VARIABILITY IN PREOPERATIVE EMERGENCY UTILIZATIONS IS ASSOCIATED WITH INITIAL PRIMARY PACEMAKER INSERTION

by

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ABSTRACT

DEBOSREE ROY. Variability in preoperative emergency room utilization is associated with initial primary pacemaker insertion (Under the direction of DR. JAMES STUDNICKI)

Implantable pacemaker insertions are recommended for treating bradycardia, heart block, or both by the Centers for Medicare and Medicaid, as well as healthcare policy groups, such as the American College of Cardiology and the American Heart Association. The incidence of pacemaker insertions has been steadily rising since the 1980s. Most surgeries are done in an inpatient setting. Bradycardia and heart block, although benign in terms of manifestation and symptom presentation on a regular basis, may present with radical symptoms such as chest pain, fatigue, or syncope without notice and may incite emergency room visits. Incidental chest pain and syncope are leading presenting conditions for emergency room visits in the United States. By way of these known etiologies and facts pertaining to emergency room use, we can justifiably assume that bradycardia and heart block leading to inpatient pacemaker insertions may have patients routing through the emergency room. We hypothesized that patients diagnosed with bradycardia, heart block, or both in the emergency room who have higher preoperative emergency room use may have a greater likelihood of receiving an eventual initial pacemaker in the inpatient setting, relative to patients with the same diagnoses, who do not visit the emergency room as often.

This retrospective case-time study used data from the Healthcare Cost and Utilization Project's (HCUP; an Agency for Healthcare Research and Quality project) State Inpatient Database (SID) and State Emergency Department Database (SEDD) from

Florida for 2011 and 2012. Patients were indexed at their first emergency room visit in 2011 and followed through to the first pacemaker insertion in the SID or censored at the end of observation (December 2012 in SID or SEDD). Patients receiving a pacemaker in the -p cases were incidence density matched with controls who did not receive a pacemaker at a 1:4 ratio on age, sex, and time under observation in the study period. Patient demographics and clinical characteristics as well as emergency room use characteristics were compared between cases and controls using descriptive and bivariate statistics. Conditional logistic regressions were used to assess marginal likelihood associated with higher emergency room use in the matched cohort.

The matching yielded a well-balanced study design and sampling. Approximately 60% of cases had 2 or more emergency room visits in the observation period, whereas only 33% of the control group had 2 or more emergency room visits in the individual case-matched observation window. Our linear regression models also corroborated the descriptive findings. Patients with higher counts of emergency room visits in the observation period were almost twice as likely to have an eventual pacemaker (OR = 1.754, 95% CI 1.536, 1.957).

Study findings helped us to reject the null hypothesis. Higher preoperative emergency room use was indeed associated with a higher likelihood of an eventual pacemaker among patients diagnosed with bradycardia, heart block, or both.

INTRODUCTION

The premise of this research rests on a pilot study conducted with the same dataset used for this study (with different years of data). The pilot study sought to classify pacemaker implantees by their preoperative emergency room use and to explore patient characteristics around those classifications. Patients diagnosed with bradycardia, heart block, or both who received a primary initial pacemaker were retrospectively studied for 1 year previous to the day of surgery. Such patients could be categorized as being (1) scheduled–patients who never visited the emergency room in the study period, (2) patients with emergency room history–patients who had evidence of emergency room visits in the observation period but had their surgery at least 1 day after their last emergency room visit in the observation period, and (3) true emergencies–patients who had their surgeries on their very first emergency room visit in the observation period. Logistic regression analysis revealed that Medicare beneficiaries with primary pacemaker were almost 65% less likely to be in the emergency room history category compared with those who had private insurance (OR = 0.35; 95% CI 0.16, 0.74). However, they had a 2-fold greater likelihood for being true emergencies than patients with private insurance (OR = 2.28; 95% CI 1.06–4.91). Patients with heart block as an inpatient discharge diagnosis were 48% more likely to be in the emergency room history category compared with those who did not have heart block alone as a discharge diagnosis (95% CI 1.06, 2.08). Conversely, patients with heart block alone (not including a diagnosis of bradycardia) were only half as likely to be in the true emergency category compared with those who did not have it (OR = 0.594; 95% CI 0.42, 0.85). Cardiac arrhythmias decreased the likelihood for patients to be in the emergency room history category by

44% (OR = 0.66; 95% CI 0.54, 0.83), although they increased the likelihood of patients to be in the true emergency category by 54% (OR = 1.54; 95% CI 1.24, 1.93). Any diagnosis for coagulopathy, conversely, decreased the likelihood for patients to be true emergencies by more than 50% (OR = 0.47; 95% CI 0.28, 0.79). Patient demographic characteristics did not have a significant effect on their likelihood of being scheduled admissions. However, not having comorbidities such as a pulmonary circulation disorder (OR = 0.48; 95% CI 0.25, 0.89) and having comorbidities such as chronic pulmonary disease and fluid and electrolyte disorders increased likelihood 67% (95% CI 1.11, 2.52) and 69% (95% CI 1.11, 2.57), respectively, for patients to be in the scheduled category.

The most logical suggestion from this pilot study was that emergency room use was important in the process of patients getting a pacemaker. Hence, to build on the pilot, we conducted the current study with the objective of testing the quantum of importance of preoperative emergency room use with regard to predicting an eventual primary initial pacemaker.

[The pilot study has been published in the *Journal of Hospital Administration*]

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CHAPTER 1: BACKGROUND

1.1. Motivation

Implantation of a cardiac pacemaker is the treatment of choice for severe or symptomatic bradycardia, heart block, or a combination of both.[1] Pacemakers are a cardiac rhythm management device; implantations usually require hospitalizations.[2] Current Centers for Medicare & Medicaid Services (CMS) guidelines also reflect that implanted cardiac pacemakers are "reasonable" treatment for nonreversible symptomatic bradycardia.[3] Use of implantable pacemakers has risen notably after clinical success in treating bradycardia and conduction disorders of the heart in multiple population based studies and small cohort studies.[4] Additionally, experience from performance and outcomes of this procedure, as well as the monitoring capacity of the device itself, have added to the existent knowledge base about indications for electrophysiological procedures to treat pace and conduction disorders of the heart.[5]

No current population-based studies indicate a national estimate for permanent pacemaker implantation. A 2008 trend study conducted in an isolated cohort reported permanent pacemaker implantation increased from 36.6 per 100,000 person-years between 1979 and 1999 to 99 per 100,000 person-years between 2000 and 2004.[6]

A 1988 population survey pegged US prevalence of implantable pacemakers at 2.6 per 1000 populations. Prevalence was higher in older adults. Age-adjusted estimates from the same survey (Medical Device Supplement to the National Health Interview

Survey[7]) were 1.5 times higher in women than men.[3] In the US Medicare population, prevalence of inpatient primary pacemaker between 1990 and 2000 increased from 325.4 to 504.4 per 100,000 beneficiaries.[7] However, the prevalence of the procedure in men was greater than that in women among Medicare beneficiaries in the same period.[8] From 1993 to 2006, 2.4 million US adults received a primary pacemaker, as estimated from national hospital inpatient discharge summaries.[3] In a study conducted with Medicare claims data, permanent pacemaker implantation increased from 325.4 per 100,000 beneficiaries in 1990 to 504.4 per 100,000 beneficiaries in 2000.[9]

The Sino-Arterial node (SAN) is the natural pacemaker of the human heart. Activity is dependent on spontaneous nodal membrane depolarization occurring between cardiac action potentials and is mediated by the autonomic nervous system. Cholinergic or β-adrenergic stimulation either accelerates or decelerates SAN function.[10]

Cardiac dysrhythmia (also known as arrhythmia or irregular heartbeat) includes any of a group of conditions in which the electrical activity of the heart is irregular or is faster or slower than normal. The heartbeat that is too slow (<60 beats per minute) is called bradycardia. Cardiac pacemaking relies on I_f current or pacemaker current.[11] The molecular constituents of pacemaker current are hyperpolarization-activated cyclic nucleotide-gated (HCN) channels.[11] Of the 2 HCN channels expressed in the human heart, dysfunction of HCN4 in mouse cardiac models (cre-lox) has been shown to contribute to severe bradycardia and atrioventricular (AV) block.[11]

The vast majority of heart blocks, also known as AV blocks, arise from pathology at the AV node. The causality of heart blocks has been a subject of investigative debate for a long time. A classic study conducted in 1969 using retrospective chart review found

bilateral bundle-branch fibrosis, cardiomyopathy, coronary artery disease, myocarditis, calcification of valves, collagen disease, amyloidosis, congenital heart disease, hemosiderosis, and luetic disease to be the most common causes of heart block, in that order.[12]

Types of blocks are as follows:

- First degree heart block, which manifests as PR prolongation
- Second degree heart block:
  - Type 1, also known as Mobitz I or Wenckebach
  - Type 2, also known as Mobitz II
- Third degree heart block, also known as complete heart block

Because bradycardia and heart block can occur separately and together and may have causal linkages between the 2, we divided the population of interest (receiving primary pacemaker) into 3 categories for retrospective analysis: (1) bradycardia, (2) heart block, and (3) both.

A 2002 consensus on guidelines for primary pacemaker reached through collaboration between the American College of Cardiology, the American Heart Association, and the North American Society for Pacing and Electrophysiology recommended appropriate clinical indications for primary pacemaker insertions. The experts participating in this consensus development thought that adults with third degree and advanced second degree AV block induced bradycardia and symptoms for heart failure that may require permanent pacing. They also thought that adults with chronic bifascular and trifascular block, as demonstrated by asymptomatic first-degree AV block, asymptomatic type-1 second degree AV block at the supra-His level, and alternating

bundle-branch block, may require permanent pacing.[13] The recommendations were elaborated on in a 2008 report on consensus development on indications for permanent pacemaker. The new recommendations for permanent pacemaker included indications for sinus node dysfunction with documented symptomatic bradycardia, which may be induced by prolonged drug therapy for chronic illnesses.[14] Changes in AV conduction in open aortic valve replacement also need to be addressed with permanent pacemaker implants.[15] (See appendix A for complete list of indications for which pacemaker insertions are recommended.) Other studies have indicated that permanent pacemakers are used to treat vasovagal (neutrally mediated) syncope[16] and sick sinus syndrome.[17,18] Most conditions that require cardiac pacing with permanent pacemakers are manifested in symptoms such as syncope, presyncope, dyspnea, and fatigue,[19] which drives emergency room use in patients with cardiac problems.[20]

Symptoms as precursors or manifestations of cardiovascular diseases are often appraised in the emergency room.[21] Emergency room referrals for hospital admissions are made after determination of a life-threatening condition.[22] Emergency rooms are major portals through which members of the community access care for urgent and complex medical needs.[23,24] Almost 50% of all nonobstetric admissions in the United States in 2006 recorded previous emergency room visits.[25] Although plenty of studies have focused on emergency room utilization to study its impact on costs,[26] few have explored the shift in the emergency room's role in the US healthcare system.[27] Almost 25% of all acute care outpatient visits in the United States take place in the emergency room.[28] This is because the emergency room is more accessible to patients, especially those suffering from acute events related to cardiac diseases. The emergency room services are available

24 hours a day, 7 days a week, regardless of insurance status; as a setting, the emergency room guarantees the best possible treatment for acute events, given its proximity to the inpatient hospital setting and allied resources.

Although the literature examining cardiac diseases and rhythm management in isolated care settings is adequate, there is a dearth of studies exploring the phenomenon from the perspective of a care continuum.

The emergency room is increasingly becoming the gateway to care in the United States. Symptoms that manifest conditions with pacing needs—such as shortness of breath, syncope, or chest pain—often prompt people to seek care in the emergency room. In fact these symptoms may qualify as precedents for emergency room visits if presented at a doctor's office or an urgent care clinic. In addition, in recent years, cardiac pacing with the use of cardiac pacemakers has increased.[29] The objective of this study is to assess the association (if any) between high emergency room use in patients with bradycardia, heart block, or both and an eventual surgical event of a primary initial pacemaker insertion in the inpatient setting.

1.2. Theoretical Framework: Access to Medical Care

Aday and Anderson, in their seminal paper published in 1975 conceptualized access in the following way:

> A basic framework for the study of access, then, may be conceptualized as proceeding from health policy objectives through the characteristics of the healthcare system and the populations at risk (inputs) to the outcomes or outputs: actual utilization of healthcare services and consumer satisfaction with these services . . .. The delivery system is characterized by two main elements-resources and organization.[30]

They further traced the process flow back to patient characteristics in need of healthcare based on Anderson and Newman's description,[31] which included predisposing,

enabling, and need components. Predisposing characteristics, which are existent before onset of illness, include age, sex, values, and so forth of patients. Enabling characteristics pertain to the means individuals have at their dispososal to seek healthcare. These include patient income, insurance, and attributes of the patient's geographical location (e.g., rural or urban dwelling). A patient's need-characteristics refer to his or her level of illness or suffering. The process is diagrammatically represented in Figure 1.

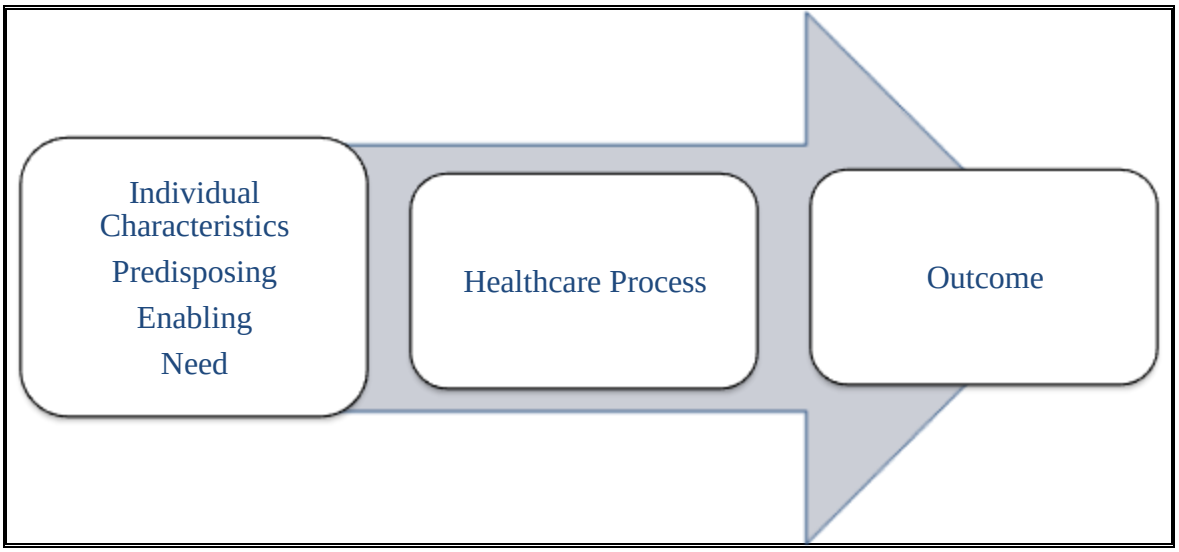

Figure 1. Schematic showing the process flow of Access to Medical Care

The original framework was adapted to suit the scope of the study, which was dependent on the availability of variables to test the hypothesis. The very premise of this study's hypothesis depends on the premise of access to care. Emergency room use is associated with low access to care. Because emergency room use is the primary exposure of interest in this study, it is imperative to look at how it mediates the outcome of an eventual primary initial pacemaker insertion in patients with certain predisposing characteristics.

In terms of this guiding theoretical model, the predisposing characteristics of the patient–characteristic component are as follows: symptomatic presentation of diseases

(bradycardia, heart block, both), presence of comorbidities (discussed in the methods section), and certain demographic characteristics (e.g., age, sex, location). The primary enabling characteristic of the patient–characteristic component is access to care, that is, the primary expected payer. The process component features emergency room use characteristics, such as number of emergency room visits, time from first emergency room visit to eventual outcome (pacemaker/no pacemaker), and duration of the first emergency room visit. The outcome component is representative of the overall outcome of the study: the likelihood of a primary initial pacemaker insertion in the inpatient setting. The ontology of the process flow that guided the study design (as guided by the theoretical model under discussion) is represented diagrammatically in Figure 2.

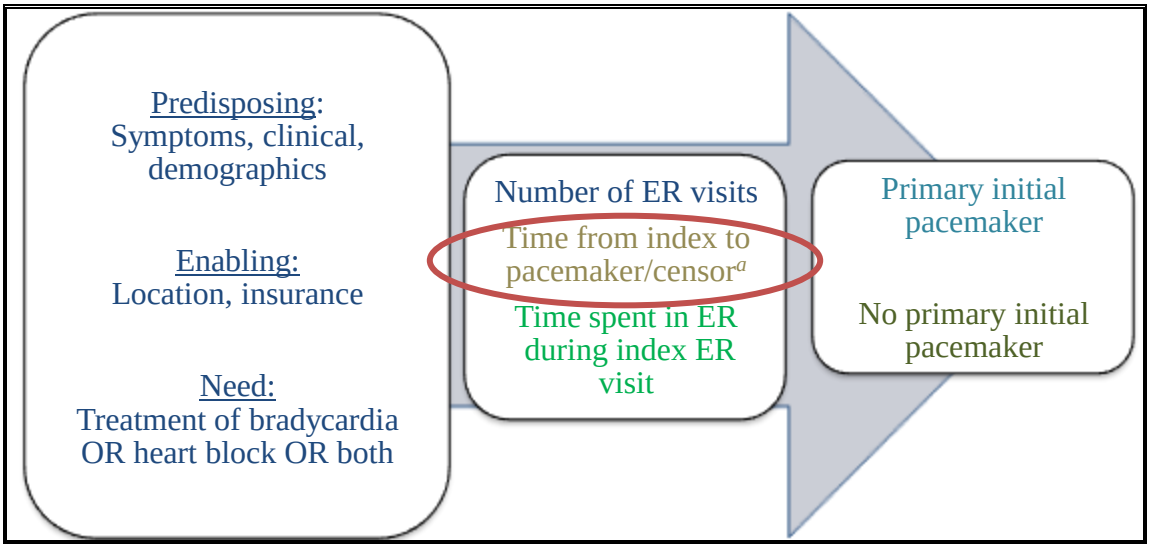

Figure 2**.** Schematic showing process flow of Access to Medical Care (adapted)

Note. ER = emergency room.

[a]Variable used for matching cases and controls, not used a predictor in models.

1.3. Hypothesis Statement

Variable preoperative emergency room use is associated with the likelihood of primary initial pacemaker insertion in the inpatient setting in patients with bradycardia, heart block, or both.

1.4. Broader Research Questions

1. What patient characteristics, clinical and demographic, are associated with inpatient primary initial pacemaker insertion among patients with bradycardia, heart block, or both who have at least 1 emergency room visit in a limited observation period?
2. In patients with bradycardia, heart block, or both, what is the difference in the emergency room use profile between those who have an inpatient primary initial pacemaker and those who do not?
3. Does higher preoperative emergency room use among patients with bradycardia, heart block, or both posit an increased likelihood for inpatient primary initial pacemaker?

CHAPTER 2: MATERIALS AND METHODS

2.1. Data Set

This study was conducted using the linked databases of Florida Healthcare Cost and Utilization Project's (HCUP; a product of AHRQ) state inpatient data (SID) and state emergency department data (SEDD) for the years 2010 and 2011. SEDD 2011 was used to create the initial base cohort. SEDD 2012, SID 2011, and SID 2012 temporally trail SEDD 2011 according to the study plan and hence were used to locate patients from the base cohort who could be observed over the study period. The data contain a complete sample of annual inpatient, emergency room, and ambulatory surgery discharges from civilian hospitals that participate in record collection. Each healthcare setting releases data in separate data files. the existence of a unique patient identifier enabled the study of patients and outcomes across the 3 settings and several years. The data are event level. There are 31 diagnosis and procedure categories attached with each inpatient discharge record, and there are 10 diagnosis and 3 procedure categories attached with each emergency room discharge record. They are presented as separate and continuous variables. The importance of a particular diagnosis or procedure is determined by its relative position in the hierarchy of diagnoses or procedures. The diagnosis variables are 5-character International Classification of Diseases, version 09 (ICD09) codes for diseases. Procedure variables are 4-character ICD09 codes for procedures.

2.2. Description and Manipulation of Variables

2.2.1. Patient Characteristics: All patient characteristic data were obtained at baseline from the index emergency room profile of patients. Race is a 6-category variable that was transformed into a 3-category variable (white, black, or other); payer is a 6-category variable that was transformed into a 3-category variable (Medicare, Medicaid, other insurance); patient location (*zipqrtl*) is a 4-category (large metropolitan, small metropolitan, non-metro urban, and rural) that is based on the 2010 Florida Department of Health's designation of rural and urban counties (density of less than 100 persons/mile^2 constitutes a rural county); age is a continuous variable. Patient clinical characteristics such as comorbidities and Charlson comorbidity score (CCI) are not mutually exclusive within the attributes themselves. Comorbidities were computed using the Elixhauser algorithm of comorbidities affecting quality of life. Only the most common comorbidities were retained for analysis. Diseases in this profile that were used for inclusion were left out of analysis. CCI is a variable consisting of the count of selective diseases (computed with the Romano adaptation of the algorithm) that each patient has. These were computed by incorporating observations for specific ICD09s if observed in any of the 10 diagnoses related data locations attached to each emergency room visit record.

2.2.2. Emergency Room Utilization: "Number of emergency room visits" is a variable that is a count of number of emergency room visits patients have made in the observation period, including those that led to an inpatient admission not leading to pacemaker insertion on the same day as the emergency room visit. This variable was as a continuous variable. It was also manipulated into 6 categories (1 emergency room visit, 2

emergency room visits, 3 emergency room visits, 4 emergency room visits, 5 emergency room visits, and 6 or more emergency room visits). The selection of categories was guided by the distribution of data (explained in the results section). Time from index emergency room to event is a continuous variable indicative of the total time spent in hours by patients on their index emergency room visit.

2.2.3. Outcome: Pacemaker is a binary variable indicative of an initial primary pacemaker insertion in the inpatient setting.

2.2.4. Temporal Variable and Manipulation: Index date is the time corresponding with the patients' index emergency room visit. This variable was derived from a variable available in the dataset called *daystoevent*. It was available in all HCUP datasets. This continuous variable consisted of a random 8-digit number assigned to a patient when he or she was first identified in a dataset or visited a healthcare facility contributing patient records to HCUP for the very first time. If he or she happened to visit the same or any other facility contributing data to the project again, the number of days between the first, the second, and subsequent visits were counted and added to the random number first assigned to her or his very first visit. This way, each visit or event irrespective of the setting (emergency room visit, inpatient admission, ambulatory surgical visit) received a unique *daystoevent* value that was also unique to the patient.

2.2.5. Other Flag Variables Pertinent to Inclusion but not in Analysis: In HCUP, patients who have an inpatient admission on the same day as an emergency room visit have their admission recorded in the in the inpatient database. However, they are identified as having a source of admission in the emergency room through a variable *hcup_ed,* which has the following values:

0 = Record does not meet the HCUP emergency room visit criterion (admission did not originate in the emergency room)

1 = Presence of emergency room revenue code (admission originated in the emergency room)

2 = Positive emergency room charge (admission originated in the emergency room)

3 = Emergency room Current Procedural Terminology (CPT) code present (admission originated in the emergency room)

4 = Condition code P7 present (Effective July 1, 2010, a new condition code, P7, must be submitted for Federal Employee Program claims when a patient is transferred or admitted to an inpatient facility from an emergency room. Currently, condition code P7 is used to identify patients who are admitted as inpatient from an emergency room on facility claims.)

Following the description, we retained observations (meeting inclusion criterion described under 'Inclusion and Exclusion') in the 2011 and 2012 SID files with *hcup_ed* flag values of 1, 2, 3, and 4 and incorporated them in our population of emergency room visits, taking into consideration that these patients had an emergency room visit that was not accounted for in their SEDD records.

2.3. Inclusion and Exclusion

All patients with at least 1 emergency room visit in 2011 with at least 1 diagnosis of bradycardia or heart block or both during the first visit included. (See Appendix B for list conditions, which, when diagnosed, has a recommended treatment with permanent pacemakers). Of these, patients who died in 2011 or had incomplete information (missing value) on for race, sex, age, insurance, or residence location were excluded. Patients who

died during any hospitalization or emergency room visit (index or subsequent) have also been excluded. The selection process is diagrammatically represented in Figure 3.

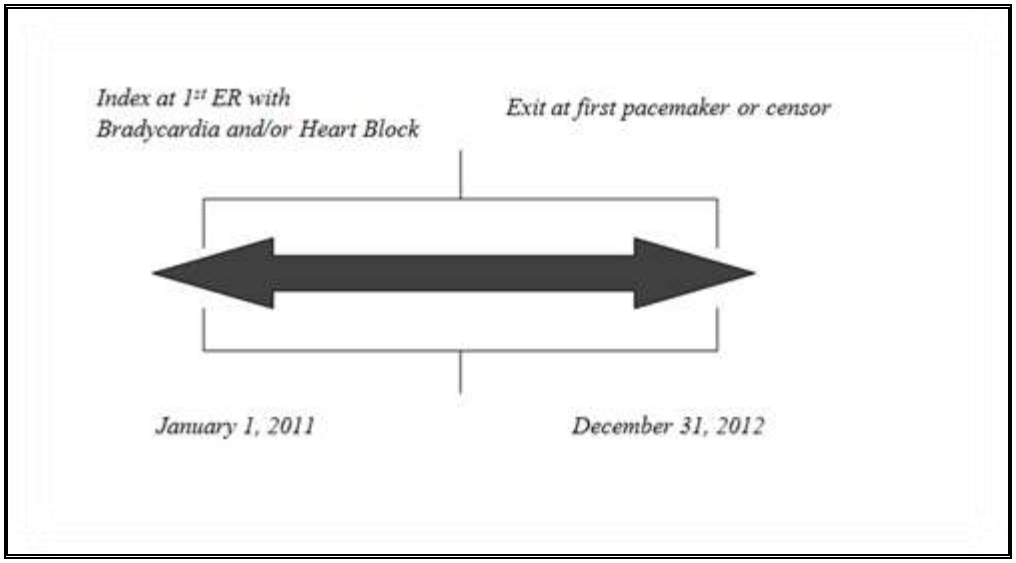

Figure 3. Schematic showing selection process

2.4. Rationale of Approach

Because our hypothesis tests the association between the exposure of 1 or multiple emergency room visits before surgery and the risk for outcome or pacemaker insertion, the study builds on a temporal follow up to an index event (first observable emergency room visit in data) to allow for observations of multiple emergency room visits subsequent to the index emergency room visit.

The outcome studied is an initial primary pacemaker in the inpatient within the conveniently chosen observation period of 730 days (or 2 data years of Florida HCUP) of the index emergency room visit. The alternative to our outcome of query is no indication for initial primary pacemaker in the inpatient within 730 days of index emergency room visit. Selected patients were indexed on the day of their first visit to the emergency room in 2011. Thereafter via unique linkages between the SEDD and the SID, they were (if

applicable) identified in the SID if they had any eventual inpatient pacemaker insertion within 730 days of their index visit. For patients identified as having an initial primary pacemaker in the observation period, the observation period automatically was truncated to the difference between date of surgery and the date of index visit. Patients who did not have an initial pacemaker insertion were censored at a date that was derived using the following formula:

Index date + {total obs. period – (middle of discharge qrtr. associated with index emergency room /total discharge qrtrs. in obs. period × 365)}

When applied to data, the formula translates to patients in the following ways:

For patients entering the study in quarter 1 of 2011 hospital year

= Index date + {730 – (1.5/8 × 365)}

For patients entering the study in quarter 2 of 2011 hospital year

= Index date + {730 – (3/8 × 365)}

For patients entering the study in quarter 3 of 2011 hospital year

= Index date + {730 – (4.5/8 × 365)}

For patients entering the study in quarter 4 of 2011 hospital year

= Index date + {730 – (6/8 × 365)}

where

Index date = the date corresponding with the patient's first emergency room visit

Quarter = time in the year (in 3 month segments) when the patient has the index emergency room visit. There were 8 quarters in the observation period, consisting of 2 years

Total days of observation = 730

Total days in the year = 365

We used the middle of the quarter (corresponding to the use of numbers 1.5, 3, 4.5, and 6, in the formula) in which the index emergency room visit took place to peg values for length of follow up, because the actual date (day and month) for index date is not available in the dataset. This deficiency is described at length under the variables of interest in the methods section.

In our data of population at start of study, *n* = 57,425, and outcome occurrence (*n* of initial primary pacemaker) *n* = 623.

Because our data have 2 units of time (in years), there are 2 likely conditional probabilities of outcome occurrence.

In our data, 491 patients met outcome by end of Year 1 and 132 patients met outcome by end of Year 2.

In our study, conditional probability of outcome for Year 1 =

π^1 = number of surgeries in Year 1/total population at risk at start of Year 1

= 491/57425 = 0.008.

Conditional probability of outcome for Year 2 =

π^2 = number of surgeries in Year 1/total population at risk at start of Year 2 =

132 /56932 = 0.002.

The cumulative probability of outcome occurrence within observation period is the product of the conditional probabilities of outcome occurrence for each year in the observation period

= $\pi^1 \times \pi^2 = 0.008 \times 0.002 = 0.000016$

The likelihood of outcome is proportional to probability of outcome with given parameter estimates for model. Natural logarithm is a monotonically increasing function, the maximum value of which is reached at the same points as the function itself. Logarithmic transformation of the likelihood of outcome is somewhat preferable to the maximum likelihood estimate itself, because it simplifies the process of drawing inference about the nature of the data.

Under this arrangement, a patient who receives a pacemaker (meets outcome) by the end of the first year of observation contributes log (π^1) to the log likelihood of outcome occurrence. Conversely, a patient who does not meet outcome at the end of the first year of observation contributes log $(1 - \pi^1)$ to the likelihood of outcome occurrence. Similarly, a patient who meets outcome in the second year contributes log $(1 - \pi^1)$ + log (π^2) to the log likelihood of outcome occurrence and a patient who does not meet outcome in the same period contributes log $(1- \pi^1)$ + log $(1- \pi^2)$.

Hence, we can calculate the total likelihood of outcome occurrence by multiplying the individual contributions to log likelihood with the frequency of patients meeting or not meeting outcome at each time point and adding the products together.

Substituting values, the total log likelihood of outcome occurrence =

$$= \quad 491 \log (0.008) + 56{,}934 \log(1 - 0.008) + 132 \log(0.002) + 56802 \log(1 - 0.002)$$

$$= \quad -1029 - 171 - 356 - 45$$

$$= \quad -1601$$

The extremely small values for both the cumulative probability and the log likelihood estimate of outcome occurrence indicate that the sample size of outcome

occurrence is not adequate for any comparison analysis with that of the rest of the cohort. This may be an affect of the brevity of the study period.

Additionally, due to limitations on follow-up imposed by secondary data, we were unable to follow all patients included in our study population in the observation period apart from patients who had an initial primary pacemaker or multiple emergency room visits or 1 or more inpatient admissions not on account of an initial primary pacemaker insertion in the observation period. Hence, a traditional observational design to look at the effect of the exposure of interest on the outcome of interest by following the cohort to all eventualities could not be adopted. Therefore, we addressed this problem with adopting a case–control approach for study design.[32]

In our study, the risk and odds parameters for outcome occurrence were as follows:

$\pi = D/N = 623/57425 = 0.011$

$\Omega = D/N - D = 623/56802 = 0.010$

where

π = the parameter for modeling risk of outcome,

Ω = parameter for modeling odds of outcome,

D = number of initial pacemakers in the study period, and

N = population/ cohort size.

We can surmise that π and Ω are approximately equal, because the probability of outcome occurrence is small. Under this condition, π and the cumulative rate of outcome occurrence (λt) are also approximately same. Here, λ is the parameter for rate of outcome

occurrence and *t* is the time period of observation. The rate parameter of outcome occurrence over the period of observation is estimated by slicing the period of observation into bands of time of equal length and estimating the common probability of outcome occurrence in each time band. In our data, if the observation period is sliced into 2 bands of equal length (1 year each), 56,934 patients have 2 time bands of observation each and 491 patients have 1 time band of observation each. The sum total of all units of observation in time bands that patients experienced =

$$(56{,}934 \times 2) + (491 \times 1) = 114{,}359$$

The probability of outcome occurrence in each time band most likely equals 623/114359 = 0.006. Hence cumulative rate of outcome occurrence is

$$\lambda t = 0.006 \times 2 = 0.0012$$

The equality of these estimates satisfies the criterion for classifying our outcome of interest as a rare event in our data.

Despite adopting a case–control design due to issues with sample size, the number of cases may have still been inadequate for analysis. To avoid this eventuality, we adopted incidence density sampling as a technique for matching cases to controls. This approach involves several consecutive short studies using patients remaining at the base of a concluded study in the immediately ensuing study. Each study provides a separate estimate of the rate ratio for outcome occurrence. If this ratio remains constant over the study period, an estimate of rate of occurrence can be aggregated, standardized, and compared between the cases and the controls.

Two assumptions (in addition to that of equality of risk, odds, and rate parameters of outcome occurrence) were made while adopting this approach:[33]

1. All patients were observed from the beginning of the study period.
2. All patients who did not meet outcome of interest in the study period remained under observation until the end of the study period.

2.5. Identifying Cases and Controls

All patients with any diagnosis for bradycardia, heart block, or both and with at least 1 emergency room visit in 2011 who had a primary initial pacemaker insertion were considered as cases. The individual window of observation in the study for cases was the difference between the day of surgery and index date (as described elsewhere). All patients with any diagnosis for bradycardia, heart block, or both and at least 1 emergency room visit in 2011 who did not get a primary initial pacemaker insertion were considered controls. Individual window of observation in the study for controls was the difference between the day of censor and the index date (as described elsewhere). Cases and controls were matched along age at index visit and window of observation in the study at a ratio of 1:4 using the following algorithm (See Appendix C for SAS code detailing this algorithm) :

Select Control if {control age = (age at index visit –1 ≤ age at index visit ≤ age at index visit + 1) of case} and (control observation window is ≤ case observation window).

A schematic representative of the matching criterion is presented in Figure 4a. The distance between index emergency room and pacemaker insertion is indicative of the time window of a case patient. Four control patients (who did not receive a pacemaker) who are of the same sex, of similar age, and have an observation window that is as long

as or greater than that of the case patient were chosen in each matched set of case and controls. Each set was assigned a number.

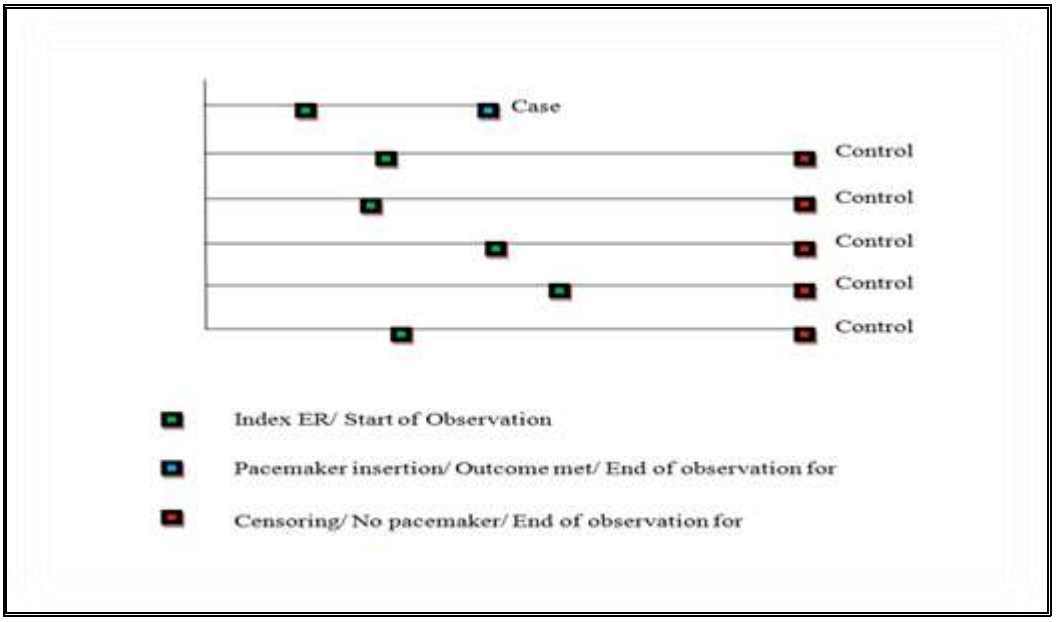

Figure 4a. Schematic showing the temporal criterion of matching

2.6. Follow-up and Observation

Follow up for controls depended on that of the case patient in each matched set of case and controls. Although all controls had a natural observation period, which varied from 1 to 730 days, the applicable observation period for controls was essentially the period of time (in days) the matched case patient was observed in the study. For example, if a case patient had an observation period of 230 days, her or his control also had an effective observation period of 230 days, regardless of how long the control patients could have been observed in the dataset. This was done because of the nature of the primary explanatory/independent variable: the number of emergency room visits, which has a significant temporal component (as explained elsewhere). Emergency room visits of controls (if any), which were observed after the observation period of their case patient, had to be discarded from the study. This was done to gain a true balanced design to

ascertain the true effect of the primary explanatory/independent variable. Truncation of observation with regard to counting the exposure (number of emergency room visits) was done manually. The truncation of observation is diagrammatically displayed in Figure 4b.

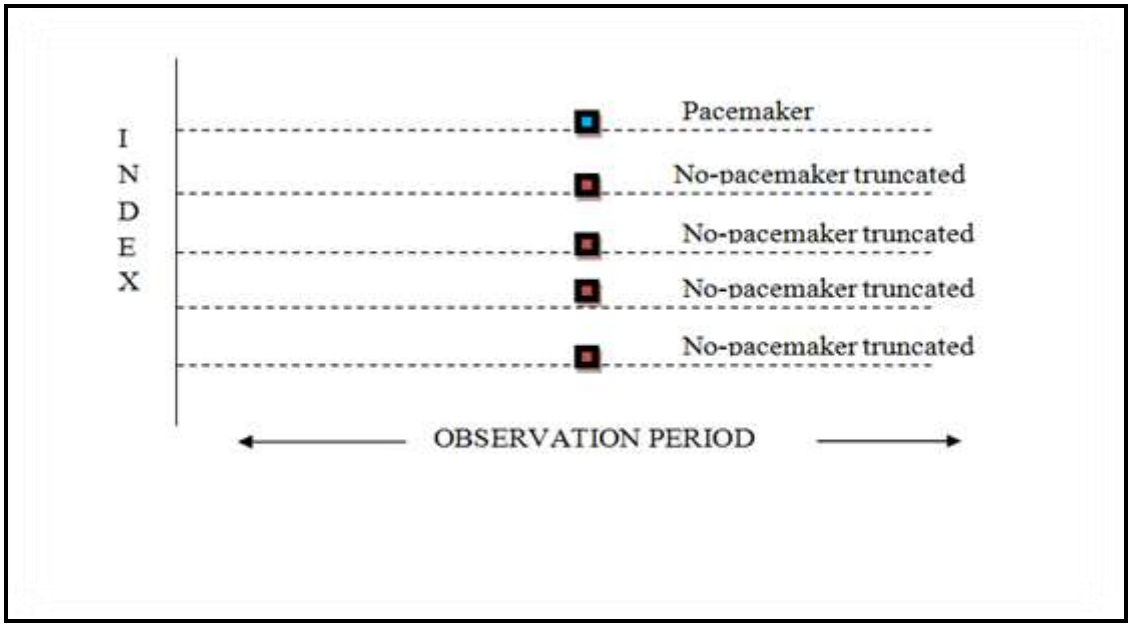

Figure 4b**.** Schematic showing the truncation of observation to suit study

2.7. Statistical Analysis Plan

2.7.1. Question 1. What patient characteristics, clinical and demographic, are associated with inpatient primary initial pacemaker insertion among patients with bradycardia, heart block, or both who had at least 1 emergency room visit in a limited observation period?

Case and control patients' demographic and baseline clinical characteristics were defined using descriptive statistics. Binomial and categorical variables were described using frequency and percentages. Continuous variables were described using measures of central tendency (means and standard deviation). The association between the binomial outcome variables and select variables of interest, which are binomial or categorical, were estimated using χ^2 tests. The probability associated with the relationship was

reported. The mean variance between the cases and controls in terms of their distribution in continuous variables was tested by *t* tests. The probability associated with the variance estimates was reported. Results were reported in tables.

2.7.2. Question 2. In patients with bradycardia, heart block, or both, what is the difference in emergency room use profile between those who have an inpatient primary initial pacemaker and those who do not?

The answer to question 2 was assessed in 2 parts. As per available data, emergency room use profile could be defined as follows:

1. For the entire observation period: Distribution of the number of visits each patient had before he or she met an outcome (pacemaker insertion for cases; censoring for controls) as presented by the variable "Number of ER visits"
2. For the index emergency room visit:
    a. The symptom that elicited the visit
    b. The duration of the visit
    c. E-codes associated with the visit

Binomial and categorical variables were described using frequency and percentages. Continuous variables were described using measures of central tendency (means and standard deviation). The association between the binomial outcome variables and select variables of interest, which are binomial or categorical, were estimated using χ^2 tests. The probability associated with the relationship was reported. The mean variance between the cases and controls in terms of their distribution in continuous variables was tested by *t* tests. The probability associated with the variance estimates was reported. Results were reported in tables.

Univariate statistics for "Number of ER visits" was also computed and its distribution displayed in graphs. The distribution of emergency room visits of cases and controls was also graphically compared using a histogram.

2.7.3. Question 3. Does higher preoperative emergency room use among patients with bradycardia, heart block, or both posit an increased likelihood for inpatient primary initial pacemaker?

The answer to question 3 was reported in 3 parts: Part 1 is the conditional logistic without adjustments, Part 2 is the conditional logistics with adjustments and outcome variable as a continuous variable, and Part 3 is the conditional logistic with adjustments and outcome variable as categorical. The sectioning pertained to the nature of the outcome variable assessed. The scope of the study delineated finding the maximum likelihood of a pacemaker being inserted given variable preoperative emergency room use by patients. Hence, both conditional logistic regressions (frequentist) and exact conditional logistic regressions were used to assess the effect of Number of ER visits on the odds/risk of getting a permanent pacemaker, because both are traditionally used to assess maximum likelihood of an event happening. The regression models were stratified by the window of time in the observation period with which cases were matched with their controls (i.e., the strata for model building was the number assigned to each matched set,which was dependent on the window of time a case and its controls observed in the study). Exact conditional logistic regressions were used for the following reasons:[34]

1. To get rid of nuisance parameters (unknown parameters) in estimating unconditional likelihood of outcome happening
2. If the analytical dataset has sparse data (multiple binary variables)

3. The degree of freedom in a model is large (which happens when some kind of matching is done)

Conditional logistic regressions were run on the premise of conditional probabilities in stratum matched samples. Conditional probabilities were fashioned after priors. For example, for a patient who visits the emergency room once, his or her probability of meeting the outcome is 0.5 (given the outcome is a binary variable). However, if he or she does not meet the outcome, his or her probability of meeting the outcome after a second emergency room visit is conditioned upon the probability of her/his meeting the outcome after the first emergency room visit (prior probability). Hence, theoretically, the probability of meeting the outcome eventually increases with each emergency room visit. This logic is described graphically in Figure 5.

Two conditional logistic regressions and 1 conditional logistic exact regressions were used to assess the effect of number of emergency room visits (first as a continuous variable and then as a categorical variable) on the likelihood of pacemaker insertion in the population of interest. Additionally, 2 more conditional logistic models were used to assess the effect of number of emergency room visits, (first as a continuous variable and then as a categorical variable) on the likelihood of a pacemaker insertion in the population of interest, with adjustments with select covariates such as patient race, primary payer, patient location, CCI score, and certain comorbidities.

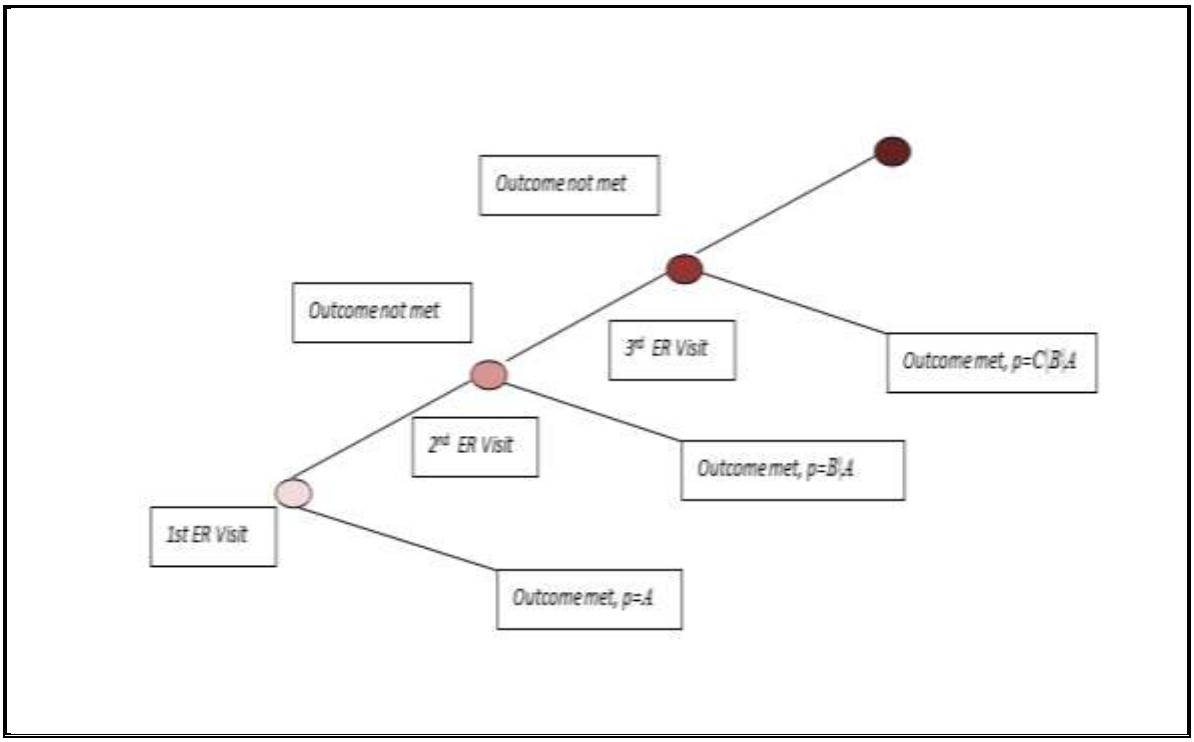

Figure 5. Schematic of conditional probability distribution guiding models

CHAPTER 3: RESULTS

3.1. Data Spread

In our unmatched cohort, of 57,425 patients indexed on their first emergency room visit in the SEDD 2011 (and with variable follow up in the SID 2011, SEDD 2012, and SID 2012), 623 patients had a primary pacemaker. Frequency of emergency room visits in the observation period of 730 days varied from 1 to 43 visits per patient. The spread is graphically represented in Figure 6.

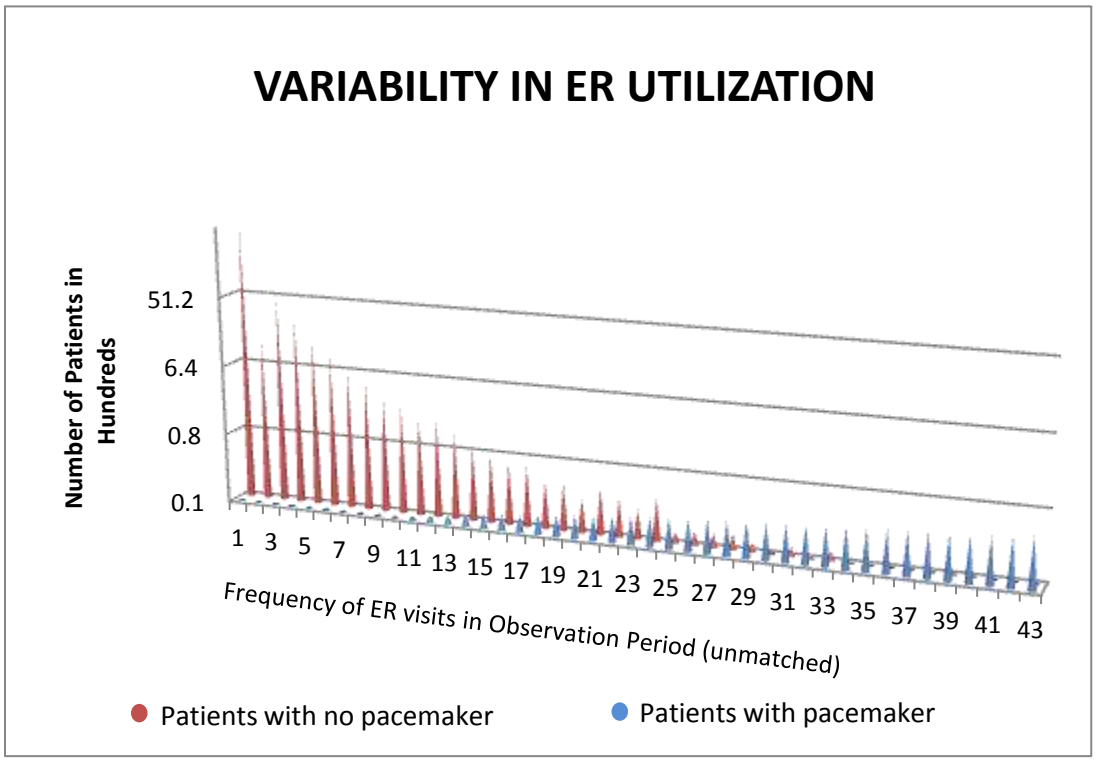

Figure 6. Histogram of patients' emergency room use (unmatched cohort)

Of the 623 patients who received a primary pacemaker (pacemaker in position 1 on the discharge record), 265 patients had an initial pacemaker. These patients were sampled for the study. (See Appendix B for a list of ICD09 procedure codes used for selection)

Incidence density matching using the algorithm adapted for the purpose (refer to the methods section; SAS code provided in Appendix C) yielded a well-balanced analytical cohort of 265 cases patients and 1084 controls. It is important to note that 20 extra controls (number of controls for 265 cases with a matching ratio of 1:4 would have yielded 1060 controls) were found from the pool and were retained for analysis.

3.2. Answer to Question 1

[Question 1: What patient characteristics, clinical and demographic, are associated with inpatient primary initial pacemaker insertion among patients with bradycardia, heart block, or both who had at least 1 emergency room visit in a limited observation period?]

We chose to run the analysis in our matched cohort, because our question was a part of a hypothesis that required testing the effect of the primary exposure (variable number of emergency room visits previous to event) on the outcome of an eventual initial pacemaker insertion in the primary setting. The nature of the hypothesis required the test to be done in a sample that was as homogeneous as possible with regard to covariates that may influence the relationship between the primary independent and the outcome variable. In our matched cohort of 265 cases and 1084 controls, patient characteristics were well balanced. Although we matched along age and sex, the distribution of other clinical and demographic characteristics were similar between the cases and the controls

(Table 1). In our descriptive exploration of association between various patient demographic and clinical characteristics with our outcome, we found that the highest proportion of patients in both cases and control were of white race (cases: 79.3%; controls: 71.6%; p =.117). The sample was also predominantly female (cases: 55.1%; controls: 57.0%; p = .2528). The mean age of case patients was 74 years (SD = 13.1) and that of controls was 74 years as well (SD = 14.2). As expected from the central tendency of age distribution in our sample, the primary expected payer was predominantly Medicare (cases: 80.7%; controls: 76.8%; p = .1617). Patient location was predominantly large metro (cases: 52.4%; controls: 55.4%, p = .3806), followed by small metro (cases: 39%; controls: 37.2%; p =.6103). Patient clinical characteristics did not vary much between the cases and the controls. Mean number of comorbidities per patient for both cases and controls were less than 1 (p = .3247). Hence, most patients from both case and control cohorts had a CCI score of 0 (cases: 57.7%; controls: 52.0%; p = .2710). Predominant comorbidities found in cases and controls were valvular disease (cases: 78.5%; controls: 79.7%; p = .6609), followed by hypertension uncomplicated (cases: 56.6%; controls: 56.1% p = .8796). Although bivariate statistical tests did not yield any statistically significant associations between any patient characteristics and the outcome variable, certain differences were discernible by studying the proportions of patients in each category. The group of pacemaker recipients (cases) were, on an overall, slightly older, had relatively more white patients, and were healthier (in terms of comorbidities) than their matched controls. The comorbidities observed in more case patients than controls were congestive heart failure (cases: 9.1%; controls: 78.7%; p = .8424), chronic

obstructive pulmonary disease (cases: 9.4%; controls: 12.9%; $p = .0713$), and uncomplicated diabetes (cases: 17.4%; controls: 19.6%; $p = 1.0000$; Table 1).

Table 1. Descriptive statistics of patient characteristics of a matched sample of patients with bradycardia, heart block or both who have at least 1 emergency room visit in the observation period of 730 days comparing those who received an initial pacemaker and those who did not.

Variable	Pacemaker $n = 265$	No Pacemaker $n = 1084$	p (χ^2/t test)
Race, *n* (%)			
White	210 (79.25)	776 (71.59)	.1117
Black	28 (10.57)	145 (13.38)	.2200
Other	24 (9.06)	139 (12.82)	.0917
Female, *n* (%)	146 (55.09)	618 (57.01)	.2528
Age, mean (*SD*)	74.3 (13.1)	73.7 (14.2)	.5431
Primary payer, n (%)			
Medicare	214 (80.75)	832 (76.75)	.1617
Medicaid	14 (5.28)	57 (5.26)	.9871
Other	25 (9.43)	103 (9.50)	.9730
Patient Location, *n* (%)			
Large metro	139 (52.45)	601 (55.44)	.3806
Small metro	103 (38.87)	403 (37.18)	.6103
Non metro urban	14 (5.28)	52 (4.80)	.7423
Rural	6 (2.26)	27 (2.49)	.8306
Avg. number of comorbidities, mean (*SD*)	0.99 (1.35)	0.94 (1.41)	.3247
Charlson Score,[a] *n* (%)			
0	153 (57.74)	564 (52.03)	.2760
1	43 (16.23)	209 (19.28)	
2	32 (12.08)	164 (15.13)	
3	18 (6.79)	90 (8.03)	
4	10 (3.77)	22 (2.03)	
5	5 (1.89)	24 (2.21)	
6	4 (1.51)	9 (0.83)	
7	0	2 (0.18)	
Selected Comorbidities, *n* (%)			
Congestive heart failure	24 (9.06)	94 (8.67)	.8424
Valvular disease	208 (78.49)	864 (79.70)	.6609
Hypertension, uncomplicated	150 (56.60)	608 (56.09)	.8796
Chronic obstructive pulmonary disease	25 (9.43)	140 (12.92)	.0713
Diabetes, uncomplicated	46 (17.36)	212 (19.56)	.4146
Hypothyroidism	4 (1.51)	16 (1.48)	1.0000
Renal failure	18 (6.79)	55 (5.07)	.2676
Fluid and electrolytes	20 (7.55)	93 (8.58)	.35867

[a]Computed using codes from the Romano adaptation of computing Charlson comorbidity index. The index takes into account 17 diseases that, when existing as comorbidities may affect survival.

3.3. Answer to Question 2

[Question 2. In patients with bradycardia, heart block, or both, what is the difference in emergency room use profile between those who have an inpatient primary initial pacemaker and those who do not?]

Emergency room use characteristics are central to the study hypothesis. For descriptive purposes, we transformed the emergency room use count into 6 categories: 1, 2, 3, 4, 5, and 6 and more emergency room visits per patient. A higher proportion of controls had a single visit to the emergency room in the observation window matching their respective cases (cases: 40.4%; controls: 67.1%, $p \leq .0001$). However, a higher proportion of cases had 2 visits (cases: 17.3%; controls: 14.4%, $p \leq .0001$), 3 visits (cases: 12.8%; controls: 4.7%, $p \leq .0001$), 4 visits (cases: 10.2%; controls: 3.8%, $p \leq .0001$), 5 visits (cases: 6.4%; controls: 1.8%, $p \leq .0001$), and 6 and more visits (cases: 12.8%; controls: 8.21%, $p < .0001$), in the matched observation windows (Table 2).

The distribution of overall number of emergency room visits was predominant in the 1 emergency room visit category for the entire cohort (Figure 7).

Table 2**.** Descriptive statistics of emergency room visit characteristics in the study period of a matched sample of patients with bradycardia, heart block or both who have at least 1 emergency room visit in the observation period of 730 days comparing those who received an initial pacemaker and those who did not.

Number of Emergency Room Visits, *n* (%)	Pacemaker *n* = 265	No Pacemaker *n* = 1084	*p* (χ^2/*t* test)
1	107 (40.38)	727 (67.06)	<.0001
2	46 (17.36)	156 (14.39)	
3	34 (12.83)	51 (4.70)	
4	27 (10.19)	41 (3.78)	
5	17 (6.42)	20 (1.85)	
6 or more	34 (12.83)	89 (8.21)	

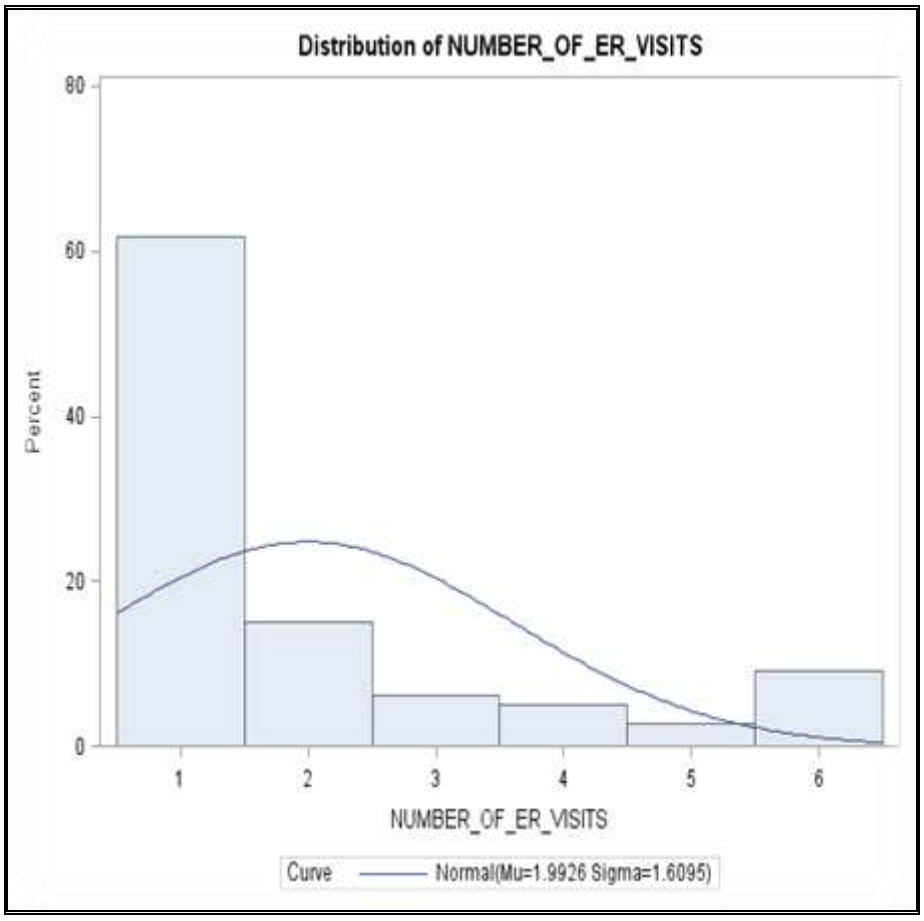

Figure 7**.** Distribution of preoperative emergency room visits

The findings from our descriptive analysis are corroborated by the graphical description of emergency room visit category distribution among cases (censor = 1) and controls (censor = 0) in Figure 8.

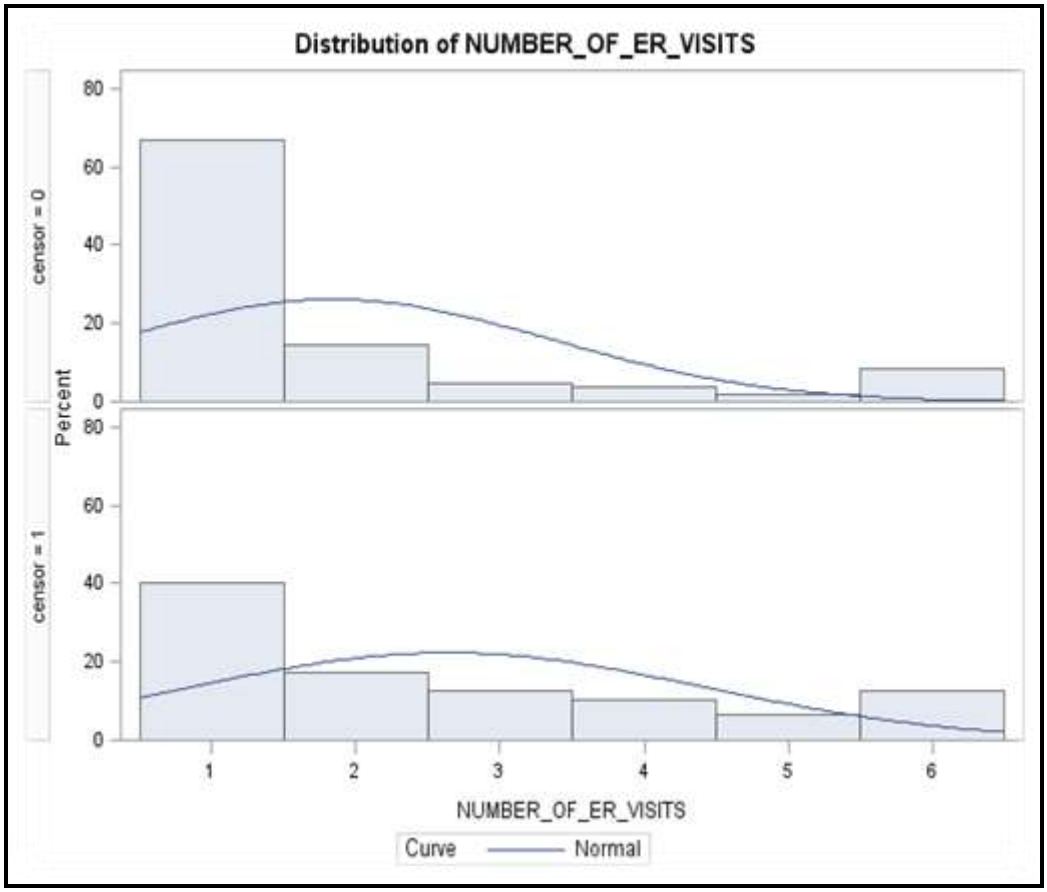

Figure 8**.** Comparative graph showing preoperative emergency room use

Other emergency room use characteristics that we could explore given the limitations of available data pertained to some description of the first emergency room visit (at which all patients were indexed). Presenting conditions preponderant in the sample were chest pain not otherwise specified (cases: 2.75%; controls: 14.29%, p = .760), chest pain, other (cases: 1.1%; controls: 7.69%, p = .760), syncope and collapse (cases: 2.75%; controls: 4.40%, p = .760), and the like. Fewer cases (compared with controls) had data pertaining to this variable; thus, we could not achieve a robust

exploration of this variable. A difference was seen in duration of visit between cases and controls. The mean duration of visit for case patients was 23.33 hours (*SD* = 27.12 hours) and that for controls was 24.5 hours (*SD* = 32.5 hours). However, this relationship was not statistically significant (*p* = .3241; Table 3).

Table 3**.** Descriptive statistics of index emergency room visit characteristics of a matched sample of patients with bradycardia, heart block or both who had at least 1 emergency room visit in the observation period of 730 days comparing those who received an initial pacemaker and those who did not.

Index Emergency Room Visit Profile	Pacemaker *n* = 265	No Pacemaker *n* = 1084	*p* (χ^2/ *t* test)
Reason for index visit, *n* (%)			.760
Chest Pain NOS	5 (2.75)	26 (14.29)	
Chest Pain NEC	2 (1.10)	14 (7.69)	
Syncope and collapse	5 (2.75)	8 (4.40)	
Malaise and fatigue	1 (0.55)	11 (6.04)	
Dizziness and giddiness	0 (0.00)	11 (6.04)	
Palpitations	1 (0.55)	5 (2.75)	
Essential hypertension	0 (0.00)	5 (2.75)	
Duration of visit (hours), mean (*SD*)	22.33 (27.12)	24.53 (32.5)	.3241
Duration of visit (hours), median	8.33	8.33	
Duration of visit (hours), mode	5.00	5.00	
Ecode present, *n* (%)	8 (3.46)	37 (4.05)	.0498
Specific ecodes, *n* (%)			—
Fall from slipping	0 (0.00)	7 (0.77)	
Fall NEC	0 (0.00)	4 (0.44)	
Accident in home	2 (0.86)	2 (0.22)	
External cause	0 (0.00)	4 (0.44)	

Note. NOS = not otherwise specified; NES = Chest Pain, other.

3.4. Answer to Question 3

[Question 3. Does higher preoperative emergency room use among patients with bradycardia, heart block, or both posit an increased likelihood for inpatient primary initial pacemaker?]

The third and final question in our study is stated to test our hypothesis. As mentioned earlier in the methods section, we ran 6 different unadjusted models with our

matched data using different manipulations of our primary independent variable and 2 different types of conditional logistic regressions. The first type of logistic regression (conditional frequentist) tested a 1-tailed hypothesis and the second type of logistic regression (conditional exact) tested a 2-tailed hypothesis. When the independent variable "Number of ER visits" was treated as a continuous variable, the likelihood of the outcome happening (likelihood of pacemaker insertion) was higher in patients with higher number of emergency room visits than those who had lower number of emergency room visits in their matched observation periods. For example, patients with a higher number of emergency room visits had 1.73 times higher likelihood of getting a pacemaker than those who had lower counts of emergency room visits according to the conditional frequentist (OR = 1.734, 95% CI 1.536, 1.957) as well as the conditional exact (OR = 1.734, 95% CI 1.537, 1.966, p = <.0001) regressions. The conditional logistic regression with the independent variable as a categorical variable also predicted higher likelihood of patients with 2 emergency room visits to have an eventual initial pacemaker as compared to those who had 1 emergency room visit in their observation windows (OR = 2.833, 95% CI 1.803, 4.452). This trend continued in all emergency room visit categories compared with the effect of a single emergency room visit. Patients who had 3 emergency room visits were 8 times as likely to get a pacemaker compared with those who had 1 emergency room visit (OR = 8.034, 95% CI 4.517, 14.288). The effect of 4 emergency room visits compared with that of 1 emergency room visit did not change significantly from the effect of 3 emergency room visits (OR = 8.736, 95% = 4.605–16.574). The effect drastically increased with 5 emergency room visits (OR = 14.181. 95% CI 5.979, 33.632) compared with the effect of 1 emergency room visit.

However, with growing effect sizes from increasing exposure (6 emergency room visits), the estimates lost statistical power as can be observed in the width of the confidence interval accompanying the estimates (Table 4).

Table 4**.** Effect of multiple preoperative emergency room use on risk for initial inpatient pacemaker for patients with bradycardia, heart block or both who have an initial pacemaker within 730 days of their index emergency room visit (unadjusted models).

Effect	Independent variable(s) type	Model type	Odds ratio	95% Confidence interval	Two-sided *p*
Number of ER visits	Continuous	Conditional Logistic	1.734	1.536, 1.957	—
Number of ER visits	Continuous	Conditional Logistic exact	1.734	1.537, 1.966	<.0001
Number of ER visits[a]	Categorical	Conditional Logistic			
2			2.833	1.803, 4.452	—
3			8.034	4.517, 14.288	—
4			8.736	4.605, 16.574	—
5			14.181	5.979, 33.632	—
6 or more			9.605	4.874, 18.928	—

[a]Reference = 1.
Note. ER = emergency room.

We ran some adjustments to our models with available patient demographic and clinical characteristics (described in earlier sections). In our first model with the primary independent variable (Number of ER visits) being continuous, we found that patients with higher counts of emergency room visits in the observation window were 1.8 times more likely to have a primary initial pacemaker in the inpatient setting compared with those who had fewer counts of emergency room visits in matching observation windows (OR = 1.799, 95% CI 1.565, 2.021). Among all covariates used in this prediction model, only CCI was a statistically significant predictor. Patients with higher CCI scores were 1.3 times less likely to get a primary initial pacemaker in the inpatient setting (OR = 0.698; 95% CI 0.489, 0.995; Table 5).

Table 5**.** Conditional Logistic Regression Model showing the effect of multiple preoperative emergency room use on risk for initial inpatient pacemaker for patients with bradycardia, heart block or both who have an initial pacemaker within 730 days of their index emergency room visit using selective adjustments (primary independent variable as a continuous variable).

Effect	Odds Ratio	95% Confidence Interval
Number of ER visits	1.799	1.565, 2.021
Patient race		
White	2.547	0.657, 9.868
Black	1.438	0.347, 5.964
Other	1.641	0.398, 6.771
Primary payer		
Medicare	2.635	1.074, 6.464
Medicaid	1.535	0.467, 5.040
Other insurance	2.337	0.948, 5.763
Patient location		
Large metro	0.153	0.006, 3.620
Small metro	0.149	0.006, 3.493
Non metro urban	0.190	0.008, 4.778
Rural	0.158	0.006, 4.287
Charlson score[a]	0.698	0.489, 0.995
Selected comorbidities		
Congestive heart failure	1.679	0.867, 3.250
Valvular disease	0.948	0.657, 1.368
Hypertension, uncomplicated	1.068	0.765, 1.490
Hypertension, complicated	0.979	0.276, 3.476
Chronic pulmonary disease	0.931	0.503, 1.723
Diabetes, uncomplicated	1.605	0.698, 3.689
Hypothyroidism	1.596	0.366, 6.971
Renal failure	3.183	0.668, 15.162
Fluid and electrolyte disorder	0.873	0.493, 1.544

[a]Computed using codes from the Romano adaptation of computable ting Charlson comorbidity index. The index takes into account 17 diseases that, when existing as comorbidities, may affect survival. *Note.* ER = emergency room

Our second adjusted model with our primary independent variable (Number of ER visits) being a categorical variable gave more precision to the predictive value of the variable as revealed in our first model. We found that compared with patients who had 1 emergency room visit in their observation window, patients with 2 emergency room visits were 2.8 times more likely to get a primary initial pacemaker in the inpatient setting (OR = 2.889; 95% CI 1.808, 4.616). We also found that patients with 3 emergency room visit were 8.3 times more likely to get a primary initial pacemaker in the inpatient setting

when compared with those who had 1 emergency room visit in their observation window (OR = 8.278; 95% CI 4.586, 14.941). The effect of higher count of emergency room visits (4, 5, 6 and more) was also higher than that of 1 emergency room visit. However, the effects ceased to be statistically significant. CCI was also predictive of the outcome at a statistical significance of alpha = 0.05. The second model, following the first, also predicted a lower likelihood of getting a primary initial pacemaker in the inpatient setting (OR = 0.691, 95% CI 0.481, 0.993; Table 6).

Table 6**.** Conditional Logistic Regression Model showing effect of multiple preoperative emergency room use on risk for initial inpatient pacemaker for patients with bradycardia, heart block, or both who have an initial pacemaker within 730 days of their index emergency room visit using selective adjustments (primary independent variables as categorical variables 1, 2,3, 4, 5, 6 and more).

Effect	**Odds Ratio**	**95% Confidence Interval**
Number of ER visits[a]		
2	2.889	1.808, 4.616
3	8.278	4.586, 14.941
4	9.793	5.003, 19.169
5	15.416	6.361, 37.364
6 or more	9.794	4.730, 20.277
Patient race		
White	3.114	0.777, 12.482
Black	1.800	0.420, 7.723
Other	2.085	0.491, 8.853
Primary payer		
Medicare	2.394	0.986, 5.816
Medicaid	1.509	0.470, 4.845
Other insurance	1.796	0.738, 4.370
Patient location		
Large metro	0.105	0.005, 2.402
Small metro	0.110	0.005, 2.479
Non metro urban	0.127	0.005, 3.064
Rural	0.139	0.005, 3.560
Charlson score[b]	0.691	0.481, 0.993
Selected comorbidities		
Congestive heart failure	1.568	0.797, 3.084
Valvular disease	0.954	0.655, 1.389
Hypertension, uncomplicated	1.101	0.783, 1.548
Hypertension, complicated	1.256	0.328, 4.815
Chronic pulmonary disease	0.970	0.515, 1.824
Diabetes, uncomplicated	1.528	0.653, 3.576
Hypothyroidism	1.561	0.353, 6.905
Renal failure	3.014	0.595, 15.268
Fluid and electrolyte disorder	1.011	0.572, 1.785

[a]Reference = 1.

[b]Computed using codes from the Romano adaptation of computing Charlson comorbidity index. The index takes into account 17 diseases that, when existing as comorbidities, may affect survival.

CHAPTER 4: DISCUSSION

This study is a first of its kind—assessing the impact of health resource utilization on the probability of a surgical event as an outcome. Pacemaker insertions are common in the United States as well as worldwide. They are considered to be the most effective way to arrest cardiac dysrhythmias, which may lead to myocardial infarctions and death. Our population of interest could be considered to be relatively healthy given that inclusion was based on bradycardia, heart block, or both (which are not life-threatening conditions individually). Heart block is found in many US adults with metabolic disorders, including those with evidence of high cholesterol and triglyceride levels, which lead to formation of plaque in the arterial walls disrupting cardiac circulation. Certain serious conditions, such as valvular disease, total heart block, or cardiomyopathy are also found in this population. These conditions are often treated with valvular repairs, coronary artery bypass graft, or transplants, all of which require opening up of the thoracic cavity. To avoid the noise that could have been introduced in the data by including patients requiring valve repair or valve transplants, coronary artery bypass, or heart transplants, we decided to introduce a case–control design in which patients were matched on age, sex, and time to event (observation window). The matching (although not done on the comorbidity profile of the patients) achieved a well-balanced sample with no statistically important associations between the serious conditions and the outcome of interest. This has been well described and proved in Table 1.

The evidence of congestive heart failure (often requiring transplants) was found in 9% of our cases and 94% of our controls. The probability of association between this disease and the outcome was statistically insignificant (p = .8424). However, valvular disease (often requiring repairs and transplants) was found in 78.5% of our cases and 79.7% of our controls (p = .6609). In both situations, higher proportions of patients with the serious conditions were cases. Because cases were predetermined to have a primary initial pacemaker, we are assured that they did not receive a more complicated procedure in the observation window (see glossary of terms for description of term "primary initial pacemaker"). Although not found to be a statistically significant predictor of the outcome later on, hypertension, chronic obstructive pulmonary disease, and diabetes were preponderant in both our case and control populations. Hypertension existed in 57% of cases, and 56% of control patients were hypertensive (p = .8796). Seventeen percent of cases, and 20% of controls had diabetes (p = .4146). This finding may be an effect of the data and general morbidity profile of the population. Hypertension and diabetes are very common comorbidities in the United States and are often recorded on summary discharges even though the encounter was not related to complications arising from these comorbidities. Additionally, hypertension is a known causative factor for heart diseases; thus, it was not surprising to find it abundantly in our population.

Aligning with our hypothesis, we found that the emergency room use characteristics (frequency/number of visits) were significantly associated with our outcome of interest (Table 2). This finding established that a relationship existed between the emergency room use characteristics and the outcome. The logistic regressions further established that the number of emergency room visits patients with bradycardia, heart

block, or both in a given period of time is strongly associated with their likelihood of getting a primary initial pacemaker. Successive iterations of the models revealed that there is difference in the likelihood of a primary initial pacemaker between patients who had 1 emergency room visit in the observation window and those who had 2 or more emergency room visits in the observation window. This finding helps us to reject the null hypothesis.

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APPENDIX A: LIST of ACC/AHA/HRS TASK FORCE CLASS I GUIDELINES

Disease	Recommendation statement	Level of evidence
SND	Permanent pacemaker implantation is indicated for SND with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms	c
	Permanent pacemaker implantation is indicated for symptomatic chronotropic incompetence	c
	Permanent pacemaker implantation is indicated for symptomatic sinus bradycardia that results from required drug therapy for medical conditions	c
AVB	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with bradycardia with symptoms (including heart failure) or ventricular arrhythmias presumed to be due to AV block.	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with arrhythmias and other medical conditions that require drug therapy that results in symptomatic bradycardia	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients in sinus rhythm, with documented periods of asystole greater than or equal to 3.0 seconds (86) or any escape rate less than 40 bpm, or with an escape rhythm that is below the AV node.	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer.	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level after catheter ablation of the AV junction.	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with postoperative AV block that is not expected to resolve after cardiac surgery	c
	Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with neuromuscular diseases with AV block, such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy, with or without symptoms	c
	Permanent pacemaker implantation is indicated for second degree AV block with associated symptomatic bradycardia regardless of type or site	c

Disease	Recommendation statement	Level of evidence
	of block	
	Permanent pacemaker implantation is indicated for asymptomatic persistent third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster if cardiomegaly or LV dysfunction is present or if the site of block is below the AV node.	c
	Permanent pacemaker implantation is indicated for second- or third-degree AV block during exercise in the absence of myocardial ischemia	c

Note. c = Means the recommendation was not unanimous. There was some ambiguity around the scientific evidence and hence all panelists did not pass the recommendations. Practitioners are advised to exercise caution when implanting this recommendation.

APPENDIX B:
ICD-9-CM/CPT

List of Different Types of Implants: Primary Pacemaker ICD-9-CM/ CPT	Description
	Primary machine
37.80	Permanent pacemaker, type not specified
37.81/33206	Single-chamber device, not specified as rate responsive
37.82/33206, 333207	Single-chamber device, rate responsive
37.83/33208	Dual-chamber device
	Wire
37.70	Insertion of lead, not otherwise specified
37.71/ 33207, 33216	Insertion of lead into ventricle
37.72/33208, 33216, 33217	Insertion of lead into atrium and ventricle
37.73/33206, 33214	Insertion of lead into atrium

List of Different Types of Implants: Initial Pacemaker

ICD-9-CM/ CPT	Description
0053–0054, 1752, 3779, 3796, 3798, 3983	Insertion of generator alone
0052, 0056, 3770–3776, 3795, 3797, 3982	Insertion of leads
0050, 0057, 1751, 3778, 3780–3789, 3981	Insertion of pacemaker

List of Indications (Primary or Secondary Diagnosis) for Inclusion

ICD-9-CM	Indication
337.00	Carotid sinus syncope or syndrome
37.34	Catheter ablation
426.00	Complete AV block
426.10	AV block unspecified
426.12	Mobitz II AV block
426.13	Other second degree AV block
427.81	SND
426.11	First degree AV block
426.20	Left bundle branch block
426.30	Other left bundle branch block
426.40	Right bundle branch block
426.50	Bundle branch block unspecified
426.51	Right bundle branch block/ left posterior fascicular block
426.52	Right bundle branch block/left anterior fascicular block
426.53	Other bilateral bundle branch block
426.54	Trifascicular block
426.60	Other heart block
426.89	Other specified conduction disorders
426.90	Unspecified conduction disorder
427.89	Other specified cardiac dysrhythmias
427.90	Unspecified cardiac dysrhythmias

APPENDIX C: SAS CODE FOR INCIDENCE DENSITY MATCHING

```
/*creating datafile with cases and changing id name*/
data cases (rename=id=pateid_case);
set source1;
where censor=1;
run;

/*matching procedure*//*Description of Variables:
pateid_case= patient id for cases (patients with pacemaker)
datediff= total time at risk or censor from index/ follow up time
ageindex= age of patient at index ER visit
rand_num= choosing controls from possible pool at random*/
proc sql;
create table join1 as select distinct
a.pateid_case, a.datediff, a.ageindex,
b.id, ranuni(12345) as rand_num
from cases a inner join source1 b
on (a.datediff) lt b.datediff
and a.pateid_case ne b.id
and a.female = b.female
and a.ageindex-1 <= b.ageindex <=a.ageindex+1
order by pateid_case, rand_num;
quit;
*Macro that selects n matches for each case*;
%Macro match(controlsnum);
data match(keep=pateid_case id);
set join1;
by pateid_case rand_num;
retain mcount;
mcount+1;
if first.pateid_case then mcount=1;
if mcount le &controlsnum;
run;
%mend match;
quit;
%match(4);
*output full dataset of matched cases and controls*;
data matched_cases_controls_all;
set match;
run;

proc printto;
run;
```

```
*select cases only from the matched file and extract tcens, other covariates from full chort*;
data matched_cases_controls;
merge matched_cases_controls_all (in=a)
work.source1(in=b keep=id datediff rename=(id=pateid_case));
by pateid_case;
if a=1 and b=1;
run;
proc sort data=matched_cases_controls;
by pateid_case;
run;


data case_id (keep= id pateid_case datediff);/*make pateid_case the identifier (pateid)*/
set matched_cases_controls;
by pateid_case;
if first.pateid_case; /*select only the 1st obs to identify a case*/
id=pateid_case; /*make the case_id as the identifier (pateid)*/
run;

data id (keep=id pateid_case matchset datediff); /*generate id to link cases with their matched sets*/
set case_id;
by pateid_case;
matchset= _N_;
run;

proc sort data=matched_cases_controls;
by id;
run;
proc sort data=case_id;
by id;
run;

*To obtain follow-up time ad if needed, generate updates of covariates for each matched control*;
data matched_cases_controls1; /*first merge cases to matched controls using control id and case id*/
merge matched_cases_controls case_id(keep=id pateid_case );
by id pateid_case;
run;

proc sort data=matched_cases_controls1;
by pateid_case;
run;
```

```
data final_matched_temp; /*assign the matchset identifier to all records and
rename it statu*/
merge matched_cases_controls1 id(keep=pateid_case datediff matchset rename=
(matchset=statu));
by pateid_case;
run;

proc sort data=final_matched_temp; /*reorder by original identifier*/
by id;
run;

data work.final_matched_all(drop=pateid_case); /*ready for analysis*/
set final_matched_temp;
if id=pateid_case then censor=1;
else censor=0;
run;


proc sort data= work.final_matched_all;
by statu id;
run;
```

APPENDIX D: GLOSSARY OF TERMS

Term	Definition
Pacemaker	A cardiac pacemaker is a device that is used to manage electrophysiological problems of the heart. It consists of two parts: the pulse generator and leads (electrodes). The pulse generator is small metal container that houses a battery and the electrical circuitry that regulates the rate of electrical pulses sent to the heart. 1 to 3 flexible, insulated wires are each placed in a chamber(s) of the heart and deliver the electrical pulses to adjust the heart rate. In addition, most pacemakers have sensors that detect body motion or breathing rate. These sensors signal the pacemaker to increase the heart rate during exercise to meet the body's increased need for blood and oxygen.
Primary pacemaker	If the pacemaker insertion is in position 1 in the patient's inpatient discharge record, it is categorized as a primary pacemaker. In common parlance, this should be the most resource-intensive procedure/ treatment the patient receives during her or his hospital stay.
Initial pacemaker	If the patient is receiving a pacemaker for the first time after a diagnosis of bradycardia or heart block, the procedure is categorized as an initial pacemaker insertion.
Inpatient setting	If the operation is conducted in a hospital operating room and involves at least 1 day of hospitalization, the procedure is categorized as being done in the inpatient setting.
Incidence density sampling	Incidence density sampling is a method of selecting controls for cases. Controls are selected from a pool that does not reach outcome of interest when the case reaches the outcome of interest in the same period of observation. A control for a certain case can subsequently be picked up as a case later when it reaches the outcome of interest.
Presenting conditions	Presenting conditions are the symptoms and complaints reported by the patient at the beginning of an encounter or the first ER visit.
Conditional logistic regression	A conditional logistic regression is a type of probabilistic model used when data are stratum matched.