THE RELATIONSHIP BETWEEN MEDICAL DEVICE RECALLS AND THE VOLUME OF MEDICAL DEVICE REPORTS (MDRs) SUBMITTED TO FDA

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INTRODUCTION:

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) is responsible for ensuring that safe and effective medical devices are available to patients and providers. CDRH strives to regulate medical devices based on valid scientific evidence while still maintaining and encouraging medical device innovation. All devices are classified based on risk into three categories: Class I (~47% of devices), Class II (~43% of devices), and Class III (~10% of devices). [1] Just over half of medical devices on the market require a premarket notification (Class II, 510(k)) or a premarket approval (Class III, PMA). While review of devices prior to marketing plays a significant role in ensuring that patients and providers have access to safe and effective medical devices, continued postmarket surveillance of devices after they reach the market is crucial to protecting public health.

The Office of Surveillance and Biometrics (OSB) within CDRH is responsible for overseeing the continued postmarket surveillance of medical devices. [2] OSB relies on five aspects of postmarket surveillance: 1) Medical Device Reporting (MDR), 2) Medical Product Safety Network (MedSun), 3) post-approval studies, 4) postmarket surveillance studies, and 5) FDA discretionary studies. [3] Each of these postmarket surveillance efforts is an enormous undertaking; however, the focus of the current work will be on Medical Device Reporting.

Medical Device Reporting Regulation

FDA's authority to require manufacturers, importers, and user facilities to submit MDRs to the agency is provided for in Section 519 of the Food Drug and Cosmetic Act (FDCA). [4] The MDR regulation (21 CFR 803) outlines adverse event reporting requirements for user facilities, manufacturers, and importers. The regulations require MDRs to be submitted electronically to FDA through the MedWatch Program (Form 3500A [5]) for device-related deaths, serious injuries, and malfunctions. While death is a medical definition, FDA clearly defines the agency's interpretation of serious injury and malfunction in 21 CFR 803.3.

A ***serious injury*** is defined as: "an injury or illness that 1) is life threatening, 2) results in permanent impairment of a body function or permanent damage to a body structure, or 3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure".

A ***malfunction*** is defined as: “the failure of a device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed.”

In clinical situations, deaths, serious injuries, and device malfunctions occur frequently; therefore, FDA is clear about under which circumstances these events should be reported.

An ***MDR reportable event*** is defined as: “an event that reasonably suggests that a device has or *may have caused or contributed* to a death or serious injury” or in the case of a device malfunction “an event that reasonably suggests that a device has malfunctioned and that the device or a similar device marketed by the manufacturer or importer *would be likely* to cause or contribute to a death or serious injury if the malfunction were to recur”.

In addition to the entities required to submit MDRs by statue, FDA encourages the submission of voluntary reports from anyone who is aware of a device-related adverse event. Voluntary reports (Form 3500 [6]) are typically submitted by patients, caregivers, healthcare professionals, and consumers.

A summary of the specific MDR reporting requirements for each type of reporter is provided in **Table 1**. FDA has also recently published a new guidance document [7] which provides an overview of the MDR regulation and updates to the 1997 guidance. [8]

Table 1. Summary of MDR Requirements.

Reporter	Types of Events to Report	Who to Report to	When to Report
Manufacturer (MFR)	Deaths, Serious Injuries, Device Malfunctions	FDA	Within 30 Calendar Days of Becoming Aware
	Events that Require Remedial Action to Prevent Unreasonable Risk of Substantial Harm	FDA	Within 5 Working Days of Becoming Aware
User Facility	Deaths	FDA and MFR	Within 10 Working Days
	Serious Injuries	MFR (FDA if Unknown)	Within 10 Working Days
Importer	Deaths and Serious Injuries	FDA and MFR	Within 30 Calendar Days
	Device Malfunctions	MFR	Within 30 Calendar Days
Voluntary	Any Type of Event	FDA	Any Time

The Manufacturer and User Facility Device Experience (MAUDE) Database

The MAUDE database stores MDRs received by FDA and provides adverse event information involving marketed medical devices. An online search of the database can be performed by the public and the data may be downloaded. [9, 10] When making decisions regarding the safety and efficacy of medical devices FDA evaluates all available data; therefore, MDR data should be interpreted within the context of other available information.

Medical Device Recalls

A medical device recall is a means by which device manufacturers and distributors remove or correct products that are in violation of the FDCA. [11] FDA formally defines a recall as “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”. [11] Recalls are typically voluntary actions taken by device manufacturers; however, FDA does have the authority to

issue a recall order under 21 CFR 810 if the manufacturer fails to recall a device that is a risk to health (21 CFR 806.2(k)). FDA has only exercised this authority in extremely rare instances.

Device recalls are classified according to the relative degree of health hazard presented by the device, with Class I being the most serious and Class III being the least serious. FDA formally defines the following three classes of medical device recalls:

Class I: A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death

Class II: A situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote

Class III: A situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences

In general, manufacturers are not required to report Class III recall activities to FDA.

FDA reviews postmarket data in order to monitor the safety and efficacy of medical devices after they reach the market. Continued surveillance of MDRs provides adverse event data to all stakeholders; including FDA, device manufacturers, and the public; which can be used to identify safety signals. MDR data, in conjunction with device recall information, may be used to indicate a public health concern related to a device or identify potential problems with a manufacturers' quality system and manufacturing practices. Understanding the relationship between device recalls and MDRs submitted to FDA could enrich the effectiveness of postmarket surveillance of medical devices and help protect public health. Therefore, the objective of this work was to examine the relationship between medical device recalls and the volume of MDRs submitted to FDA for medical devices in three different product areas.

METHODS:

Three major device areas were selected randomly for investigation: cardiovascular, orthopaedics, and respiratory devices. One FDA device classification product code was then identified within each major device area for a case study. For each classification product code the following steps were performed:

1. The Medical Device Recalls database [12] was searched using the product code.
2. The medical device with the largest number of recalls over the time period from October 2011 to October 2016 was selected for further investigation.
3. The MAUDE database [9, 10] was searched for MDRs submitted to FDA for the targeted device over the same five year period using the Brand Name and Product Code.
4. MDRs were exported to an Excel spreadsheet for further analysis.
5. The volume of MDRs received by FDA was plotted by month over the five year time period.
6. The time in months from the local maximum volume of MDRs to the device recall date was calculated for each recall.

RESULTS:

The three devices chosen for investigation demonstrated a vastly different MDR profile over the same five year time frame. The results of each of the three cases are presented below.

Case 1 - Cardiovascular Device

In the cardiovascular device area a class II medical device with three recalls over the five year time period was selected for investigation. A summary of these recalls in provided in **Table 2**.

Table 2. Recalls for Cardiovascular Device.

Recall Identifier	Month of Recall During Five Year (60 Month) Period	Recall Classification
CV-1	Month 25	Class II
CV-2	Month 43	Class I
CV-3	Month 58	Class II

A total of 139 MDRs were identified in the MAUDE database for the cardiovascular device over the five year time period. These MDRs included 6 deaths, 74 serious injuries, and 59 device malfunctions. (**Figure 1**)

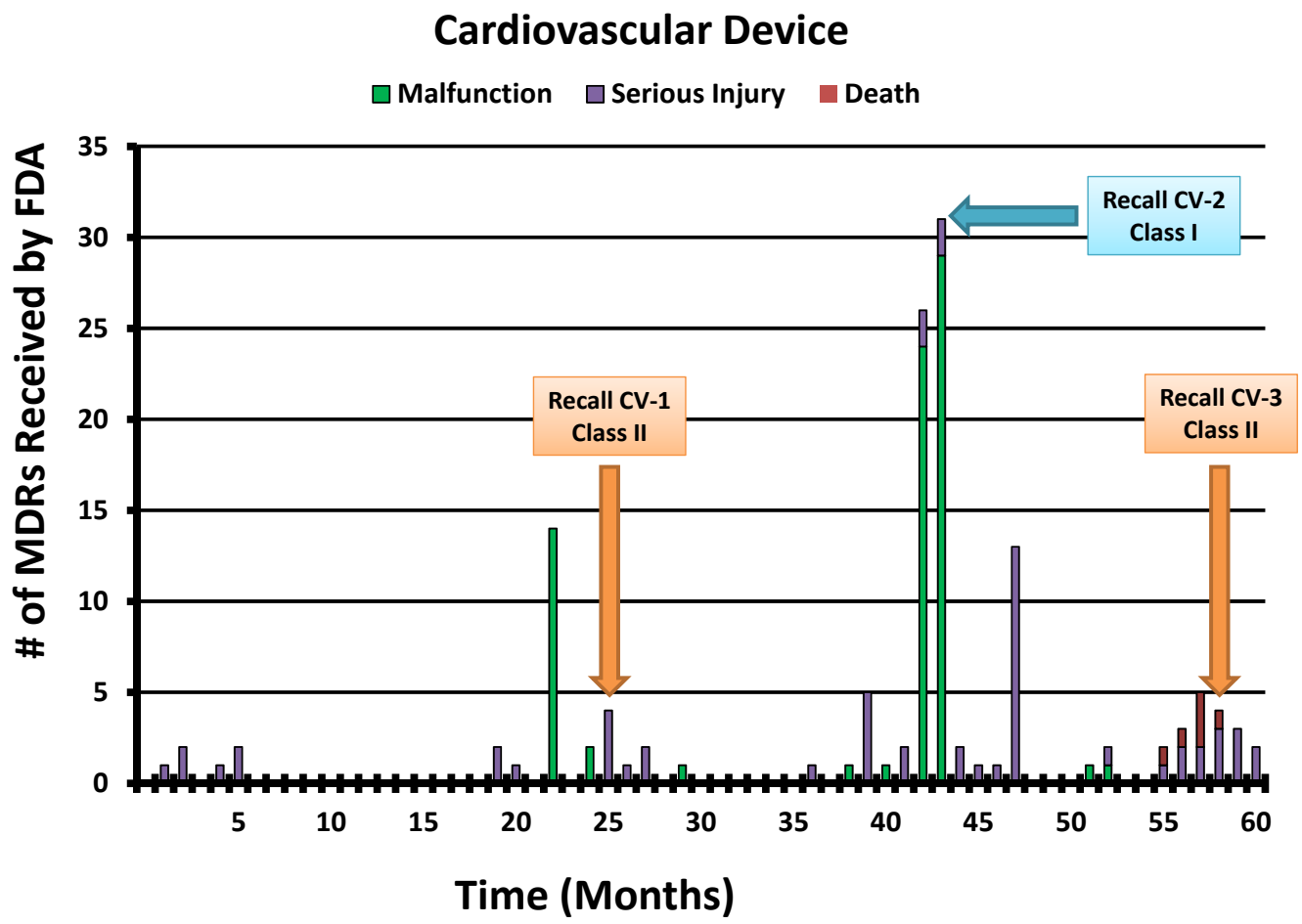

Figure 1. Volume of MDRs submitted to FDA over a 5 year time frame for the cardiovascular device.

The volume of MDRs over the five year time period exhibited three local maxima. These maxima occurred in months 22, 43, and 57 and correspond to a total of 14, 31, and 5 MDRs, respectively. The largest volume of MDRs for this device was submitted in month 43, the same month in which the Class I recall (CV-2) occurred. The smaller two peaks in MDR volume occurred 3 months (CV-1) and 1 month (CV-3) prior to the Class II recalls.

It appears that the Class I recall (CV-2) was associated with the highest volume of MDRs which consisted mostly of device malfunctions and a small number of serious injury reports. While the CV-1 recall occurred several months following the first peak in MDR volume, this peak consisted of only device malfunctions. Four serious injury reports were received in the same month as the CV-1 recall. Finally, the CV-3 recall was associated with the smallest peak in MDRs; however, this peak included a series of 6 patient deaths received over a 4 month time period.

Case 2 - Orthopaedic Device

In the orthopaedic device area a class II medical device with two recalls over the five year time period was selected for investigation. A summary of these recalls in provided in **Table 3**.

Table 3. Recalls for Orthopaedic Device.

Recall Identifier	Month of Recall During Five Year (60 Month) Period	Recall Classification
O-1	Month 36	Class II
O-2	Month 40	Class II

A total of 19 MDRs were identified in the MAUDE database for the orthopaedic device over the five year time period. These MDRs included 2 serious injuries, and 17 device malfunctions. (**Figure 2**)

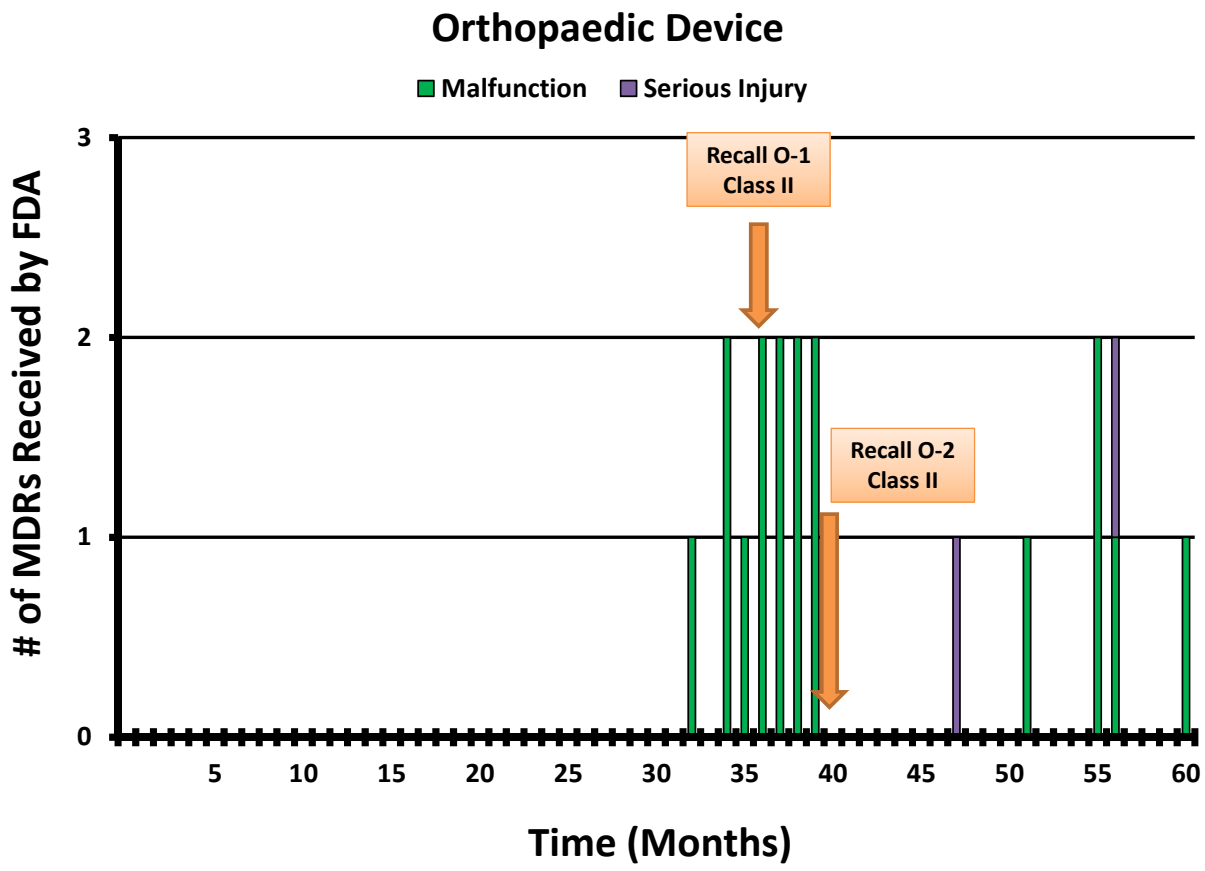

Figure 2. Volume of MDRs submitted to FDA over a 5 year time frame for the orthopaedic device.

The overall volume of MDRs submitted to FDA for the orthopaedic device was an order of magnitude smaller than the volume submitted for the cardiovascular device. There were no patient deaths reported for this device and the majority of MDRs were for device malfunctions. Due to the small volume of MDRs, a relative maximum was not apparent and the largest number of MDRs submitted in one month was only two. The first Class II recall (O-1) occurred in month 36, which was four months after the first MDR was received. The second Class II recall (O-2) occurred in month 40 after 12 MDRs had been received. Following the second recall no MDRs were submitted to FDA for this device for the next six months. Based on this data it is possible that the initial recall did not completely address the device problem; and therefore, the firm initiated a second recall which appears to have been effective.

Case 3 - Respiratory Device Area

In the respiratory device area a class I medical device with one recall over the five year time period was selected for investigation. A summary of this recall in provided in **Table 4**.

Table 4. Recalls for Respiratory Device.

Recall Identifier	Month of Recall During Five Year (60 Month) Period	Recall Classification
R-1	Month 48	Class I

A total of 12 MDRs were identified in the MAUDE database for the respiratory device over the five year time period. These MDRs included 8 serious injuries, and 4 device malfunctions. (**Figure 3**)

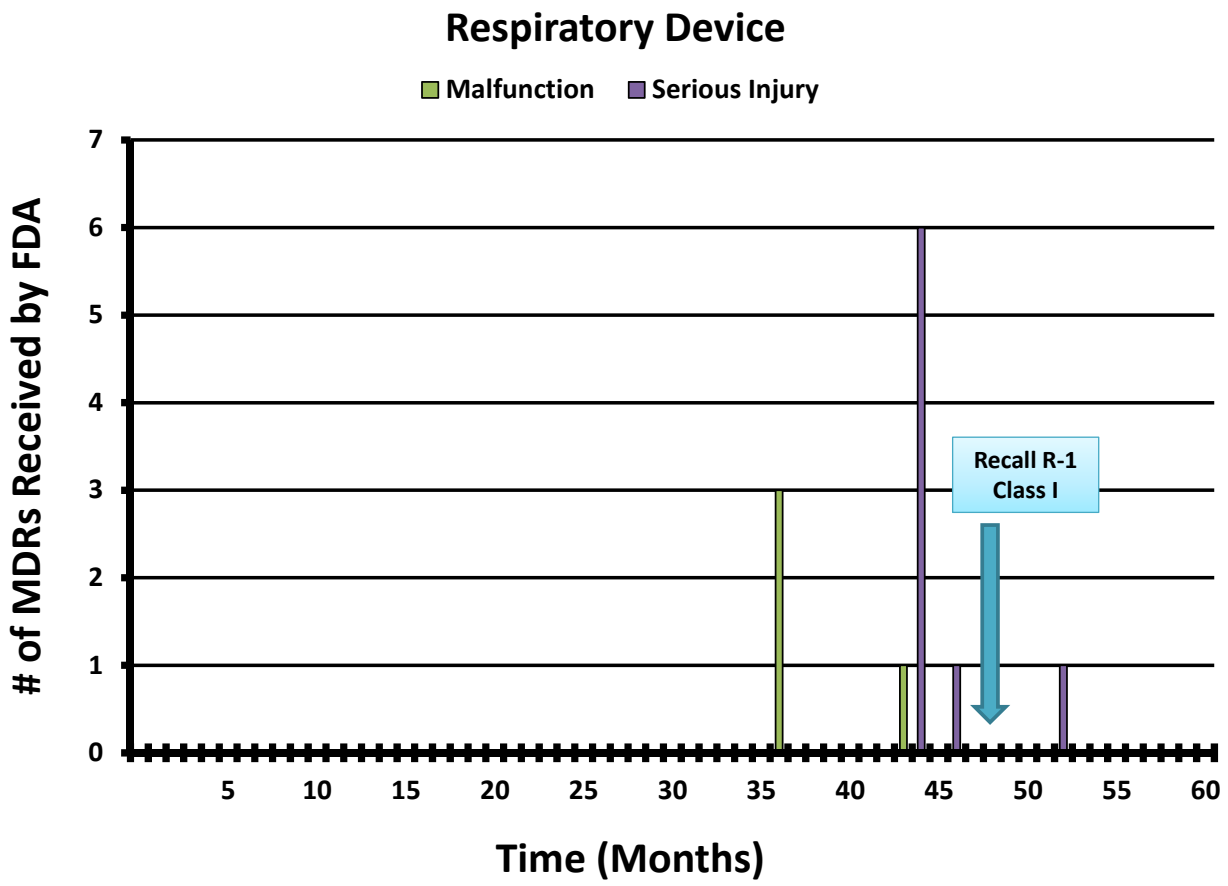

Figure 3. Volume of MDRs submitted to FDA over a 5 year time frame for the respiratory device.

The volume of MDRs submitted to FDA for the respiratory device was on the same order of magnitude as the orthopaedic device. There were no patient deaths and the majority of MDRs were for serious injury events. The maximum number of MDRs received in one month was six injury reports and this occurred four months prior to the Class I recall (R-1).

DISCUSSION:

This study examined the relationship between medical device recalls and the volume of MDRs submitted to FDA for medical devices in three different product areas. Two Class II and one Class III device in the cardiovascular, orthopaedic, and respiratory device area, respectively, were chosen at random for further investigation. The volume of MDRs received by FDA over a five year time period was plotted in conjunction with any recalls associated with the devices.

Even though the same five year time frame was evaluated, each of the three devices demonstrated a vastly different MDR profile.

The greatest number of MDRs was received for the cardiovascular device. Cardiovascular procedures are typically performed in high-risk situations, often with manufacturer representatives present. In addition, the number of devices sold in this area can be substantially higher than other device areas depending on the particular product. These factors may contribute to the larger volume of MDRs received in this device area.

Regardless of the device area, a recall may be associated with an increase in the number of MDRs submitted to FDA. The magnitude of the increase is highly variable and dependent upon the particular device. The cardiovascular device, which demonstrated a higher overall volume of MDRs, suggests that a greater increase may be required in order to identify a safety issue. In other words, a detectable increase in MDRs above the normal “noise” within the MDR profile may be indicative that a safety issue may be present. However, with other devices that do not typically stimulate MDRs on a regular basis, simply the presence of MDRs (e.g. orthopaedic device) may indicate a potential problem.

Another factor worth noting is the type of MDR received (death, serious injury, or device malfunction). The cardiovascular device demonstrates that a large volume of MDRs is not necessarily required to suggest a potential safety issue or initiate a device recall. If the severity of the events is high, either directly resulting in an increased number of patient deaths or situations in which patient death is likely, this may be sufficient evidence to suggest a problem or support a recall. In addition, if a device’s MDR profile typically consists of device malfunctions (e.g. respiratory device), and then FDA receives several serious injury reports this may warrant further investigation.

Even though MDR data is extremely important, it is only one aspect of FDAs multifaceted postmarket surveillance system which continues to grow and evolve year after year. [13] It is important to remember that this data is interpreted within the context of all other information available including post-approval studies, postmarket surveillance studies, MedSun reports, and device and market share information.

As a passive surveillance system, MDR reporting provides a qualitative snapshot of adverse events for a specific device or device type. It enables FDA to detect problems with medical

devices when they are used by “real people” in “real world” clinical situations and identifies rare and unexpected events, long-term events, events involving vulnerable populations, off-label use, and user errors or human factors issues.

As a passive surveillance system, MDR reporting is subject to limitations. [9, 10] Adverse events are under-reported due to a lack of awareness. Many healthcare providers are unaware of reporting requirements or the role they may play in reporting adverse events to FDA and how the process impacts public safety.

Establishing a cause-and-effect relationship between a medical device and an adverse event is extremely difficult for a number of reasons. For example, multiple devices are used in a single procedure or in life-sustaining or life-supporting situations on very sick patients with multiple comorbidities. Further, reports that are submitted are often incomplete and lack vital information regarding the adverse event. The circumstances surrounding the event and important patient details are frequently neglected. Finally, the adverse events are not verified, and many times the device is not evaluated.

Another limitation of MAUDE data is reporting biases including variation in the reporting practices between device manufacturers and the impact of the media and regulatory actions. MAUDE data is commonly misinterpreted and used to draw conclusions regarding the frequency and severity of issues associated with devices. MDR data cannot be used to establish rates of events or compare rate data over time or between devices, even for similar devices with the same intended use. For these reasons, trends in MDR data should be interpreted cautiously. Despite these limitations, MDR data provides useful information about the postmarket behavior of medical devices and assists in continuous monitoring of devices after they reach the market.

In conclusion, this study provided a first step towards investigating the relationship between MDR and recall data. A deeper evaluation is necessary and should include multiple devices within each device area as well as expanding into other device areas. Based on these preliminary results it is evident that each device exhibits a very unique MDR profile which can be used, in conjunction with other sources of information, to gain insight into the postmarket experience of the specific device. Therefore, it is important to examine the entire device profile when reviewing postmarket data and identifying safety signals for medical devices.

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