [cited 2023 May 3]. Medical Device Reporting: Electronic Submission Requirements. Available from: https://www.federalregister.gov/documents/2014/02/14/2014-03279/medical-device-reporting-electronic-submission-requirements
21. Zuckerman DM, Brown P, Nissen SE. Medical Device Recalls and the FDA Approval Process. Archives of Internal Medicine. 2011 Jun 13;171(11):1006–11.
22. Dubin JR, Simon SD, Norrell K, Perera J, Gowen J, Cil A. Risk of Recall Among Medical Devices Undergoing US Food and Drug Administration 510(k) Clearance and Premarket Approval, 2008-2017. JAMA Netw Open. 2021 May 3;4(5):e217274.
23. FDA [Internet]. FDA; 2023 [cited 2023 Oct 5]. Examples of Reported Infusion Pump Problems. Available from: https://www.fda.gov/medical-devices/infusion-pumps/examples-reported-infusion-pump-problems
24. Craig A, O'Meley P, Carter P. The Need for Greater Reporting of Medical Device Incidents. EMJ. 2019 Oct 1;3(1):56–63.
25. 2Knisely BM, Levine C, Kharod KC, Vaughn-Cooke M. An Analysis of FDA Adverse Event Reporting Data for Trends in Medical Device Use Error. Proceedings of the International Symposium on Human Factors and Ergonomics in Health Care. 2020 Sep 1;9(1):130–4.