FDA Executive Summary

Prepared for the June 3-4, 2021 Meeting of the Neurological Devices Advisory Panel

Classification of Acupressure Devices

Product Code: MVV

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1. Introduction

Per Section 513(b) of the Food, Drug, and Cosmetic Act (the Act), the Food and Drug Administration (FDA) is convening the Neurological Devices Advisory Panel (the Panel) for the purpose of obtaining recommendations regarding the classification of acupressure devices, a pre-amendments device type which remains unclassified. Specifically, the FDA will ask the Panel to provide recommendations regarding the regulatory classification of acupressure devices under product code "MVV". The device names and associated product codes are developed by the Center for Devices and Radiological Health (CDRH) in order to identify the generic category of a device for FDA. While most of these product codes are associated with a device classification regulation, some product codes, including "MVV" remain unclassified.

FDA is holding this Panel meeting to obtain input on the risks to health and benefits of the acupressure devices under product code "MVV." The Panel will discuss whether the acupressure devices under product code "MVV" should be classified into class I (subject only to General Controls).

1.1 Current Regulatory Pathways

Acupressure devices are a pre-amendments, unclassified device type. This means that this device type was marketed prior to the Medical Device Amendments of 1976, but was not classified by the original classification panels. Currently these devices are being regulated through the 510(k) pathway, and are cleared for marketing if their intended use and technological characteristics are "substantially equivalent" to a legally marketed predicate device. Since these devices are unclassified, there is no regulation associated with the product code.

1.2 Device Description

Acupressure devices are used to apply pressure to the Pericardium (P6 or PC6) or "Nei-Kuan" acupuncture point on the inner wrist. Application of consistent pressure at this point is applied through elastic or applied force via a wrist band, strap, or adhesive strip. A raised wooden or plastic bead/button is often embedded within the band, strap, or strip, which creates a resistive force against the inner wrist. In some devices the amount of pressure can be adjusted manually by adjusting the circumference of the wrist band/strap, or by adjusting the diameter of the bead or button.

2. Regulatory History

The Sea-Band manufactured by UK Ltd was the first device under product code MVV to be cleared by FDA on January 7, 2004. The FDA determined that the Sea-Band was substantially equivalent to pre-amendments, unclassified acupressure devices. Since this 510(k) clearance, 10 devices have been cleared under the unclassified product code MVV (see Table 1).

Table 1: 510(k) clearances for acupressure devices under product code "MVV"

510(k) Number	Trade Name	Sponsor
K900588	Acu-Band Acupressure Wrist Device	Euro-Am Pharma Inc.
K033268	Sea-Band	Sea-Band UK Ltd.
K041766	EZY-Travel Wristband	Apothecary Products, Inc.
K041877	Acu-Strap Motion Sickness Band	Health ENT., Inc.
K051397	Biobands	Biobands Distributors, Inc.
K053509	Acuband Acupressure Wrist Band Device	Acuband Inc.
K070766	PSI Bands	PSI Health Solutions, Inc.
K110563	Pressure Right, Single-Use, Disposable, Pressure-Sensitive Emetic-Management Wrist Strap	Therapeutics 101, Inc. (DBA Pressure Point, Inc.)
K110821	Barf Bands	Doodlebug Products, LLC
K142471	Pressure Right, Single-Use, Disposable, Acupressure, Pressure-Sensitive Wrist Strap	Pressure Point Inc.
K193374	TumEase Acupressure Bracelets	MumEase LLC

3. Indications for Use

The Indications for Use (IFU) statement identifies the condition and patient population for which a device should be appropriately used. Acupressure devices are used in the treatment of nausea/emesis due to causes including motion sickness, pregnancy, chemotherapy, and post-operative anesthesia. The IFU statements for the cleared devices under product code MVV are specified in Table 2 below. All of the devices are cleared for over-the-counter (OTC) use.

Table 2: Indications for Use (IFUs) for acupressure devices under product code "MVV"

510(k) Submission #	Indications for Use
K033268	The Sea-Band limited "Sea-Band" is indicated for the relief of nausea. Nausea is a symptom that may be experienced due to a variety of causes, for example: - travel/motion - pregnancy (morning sickness) - chemotherapy - post-operative

K041766	For the relief of nausea. Nausea may be caused by motion, morning sickness, chemotherapy or anesthesia.
K041877	The Acu-Strap travel and motion sickness band is intended for the relief of nausea. Nausea may be experienced due to travel (motion sickness), pregnancy (morning sickness), anesthesia or chemotherapy.
K051397	Biobands is indicated for the relief of nausea. Nausea may be experienced due to a variety of causes, including travel (motion sickness), pregnancy (morning sickness), anesthesia (post-operative) or chemotherapy.
K053509	Acuband are indicated for the relief of nausea. Nausea is a symptom which can be experienced by causes such as motion sickness, morning sickness (pregnancy), chemotherapy and post-operative from anesthesia.
K070766	PSI Bands are indicated for the relief of nausea. Nausea is a symptom that may be experienced due to a variety of causes, for example: - pregnancy (morning sickness) - motion sickness - anesthesia - chemotherapy PSI Bands are intended for over-the-counter use
K110563	The Pressure Right, Single-Use Disposable, Pressure-Sensitive Emetic-Management Wrist Strip is indicated for the relief of emetic (nausea and vomiting) symptoms associated with post-operative anesthesia.
K110821	The Barf Band is indicated for the relief of nausea. Nausea is a symptom that may be experienced due to a variety of causes, for example; pregnancy (morning sickness), motion sickness, anesthesia and chemotherapy.
K142471	Pressure Right® is a drug-free, Single-Use, Pressure-Sensitive Acupressure Wrist Strip, externally applied, which is indicated for relief of nausea symptoms associated with chemotherapy, post-operative, pregnancy (morning sickness) and travel/motion. For Over-the-Counter (OTC) use.
K193374	The Acupressure Bracelets are intended to reduce symptoms of nausea. Nausea may be experienced due to Travel/Motion, Pregnancy/Morning Sickness, Chemotherapy, and Anesthesia (post-procedure).

4. Clinical Background

4.1 Disease Characteristics

Nausea is an unpleasant sensation of needing to vomit and can occur independently or accompany gastric emesis. The pathophysiology of nausea involves a disturbance of the normal rhythmic three cycle per minute gastric myoelectrical activity controlled by the enteric brain neurons and the autonomic nervous system innervating smooth muscles cells of the GI tract.

Vomiting is reflexive emesis activated by neuronal stimuli responsive to chemoreceptor triggers in the brain. Five principle neurotransmitter receptors have been found to mediate vomiting: M1 muscarinic, D2 dopamine, 5-HT(3), H(1) histamine, and NK1 neurokinin receptors. Emesis occurs upon relaxation of the gastric and esophageal sphincter, contraction of the proximal small bowel and abdominal muscles.

4.2 Patient Outcomes

History and physical examination can, in most cases, determine the cause of nausea and vomiting. The need for additional testing is guided by factors such as symptom duration, frequency, severity and characteristics such as the presence or absence of abdominal pain or abdominal distention. Additional testing may include endoscopy to identify gastric obstructions or other gastric disorders requiring specific therapy.

Gastric emptying can be assessed with scintigraphy tests. The underlying cause of nausea and vomiting symptoms can include the following diagnoses and conditions (not all inclusive): acute gastritis, postoperative nausea and vomiting, vestibular neuritis, chemotherapy-induced nausea and vomiting, pregnancy related nausea and vomiting, gastroparesis, gastroesophageal reflux, gastric outlet obstruction, intestinal pseudo-obstruction, and functional nausea and vomiting disorders.

4.3 Currently Available Treatment

The management of nausea and vomiting primarily relies on drug treatment in standard practice. Antiemetic and prokinetic medications are useful in acute and chronic nausea and vomiting and include prochlorperazine, metoclopramide, domperidone, erythromycin, bethanechol and serotonin antagonists. Other drug classes used to treat chronic nausea and vomiting symptoms include antidepressants, which can be used when other anti-nausea drugs are ineffective.

Gastric electrical stimulation via implanted electrodes have been applied to select patients who are refractory to conventional therapy for nausea and vomiting. However, the device is available in the United States only for humanitarian use[1]. Surgical options for the treatment of nausea and vomiting include gastrostomy,

[1] H990014, Gastric Electrical Stimulation (GES) (https://www.accessdata.fda.gov/cdrh_docs/pdf/H990014A.pdf)

pyloroplasty, jejunostomy and gastrectomy in patients with diabetic, postsurgical and idiopathic gastroparesis, but these treatments have not been studied under well controlled conditions and remain options of last resort.

4.4 Risks

FDA has identified the following risks to health associated with acupressure devices:

Table 3: Risks to Health and Descriptions/Examples for Acupressure Devices

Identified Risk	Description/Examples
Pain or discomfort	This can result from bruising, swelling and tenderness under the wrist band and at the pressure point, particularly if applied too tightly
Skin irritation	This can result from improper cleaning and from pressure/contact with the wrist band

The Panel will be asked whether this list is a complete and accurate list of the risks to health presented by acupressure devices under product code "MVV" and whether any other risks should be included in the overall risk assessment of the device type.

5. Literature Review

5.1 Methods

A systematic literature review was conducted to gather any published literature regarding the safety and effectiveness of acupressure wristband devices that are under the product code "MVV". Online literature searches were performed in two electronic databases (Embase and PubMed) using the following search terms: "acupressure AND nausea". **Appendix A** contains a table listing all search terms and filters utilized for Embase and PubMed. The search was limited to human clinical studies published in the English language, with publication dates between January 1, 2010 and December 31, 2020. Database filters were used to exclude non-original human clinical studies such as conference abstracts/proceedings, commentaries, and editorials.

An initial search was performed on May 1, 2020 using publication dates between January 1, 2010 and May 1, 2020. Two supplementary searches were performed on September 1, 2020 and March 9, 2021 to capture any additional articles published between May 1, 2020 and December 31, 2020. The flow diagram in **Appendix B** represents the total number of articles and exclusion criterium obtained from both searches.

5.2 Results

The search yielded 253 initial literature references. After duplicate articles were removed between databases, a total of 202 articles remained. Following a review of the titles and abstracts, a total of 90 articles remained for full-text review. Of these, 28 articles were determined to be relevant to the safety and effectiveness of acupressure wristbands (**Appendix B**). The number of each excluded criterium is also summarized in the flow diagram in **Appendix B**. The selected studies consisted of 26 randomized controlled trials (RCT)[1-26] and two prospective cohort studies[27,28]. The indication for use of the acupressure wristbands for all 28 studies is for the relief of nausea and vomiting. The studies included the following patient populations: post-operative patients (13 studies)[5,6,8,11,12,14,17-19,23-25,27], chemotherapy patients (9 studies)[4,7,9,10,13,16,20,26,28], women in early pregnancy (2 studies)[15,21], hyperemesis gravidarum patients (1 study)[1], labor and delivery patients (1 study)[22], hemodialysis patients (1 study)[3], and patients suffering from vertigo and neurovegetative symptoms (1 study)[2].

5.3 Adverse Events Associated with Acupressure Devices

Of the 28 studies, a total of 5 studies reported on adverse events associated with the use of acupressure wristbands. From the 13 studies in which the acupressure wristbands were used to prevent or relieve nausea and vomiting in post-operative patients, two studies reported on safety outcomes attributed to the use of the device and these consisted of redness, swelling, tenderness, bruising, paresthesia, discomfort and pain[14,17]. The authors of two studies, in which the acupressure wristbands were used to relieve nausea in chemotherapy patients, reported on safety outcomes attributed to the use of the device, e.g., a feeling of acupressure wristbands tightness, discomfort, and itchiness[13,26]. The authors of the study in which acupressure wristbands were used in hyperemesis gravidarum patients reported that in the treatment group (n = 60), three (2%) of the women developed redness over the Neiguan acupressure point after wearing the acupressure wristbands for 12 hours daily for 3 weeks[1].

5.4 Effectiveness Associated with Acupressure Devices

Post-Operative

There were 13 studies in which acupressure wristbands were used to prevent or relieve nausea and vomiting in post-operative patients. These studies consisted of 12 randomized controlled trials[5,6,8,11,12,14,17-19,23-25] and one prospective cohort study[27]. The acupressure wristbands were compared to the use of a sham wristband in ten of these studies[5,8,11,12,14,17,18,24,25,27], to antiemetic medication in two studies[6,23], and to electrostimulation in one study[19]. Six of the 13 studies found the use of acupressure wristbands statistically significant in relieving or preventing both nausea and vomiting in post-operative patients as compared to the comparator ($p < 0.05$)[6,8,12,18,19,24]. Two of the studies found that acupressure wristbands were

statistically significant in the prevention or relief of nausea; but not vomiting[23,27]. One study found that there was statistically significant reduction in nausea and vomiting with the use of acupressure wristbands compared to the use of sham wristbands ($p < 0.05$), but not compared to the control (no bands).[5] Four of the studies found that acupressure wristbands had no statistically significant effects in relieving neither nausea or vomiting in post-operative patients as compared to the sham wristband ($p > 0.05$)[11,14,17,25].

Chemotherapy

There were 9 studies in which acupressure wristbands were used in cancer patients undergoing chemotherapy to prevent or relieve chemotherapy induced nausea and vomiting. These studies consisted of 8 randomized controlled trials[4,7,9,10,13,16,20,26] and one prospective cohort study[28]. Five of these studies compared the use of acupressure wristbands to sham wristband devices[7,9,13,16,26], one compared to manually applied acupressure[4], and two compared to no applied acupressure[10,28]. One study compared the effects of acupressure wristbands on chemotherapy-induced nausea when provided with relaxing music paired with reading expectancy-enhancing handouts versus relaxing music paired with expectancy-neutral handouts versus the absence of music and wristband use[20]. Three of these studies found that the use of acupressure wristbands when used for four or more consecutive days following chemotherapy prevented or reduced the incidence and severity of both nausea and vomiting ($p < 0.05$)[4,10,20]. One study found that the use of acupressure wristbands was statistically significant in the prevention or relief of nausea ($p < 0.05$); but not vomiting ($p > 0.05$).[28] Five studies found that the use of acupressure wristbands had no statistically significant effects in reducing the incidence of nausea and vomiting in chemotherapy patients as compared to sham wristband devices ($p > 0.05$)[7,9,13,16,26].

Early Pregnancy

There were two randomized controlled trials[15,21] in which acupressure wristbands were used in subjects experiencing early pregnancy nausea and vomiting. One study compared the effects of the acupressure wristbands against the use of ginger[21] and the other compared to the use of sham wristbands[15]. One study reported a statistically significant reduction in the incidence of nausea and vomiting with the use of acupressure wristbands as compared to the use of sham wristbands ($p < 0.05$)[15]. The other study found that the mean differences in vomiting, nausea, retching, and total scores between the acupressure wristband and control group (no band) were statistically significant ($p < 0.05$); however, the difference in vomiting between the acupressure wristband and ginger group was not statistically different ($p = 0.98$)[21].

Hyperemesis Gravidarum

One randomized controlled trial studied the effects of acupressure wristbands in the reduction of nausea and vomiting in hyperemesis gravidarum as compared to the use of a sham wristbands[1]. The study reported a statistically significant reduction in

nausea and vomiting with the use of acupressure wristbands as compared to the sham wristbands ($p < 0.05$).

Labor and Delivery

One randomized controlled trial studied the effects of acupressure wristbands compared to the use of sham wristbands in the reduction of the incidence of nausea and vomiting in women two hours post labor and delivery[22]. The authors reported no statistically significant reduction of nausea and vomiting with the use of the acupressure wristbands compared to the use of sham wristbands ($p > 0.05$), and that 8% of the women reported discomfort from the acupressure band.

Hemodialysis

One randomized controlled trial studied the effects of the acupressure wristbands compared to the use of sham wristbands in the reduction of nausea and vomiting in patients undergoing hemodialysis[3]. The authors reported a statistically significant reduction in nausea and vomiting with the use of acupressure wristbands as compared to the sham wristbands ($p < 0.05$).

Vertigo and Neurovegetative Symptoms

One randomized controlled trial studied the effects of the acupressure wristbands compared to the use of sham wristbands in the reduction of nausea and vomiting in patients suffering from vertigo and neurovegetative symptoms[2]. The authors reported that 85% of the treatment group reported improvement in symptoms, which was statistically significant for the neurovegetative symptoms ($p < 0.05$), but not for vertigo.

5.5 Overall Literature Review Conclusions

The majority (82.2%) of publications did not report on adverse events or safety risks with the use of the device. The adverse events from the five clinical studies that reported safety events were all mild in nature and resolved after removal of the acupressure wristbands, without additional treatment. Reported adverse events included redness, swelling, discomfort, itch, and band tightness. Clinical evidence from the published literature shows mixed results for the effectiveness of acupressure wristbands in the prevention or reduction of nausea and vomiting. Overall, 18 of the 28 (64%) studies reported a statistically significant prevention or reduction in nausea and/or vomiting with use of acupressure wristbands ($p < 0.05$). In summary, based in the peer reviewed medical literature, acupressure wristbands are safe and more effective in some patients than others. The reasons for the variation in effectiveness are not well understood.

6. Risks to Health Identified through Medical Device Reports (MDRs)

6.1 Overview of the MDR System

The MDR system provides FDA with information on medical device performance from patients, health care professionals, consumers and mandatory reporters (manufacturers, importers and device user facilities). The FDA receives MDRs of suspected device-associated deaths, serious injuries, and certain malfunctions. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDRs can be used effectively to:

- Establish a qualitative snapshot of adverse events for a specific device or device type
- Detect actual or potential device problems used in a "real world" setting/environment

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the submission of incomplete, inaccurate, untimely, unverified, duplicated or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about the frequency of device use. Finally, the existence of an adverse event report does not definitely establish a causal link between the device and the reported event. Because of these limitations, MDRs comprise only one of the FDA's tools for assessing device performance. As such, MDR numbers and data should be taken in the context of the other available scientific information.

6.2 MDR Data: Acupressure Devices (Product Code MVV)

Individual MDRs for acupressure devices are reported through FDA's Manufacturer and User Facility Device Experience (MAUDE) Database, which houses mandatory reports from medical device manufacturers, importers and user facilities, as well as voluntary reports from entities such as health care professionals, patients and consumers.

The Agency searched the Medical Device Reports (MDR) database on March 9, 2021 to identify adverse events related to the use of acupressure devices (product code MVV) entered between January 1, 1991 and December 31, 2020. The search did not identify any relevant MDRs for acupressure devices.

7. Recall History

7.1 Overview of Recall Database

The Medical Device Recall database contains Medical Device Recalls classified since November 2002. Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA. The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated. FDA recall classification may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall. Therefore, the recall information posting date ("create date") identified on the database indicates the date FDA classified the recall, it does not necessarily mean that the recall is new.

7.2 Recall Results: Acupressure Devices

One Class II[2] recall has been identified in the Medical Recall Database with the product code "MVV". Psi Bands acupressure/acustimulation wrist bands in the following colors: Racer Black (UPC 859570001036), Daisy Chain (UPC 859570001029), Color Play (UPC 859570001043) and Cherry Blossom (UPC 859570001012) were recalled in 2007 because the firm was marketing their devices before its 510(k) submission received clearance.

8. Summary

In light of the information available, the Panel will be asked to comment on whether acupressure devices under product codes "MVV"

meet the statutory definition of a Class III device:

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, and

- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury

or would be more appropriately regulated as Class II, in which:

- general and special controls, which may include performance standards, postmarket surveillance, patient registries and/or development of guidelines, are sufficient to provide reasonable assurance of safety and effectiveness;

or as Class I, in which:

[2] Recalls are classified into a numerical designation (I, II, or III) by the FDA to indicate the relative degree of health hazard presented by the product being recalled. A Class II recall is 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.

- the device is subject only to general controls, which include registration and listing, good manufacturing practices (GMPs), prohibition against adulteration and misbranding, and labeling devices according to FDA regulations.

For the purposes of classification, FDA considers the following items, among other relevant factors, as outlined in 21 CFR 860.7(b):

1. The persons for whose use the device is represented or intended;

2. The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;

3. The probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and

4. The reliability of the device.

8.1 Special Controls

For acupressure devices with the intended use of treatment of nausea/emesis due to causes including motion sickness, pregnancy, chemotherapy, and post-operative anesthesia, FDA does not believe that special controls will be required and that general controls will be sufficient to provide a reasonable assurance of the safety and effectiveness of “acupressure device for nausea”.

8.2 Overview of Proposed Classification/FDA Recommendation

Based on the safety and effectiveness information gathered by the FDA, the identified risks to health and recommended mitigation measures, we recommend that acupressure devices indicated for the relief of nausea resulting from motion, pregnancy (morning sickness), post-operative anesthesia, or chemotherapy be regulated as Class I [exempt] devices.

890.5872 Acupressure device for nausea.

(a) *Identification.*

An acupressure device is used to apply pressure to the Pericardium 6 (P6 or PC6) acupuncture point on the inner wrist(s) for the relief of nausea resulting from motion, pregnancy (morning sickness), post-operative anesthesia, or chemotherapy. Application of consistent pressure at this point is applied through elastic or applied force via a bead or button embedded in a wrist band, strap, or adhesive strip.

(b) *Classification.*

Class I (general controls).

Based on the available scientific evidence, the FDA will ask the Panel for their recommendation on the appropriate classification of the acupressure devices under product code "MVV."

Appendix A: Literature Search Terms and Filters for Acupressure Devices

Table 4: Search terms for Embase and PubMed

AND	OR
Acupressure	
Nausea	

Table 5: Search filters for Embase

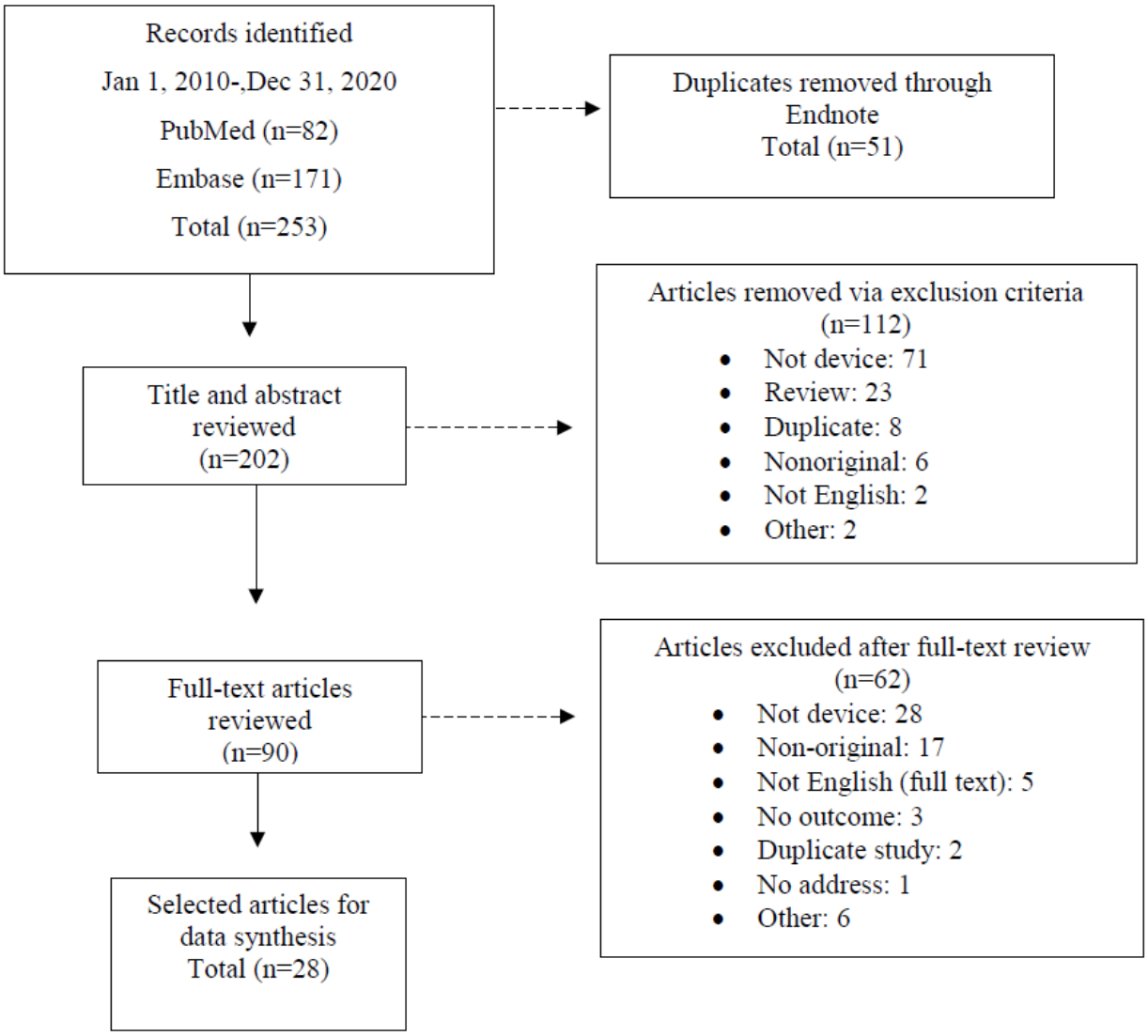
AND	OR
Publication year 2010-2020	
Case control study	Case report
	Case study
	Clinical article
	Clinical trial
	Clinical trial topic
	Cohort analysis
	Comparative effectiveness
	Comparative study
	Control group
	Controlled clinical trial
	Controlled study
	Cross sectional study
	Crossover procedure
	Double blind procedure
	Evidence based medicine
	Evidence based practice
	Experimental study
	Feasibility study
	Human
	Intermethod comparison
	Intervention study
	Longitudinal study
	Major clinical study
	Meta-analysis
	Meta-analysis topic
	Multicenter study
	Multicenter study topic
	Observational study
	Phase 2 clinical trial topic
	Prospective study
	Qualitative research

	Quality control
	Randomized controlled trial
	Randomized controlled trial topic
	Retrospective study
	Single blind procedure
	Systematic review
	Systematic review topic
Article	

Table 6: Search filters for PubMed

AND	OR
Clinical trial	Meta-analysis
	Randomized controlled trial
	Systematic review
Publication year 2010-2020	

Appendix B: Flow Diagram of Systematic Literature Review Search Results



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