OPTIMIZING IMPLANTED CARDIAC DEVICE FOLLOW-UP CARE

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Cardiovascular implantable electronic devices (CIEDs) are life-saving devices programmed to detect cardiac arrhythmias and intervene with pacing or shocks to avoid cardiac death. Currently, three to four million Americans rely on CIEDs and this number is growing rapidly with approximately 400,000 new device implantations each year. Worldwide, around one million new device implantations are performed annually.

CIEDs consist of battery-powered pulse generators connected to the heart by one or more electrode wires, called "leads," embedded within a patient's vein. To achieve the maximum possible clinical benefit, modern CIEDs can automatically transmit data to the clinician's office through various media, such as email and text messaging, to allow for remote monitoring.

This dissertation concentrates on improving the quality of care of patients with CIEDs, i.e., maximizing the expected lifetime of these patients, by focusing on three major challenges inherent to these devices: (*i*) cardiac leads fail stochastically and it is not clear whether to abandon them or to extract them, either immediately or at a later time; (*ii*) the average life span of CIED batteries is not as long as the average patient's expected lifetime and it is not clear when to replace the battery-powered pulse generators; (*iii*) the remote monitoring of CIEDs can adversely affect the battery's remaining lifetime and it is not clear how frequently the remote transmissions should be performed.

We use methodologies including Markov decision processes as well as applied probability and statistics to formulate and analyze decision models that enable clinicians to provide patients with better quality of care. Using clinical data and expert opinion, we carefully calibrate the models concerning challenges (*i*) and (*ii*); for (*iii*), we provide insightful numerical

examples for a stylized model. Our results suggest that behaving optimally can significantly extend patients' lives while simultaneously decreasing the burden on the healthcare system by reducing the number of surgeries, in-office visits, and so on, without compromising the patients' well-being.

Keywords: Markov decision processes (MDPs), medical decision making, cardiovascular implantable electronic devices (CIEDs), maintenance optimization, optimal replacement, threshold policy, virtual age, remote transmission, finite horizon

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PREFACE

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1.0 INTRODUCTION

This dissertation addresses the optimization of implanted cardiac device follow-up care. Currently, three to four million Americans rely on cardiovascular implantable electronic devices (CIEDs), i.e., pacemakers, implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices. This number is growing rapidly with approximately 400,000 new device implantations each year (Buch et al. 2011). Worldwide, around one million new device implantations are performed annually (Neelankavil et al. 2013).

CIEDs are comprised of battery-powered pulse generators and electrode wires, called "leads," which are embedded within a patient's vein and are connected to the heart. CIEDs continuously monitor the patient rhythm for cardiac arrhythmias, which they treat with pacing or shock therapy to avoid cardiac death. To improve the clinical benefits of these life-saving devices, modern CIEDs can automatically transmit data to the clinician's office through various media, such as email and text messaging, to allow for remote monitoring.

The term CIED captures a wide variety of devices including pacemakers, ICDs and CRT devices. Pacemakers are used for bradyarrhythmia treatment, i.e., they detect slow rhythms and send an electronic impulse to the heart to maintain a normal rhythm. ICDs are mainly used for tachyarrhythmia management, i.e., they detect a very fast, potentially lethal heart rhythm, and deliver a shock(s) or charge(s) to the heart muscle to restore a normal rhythm. Both pacemakers and ICDs can be of single-chamber or dual-chamber type. Single- and dual-chamber devices are connected to the heart with one and two leads, respectively, delivering the therapy to the respective heart chamber(s). Because of the extra lead attaching the device to one of the heart's upper chambers, dual-chamber ICDs can also function as pacemakers, i.e., they can treat bradyarrhythmia.

CRT devices are used to coordinate the contraction of heart chambers in both sides of the heart to improve the blood flow into the body. That is, instead of only sending impulses to the right side of the heart, as other standard CIEDs do, they also send electronic impulses to the lower left chamber of the heart to help the chambers beat synchronously. CRT devices are of two major types. CRT devices that are only capable of pacing the heart are called CRT-P and those that are also equipped with an integrated defibrillator are called CRT-D.

This dissertation concentrates on improving the quality of care of CIED patients, i.e., maximizing the expected lifetime of the patients, by focusing on three major challenges inherent to CIEDs:

(i) cardiac leads fail stochastically and it is not clear whether to abandon them or to extract them, either immediately or at a later time;

(ii) the average life span of CIED batteries is not as long as the average patient's expected lifetime and it is not clear when to replace the battery-powered pulse generators;

(iii) the remote monitoring of CIEDs can adversely affect the battery's remaining lifetime and it is not clear how frequently the remote transmissions should be performed.

Unfortunately, little work has been done to assess how the decision making processes regarding the follow-up care of patients with CIEDs may be improved, let alone optimized. As a result, current practice varies widely from clinic to clinic. However, there is a growing need for healthcare providers to justify their actions and policies. Indeed, the results established through my research will significantly impact society by informing clinical practice, reducing healthcare expenditures and improving patient safety.

In this dissertation, we use Markov decision processes (MDPs) as well as applied probability and statistics to address the three major challenges inherent to CIEDs. More specifically, in Chapter 2, we address the maintenance of cardiac leads, "the weakest link" in CIED treatment, for four major device types. Chapter 3 addresses the mismatch between the average patient's expected lifetime and the average device's lifespan. Next, in Chapter 4, we obtain lifetime-reward-maximizing policies for performing life-depleting data transmissions under various settings. Finally, we conclude in Chapter 5.

2.0 DYNAMIC ABANDON/EXTRACT DECISIONS FOR FAILED CARDIAC LEADS

2.1 INTRODUCTION

As discussed in Section 1, CIEDs including pacemakers, ICDs and CRT devices are implanted in the patient's chest and attached to wires called "leads" connected to the heart. These leads, which consist of small sensors that monitor the heart rhythm and deliver therapy to the heart, fail stochastically at a significant, increasing rate over time (Dorwarth et al. 2003, Gradaus et al. 2003, Kleemann et al. 2007). In fact, lead failure rates are so pronounced that cardiac leads are often referred to as "the weakest link" in CIED treatment (Bongiorni et al. 2012, Maisel 2007).

Depending on the type of CIED, one, two or three functioning leads must be in place at all times to properly deliver the required therapy. Therefore, whenever one lead fails or multiple leads fail simultaneously, to ensure the functionality of the device the patient undergoes a surgical lead replacement procedure. During the procedure, the patient receives new, functioning lead(s). Implanting new leads carries rare, but life-threatening risks. Furthermore, during each lead replacement procedure, the physician has the option of extracting one or more of the failed leads, including the previously abandoned ones. Extracting leads also carries life-threatening risks. However, if extraction is postponed, it becomes more difficult as fibrosis start to grow around leads attaching them to the adjacent heart and blood vessels (Buch et al. 2011, Pérez Baztarrica et al. 2012). Hence, the risk of complications, and consequently death, following lead extraction increases in the dwell time of the lead.

Although lead extraction involves risks (Henrikson and Brinker 2008c, Henrikson et al. 2010), there are situations in which the extraction of one or more leads is mandatory, namely, reaching a physical constraint or developing an infection. More specifically, the total num-

ber of implanted leads (including failed and functioning leads) is subject to a maximum limit, typically five, due to physical space constraints (Buch et al. 2011, Wilkoff et al. 2009). Hence, lead extraction is mandatory if this limit is reached with fewer functioning leads than required by the device. Furthermore, patients are at risk of developing life-threatening infections which prompt mandatory device extraction(s), i.e., extraction of all parts of the CIED including all leads. One major cause of infection is the lead replacement procedure itself; patients may develop a lead replacement procedure-induced infection shortly after lead addition with or without extraction. However, patients may also acquire "unrelated" infections due to a wide array of other reasons, from generator replacement surgeries to a simple scratch (Uslan et al. 2007). If an infection occurs, either lead replacement procedure-induced or unrelated, the entire CIED including all implanted leads must be extracted (Henrikson and Brinker 2008a). When the infection is cleared, the patient receives a new device (with new lead(s)), typically within a few days to a month after extraction (Bongiorni et al. 2012, Chua et al. 2000, Sohail et al. 2007a). Hence, choosing to abandon leads, i.e., leave leads in place at the time of failure, may result in risky, mandatory future extractions.

Therefore, at the time of each lead failure a trade-off exists between abandoning the failed lead(s) to minimize the short-term risks of complication and extracting one or more of the failed leads to minimize the long-term risks of mandatory lead extractions. For instance, although abandoning a failed lead lowers the short term risks of complication, extracting a "young" failed lead now to "save space" or to avoid having to extract the lead due to infection when it is "old" in the future, may increase the benefits in the long run (Buch et al. 2011).

The decision to abandon versus extract a failed lead persistently challenges clinicians (Henrikson 2010, Maytin and Epstein 2010). In fact, there are no clear guidelines concerning CIED lead maintenance and as a result, surveys of the current practice show a large variation from clinic to clinic (Henrikson et al. 2010, Xu et al. 2009); some clinics favor extracting the failed leads over abandoning them (Bongiorni et al. 2008, Jones IV et al. 2008, Kennergren et al. 2009), whereas some clinics are more inclined to abandon the failed leads unless an extraction is mandatory (Glikson et al. 2009, Venkataraman et al. 2009). Although clinical aspects of lead extraction are widely discussed in the literature (Bode et al. 2012, Bongiorni et al. 2008, Bracke 2009, Buch et al. 2011, Gradaus et al. 2003, Glikson et al. 2009, Henrikson and Brinker 2008b, Henrikson 2010, Jones IV et al. 2008, Kennergren et al. 2009, Levine 2000, Maytin and Epstein 2010, Venkataraman et al. 2009, Xu et al. 2009), to

the best of our knowledge, there is no work that compares the risks involved in making such decisions from a quantitative perspective.

In this chapter, we formulate a collection of mathematical models to adaptively determine the optimal treatment actions as a function of patient age and the age of every implanted lead at the time of lead failure(s), given the individual's clinical characteristics and device specifications. More specifically, we use four Markov decision process (MDP) models to maximize the total expected lifetime of any given patient wearing either one of the four most popular types of CIEDs, i.e., single-chamber pacemakers, dual-chamber ICDs, dual-chamber pacemakers and CRT defibrillator (CRT-D) devices. First, we develop a model for single-chamber pacemakers which require exactly one working lead (of pacemaker type) to function at all times. Next, we generalize our model to dual-chamber ICDs which require two functioning leads, one pacemaker lead and one ICD lead. Pacemaker leads can only deliver pacing therapy, whereas ICD leads have the additional function of delivering defibrillation shocks to the patient's heart. We next simplify the model for dual-chamber ICDs to dual-chamber pacemakers, with two identical pacemaker leads. Finally, we develop a model for CRT-D devices that engage three chambers of the heart and require two pacemaker leads and one ICD lead. We calibrate all these models using clinical data and execute numerical experiments to determine patient-specific optimal policies as a function of patient age and the age of every implanted lead. We then use several performance measures to compare these policies with the ones commonly used in practice.

In terms of the operations research literature, the problem of interest touches on multiple bodies of work within the reliability and maintenance optimization area including opportunistic maintenance optimization, k-out-of-n systems and damage-inducing maintenance activities. Most relevant to our problem is the so-called opportunistic maintenance optimization literature. Opportunistic maintenance, surveyed by Nicolai and Dekker (2006) and Wang (2002), explores the opportunity of performing preventive maintenance (PM) on functioning components of multi-component systems while its failed component(s) are being repaired to exploit economies of scale. In our problem, the opportunity lies in the possibility of "preventively" extracting one or more of the failed leads at the time of each lead addition, before such action may become mandatory due to the space constraint or an infection. In our context, the "cost" of PM is the risk of death from extracting the lead(s).

The problem at hand can be loosely viewed as a k-out-of-n system, in which the system functions while at least k out of n typically identical components remain non-failed

(Nicolai and Dekker 2006). In the context of this problem, n corresponds to the maximum number of "positions" in the vein, i.e., five, and k is the number of required functioning leads, i.e., $k = 1, 2, 3$ for single-chamber, dual-chamber and CRT-D devices, respectively. Despite the cosmetic similarity of this problem with traditional k-out-of-n systems, our system is different from these systems in important ways. In k-out-of-n systems, the status of the n components is binary, i.e., the components are either failed or working. In this problem, their status is expanded to include "empty" as well, which changes the underlying dynamics of the system altogether. Additionally, the working components are not necessarily identical in all the systems considered, e.g., in dual-chamber ICDs.

Lastly, the problem of interest shares a common feature with the damage-inducing maintenance literature, surveyed by Pham and Wang (1996). In practice, a maintenance action may degrade the system or cause a breakdown, typically due to human error. Similarly, in our problem the corrective action of adding a lead or the preventive action of extracting a failed lead may give rise to life-threatening complications. Additionally, infection may occur as a result of surgery, which may cause premature problem termination due to patient death.

In summary, despite a few attributes that our problem shares with bodies of work within the reliability and maintenance optimization area, it does not entirely align with any of them as it encompasses a unique combination of features, mainly due to the problem's context and consequently, its objective. Our problem is motivated by the need to manage failed cardiac leads and its objective function strives to maximize the patient's total expected lifetime, whereas, in a typical maintenance optimization, the objective is to minimize the cost or maximize the availability of machinery. Furthermore, our problem, which, different from typical maintenance optimization problems, has a finite horizon to begin with, may be prematurely terminated as the patient may die from various reasons, including the corrective action itself.

The remainder of this chapter is organized as follows. In Section 2.2, we formulate four models for the four most prevalent implanted cardiac devices. Next, to put the results in perspective, we open Section 2.3 with an example optimal policy, which we compare and contrast with the policies commonly used in practice. We continue Section 2.3 with presenting three heuristic policies as benchmarks. In Section 2.4, we calibrate the developed models using clinical data, the existing medical literature and expert opinion and design a large numerical experiment by establishing patient classes. In Section 2.5, we report the comprehensive results of our experiment, including the optimal lead abandon/extract policies for various patient classes. Finally, we conclude in Section 2.6.

2.2 MODEL FORMULATION

In this section, we first formulate an MDP model for single-chamber devices (Section 2.2.1). We then expand this model to account for dual-chamber devices with both identical and heterogeneous leads (Section 2.2.2). Finally, we generalize our model to consider the most prevalent type of three-chamber cardiac devices, i.e., CRT-D devices (Section 2.2.3).

2.2.1 Single-Chamber Devices

Let $s_t = (\ell, \theta)$ denote the state of the process for a patient of age t, $\underline{T} \leq t \leq \overline{T}$, where $\underline{T}$ and $\overline{T}$ are the minimum and maximum ages, respectively, ℓ is the ordered vector of ages for the leads currently implanted (both functioning and failed) and θ indicates whether the decision epoch is due to a failure or an infection. That is, $\ell = [\ell_{(1)}, \ell_{(2)}, \ldots, \ell_{(L)}]$, where L denotes the maximum number of leads that may be simultaneously implanted at any given time due to space limitations, and $\ell_{(i)}$, $i \in \{1, \ldots, L\}$, denotes the age of the i^{th} oldest lead, if present, and is assigned the value -1, otherwise. Note that the vector ℓ includes lead ages only and not any additional information on leads' "positions" within the vein as the latter do not have any significant effect on the dynamics of the problem. When $\theta = 1$, the decision epoch is due to a failure and a decision must be made; when $\theta = 0$, the "decision epoch" is due to an infection and the entire CIED must be replaced, but no decisions must be made. We introduce these "false" $\theta = 0$ decision epochs strictly for mathematical convenience.

At every failure decision epoch, a new lead must be implanted for the device to function; hence, the decision to be made is simply which lead(s) to extract. That is, the available actions in state s_t, A_{s_t}, correspond to the set of all possible subsets of the lead indices to be removed, i.e., $a \subseteq \{1, 2, \ldots, L\}$ for all $a \in A_{s_t}$. However, not all combinations of lead indices constitute a feasible action, e.g., a lead that is nonexistent may not be extracted. For $\theta = 1$,

$$A_{(\ell,1)} = \left\{ a \;\; : \;\; \sum_{i=1}^{L} \mathbb{1}_{\{\ell_{(i)}=-1\}} + |a| \geq 1, \quad \mathbb{1}_{\{\ell_{(i)}=-1\}} \cdot \mathbb{1}_{\{i \in a\}} = 0, \;\; i = 2, \ldots, L \right\}, \quad (2.1)$$

where the first constraint in (2.1) guarantees that at least one position is available for implanting the new lead, and the second constraint in (2.1) prohibits the extraction of all nonexistent leads. For $\theta = 0$, the only possible action is to extract all existing leads, i.e.,

$$A_{(\ell,0)} = \{a : \mathbb{1}_{\{\ell_{(i)}>-1\}} \cdot \mathbb{1}_{\{i \in a\}} = 1, i = 1, 2, \ldots, L\} \equiv \{\bar{a}(\ell)\}. \quad (2.2)$$

Let β_1 denote the probability of death following lead addition and $\beta_{-1}(\ell_{(\cdot)})$ denote the probability of death following extraction of a lead of age $\ell_{(\cdot)}$. Let $\mu(\ell, a)$ denote the probability of surviving the lead replacement procedure-induced complications starting from state $(\ell, \cdot)$ under action a. We assume procedural complications related to different leads are independent. Hence,

$$\mu(\ell, a) = (1 - \beta_1) \cdot \prod_{i \in a} \left(1 - \beta_{-1}(\ell_{(i)})\right). \tag{2.3}$$

Next, let the random variable X with p.m.f. p_X, c.d.f. F_X and survival function $\bar{F}_X$ denote the time to failure for a new lead, i.e., a lead of age 0. We assume that all leads survive up to a specified maximum age, $\bar{\ell} \geq \overline{T} - \underline{T}$, with some positive probability, i.e., $p_X(x) > 0 \;\; \forall x < \bar{\ell}$.

We make several assumptions regarding the order of events between decision epochs. First, we assume that failures, when they occur, do so at the end of the year. As discussed in Section 2.1, patients may develop an infection following a lead replacement procedure or acquire an "unrelated" infection. Because lead replacement procedure-induced infections typically develop within two to three months following the procedure (Kleemann et al. 2010) and the model is formulated in yearly time increments, we assume lead replacement procedure-induced infections occur immediately after the procedure. In agreement with the published clinical literature, e.g., Chua et al. (2000), we also assume that once an infection is cleared, another infection may not immediately develop. Consistent with the failure assumption, we let unrelated infections, if they occur, do so at the end of the year, but assume that failures precede unrelated infections, i.e., if a failure occurs in a given year, the patient may experience a lead replacement procedure-induced infection, but not an unrelated infection in that year.

Let $\lambda(t)$ denote the likelihood of surviving the competing risks of death (e.g., due to comorbidities) between ages $t-1$ and t. Thus, the likelihood of surviving these competing risks for m periods starting from age t is given by

$$\bar{\lambda}(t, m) \equiv \prod_{j=t+1}^{t+m} \lambda(j). \tag{2.4}$$

Next, let κ denote the annual probability of acquiring an unrelated infection. Given that the next decision epoch is due to an unrelated infection, let $\rho(m)$ denote the probability that this decision epoch occurs in m years; similarly, given that the next failure occurs in n years, let $\eta(n)$ denote the probability that the next decision epoch is due to a failure, i.e.,

$$\rho(m) = \bar{\lambda}(t, m) \cdot (1 - \kappa)^{m-1} \cdot \kappa \qquad \text{and} \qquad \eta(n) = \bar{\lambda}(t, n) \cdot (1 - \kappa)^{n-1}. \tag{2.5}$$

Finally, let γ be the probability that the patient survives the risk of sudden cardiac death at the time of a lead failure; α denote the probability of developing a lead replacement procedure-induced infection; and δ be the probability that the patient survives the risk of death due to acquiring an infection (separate from any required lead procedures).

Now consider $V_t(\ell, \theta)$, the maximum total expected reward starting from state $s_t = (\ell, \theta)$. Clearly, the maximum total expected reward for a patient of age $\overline{T}$ is simply zero, i.e., $V_{\overline{T}}(\ell, \theta) = 0$.

Decision epoch due to infection. For $t < \overline{T}$, first consider the case in which $\theta = 0$, i.e., the decision epoch is due to an infection. Let $\ell'(m)$ denote the lead age vector m years after an infection, i.e., $\ell'(m) = [m, -1, -1, -1, -1]$. Given that the next failure is in n years, let $r_t(n)$ denote the immediate expected reward starting from patient age t, i.e.,

$$r_t(n) = \sum_{m=1}^{n} \bar{\lambda}(t, m) \cdot (1 - \kappa)^{m-1}. \tag{2.6}$$

Additionally, let the function $\nu_t(n)$ denote the total expected reward obtained starting from state $s_t = (\ell, 0)$, conditional on surviving the infection and the requisite lead procedures, weighted by the likelihood of the next lead failure occurring in n periods, i.e.,

$$\nu_t(n) = \begin{cases} p_X(n) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), 0) \\ \qquad\qquad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell'(n), 1) \Big), & \text{if } n < \overline{T} - t, \\ \bar{F}_X(n-1) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), 0) \Big), & \text{if } n = \overline{T} - t. \end{cases} \tag{2.7}$$

Starting from patient age t, the first expression in equation (2.7) gives the total expected reward when the next failure occurs in n years at patient age $t + n < \overline{T}$. First, the patient earns the immediate expected reward $r_t(n)$ corresponding to the expected number of years survived, possibly fewer than n years. If an unrelated infection occurs in $m < n$ years, the total expected reward to go is $V_{t+m}(\ell'(m), 0)$. Note that $m \neq n$ as we assume that failures precede unrelated infections within each period. Finally, given that the patient survives all risks to experience a failure at age $t + n$, the total expected reward to go is $V_{t+n}(\ell'(n), 1)$. Starting from patient age t, the second expression in equation (2.7) gives the total expected reward if the next failure occurs at or after the patient's maximum age. In this case, the patient reaches the maximum age $\overline{T}$ and the problem terminates before the next lead failure

occurs. Similar to the first expression in equation (2.7), the patient earns the immediate expected reward $r_t(n)$, plus the total expected reward to go associated with possibly developing an infection prior to the maximum age. Lastly, note that because all leads are extracted due to an infection, $\nu_t(n)$ is only a function of the patient age t and the time to next failure n, and not the ages of the leads. Hence, for $t < \overline{T}$, using (2.3)-(2.7) the maximum total expected reward at a decision epoch with $\theta = 0$ is given by

$$V_t(\ell, 0) \quad = \quad \delta \cdot \mu(\ell, \bar{a}(\ell)) \cdot \sum_{n=1}^{\overline{T}-t} \nu_t(n). \tag{2.8}$$

Decision epoch due to failure. Next, for $t < \overline{T}$, consider the case in which $\theta = 1$, i.e., the decision epoch is due to a failure. Starting from state $s_t = (\ell, 1)$, suppose action a is taken and the next decision epoch occurs m years later. Let $\ell''(a, m)$ denote the lead age vector at this decision epoch, i.e., $\ell''(a, m) = [\ell''_{(1)}, \ell''_{(2)}, \ldots, \ell''_{(L)}]$, where $\ell''_{(i)}$, $i \in \{1, \ldots, L\}$, denotes the age of the i^{th} oldest lead at patient age $t + m$, if present, and assumes the value -1, otherwise. Furthermore, let

$$\psi(\ell, a, m) \equiv \left\{ \ell_{(i)} + m : \ 1 \leq i \leq L, i \notin a, \ell_{(i)} \neq -1 \right\} \cup \{m\}, \tag{2.9}$$

i.e., $\psi(\ell, a, m)$ is the set of lead ages at patient age $t + m$ after taking action a in state $s_t = (\ell, 1)$. The vector $\ell''(a, m)$ is hence given by the non-increasingly ordered members of the set $\psi(\ell, a, m)$, with the unfilled components of vector $\ell''(a, m)$ set to -1. For example, let $\bar{\ell} = 40$ and consider a decision epoch at which the process is in state $s_{60} = ([9, 5, 3, -1, -1], 1)$. Because all three implanted leads are failed, $a \subseteq \{1, 2, 3\}$. Now suppose action $a = \{2\}$ is taken and the newly implanted lead fails 4 years later. Therefore, from equation (2.9), we have $\psi([9, 5, 3, -1, -1], \{2\}, 4) = \{13, 4, 7\}$ and at the next decision epoch, the process is in state $s_{64} = ([13, 7, 4, -1, -1], \cdot)$, i.e., $\ell''_{(1)} = 13$, $\ell''_{(2)} = 7$, $\ell''_{(3)} = 4$ and $\ell''_{(4)} = \ell''_{(5)} = -1$.

Now, let $u_t(\ell, a, n)$ denote the total expected reward obtained starting from state $s_t = (\ell, 1)$ under action a, conditional on the next lead failure occurring in n periods and weighted by its likelihood, i.e.,

$$u_t(\ell, a, n) = \begin{cases} p_X(n) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), 0) \\ \qquad\qquad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a, n), 1) \Big), & \text{if } n < \overline{T} - t, \\ \bar{F}_X(n-1) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), 0) \Big), & \text{if } n = \overline{T} - t. \end{cases} \tag{2.10}$$

Equation (2.10) is similar in structure to equation (2.7); the only difference is in the lead age vector at the next decision epoch, i.e., $\ell''(a,m)$ and $\ell''(a,n)$ in equation (2.10) as opposed to $\ell'(m)$ and $\ell'(n)$ in equation (2.7). Therefore, when $\theta = 1$ the maximum total expected reward is given by

$$V_t(\ell,1) = \max_{a \in A_{(\ell,1)}} \left\{ \mu(\ell,a) \cdot \left((1-\alpha) \cdot \sum_{n=1}^{\overline{T}-t} u_t(\ell,a,n) + \alpha \cdot V_t(\ell''(a,0),0) \right) \right\}, \tag{2.11}$$

where $\mu(\ell,a)$ and $V_t(\ell''(a,0),0)$ are given by (2.3) and (2.8), respectively. At a decision epoch with $\theta = 1$, a new lead is added and a subset of the failed leads may be extracted. Given that the patient survives the lead replacement procedure-induced complications, if no lead replacement procedure-induced infection occurs and the next failure occurs in n years, $n = 1, \ldots, \overline{T} - t$, the patient earns the total expected reward of $u_t(\ell,a,n)$, given by equation (2.10). Otherwise, if a lead replacement procedure-induced infection occurs, the process instantaneously enters state $(\ell''(a,0),0)$ at which point the patient receives the total expected reward of $V_t(\ell''(a,0),0)$, given by equation (2.8).

2.2.2 Dual-Chamber Devices

In this section, we generalize the model developed in Section 2.2.1 to account for dual-chamber devices. First, we formulate a model for dual-chamber ICDs, with two heterogenous leads, in Section 2.2.2.1. Then, we simplify this model in Section 2.2.2.2 to obtain a formulation for dual-chamber pacemakers, in which we exploit the fact that the leads are identical to reduce the size of the state space.

2.2.2.1 Dual-Chamber Devices with Heterogeneous Leads

Here, we consider dual-chamber ICDs which, to function, require exactly two working, heterogenous leads at all times. In the remainder of the chapter, for simplicity, we refer to pacemaker and ICD leads as 'P' and 'D' leads, respectively. First, we augment the state definition from Section 2.2.1 to include w (i.e., $s_t = (\ell, w, \theta)$), where $w \in W = \{0,1,2\}$

indicates the working lead at the time of lead failure with the value zero corresponding to the simultaneous failure of both leads. That is,

$$w = \begin{cases} 0, & \text{none of the leads are functional,} \\ 1, & \text{a P lead is functional,} \\ 2, & \text{a D lead is functional.} \end{cases} \tag{2.12}$$

Furthermore, we redefine the lead age vector to be $\ell = [(\ell_{(1)}, \ell_{(2)}), \ell_{(3)}, \ldots, \ell_{(L)}]$, where components $\ell_{(1)}$ and $\ell_{(2)}$ denote the ages of the "current," i.e., not previously abandoned, P and D leads, respectively, and $\ell_{(i)}$, $i \in \{3, \ldots, L\}$, denotes the age of the i^{th} oldest, previously abandoned lead, if present, and is assigned the value -1, otherwise. Because all failed leads may be treated identically, the values of $\ell_{(i)}$, $i \in \{3, \ldots, L\}$, are ordered non-increasingly in vector ℓ regardless of their associated lead types. Note that in this redefined lead age vector, at least one of the current P and D leads is always the youngest lead. For example, consider $s_{60} = ([(3, 8), 5, 4, -1], 2, \cdot)$. In this state, the patient and the current P and D leads are 60, 3 and 8 years old, respectively, and the only working lead is the D lead. The current P lead is added last, hence is the youngest lead, and two previously abandoned leads of ages 5 and 4 are also present.

Let the random variable X_j, $j = 1, 2$, with p.m.f. p_{X_j}, c.d.f. F_{X_j} and survival function $\bar{F}_{X_j}$ denote the time to failure for a new P lead and a new D lead, respectively. Similar to Section 2.2.1, we assume that all leads survive up to a specified maximum age, $\bar{\ell} \geq \bar{T} - \underline{T}$, with some positive probability. Furthermore, consistent with Section 2.2.1, we assume that failures and infections, if they occur, do so at the end of each year.

For dual-chamber ICDs, at every failure decision epoch, the value of w determines the number and type(s) of the lead(s) that must be implanted. Let $\phi(w, \theta)$ denote the required number of leads to add in state (ℓ, w, θ), i.e.,

$$\phi(w, \theta) = \begin{cases} 2, & \text{if } \theta = 0, \\ 2 - \mathbb{1}_{\{w>0\}}, & \text{otherwise.} \end{cases} \tag{2.13}$$

Analogous to Section 2.2.1, A_{s_t} corresponds to the set of all possible subsets of the lead indices to be removed; however, not all combinations of lead indices constitute a feasible action. For $\theta = 1$, we redefine A_{s_t} in equation (2.1) to be

$$A_{(\ell,w,1)} = \Bigg\{ a : \quad \sum_{i=1}^{L} \mathbb{1}_{\{\ell_{(i)}=-1\}} + |a| \geq \phi(w,1), \text{if } w > 0 : \mathbb{1}_{\{w \in a\}} = 0, \\ \mathbb{1}_{\{\ell_{(i)}=-1\}} \cdot \mathbb{1}_{\{i \in a\}} = 0, \;\; i = 3, \ldots, L \Bigg\}, \tag{2.14}$$

where the first constraint in (2.14) guarantees that enough positions are available for implanting the new lead(s), the second constraint in (2.14) prevents the extraction of a working lead and the last constraint in (2.14) prohibits the extraction of nonexistent leads. For $\theta = 0$, because the only possible action is again to extract all existing leads, A_{s_t} remains unchanged and is given by equation (2.2), i.e., $A_{(\ell,w,0)} = A_{(\ell,0)} = \{\bar{a}(\ell)\}$.

Next, we redefine $\mu(\cdot, a)$, previously given by (2.3), to denote the probability of surviving the lead replacement procedure-induced complications starting from state (ℓ, w, θ) under action a, i.e.,

$$\mu((\ell, w, \theta), a) = (1 - \beta_1)^{\phi(w,\theta)} \cdot \prod_{i \in a} \big(1 - \beta_{-1}(\ell_{(i)})\big), \tag{2.15}$$

where $\phi(w, \theta)$ is given by equation (2.13). Lastly, we redefine $V_t(\ell, w, \theta)$ to denote the maximum total expected reward starting from state $s_t = (\ell, w, \theta)$. Clearly,

$$V_{\overline{T}}(\ell, w, \theta) = 0. \tag{2.16}$$

Decision epoch due to infection. For $t < \overline{T}$, first consider the case in which $\theta = 0$. Redefine $\ell'(m)$ to denote the lead age vector m years after an infection for a dual-chamber ICD, i.e., $\ell'(m) = [(m, m), -1, -1, -1]$. Also, redefine $\nu_t(n)$, previously given by equation (2.7), to denote the total expected reward obtained starting from state $s_t = (\ell, w, 0)$, conditional on surviving the infection and the requisite lead procedures, weighted by the likelihood of the next lead failure occurring in n periods, i.e.,

$$\nu_t(n) \;\; = \;\; \begin{cases} \sum_{i \in \{0,1,2\}} \varphi_i(t, n), & \text{if } n < \overline{T} - t, \\ \varphi_\Delta(t, n), & \text{if } n = \overline{T} - t, \end{cases} \tag{2.17}$$

where

$$\begin{aligned}\varphi_i(t,n) &= p_{X_1}(n)^{\mathbb{1}_{\{i\in\{0,2\}\}}} \cdot p_{X_2}(n)^{\mathbb{1}_{\{i\in\{0,1\}\}}} \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i\in\{1\}\}}} \cdot \bar{F}_{X_2}(n)^{\mathbb{1}_{\{i\in\{2\}\}}} \\ &\quad \cdot\Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), w, 0) \\ &\quad +\eta(n) \cdot \gamma \cdot V_{t+n}(\ell'(n), i, 1)\Bigg), \quad i \in \{0,1,2\} \qquad (2.18a) \\ \varphi_\Delta(t,n) &= \bar{F}_{X_1}(n-1) \cdot \bar{F}_{X_2}(n-1) \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), w, 0)\Bigg). \qquad (2.18b)\end{aligned}$$

The probabilities $\rho(m)$ and $\eta(n)$ and the immediate expected reward, $r_t(n)$, are given by equations (2.5) and (2.6), respectively. Starting from patient age t, for $i \in \{0,1,2\}$, equation (2.18a) gives the total expected reward when the next failure occurs in n years at patient age $t+n < \overline{T}$. More specifically, equations (2.18a) corresponds to the total expected reward obtained when the next failure is caused by the simultaneous failure of both working leads ($i = 0$), the failure of the working D lead ($i = 1$), and the failure of the working P lead ($i = 2$), respectively, at patient age $t+n$. Starting from patient age t, equation (2.18b), analogous to the second expression in equation (2.7), gives the total expected reward if the next failure occurs at or after the patient's maximum age. Finally, for $t < \overline{T}$, the maximum total expected reward at a decision epoch with $\theta = 0$ is given by

$$V_t(\ell, w, 0) = \delta \cdot \mu((\ell, w, 0), \bar{a}(\ell)) \cdot \sum_{n=1}^{\overline{T}-t} \nu_t(n), \qquad \forall w \in W. \qquad (2.19)$$

Decision epoch due to failure. Next, for $t < \overline{T}$, consider the case in which $\theta = 1$. We redefine $\ell''(a,m)$ from Section 2.2.1 to denote the lead age vector m years after a transition from state $s_t = (\ell, w, 1)$ under action a, i.e., $\ell''(a,m) = [(\ell''_{(1)}, \ell''_{(2)}), \ldots, \ell''_{(L)}]$, where $\ell''_{(1)}$ and $\ell''_{(2)}$ denote the ages of the current P and D leads at patient age $t+m$, respectively, and $\ell''_{(i)}$, $i \in \{3, \ldots, L\}$, denotes the age of the i^{th} oldest, previously abandoned lead at patient age $t+m$, if present, and assumes the value -1, otherwise. For $j = 1, 2$, we have

$$\ell''_{(j)} = \begin{cases} m, & \text{if } j \neq w, \\ \ell_{(j)} + m, & \text{otherwise.} \end{cases} \qquad (2.20)$$

We augment the set definition previously given by (2.9) to include w (i.e., $\psi(\ell, a, m, w)$) and redefine it to be the set of the ages of previously abandoned leads at patient age $t+m$ after taking action a in state $s_t = (\ell, w, 1)$, i.e.,

$$\psi(\ell, a, m, w) = \Big\{ \ell_{(i)} + m : 1 \leq i \leq L, i \notin a, \ell_i \neq -1, i \neq w \Big\}. \tag{2.21}$$

Hence, the first two components of vector $\ell''(a, m)$ are given by equation (2.20) and its remaining components are given by the non-increasingly ordered members of the set $\psi(\ell, a, m, w)$, with the unfilled components set to -1. For example, let $\bar{\ell} = 40$ and consider a decision epoch at which the process is in state $s_{60} = ([(3, 8), 5, 4, -1], 1, 1)$, i.e., $\ell_{(1)} = 3$, $\ell_{(2)} = 8$, $\ell_{(3)} = 5$, $\ell_{(4)} = 4$, $\ell_{(5)} = -1$, $w = 1$ and $\theta = 1$. Because the only working lead is the current P lead, $a \subseteq \{2, 3, 4\}$. Now, suppose action $a = \{3\}$ is taken and the newly implanted D lead fails 3 years later. Therefore, from equation (2.20), $\ell''_{(1)} = 6$ and $\ell''_{(2)} = 3$ and from equation (2.21), $\psi([(3, 8), 5, 4, -1], \{3\}, 3) = \{11, 7\}$; hence, at the next decision epoch, the process is in state $s_{63} = ([(6, 3), 11, 7, -1], \cdot, \cdot)$, i.e., $\ell''_{(1)} = 6$, $\ell''_{(2)} = 3$, $\ell''_{(3)} = 11$, $\ell''_{(4)} = 7$, $\ell''_{(5)} = -1$.

Now, we redefine $u_t(\ell, w, a, n)$, previously given by equation (2.10), to denote the total expected reward obtained starting from state $s_t = (\ell, w, 1)$ under action a, conditional on the next lead failure occurring in n periods and weighted by its likelihood, i.e.,

$$u_t(\ell, w, a, n) = \begin{cases} \sum_{i \in \{0,1,2\}} \upsilon_i(t, \ell, w, a, n), & \text{if } n < \overline{T} - t, \\ \upsilon_\Delta(t, \ell, w, a, n), & \text{if } n = \overline{T} - t, \end{cases} \tag{2.22}$$

where for $w = 0$, $\upsilon_i(t, \ell, 0, a, n), i \in \{0, 1, 2, \Delta\}$, is given by an equation similar to equation (2.18), in which $\ell'(m)$ and $\ell'(n)$ are substituted with $\ell''(a, m)$ and $\ell''(a, n)$, respectively, and for $w > 0$, $\upsilon_i(t, \ell, w, a, n), i \in \{0, 1, 2, \Delta\}$, is given as follows. Namely, if $w > 0$, let

$\bar{w} = 1 + \mathbb{1}_{\{w=1\}}$; hence,

$$\begin{aligned} \upsilon_i(t,\ell,w,a,n) &= \Pr(X_w = \ell_{(w)} + n | X_w > \ell_{(w)})^{\mathbb{1}_{\{i\in\{0,2\}\}}} \cdot p_{X_{\bar{w}}}(n)^{\mathbb{1}_{\{i\in\{0,1\}\}}} \\ &\quad \cdot \Pr(X_w > \ell_{(w)} + n | X_w > \ell_{(w)})^{\mathbb{1}_{\{i\in\{1\}\}}} \cdot \bar{F}_{X_{\bar{w}}}(n)^{\mathbb{1}_{\{i\in\{2\}\}}} \\ &\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \\ &\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a,n), 0 + \mathbb{1}_{\{i\in\{1\}\}} \cdot w + \mathbb{1}_{\{i\in\{2\}\}} \cdot \bar{w}, 1) \Bigg), \ i \in \{0,1,2\} \end{aligned} \tag{2.23a}$$

$$\begin{aligned} \upsilon_\Delta(t,\ell,w,a,n) &= \Pr(X_w > \ell_{(w)} + n - 1 | X_w > \ell_{(w)}) \cdot \bar{F}_{X_{\bar{w}}}(n-1) \\ &\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \Bigg). \end{aligned} \tag{2.23b}$$

That is, when w is positive, either the current P or the current D lead is working; hence, to ensure the functionality of the device, a new lead of the other type must be added. Starting from patient age t, equation (2.23a) gives the total expected reward when the next failure occurs in n years at patient age $t + n < \overline{T}$. More specifically, when $i = 0$, equation (2.23a) corresponds to the total expected reward obtained when the next failure is caused by the simultaneous failure of both working leads at patient age $t + n$. When $i = 1$ and $w = 1$ ($w = 2$), the current P lead (the current D lead) is functional at patient age t and equation (2.23a) corresponds to the total expected reward obtained when the next failure is caused by the failure of the newly implanted lead at patient age t, which is of type D (respectively, P). Similarly, when $i = 2$ and $w = 1$ ($w = 2$), the current P lead (the current D lead) is functional at patient age t and equation (2.23a) corresponds to the total expected reward obtained when the next failure is caused by the failure of this lead at patient age $t + n$. Lastly, starting from patient age t, equation (2.23b) gives the total expected reward if the next failure occurs at or after the patient's maximum age. Therefore, when $\theta = 1$, the maximum total expected reward is given by

$$\begin{aligned} V_t(\ell,w,1) = \max_{a\in A_{(\ell,w,1)}} \Bigg\{ \mu((\ell,w,1),a) \cdot \Bigg((1-\alpha) \cdot \sum_{n=1}^{\overline{T}-t} u_t(\ell,w,a,n) \\ + \alpha \cdot V_t(\ell''(a,0),w,0) \Bigg) \Bigg\}, \end{aligned} \tag{2.24}$$

where $\mu((\ell,w,1),a)$ and $V_t(\ell''(a,0),w,0)$ are given by equations (2.15) and (2.19), respectively.

2.2.2.2 Dual-Chamber Devices with Identical Leads

In this section, we consider dual-chamber pacemakers which require exactly two functioning pacemaker leads at all points in time. To formulate a model for dual-chamber pacemakers, we simplify the model formulated for dual-chamber ICDs in Section 2.2.2.1. For the sake of brevity, we only include the state and action space definitions in this section. The complete discussion on the model formulation is included in Appendix A.1.

We redefine the lead age vector from Section 2.2.2.1 to be $\ell = [(\ell_{(1)}, \ell_{(2)}), \ldots, \ell_{(L)}]$, where $\ell_{(1)}$ and $\ell_{(2)}$ denote the ages of the current P leads. Because the two current leads are identical, we let $\ell_{(1)}$ and $\ell_{(2)}$ be ordered non-increasingly to reduce the size of the state space. Next, we modify the definition of $w \in W = \{0, 1, 2\}$ to indicate the working lead at the time of lead failure with the value zero corresponding to the simultaneous failure of both leads, i.e.,

$$w = \begin{cases} 0, & \text{none of the leads are functional,} \\ 1, & \text{the older, current P lead is functional,} \\ 2, & \text{the younger, current P lead is functional.} \end{cases} \tag{2.25}$$

The action space, A_{s_t}, remains the same as in Section 2.2.2.1.

2.2.3 CRT-D Devices

In this section, we consider CRT-D devices that require exactly two functioning pacemaker leads and one functioning ICD lead at all points in time. We formulate a model for CRT-D devices by generalizing the models presented in Section 2.2.2. For the sake of brevity, we only include the state and action space definitions in this section. The complete discussion on the model formulation is included in Appendix A.2.

We redefine the lead age vector from Section 2.2.2 to be $\ell = [(\ell_{(1)}, \ell_{(2)}, \ell_{(3)}), \ldots, \ell_{(L)}]$, where $\ell_{(1)}$ and $\ell_{(2)}$ denote the ages of the current P leads, when ordered non-increasingly, $\ell_{(3)}$ denotes the age of the current D lead, and $\ell_{(i)}$, $i \in \{4, \ldots, L\}$, denotes the age of the i^{th} oldest, previously abandoned lead, if present, and is assigned the value -1, otherwise. Next,

we modify the definition of $w \in W = \{0, 1, 2, \ldots, 6\}$ to indicate the working lead(s) at the time of lead failure, i.e.,

$$w = \begin{cases} 0 & \text{none of the leads are functional,} \\ 1, & \text{the older, current P lead is functional,} \\ 2, & \text{the younger, current P lead is functional,} \\ 3 & \text{the current D lead is functional,} \\ \bar{3}, & \text{both current P leads are functional,} \\ \bar{2}, & \text{the older, current P lead and the current D lead are functional,} \\ \bar{1}, & \text{the younger, current P lead and the current D lead are functional.} \end{cases} \tag{2.26}$$

For example, consider $s_{60} = ([(6, 3, 4), 9, -1], \bar{2}, \cdot)$. From this example, the patient, the current P leads and the current D lead are 60, 6, 3 and 4 years old, respectively, and the only working leads are the older, current P lead and the current D lead. One previously abandoned lead of age 9 is also present.

Similar dual-chamber ICDs, the value of w determines the number and type(s) of the lead(s) that must be implanted for CRT-D devices. Redefine $\phi(w, \theta)$ to denote the required number of leads to add in state (ℓ, w, θ), i.e.,

$$\phi(w, \theta) = \begin{cases} 3, & \text{if } \theta = 0, \\ 3 - \mathbb{1}_{\{w \in \{1,2,3\}\}} - 2 \cdot \mathbb{1}_{\{w \in \{\bar{3},\bar{2},\bar{1}\}\}}, & \text{otherwise.} \end{cases} \tag{2.27}$$

Analogous to Sections 2.2.1 and 2.2.2, A_{s_t} corresponds to the set of all possible subsets of the lead indices to be removed; however, not all combinations of lead indices constitute a feasible action. For $\theta = 1$, let the set $B(w)$, $w \in \{\bar{3}, \bar{2}, \bar{1}\}$, denote the indices of the working leads when exactly two leads are functional, i.e.,

$$B(w) = \left\{ b : b \in \{1, 2, 3\}, \mathbb{1}_{\{w=\bar{3}\}} \cdot \mathbb{1}_{\{b=3\}} = 0, \mathbb{1}_{\{w=\bar{2}\}} \cdot \mathbb{1}_{\{b=2\}} = 0, \mathbb{1}_{\{w=\bar{1}\}} \cdot \mathbb{1}_{\{b=1\}} = 0 \right\}. \tag{2.28}$$

Hence,

$$A_{(\ell,w,1)} = \Bigg\{ a \;\; : \;\; \sum_{i=1}^{L} \mathbb{1}_{\{\ell_{(i)}=-1\}} + |a| \geq \phi(w,1), \tag{2.29a}$$

$$\text{if } w \in \{1,2,3\} : \; \mathbb{1}_{\{w \in a\}} = 0, \;\; \text{if } w \in \{\bar{3},\bar{2},\bar{1}\} : \; \mathbb{1}_{\{B(w) \cap a = \emptyset\}} = 1, \tag{2.29b}$$

$$\mathbb{1}_{\{\ell_{(i)}=-1\}} \cdot \mathbb{1}_{\{i \in a\}} = 0, \;\; i = 4, \ldots, L \Bigg\}, \tag{2.29c}$$

where the constraint in (2.29a) guarantees that enough positions are available for implanting new lead(s), the constraints in (2.29b) prevent the extraction of a working lead and lastly, the constraint in (2.29c) prohibits the extraction of all nonexistent leads. For $\theta = 0$, A_{s_t} remains unchanged and is given by equation (2.2), i.e., $A_{(\ell,w,0)} = A_{(\ell,0)}$.

2.3 LEAD MAINTENANCE POLICIES

In this section, we first present an example optimal policy. We discuss several interesting properties of this policy that are consistently observed throughout our numerical experimentation. Next, we review the policies commonly used in current practice. Finally, inspired by current practice, we introduce three heuristic policies which later act as benchmarks.

An example optimal policy. Figures 1a-1e illustrate the optimal lead abandon/extract policy for an example single-chamber pacemaker patient. In these figures, the dark and light squares correspond to the states in which it is optimal to extract and abandon the lead, respectively. The blank squares correspond to the states that are unreachable considering the parameter settings or problem dynamics, e.g., a 31-year-old patient may not have a lead of two years or older when $\underline{T} = 31$.

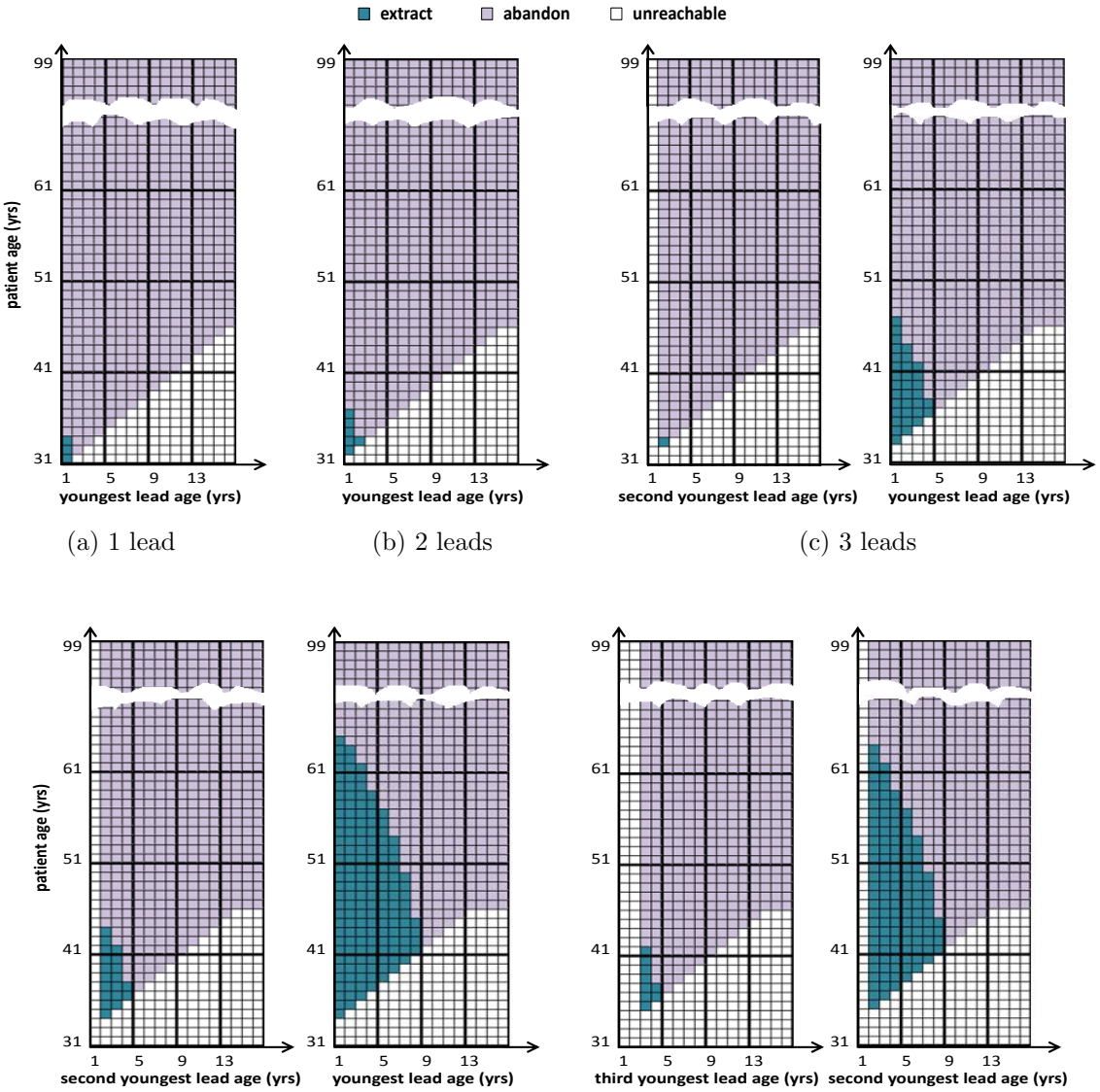
Figures 1a-1e show the optimal abandon/extract policy as a function of the lead age and the patient age when exactly one–five leads are implanted, respectively. The plots that do not carry any information are removed from Figure 1. That is, the plots corresponding to the second youngest lead (the older of the two) in Figure 1b, the third youngest lead in Figure 1c, the third and fourth youngest leads in Figure 1d, and the fourth and fifth youngest leads in Figure 1e are removed as it is never optimal to extract these leads. Similarly, the plot corresponding to the youngest lead in Figure 1e is removed as it is always optimal to extract

this lead. Recall that the number of implanted leads is limited to five, hence in Figure 1e the youngest lead is always extracted to make room for adding a new lead.

As seen in Figure 1, the optimal action is to extract a lead when the lead and patient are both "young." The former is due to the fact that the risk of death following lead extraction increases in lead age and the latter is mainly because younger patients are more likely to eventually reach the maximum number of implanted leads, and hence require a "forced" extraction. Interestingly, we observe that under the optimal policy, the abandon/extract decision for each lead only depends on its age, patient age, its age rank among the lead ages and the total number of implanted leads, i.e., the decision does not depend on the exact ages of all implanted leads. Additionally, the decision is of threshold type in the lead age, patient age and the lead's age rank among the lead ages, hence making it easier to implement.

Throughout the numerical experimentation, we consistently observe that, similar to single-chamber devices, in multi-chamber devices the abandon/extract decision for each lead also depends on its age, patient age, its age rank among the lead ages and the total number of implanted leads. Recall that in multi-chamber devices, not all required, working leads may be failed at the time of a lead failure. As a result, different from single-chamber devices, we observe that in multi-chamber devices the abandon/extract decision for each lead also depends on the age of the working lead(s). Clearly, the "older" the working lead(s), the larger their hazard rate(s); hence, consistent with the intuition, we observe that the optimal policy prescribes to extract failed leads at "younger" ages when working leads are "older," in anticipation that the next failure occurs shortly.

Current clinical practice. In contrast to patient-specific optimal policies generated by the models in Section 2.2, the policies used in clinical practice are overly simplified; they not only fail to take into account both sides of the trade-off with which decision makers are generally faced, but are not tailored to individuals. Recall from Section 2.1 that at the time of each lead failure a trade-off exists between abandoning the failed lead(s) to minimize the short-term risks of complication and extracting one or more of the failed leads to minimize the long-term risks of mandatory lead extractions. Despite this trade-off and regardless of important patient/device characteristics, two current approaches to lead maintenance include either extracting all failed leads (see Bongiorni et al. (2008), Jones IV et al. (2008), Kennergren et al. (2009)), or abandoning all failed leads unless an extraction is mandatory (see Glikson et al. (2009), Venkataraman et al. (2009)). In the following, inspired by the approaches used in various clinics, we introduce three heuristic policies which we later use as benchmarks.



(a) 1 lead (b) 2 leads (c) 3 leads

(d) 4 leads (e) 5 leads

Figure 1: Optimal lead maintenance policy for a single-chamber device when $\underline{T} = 31$, $\overline{T} = 100$, $p_X(x)$ is obtained using the hazard function in Table 20 (in Appendix A.3) for $\omega = 0.55$, $\alpha = 0.03$, $\kappa = 0.015$, $\beta_1 = 0.00075$, $\beta_{-1}(\ell)$ is of type "average" in Table 21 (in Appendix A.3), and $\delta = 0.98$.

Table 1: Three heuristic lead maintenance policies when a decision epoch is due to a failure ($\theta = 1$).

Heuristic policies	Description
$\mathcal{C}$	Only add lead(s) if possible. If not possible, extract the youngest failed lead(s) only.
$\mathcal{H}$	Only add lead(s) if possible. If not possible, extract all failed leads.
$\mathcal{A}$	Extract all failed leads.

As discussed in Sections 2.1 and 2.2, if a decision epoch is due to an infection, i.e., $\theta = 0$, the extraction of all leads is mandatory. Hence, what differentiates various policies is their recommendation on which leads to abandon/extract when a decision epoch is due to a failure, i.e., $\theta = 1$. Here, we introduce three policies, referred to as policies $\mathcal{C}$, $\mathcal{H}$, and $\mathcal{A}$ for "conservative," "hybrid" and "aggressive," respectively. Policies $\mathcal{C}$ and $\mathcal{A}$ are widely used in practice.

Physicians are typically reluctant to extract leads due to the risks involved. Therefore, many tend to abandon failed leads until extraction becomes inevitable due to reaching the physical space constraint with fewer functioning leads than required by the device. Once mandatory, depending on the device type and the number of working leads, one to three leads are extracted to make space for implanting the required number of new leads. Clearly, to reduce the risk of death, the lead(s) that are extracted are the youngest(s). We capture this "conservative" lead maintenance scheme in policy $\mathcal{C}$. Policy $\mathcal{H}$ is similar to policy $\mathcal{C}$ in that extraction decisions are not made until the space constraint is reached; however, under policy $\mathcal{H}$, once mandatory, all failed leads are extracted. Finally, policy $\mathcal{A}$ is "aggressive" in that it advises to extract all failed leads at every decision epoch. Table 1 summarizes the three heuristic lead abandon/extract policies. In the remainder of this chapter, we denote the total expected reward obtained under policy $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$ by $V_{t,\pi}(\ell, \theta)$ for single-chamber devices and $V_{t,\pi}(\ell, w, \theta)$ for multi-chamber devices.

2.4 MODEL CALIBRATION AND EXPERIMENTAL DESIGN

In this section, we use a combination of the existing medical literature, clinical data and expert opinion to calibrate the mathematical models formulated in Section 2.2. We

Table 2: Experimental-design factors and their corresponding levels. The values of $p_X(x)$(or $p_{X_1}(x)$) and $p_{X_2}(x)$ are obtained using the hazard function values for pacemaker and ICD leads, respectively, presented in Table 20 in Appendix A.3. For the values of $\beta_{-1}(\ell)$, refer to Table 21 in Appendix A.3.

Factor	No. of levels	Levels
$p_X(x)$(or $p_{X_1}(x)$)	3	for $\omega \in \{0.45, 0.5, 0.55\}$
$p_{X_2}(x)$	3	for $\omega \in \{0.4, 0.45, 0.5\}$
α	4	0.01, 0.02, 0.03, 0.04
κ (for PM1 and PM2)	3	0.005,0.01,0.015
κ (for ICD)	4	0.005,0.01,0.015,0.02
κ (for CRT-D)	5	0.005,0.01,0.015,0.02,0.025
β_1	3	0.00075, 0.001, 0.00125
$\beta_{-1}(\ell)$	3	low, average, high
δ	3	0.94,0.96,0.98

then design a large numerical experiment to analyze the effects of the patient-specific parameters on the optimal policy. In the remainder of the chapter, for simplicity we refer to single-chamber and dual-chamber pacemakers (i.e., dual-chamber devices with identical leads) with acronyms PM1 and PM2, respectively. Table 2 summarizes the factors of the experiment and their corresponding levels that are estimated and thoroughly discussed in this section and Appendix A.3.

Maximum number of leads, L. From the clinical guidelines (Buch et al. 2011, Wilkoff et al. 2009), the maximum number of leads implanted at any given point in time should be limited to five, i.e., $L = 5$.

Probability of surviving the risk of sudden cardiac death due to lead failure, γ. Based on expert opinion, this probability is very close to one. To the best of our knowledge, there are no published data on the probability of surviving the risk of sudden cardiac death due to lead failure. Therefore, we use recalled lead-induced deaths as a proxy for this probability. A recall is typically issued in response to increased rates of lead failure, fracture or externalization. As a result, recalled leads may be extracted before they fail; however,

for the purpose of estimating γ, we assume patients continue using these leads until they fail. According to a report by Samsel 2009, out of patients with 268,000 recalled leads, 9 (equivalently, 0.005%) instances of death may be attributed to lead fracture. Therefore, we let $\gamma = 0.99995$.

Minimum patient age at the time of lead failure, $\underline{T}$; maximum patient age at the time of lead failure, $\overline{T}$; maximum lead age, $\bar{\ell}$. In most clinical studies, the mean age at initial CIED implantation is between 57 and 76 years (Johansen et al. 2011, Lee et al. 2010, Remmelts et al. 2009, Saxon et al. 2010). To obtain comprehensive results for a wide range of adult cardiac patients, we consider individuals who undergo initial implantation at or after age 30 and assume no patient survives beyond 100 years. That is, $\underline{T} = 31$ and $\overline{T} = 100$. Recall from Section 2.2 that we assume $\bar{\ell} \geq \overline{T} - \underline{T}$; hence, without loss of generality, we let $\bar{\ell} = 69$.

Probability of surviving the competing risks of death, $\lambda(\ell)$. To estimate values of $\lambda(\ell)$, we use the United States total population life table provided by the Centers for Disease Control and Prevention (CDC) (Arias 2012). Pacemaker patients live almost as long as the average population (Brunner et al. 2004, Udo 2013); hence, for these patients the values of $\lambda(\ell)$ directly follow from the life table. Patients with ICD and CRT-D devices, however, have shorter life expectancies than the average population. Therefore, to obtain values of $\lambda(\ell)$ for each subpopulation of interest, we use the disease-specific excess rate of mortality to decrease the survival probabilities of the total population. More specifically, the per-year survival probability of patients with a particular disease is set equal to the complement of the probability of death from competing risks for the average population in that year, plus the disease-specific excess rate of mortality. We estimate the annual excess rate of mortality for patients with ICD and CRT-D devices by applying the DEALE method (Beck et al. 1982) to single-point survival data reported by Saxon et al. (2010). The estimated rates are 0.025 and 0.075, respectively. Further details are included in Appendix A.3.

Distribution of the time to failure of a new lead, $p_X(x)$ (or $p_{X_1}(x)$) and $p_{X_2}(x)$. Because advances in technology have not necessarily translated into higher lead reliability (Emory Healthcare 2012), we may safely use longitudinal studies as a means of estimating $p_X(x)$. More specifically, here we use a combination of manufacturers' reports on lead survival probabilities in the past decade or so, expert opinion and mathematical modeling tools to estimate the distribution of the time to failure for both pacemaker and ICD leads. We assume that leads fail at a constant rate for all $\ell \geq \underline{\ell}$. This assumption alleviates the

problem of data sparsity for leads older than 12-14 years, for which annual lead survival probabilities are not readily available. Additionally, the assumption reduces the computational burden and memory requirements by limiting the maximum lead age to $\underline{\ell}$. Considering the specifications of our computers, we let $\underline{\ell} = 16$ years in the remainder of the chapter.

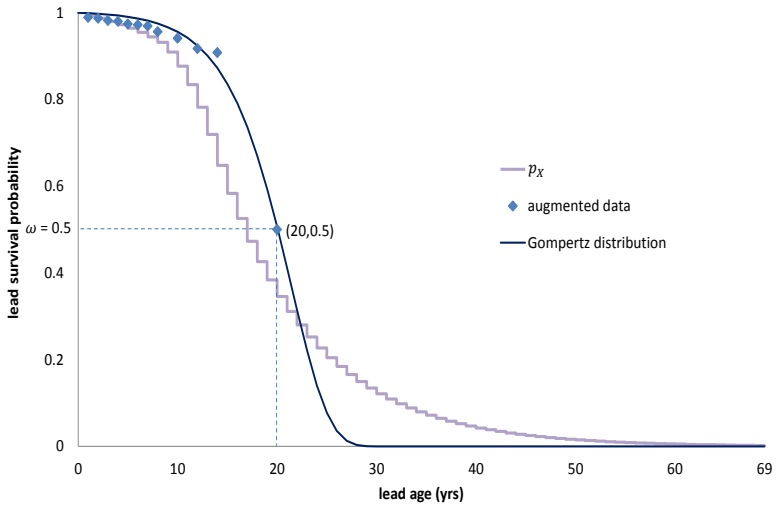
Note that to exploit the constant hazard property of $p_X(x)$ after age $\underline{\ell}$, we update the models in Section 2.2. That is, we slightly modify the models to limit the lead age to $\underline{\ell}$. For instance, in Section 2.2.1, we alter $\ell'(m)$, previously defined as $\ell'(m) = [m, -1, -1, -1, -1]$, to $\ell'(m) = [\min\{\underline{\ell}, m\}, -1, -1, -1, -1]$ and substitute $\ell_{(i)} + m$ with $\min\{\ell_{(i)} + m, \underline{\ell}\}$ in equation (2.9). We make a series of similar changes to the models in Sections 2.2.2 and 2.2.3.

We obtain annual lead survival probabilities using a combination of manufacturers' reports and expert opinion. For pacemaker and ICD leads, we use publicly available empirical data on Medtronic CapSureFix model 4068 and Medtronic Transvene model 6936/6966, respectively (Medtronic August 06, 2012). These models are widely used in practice and their survival probabilities are recorded for a substantial length of time (i.e., almost 14 years). From the data, the ICD lead is much less reliable than the pacemaker lead, which is because ICDs leads are generally more technologically complex than pacemaker leads (Schiariti et al. 2011, Van Dessel 2010). To more accurately predict the behavior of these survival probabilities for older leads, we then use expert opinion to add a point estimate, ω, at lead age 20 to each dataset. To account for disparity in lead technology, we use a range of values for ω, i.e., $\omega \in \{0.45, 0.5, 0.55\}$ for pacemaker leads and $\omega \in \{0.4, 0.45, 0.5\}$ for ICD leads.

Next, to obtain $p_X(x)$, we fit a Gompertz distribution (Cox and Oakes 1984) to the appended data and discretize to obtain a p.m.f., $p_{\tilde{X}}(x)$, which we then adjust so that it exhibits constant hazard after age $\underline{\ell}$. Further details are included in Appendix A.3.

Figure 2a plots the augmented data, the Gompertz distribution and the estimated survival distribution, p_X, for a pacemaker lead when $\omega = 0.5$. Figure 2b reports the corresponding p.m.f., c.d.f. and hazard function for the lead represented in Figure 2a.

Probability of lead replacement procedure-induced infection, α. The *overall* incidence rate of infection among patients with cardiac devices is widely published in the clinical literature (Baddour et al. 2003, Chua et al. 2000, Kleemann et al. 2010, Voigt et al. 2010, Kirmani et al. 2012). However, the incidence rate of infection that is specifically caused by lead replacement is not typically reported. According to Kleemann et al. (2010), the incidence rate of generator replacement- and lead replacement procedure-induced infection are approximately equal. In the following, we use this fact to estimate α.



(a)

Lead age (yrs)	Estimated hazard function, h_X	Estimated p.m.f., p_X	Estimated c.d.f., F_X
0	0.000000	0.000000	0.000000
1	0.006197	0.006197	0.006197
2	0.006597	0.006556	0.012753
3	0.007114	0.007023	0.019776
4	0.007783	0.007629	0.027406
5	0.008651	0.008414	0.035819
6	0.009779	0.009429	0.045248
7	0.011247	0.010738	0.055986
8	0.013160	0.012423	0.068409
9	0.024070	0.022423	0.090832
10	0.035662	0.032423	0.123255
11	0.048387	0.042423	0.165678
12	0.062833	0.052423	0.218102
13	0.079835	0.062423	0.280525
14	0.099492	0.071582	0.352107
15	0.099492	0.064460	0.416567
16	0.099492	0.058047	0.474615
17	0.099492	0.052272	0.526886
⋮	⋮	⋮	⋮
68	0.099492	0.000250	0.997741
69	1.000000	0.002259	1.000000

(b)

Figure 2: An estimated pacemaker lead failure distribution when $\omega = 0.5$.

In a study by Poole et al. (2010), 0.7% (0.5%) of patients who underwent generator replacement with (respectively, without) lead addition acquired infection that resulted in device removal. In a study by Kleemann et al. (2010), out of 122 patients who underwent lead replacement and/or generator replacement, five (4%) acquired infection.

The rate of infection is a function of the patient's comorbidities (Kleemann et al. 2010) and the type of the device (Baddour et al. 2003, Uslan et al. 2007). Duration of surgery and the number of implanted leads are also conjectured to be risk factors for infection (Kleemann et al. 2010, Sohail et al. 2007b). Hence, to account for a wide range of patients and device types, we let $\alpha \in \{0.01, 0.02, 0.03, 0.04\}$.

Annual probability of acquiring unrelated infection, κ. Recall from Section 2.1 that patients may acquire unrelated infections due to a wide range of reasons unrelated to lead replacement procedures (e.g., generator replacements, procedures to treat comorbidities). The prominent cause of these infections is, however, generator replacement surgery (Kleemann et al. 2010). As mentioned above, according to Kleemann et al. (2010), the likelihood of infection as a result of generator and lead replacements are approximately equal.

Hence, we reuse the estimated range of values of α, i.e., $\{0.01, 0.02, 0.03, 0.04\}$, for the likelihood of infection following generator replacement surgery.

To convert these values to annual probabilities, we first obtain each device's average life span. On average, pacemaker generators last between 5 and 8 years (Wood and Ellenbogen 2002). ICD generators life span is on the order of 2.5 to 6 years (Hauser et al. 2006, Thijssen et al. 2012). CRT-D generators typically have a shorter life expectancy than ICD generators with a reported 2 to 5 years of life (Hauser et al. 2006, Thijssen et al. 2012). However, more recent data for CRT-D generators have demonstrated improved longevity (Thijssen et al. 2012); Alam et al. (2014) report four-year survival rates of 67%-94% for CRT-D generators by different manufacturers. Hence, we use an average life expectancy of 2 to 6 years for CRT-D generators.

To obtain point estimates for the annual probability of generator replacement-induced infection for each CIED type, we divide the rate of infection following these replacements by the device's average life span. As a result, the annual probability of generator replacement-induced infection for pacemaker (single- or dual-chamber), ICD and CRT-D devices are in the ranges of 0.001-0.008, 0.002-0.016 and 0.002-0.020, respectively.

Based on expert opinion, the risk of acquiring unrelated infection due to reasons other than generator replacement is quite low; the cause of approximately 90% of unrelated infections is generator replacement surgery. Therefore, to consider a wide range of cases, we let κ assume values in $\{0.005,0.01,0.015\}$, $\{0.005,0.01,0.015,0.02\}$ and $\{0.005,0.01,0.015,0.02,0.025\}$ for pacemaker (i.e., PM1 and PM2), ICD and CRT-D devices, respectively.

Probability of death following lead addition, β_1. We let the probability of death following lead addition include all immediate and short-term complications that cause patient death. Based on expert opinion, this probability is fairly low and on the order of 0.1%. To capture the variability of this probability for a wide range of patients and devices, we let $\beta_1 \in \{0.00075, 0.001, 0.00125\}$.

Probability of death following extraction of a lead of age ℓ, $\beta_{-1}(\ell)$. As discussed in Section 2.1, the probability of death following lead extraction increases in lead dwell time (Buch et al. 2011, Pérez Baztarrica et al. 2012); however, in the literature, this probability is generally reported in a form of a constant or a range, e.g., according to Henrikson et al. (2011), the rate of mortality following lead extraction is between 0.2% and 0.8%. Therefore, we use the clinical literature to estimate the probability of death following lead extraction as a function of lead dwell time as follows.

Table 3 summarizes the published data on lead extraction procedure-induced mortality (see Appendix A.3 for the details). To estimate $\beta_{-1}(\ell)$, we fit a Gompertz function to the observed probability of death following lead extraction as a function of mean lead dwell time as reported in Table 3. We use a Gompertz function because the main cause of increased rate of complication in lead dwell time is the growth of fibrosis around the leads attaching them to the adjacent heart and blood vessels (Pérez Baztarrica et al. 2012) and the Gompertz function can aptly describe tissue growth (Waliszewski and Konarski 2005). Finally, because $\underline{\ell}$ is the maximum lead age that is used in computations, we truncate the function at lead age $\underline{\ell}$.

The probability of major complications, and consequently death, also varies based on patient characteristics and surgeon expertise (Pérez Baztarrica et al. 2012). To capture a wide range of scenarios, we shift the Gompertz function by $\pm 10\%$ of its mid-range value, $\beta_{-1}(\underline{\ell}/2) = \beta_{-1}(8)$, i.e., for all $\ell \leq \underline{\ell}$, we increase/decrese the estimated $\beta_{-1}(\ell)$ values by $0.1 \times \beta_{-1}(8) = 0.000511$. We refer to the three resulting functions as "low," "average" and "high." Table 21 in Appendix A.3 reports the estimated probabilities. It is worth mentioning that the final probabilities are consistent with the published range of lead extraction mortality risks, e.g., the 0.2% to 0.8% rate of mortality following lead extraction as reported by Henrikson et al. (2011).

We use the estimated values of $\beta_{-1}(\ell)$ (and β_1) for individual leads to estimate the probability of surviving the lead replacement procedure-induced complications when implementing action a in state $(\ell, \cdot)$, $\mu(\ell, a)$, by assuming that complications associated with different leads are independent. We make this assumption for two reasons (1) no data exist on interactions between procedural outcomes and (2) based on expert opinion, this assumption does not compromise the clinical implications of the model.

Probability of surviving infection, δ. The probability of surviving infection depends on the type of the infection (e.g., localized versus systemic) and can vary dramatically from one type to another. For instance, infective endocarditis, i.e., infection of the endocardial surface of the heart, which causes 10%-23% of CIED infection incidents (Kantharia et al. 2000, Sohail et al. 2008, Uslan and Baddour 2006) is associated with an in-hospital mortality rate of 7.6%-14% (Klug et al. 1997, Sohail et al. 2008); however, not all types of infection are as risky. In the following, we estimate the average probability of surviving infection, δ.

Recall from Section 2.1 that whenever an infection occurs, the entire CIED is extracted and new leads are implanted after the infection is cleared. To the best of our knowledge, there are no published data on the probability of death due to the infection alone; rather, the

Table 3: Observed lead extraction mortality from clinical literature.

Reference	Mean lead dwell time (yrs)	Number of extractions	Number of patients	Number of reported deaths	Pr. of death following lead extraction
Byrd et al. (1999)	3.92	3,540	2,338	1	0.000282
Epstein et al. (1999)	6.92	413	248	7	0.016949
Epstein et al. (1999)	5.25	201	177	1	0.004975
Epstein et al. (1999)	6.58	671	438	6	0.008942
Kennergren (1999)	5.69	179	149	0	0.000000
Wilkoff et al. (1999)	5.42	244	153	1	0.004098
Byrd et al. (2002)	6.33	2,561	1,684	13	0.005076
Saad et al. (2003)	2.45	161	161	1	0.006211
Roux et al. (2007)	7.8	270	175	1	0.003704
Bongiorni et al. (2008)	5.78	2,065	1,193	3	0.001453
Jones IV et al. (2008)	7.5	975	498	0	0.000000
Agarwal et al. (2009)	5.7	456	212	1	0.002193
Kennergren et al. (2009)	5.75	1,032	592	2	0.001938
Wazni et al. (2010)	6.84	2,405	1,449	4	0.001663

published probabilities always include the risks involved in extracting the leads and adding new ones. Therefore, in the following we use the estimated probabilities of death following lead addition/extraction to estimate the probability of death due to the infection alone.

From a study by Sohail et al. (2007a), almost 95% of 189 patients with infected pacemaker or ICD devices survived the risk of death from infection, extraction of on average 1.6 leads (details in Appendix A.3), each with a risk of death ranging between 0.2% to 1.2% (Table 21), or addition of one to two leads, each with a risk of death around 0.1% as estimated earlier in this section. Hence, because the devices in Sohail et al. (2007a) are of single- or dual-chamber types, we expect δ to be between

$$\frac{0.95}{(1-0.002)^{1.6}\cdot(1-0.001)^{1}} \simeq 0.95 \tag{2.30}$$

and

$$\frac{0.95}{(1-0.012)^{1.6}\cdot(1-0.001)^{2}} \simeq 0.97. \tag{2.31}$$

Clearly, the number and ages of the leads as well as the infection types and underlying conditions may vary from one patient to another. Therefore, to capture a wide variety of patients we let δ assume multiple values in our numerical experiment, i.e., $\delta \in \{0.94, 0.96, 0.98\}$.

2.5 COMPUTATIONAL STUDY

In this section, we first define additional metrics that facilitate policy comparisons (Section 2.5.1). Next, we report the results obtained under the optimal policy and compare them with those obtained under the three heuristic polices defined in Section 2.3 (Section 2.5.2). Finally, we conduct extensive sensitivity analyses to examine how parameter changes affect the results (Section 2.5.3). All of the computational results reported in this section are obtained by executing the backward induction algorithm (see Puterman (1994), page 92).

2.5.1 Additional Metrics

For single-chamber devices, let the optimal action in state $s_t = (\ell, 1)$ be denoted by $a_{t,*}(\ell)$. Similarly, for multi-chamber devices, let the optimal action in state $s_t = (\ell, w, 1)$ be denoted by $a_{t,*}(\ell, w)$. For each policy $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$, let $a_{t,\pi}(\ell)$ and $a_{t,\pi}(\ell, w)$ denote the corresponding actions for single- and multi-chamber devices, respectively.

Probability of death due to CIED-related causes, $\chi_t(s)$. In addition to expected lifetime, we are interested to learn how the probability of death due to CIED-related causes changes under various lead maintenance policies. To obtain this probability, we first calculate the probability of death from competing risks and then report its complement as $\chi_t(s)$. For each device type, we redefine the reward functions provided in Section 2.2 and use the finite-horizon policy evaluation algorithm to recursively evaluate the expected reward of any given policy (see Puterman (1994), page 80). To avoid repetition, here we only present the equations used to obtain the metric for PM1. The methods are analogous for PM2, ICD and CRT-D.

Let $\underline{\lambda}(t, m)$ denote the likelihood of death due to competing risks after exactly m periods for a patient of age t, i.e.,

$$\underline{\lambda}(t, m) = \bar{\lambda}(t, m-1) \cdot (1 - \lambda(t+m)), \tag{2.32}$$

and redefine $r_t(n)$ to denote the immediate probability of death due to non CIED-related causes starting from patient age t, given that the next failure is in n years, i.e.,

$$r_t(n) = \sum_{m=1}^{n} \underline{\lambda}(t, m) \cdot (1 - \kappa)^{m-1}. \tag{2.33}$$

Additionally, redefine $V_t(\ell, \theta)$ to denote the probability of death due to non CIED-related causes starting from state $s_t = (\ell, \theta)$. Clearly, $V_{\overline{T}}(\ell, \theta) = 1$. Finally, modify $\nu_t(n)$ and $u_t(\ell, a, n)$, given by equations (2.7) and (2.10), for PM1, as follows:

$$\nu_t(n) = \begin{cases} p_X(n) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), 0) \\ \qquad +\eta(n) \cdot \gamma \cdot V_{t+n}(\ell'(n), 1) \Big), & \text{if } n < \overline{T} - t, \\ \bar{F}_X(n-1) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), 0) + \eta(n) \cdot \gamma \Big), & \text{if } n = \overline{T} - t, \end{cases} \tag{2.34}$$

and

$$u_t(\ell, a, n) = \begin{cases} p_X(n) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), 0) \\ \qquad +\eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a, n), 1) \Big), & \text{if } n < \overline{T} - t, \\ \bar{F}_X(n-1) \cdot \Big(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), 0) \\ \qquad +\eta(n) \cdot \gamma \Big), & \text{if } n = \overline{T} - t, \end{cases} \tag{2.35}$$

where $r_t(n)$ is given by equation (2.33).

For $t < \overline{T}$, when $\theta = 0$, $V_t(\ell, 0)$ is given by equation (2.8), in which $r_t(n)$ and $\nu_t(n)$ are given by equations (2.33) and (2.34), respectively. When $\theta = 1$, $V_t(\ell, 1)$ is given by (2.11), where in each state $s_t = (\ell, 1)$ the action is predetermined for any given policy, i.e., the action is $a_{t,\pi}(\ell)$ where $\pi \in \{*, \mathcal{C}, \mathcal{H}, \mathcal{A}\}$, and $r_t(n)$ and $u_t(\ell, a, n)$ are given by equations (2.33) and (2.35), respectively. Finally, the probability of death due to CIED-related causes starting from state s_t, denoted by $\chi_t(s)$, is given by

$$\chi_t(s) = 1 - V_t(s). \tag{2.36}$$

Average difference between the total expected life years under the optimal and heuristic policies starting from first failure, $\Gamma_{t_1,t_2,d,\pi}(\ell, y)$. This metric measures the increase in total expected lifetime that patients earn by following the optimal policy as opposed to a given heuristic policy, starting from the first lead failure after implantation. Let $\Gamma_{t_1,t_2,d,\pi}(\ell, y)$ denote the difference between the total expected lifetime under the optimal policy and heuristic policy $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$ averaged over all patient ages between t_1 and

t_2 for device type $d \in \{\text{PM1}, \text{PM2}, \text{ICD}, \text{CRT-D}\}$ and first lead failure ℓ years after initial implantation at which point y leads are functional. For PM1, y is always zero and we have

$$\Gamma_{t_1,t_2,\text{PM1},\pi}(\ell, 0) = \frac{1}{t_2 - t_1 + 1} \cdot \sum_{t=t_1}^{t_2} \Big(V_t([\ell, -1, -1, -1, -1], 1) - V_{t,\pi}([\ell, -1, -1, -1, -1], 1) \Big), \tag{2.37}$$

where $V_t(s)$ is given by equation (2.11). For PM2, ICD, and CRT-D, the value of $\Gamma_{t_1,t_2,d,\pi}(\ell, y)$ is obtained from an equation analogous to (2.37) in which the value of y, the state s and the functions $V_t(s)$ and $V_{t,\pi}(s)$ are adjusted to reflect the device type.

Maximum difference between the total expected life years under the optimal and heuristic policies, $\Phi_{t_1,t_2,d,\pi}(j, y)$. We are also interested in comparing the maximum benefit an individual receives from following the optimal policy as opposed to a given heuristic policy, starting from any given state in which the device is failed. We introduce $\Phi_{t_1,t_2,d,\pi}(j, y)$, which denotes the maximum difference between the total expected reward obtained under the optimal policy and the heuristic policy $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$ across all states in which the device is failed, y out of j implanted leads are functional, the patient is between t_1 and t_2 years old and has a cardiac device of type $d \in \{\text{PM1}, \text{PM2}, \text{ICD}, \text{CRT-D}\}$, i.e., for PM1,

$$\Phi_{t_1,t_2,\text{PM1},\pi}(j, 0) = \max_{t \in \{t_1,\ldots,t_2\}} \left\{ V_t(\ell, 1) - V_{t,\pi}(\ell, 1) : \sum_i \mathbb{1}_{\{\ell_i > 0\}} = j \right\} \tag{2.38}$$

and for multi-chamber devices, $d \in \{\text{PM2}, \text{ICD}, \text{CRT-D}\}$,

$$\Phi_{t_1,t_2,d,\pi}(j, y) = \max_{t \in \{t_1,\ldots,t_2\}} \left\{ V_t(\ell, w, 1) - V_{t,\pi}(\ell, w, 1) : \sum_i \mathbb{1}_{\{\ell_i > 0\}} = j, \; y = \mathbb{1}_{\{w \in \{1,2,3\}\}} + 2 \cdot \mathbb{1}_{\{w \in \{\bar{3},\bar{2},\bar{1}\}\}} \right\}, \tag{2.39}$$

where $V_t(s)$ is given by equation (2.11) for PM1 and equation (2.24) for PM2, ICD, and CRT-D.

Maximum percentage difference between the probability of death due to CIED-related causes under the optimal and heuristic policies, $\Xi_{t_1,t_2,d,\pi}(j, y)$. Finally, we introduce $\Xi_{t_1,t_2,d,\pi}(j, y)$, which allows to compare the percentage difference in the probability of death due to device related causes under the optimal policy and the heuristic policy $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$ across all states in which the device is failed, y out of j implanted leads

are functional, and the patient is between t_1 and t_2 years old and has a cardiac device of type $d \in \{\text{PM1}, \text{PM2}, \text{ICD}, \text{CRT-D}\}$. The formulations are analogous to those of $\Phi_{t_1,t_2,d,\pi}(j, y)$ in equations (2.38) and (2.39), except that the function $V_t(s)$ in (2.38) and (2.39) is substituted with $\chi_t(s)$, given by equation (2.36), and percentage differences are calculated.

2.5.2 Policy Comparisons

In this section we compare the performance of the optimal policy to that of the three heuristic policies. We present insightful numerical results using the metrics defined in Section 2.5.1 for various device types and discuss the intuition behind the observations.

Figure 3 plots the increase in expected lifetime that a patient gains by following the optimal policy as opposed to the three heuristic policies as a function of the time of the first lead failure when $\underline{T} = 31$, $\overline{T} = 100$ and the other parameters assume their average values as given by Table 4. In Figure 3, we present the results for device types of PM1 and PM2 (rows) and three patient age groups (columns). That is, the figures in the first column report $\Gamma_{30,49,\text{PM1},\pi}(\ell, 0)$, $\Gamma_{30,49,\text{PM2},\pi}(\ell, 1)$ and $\Gamma_{30,49,\text{PM2},\pi}(\ell, 0)$ for all $\pi \in \{\mathcal{C}, \mathcal{H}, \mathcal{A}\}$ and $\ell = \{1, \ldots, 16\}$, respectively from top to bottom.

In each row, as intuition would suggest, the older the patients (left to right), the less significant the results. Clearly, younger patients have longer remaining expected lifetimes and experience more lead failures; hence, they benefit more from following the optimal policy, which aims to balance the risks involved in "elective" versus "forced" lead extractions.

In each column of Figure 3, the increase in expected lifetime for any given lead dwell time increases from top to bottom. Clearly, for PM1, only one lead is in place at the time of the first lead failure, as opposed to two leads for PM2. Hence, because patients with PM1 are less likely to the reach the space constraint of five in comparison to patients with PM2, it is less important for them to follow the optimal policy as opposed to a heuristic policy. With PM2, a patient is intuitively worse off at the time of simultaneous lead failure as opposed to single lead failure, hence the improved effect of following the optimal policy as opposed to a heuristic policy in the third row. The results for ICD and CRT-D are similar in spirit to the results for PM1 and PM2. Generally speaking, the greater the number of failed leads or the greater the number of leads that the device requires, the more beneficial it is to follow the optimal policy. However, because patients with ICD and CRT-D have more severe heart disease than patients with PM1 and PM2, the increase in expected life days is less pronounced compared to PM2.

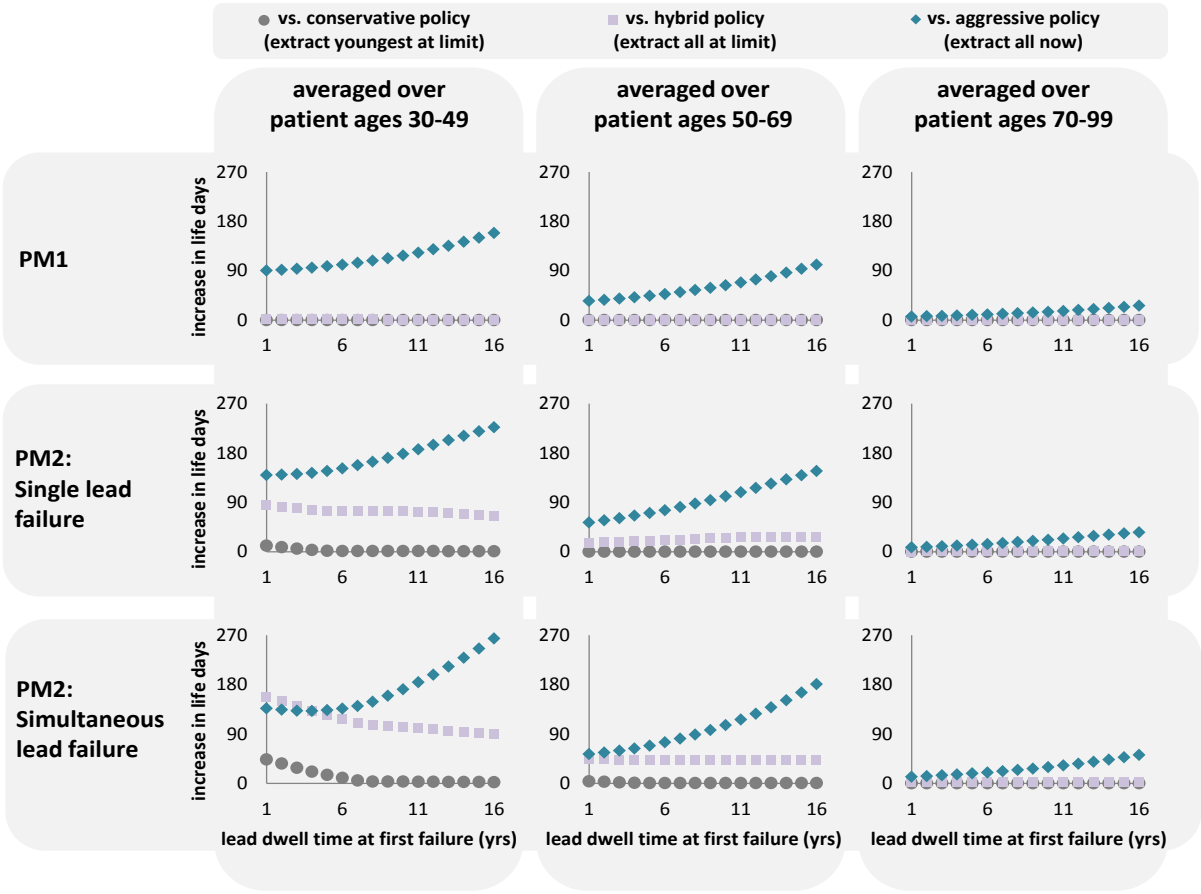


Figure 3: Average increase in expected lifetime, $\Gamma_{t_1,t_2,d,\pi}(\ell, y)$, gained by following the optimal policy as opposed to the three heuristic policies starting from the first failure when $\underline{T} = 31$, $\overline{T} = 100$ and the other parameters are given by Table 4.

Table 4: Parameter values for Figures 3-5. For $p_X(x)$ and $\beta_{-1}(\ell)$ values refer to Tables 20 and 21 in Appendix A.3, respectively.

Device Type	$p_X(x), p_{X_1}(x)$	$p_{X_2}(x)$	α	κ	β_1	$\beta_{-1}(\ell)$	δ
PM1	ω=0.5	-	0.03	0.01	0.001	average	0.96
PM2	ω=0.5	-	0.03	0.01	0.001	average	0.96
ICD	ω=0.5	ω=0.45	0.03	0.01	0.001	average	0.96
CRT-D	ω=0.5	ω=0.45	0.03	0.015	0.001	average	0.96

Figure 3 also suggests that the increase in expected life days under the optimal policy as opposed to the conservative policy is relatively small (i.e., on the order of zero to 43 days); the performance of the conservative policy is close to optimal. On the other hand, compared to the aggressive policy, the expected lifetime can increase by up to nine months under the optimal policy. Overall, the aggressive policy is almost always the worst performing policy. Moreover, its performance worsens in the time of the first lead failure due to the fact that the probability of death following lead extraction increases in lead dwell time.

Additionally, in Figure 3 the hybrid policy, which typically performs at least as well as the aggressive policy, underperforms the aggressive policy in the case of PM2 with simultaneous lead failure when the leads and the patient are young on the order of 1-3 years and 30-49 years, respectively. In these cases, under the hybrid policy both failed leads are abandoned and two new leads are added, which leaves the patient with four leads in place at a very young age. It is not unlikely that this young patient would experience two additional lead failures that would prompt the extraction of all implanted leads under the hybrid policy, which can be very dangerous.

The results in Figure 3 assume that patients follow a certain policy from implantation. Next, consider the case in which patients may switch between follow-up policies, which is often the case in practice; hence, patients can reach a wide combination of lead ages at the time of lead failure. Figure 4 plots the maximum increase taken over all reachable combinations of lead ages in expected lifetime gained by following the optimal policy as opposed to the three heuristic policies, stratified across the number of implanted leads and the patient age group when $\underline{T} = 31$, $\overline{T} = 100$ and the other parameters are given by Table 4.

Figure 4 reports these results for all four device types (rows) and three heuristic policies (columns). For instance, the first three plots in the first column report $\Phi_{t_1,t_2,\text{PM1},\mathcal{C}}(j,0)$ for all $(t_1,t_2) \in \{(30,49), (50,69), (70,99)\}$ and $j = \{1,\ldots, 5\}$, and $\Phi_{t_1,t_2,\text{PM2},\mathcal{C}}(j,1)$ and $\Phi_{t_1,t_2,\text{PM2},\mathcal{C}}(j,0)$ for all $(t_1,t_2) \in \{(30,49), (50,69), (70,99)\}$ and $j = \{2,\ldots, 5\}$, respectively from top to bottom. ICD with simultaneous lead failure, CRT-D with double lead failure and CRT-D with triple lead failure are not included in Figure 4, but behave similarly.

Consistent with the results in Figure 3, in Figure 4 the largest increase in the expected lifetime gained by following the optimal policy as opposed to a heuristic policy is always obtained by younger patients. In fact, in Figure 4, the maximum reward reported for each combination of number of implanted leads and patient age group (corresponding to the height of each bar in the plots) is generally attained by the youngest patients in that subcategory. For instance, in Figure 4, for 50- to 69-year-old patients with PM1, the maximum reward $\Phi_{50,69,\text{PM1},\pi}(j,0)$ is always obtained by 50-year-old patients, regardless of the policy and the number of implanted leads. However, this observation may not always be generalized, especially when some states are unreachable. For instance, for 30- to 49-year-old patients with PM1 who follow the optimal policy as opposed to the hybrid policy, the maximum reward $\Phi_{30,49,\text{PM1},\mathcal{H}}(j,0)$ is obtained by the youngest patients when $j \in \{1,\ldots,4\}$ and by 46-year-old patients when $j = 5$. That is, $\Phi_{30,49,\text{PM1},\mathcal{H}}(5,0) = 390.6$, reported in the top plot of the second column, is obtained by a 46-year-old patient, not a 35-year-old one.

Unlike Figure 3, in Figure 4 the increase in expected lifetime can be quite significant for older patients. Additionally, from Figure 4, we observe that it is especially important to make the abandon/extract decisions optimally when more leads are in place; the lifetime extension can be well more than one year. Lastly, note that the lifetime extension for patients with ICD and CRT-D seems to be low in comparison to PM1 and PM2. The reason behind this observation is that patients with these two device types have shorter life expectancies than patients with PM1 and PM2 and thus have fewer remaining life years during which to benefit from implementing the optimal policy.

Finally, Figure 5 is structured the same as Figure 4, but plots the maximum percentage decrease in the probability of device related death. For instance, the first three figures in the first column report $\Xi_{t_1,t_2,\text{PM1},\mathcal{C}}(j,0)$ for all $(t_1,t_2) \in \{(30,49), (50,69), (70,99)\}$ and $j = \{1,\ldots, 5\}$, and $\Xi_{t_1,t_2,\text{PM2},\mathcal{C}}(j,1)$ and $\Xi_{t_1,t_2,\text{PM2},\mathcal{C}}(j,0)$ for all $(t_1,t_2) \in \{(30,49), (50,69), (70,99)\}$ and $j = \{2,\ldots, 5\}$, respectively, from top to bottom. In contrast to Figures 3 and 4, in Figure 5 older patients, not younger ones, who follow the optimal policy as opposed

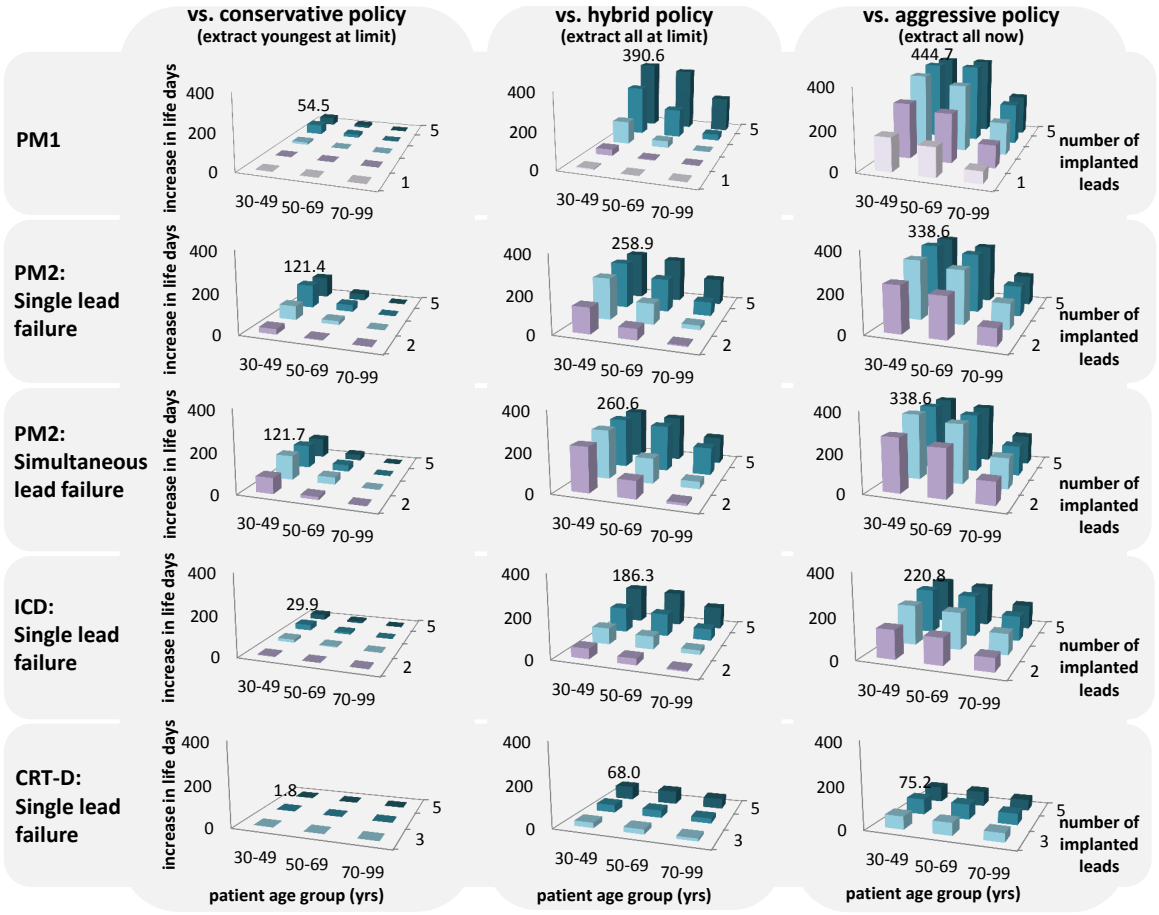


Figure 4: Maximum increase in expected lifetime over all starting states, $\Phi_{t_1,t_2,d,\pi}(j,y)$, gained by following the optimal policy as opposed to the three heuristic policies, stratified across patient age groups and number of implanted leads when $\underline{T} = 31$, $\overline{T} = 100$ and the other parameters are given by Table 4.

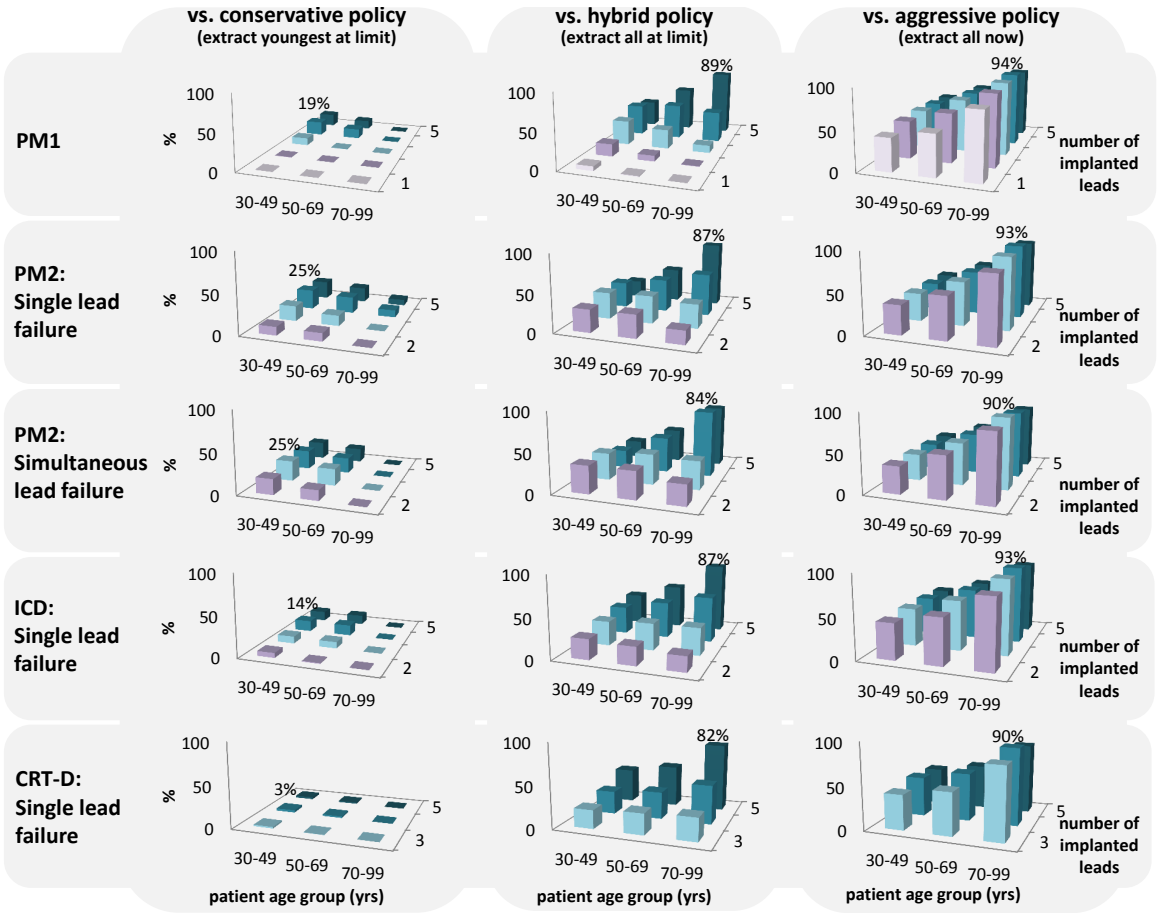


Figure 5: Maximum percentage decrease in probability of device related death over all starting states, $\Xi_{t_1,t_2,d,\pi}(j,y)$, realized by following the optimal policy as opposed to the three heuristic policies starting from any combination of lead ages at the time of a lead failure, stratified across patient age groups and number of implanted leads when $\underline{T} = 31$, $\overline{T} = 100$ and the other parameters are given by Table 4.

Table 5: Sensitivity analysis for a single-chamber device, starting from state (40,[6,2,1,-1,-1]).

Parameter	Levels	Increase in the expected number of life days under the optimal policy as opposed to conservative			hybrid			aggressive		
		Min	Mean	Max	Min	Mean	Max	Min	Mean	Max
$p_X(x)$	$\omega = 0.45$	0.62	4.65	12.96	69.82	85.68	105.63	81.21	125.82	182.13
	$\omega = 0.5$	0.62	4.23	12.41	67.31	82.89	102.49	79.53	124.14	180.67
	$\omega = 0.55$	0.58	3.75	11.83	64.35	79.53	98.70	77.67	122.27	179.07
α	0.01	0.62	3.94	12.37	69.90	86.30	105.63	84.57	129.01	182.13
	0.02	0.62	4.12	12.59	68.00	83.86	102.27	82.27	125.68	177.50
	0.03	0.58	4.30	12.74	66.14	81.48	98.99	79.97	122.41	172.94
	0.04	0.62	4.48	12.96	64.35	79.15	95.78	77.67	119.20	168.52
κ	0.005	0.58	1.69	5.18	84.28	94.31	105.63	123.77	151.86	182.13
	0.01	0.62	3.91	9.38	73.77	81.57	89.02	98.99	122.26	147.64
	0.015	0.95	7.04	12.96	64.35	72.22	79.86	77.67	98.11	119.43
β_1	0.00075	0.58	4.22	12.96	64.46	82.77	105.63	77.78	124.13	182.13
	0.0010	0.58	4.21	12.96	64.42	82.70	105.52	77.75	124.08	182.06
	0.00125	0.58	4.20	12.92	64.35	82.62	105.45	77.67	124.02	181.95
$\beta_{-1}(\ell)$	low	2.04	7.75	12.96	68.04	82.74	100.08	77.67	106.87	138.85
	average	0.73	3.62	8.40	66.17	82.11	101.32	91.69	123.50	159.10
	high	0.58	1.26	3.98	64.35	83.24	105.63	105.67	141.86	182.13
δ	0.94	0.58	3.97	12.01	64.35	82.46	105.59	79.17	124.62	182.13
	0.96	0.58	4.21	12.45	64.79	82.70	105.59	78.44	124.08	181.73
	0.98	0.58	4.46	12.96	65.23	82.94	105.63	77.67	123.53	181.33

to the hybrid or aggressive policy gain the most benefit; they may experience a dramatic drop, by up to 90% or more, in the risk of death from device related causes. In other words, under the optimal as opposed to hybrid and aggressive policies, older patients may live a life that is much less affected by their implanted cardiac device. Note that in Figure 5 the maximum percentage decrease for each combination of number of implanted leads and patient age group (corresponding to the height of each bar in the plots) is not necessarily attained by the oldest patients in that subcategory. For instance, $\Xi_{30,49,\text{PM1},\mathcal{C}}(4,0) = 19\%$ and $\Xi_{50,69,\text{PM1},\mathcal{H}}(4,0) = 48\%$ are obtained by 38- and 63-year-old patients, respectively.

2.5.3 Sensitivity Analysis

In this section, we present some sensitivity analyses to assess the robustness of our results with respect to the key problem parameters. We limit our analysis to single-chamber devices but anticipate similar results for dual-chamber and CRT-D device.

Table 5 presents the sensitivity analysis for single-chamber devices, starting from state (40,[6,2,1,-1,-1]). For each parameter, the table reports the minimum, mean and maximum

increase in the expected lifetime obtained under the optimal policy as opposed to the three heuristic policies, averaged across all other parameter combinations. For most parameters, the results appear to be insensitive to moderate changes. For instance, the changes in the increase in expected lifetime across various values of β_1 and δ is on the order of one day. The increase in expected lifetime is most sensitive with respect to the annual probability of acquiring unrelated infection, κ, and the probability of death following extraction of a lead of age ℓ, $\beta_{-1}(\ell)$. The maximum difference between the obtained increase in expected lifetime across various levels of these two parameters is on the order of two and one months, respectively.

The results provided by Table 5 are consistent for a representative sample of ten starting states. These additional analyses are not included for sake of brevity.

2.6 CONCLUSION

Cardiac leads are often referred to as "the weakest link" in implantable cardiac device care. Despite their importance, lead maintenance philosophies vary widely from practice to practice. We develop an approach that assists clinicians in making patient-specific lead abandon/extact decisions to maximize patients lifetime. More specifically, we develop novel MDP models that dynamically determine which leads to extract at the time of lead failure as a function of patient age and lead ages for four major device types. We observe that under the optimal policy, the decision to abandon or extract each lead only depends on its age, patient age, its age rank among the lead ages, the total number of implanted leads and, in the case of multi-chamber devices, the age of the working lead(s). In other words, the decisions do not depend on the exact ages of all implanted leads, which simplifies the implementation of the policy.

Following the optimal policy as opposed to commonly used heuristic policies both extends the expected lifetime and decreases the average likelihood of device related death for all patient subgroups. A "conservative" lead maintenance scheme that recommends extracting the youngest failed lead(s) only when an extraction is required due to space considerations typically preforms close to optimal; however, by following the optimal policy as opposed to this policy, an average patient may gain four additional expected life months. The benefit

of following the optimal policy as opposed to other commonly used heuristic policies can be more dramatic; average patients may gain an expected lifetime extension of up to 1.2 years. Generally speaking, younger patients benefit from following the optimal policy in the form of gaining lifetime extension. For older patient, this benefit is in the form of avoiding device related death; by following the optimal policy as opposed to the heuristic policies, older patients may see a dramatic drop of up to 94% in the risk of death from device related causes.

3.0 OPTIMAL IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD) GENERATOR REPLACEMENT

3.1 INTRODUCTION

Over 650,000 people in the United States currently rely on CIEDs for defibrillation and/or pacing, and this number is growing exponentially (Meier 2010, Stellbrink and Trappe 2007, Stoepel et al. 2009) with approximately 10,000 new implantations occurring per month (Meier 2010). Recall from Section 1 that dual-chamber ICDs are used to prevent bradycardia, i.e., a slow heart rate, and manage tachycardia, i.e., a fast or irregular heart rate. More specifically, the device can detect slow rhythms and send small electronic impulses to the heart to make it beat faster. Additionally, it can detect dangerously fast, potentially lethal rhythms, and deliver a "shock(s)" or "charge(s)" in an attempt to restore normal rhythm (Neighmond 2006).

ICDs are typically powered by lithium/silver vanadium oxide or lithium/manganese dioxide batteries (Crespi et al. 2001, Drews et al. 2001). One major drawback of these batteries is their limited lifetimes. In fact, ICD battery lifetimes do not typically exceed the patient's remaining lifetime at the time of initial implantation (Hauser 2005). Therefore, most patients undergo multiple generator replacement surgeries during the course of their lives due to battery depletion (Hauser 2005, Stiles 2005, Thijssen et al. 2012).

Like any surgery, ICD generator replacement involves risks, is costly and can cause patient anxiety. Some studies report the rate of major complications, e.g., pocket infection requiring dangerous lead extraction, to be as high as 4.1% and 5.8% (Costea et al. 2008, Gould and Krahn 2006). Klug et al. (2007) and Lekkerkerker et al. (2009) demonstrate an association between ICD generator replacement and the occurrence of infection. In a study by Gould and Krahn (2006), major complications resulted in death in 0.38% of ICD generator replacements. Krahn et al. (2011) report a major complication rate of 2.6% and associate

these complications with a mortality rate as high as 8.7% in the six months following surgery. In terms of cost, each replacement is on the order of $24,000 (BIOTRONIK, Inc. 2012 and St. Jude Medical, Inc. 2012). Moreover, any operation, ICD generator replacement included, can cause anxiety both preoperatively and postoperatively (Mitchell 2003). For some or all of these reasons, many experts argue that it would be ideal to perform two or fewer replacements in a typical patient's lifetime instead of the current three to four (Stiles 2005).

Although generator replacement involves risks, not performing replacements early enough exposes the patient to other risks. The main function of an ICD is to deliver as many full-energy charges as needed (possibly more than one per episode) to regulate dangerously fast heart rhythms and hence prevent cardiac arrest. Because each full-energy charge consumes almost one month of the average generator lifetime (SECURA manual, Medtronic 2012c), determining the replacement time is a sensitive issue. Manufacturers recommend that ICDs be replaced when they reach the recommended replacement time (RRT). At RRT, the device has enough energy remaining to emit pacing pulses 100% of the time for an additional three months and to deliver six full-energy charges (Medtronic 2012c). Once RRT is reached, the device emits the RRT signal indicating that the "end of service (EOS)" will be reached shortly and a generator replacement needs to be scheduled. Although the time it takes different patients to reach RRT depends on each individual's battery consumption rate, the RRT itself is not tailored for individuals. Clearly, there is a trade-off between prematurely exposing the patient to the risk of replacement and allowing for the possibility that the device is unable to deliver charges/therapy when needed.

In this chapter, we focus on obtaining an optimal ICD replacement time given a set of patient characteristics. More specifically, we use a finite horizon MDP model to investigate the degree to which unnecessarily "conservative" (i.e., "early") generator replacements may be delayed to maximize the patient's total expected life years. Furthermore, we examine the impact of our approach on reducing the expected number of replacements during the patient's lifetime. In current practice, replacement decisions are based solely on the estimated remaining longevity of the device. In contrast, our approach allows clinicians to make replacement decisions dynamically as a function of both patient age and the remaining energy stored in the battery, i.e., remaining battery capacity.

The burden that ICD generator replacement places on patients and the health care system at large is widely discussed in the clinical literature (Biffi et al. 2011, 2008, Hauser 2005, Ramachandra 2010). However, to the best of our knowledge, no research addresses this

issue from a mathematical/optimization perspective. There exists a somewhat relevant body of work that considers using slightly larger batteries with higher capacities to extend ICD generator longevity (Hauser 2005, Ramachandra 2010, Russo 2012, Thijssen et al. 2012). However, these works are descriptive in nature and do not involve mathematical models or decision making. Furthermore, in contrast to this chapter, in which the objective is to maximize the patient's benefit using the ICD technology currently available, these works propose hardware changes.

The most relevant literature is in reliability and maintenance modeling, more specifically damage models in which a device fails if the cumulative damage exceeds a damage level (see references in Nakagawa 2007). Similar to these models, we introduce a system, i.e., an ICD generator, whose battery is subject to depletion and fails if its battery capacity is exhausted. In this context, depletion is equivalent to damage and the system fails if the total amount of battery depletion, i.e., the cumulative damage, exceeds the initial battery capacity, i.e., the damage level. In our model, depletion is caused by both randomly demanded charges as well as continuous monitoring and pacing. The former corresponds to random shocks/damage and is incorporated in most damage models (Nakagawa 2007); the latter corresponds to "graceful" system deterioration over time and is considered in some damage models, e.g., Satow et al. (2000). Typically in damage models, costs are associated with replacements and failures, and the objective is to minimize the cost rate over an infinite horizon (Nakagawa 2007, Ito and Nakagawa 2011 and Zhao et al. 2011). In contrast, we consider a finite horizon problem in which the objective is to avoid premature problem termination caused by either replacement or failures. Also, rather than incurring an economic cost, a failure terminates the ICD replacement problem, i.e., results in the patient's death.

The remainder of the chapter is organized as follows. In Section 3.2, we present the model formulation and an insightful example of an optimal policy. Section 3.3 examines the structural properties of the model and optimal policy. In Section 3.4, we calibrate the model and obtain the transition probabilities for various classes of patients using both data from the existing literature as well as from a clinical dataset. In Section 3.5, we report the results from a large computational study to compare and contrast the total expected reward and the total expected number of replacements under the optimal policy and current practice. Lastly, we conclude in Section 3.6.

3.2 MODEL FORMULATION

Consider an ICD pulse generator battery with a known, deterministic initial useful capacity $\bar{u}$. Let the random variable D, with p.m.f. p_D and c.d.f. F_D, denote the number of charges demanded per period, e.g., per week. Furthermore, let δ and δ_c denote the amount of capacity consumed by the ICD per period excluding any charges and per charge, respectively. Assume that the periods are defined such that $\delta < \delta_c$, and note that for a given set of patient characteristics, the parameter δ is constant over time.

Let $g(u)$ be the maximum number of charges that may be delivered in any given period starting with a remaining battery capacity of u. Assuming that the demands for charges occur all at once at the end of each period,

$$g(u) = \left\lfloor \frac{u - \delta}{\delta_c} \right\rfloor . \tag{3.1}$$

Let $\underline{\ell} \geq 0$ denote the age of the patient at the time of initial implantation and $\bar{\ell} > \underline{\ell}$ be the maximum reachable age. Let the pair (ℓ, u) correspond to the state of the process where $\underline{\ell} \leq \ell \leq \bar{\ell}$ and $u \leq \bar{u}$ denote the patient age and the remaining capacity of the battery, respectively.

A decision is made at the beginning of every period to either "replace" the battery or to take no action, i.e., "wait." We assume that replacement takes one period during which no charges occur. Consequently, the patient may die due to replacement induced complications at the end of the period. Recall that the demand for charges also occur at the end of each period. Therefore, upon every decision the patient earns one period of lifetime independent of the action taken. The objective is to make decisions dynamically throughout the patient's lifetime to maximize the patient's total expected lifetime.

Replacement procedures are not perfect; as a result of a procedure, the patient may suffer from recoverable complications or die. Let $\alpha_\Delta(\ell)$ denote the probability of replacement induced death for a patient of age ℓ. We assume that $\alpha_\Delta(\ell)$ is non-decreasing in patient age, ℓ, and procedure-related deaths occur immediately after surgery. Finally, in any period, a patient may die due to competing risks of death, e.g., comorbidities and unrelated causes. Let $\lambda(\ell)$ be the per period probability of surviving the competing risks of death for a patient of age ℓ, $0 \leq \lambda(\ell) < 1$. We assume that $\lambda(\ell)$ is non-increasing in patient age, ℓ.

Let $V(\ell, u)$ denote the maximum total expected reward starting from state (ℓ, u) (see Bellman (1957)), i.e.,

$$V(\ell, u) = \begin{cases} 0, & \text{if } \ell = \bar{\ell}, \text{ or } u \leq 0, \\ \max\{R(\ell), C(\ell, u)\}, & \text{otherwise,} \end{cases} \tag{3.2}$$

where $R(\ell)$ is the reward obtained under the action "replace,"

$$R(\ell) = 1 + (1 - \alpha_\Delta(\ell)) \cdot \lambda(\ell) \cdot V(\ell + 1, \bar{u}), \tag{3.3}$$

and $C(\ell, u)$ is the reward obtained under the action "wait,"

$$C(\ell, u) = 1 + \sum_{d=0}^{g(u)} \lambda(\ell) \cdot V(\ell + 1, u - \delta - d \cdot \delta_c) \cdot p_D(d). \tag{3.4}$$

Independent of the decision (hence in both equations (3.3) and (3.4)), the patient instantaneously earns one period of life. Whenever the decision is to "replace" the generator (equation (3.3)), if the procedure is successful, then the patient continues with a new generator with an initial capacity of $\bar{u}$. When the decision is to "wait" (equation (3.4)), the patient survives if death due to other causes is averted and the remaining battery capacity is enough to deliver the charges demanded during the period; otherwise, the process terminates, i.e., the patient dies.

Figure 6 displays an example optimal policy for $\bar{u} = 1.06$ ampere hours (Ah), $\bar{\ell} = 6240$ weeks (120 years), $\underline{\ell} = 2600$ weeks (50 years), $\alpha_\Delta(\ell) = 0.02$, $\delta = 0.00265$ Ah, $\delta_c = 0.008053$ Ah and the distribution of charges given by Table 6. For this example, the optimal policy is of threshold form. That is, there exists a replacement threshold such that for any state (ℓ, u) on or below the threshold, the optimal action is to "replace" the generator and for any state (ℓ, u) above the threshold, the optimal action is to "wait." The sample path realization in Figure 6 demonstrates possible ICD generator usage dynamics for a patient who receives a new ICD at the age of 50. The slope of the non-vertical pieces of the sample path is δ and the vertical decrements, which are integer multiples of δ_c, indicate the amount of capacity consumed due to delivering charges. The optimal policy advises a generator replacement once the sample path crosses the optimal threshold. From Figure 6, this patient undergoes the first generator replacement surgery after almost 6 years at the age of 56.1. Once the device is replaced, the patient receives a new ICD generator and continues to receive therapy.

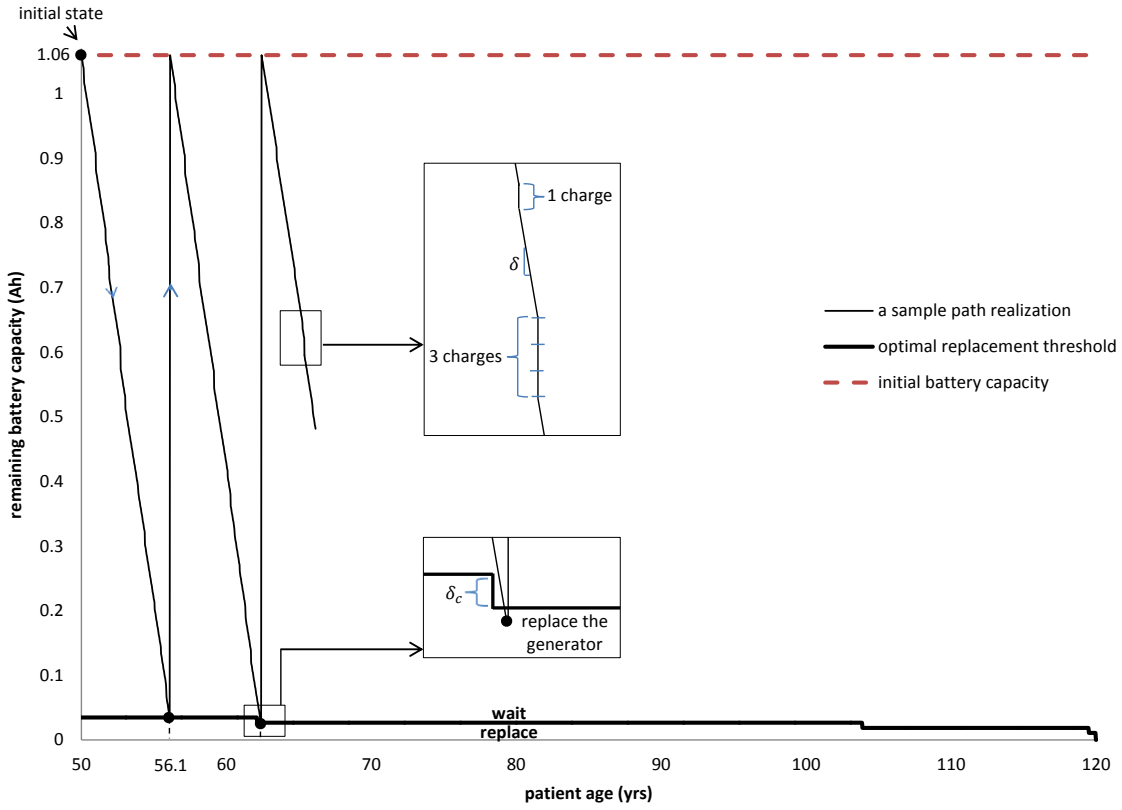


Figure 6: An example optimal policy and sample path for $\bar{u} = 1.06$ Ah, $\bar{\ell} = 6240$ weeks (120 years), $\underline{\ell} = 2600$ weeks (50 years), $\alpha_\Delta(\ell) = 0.02$, $\delta = 0.00265$ Ah, $\delta_c = 0.008053$ Ah and the distribution of charges given by Table 6.

Table 6: Distribution of charges per week.

d	0	1	2	3	4	5	6	7	≥ 8
$p_D(d)$	0.953759	0.045199	0.000817	0.000154	0.000044	0.000021	0.000005	0.000001	0

In Figure 6, the optimal replacement threshold decreases as the patient ages, advising less conservative replacement actions. The downward steps in the optimal replacement threshold are of size δ_c, the amount of energy consumed per charge. Hence, these downward steps reflect the policy's tendency to retain less battery capacity (in integer multiples of the capacity consumed per charge) as the patient ages. That is, the downward steps help delay the replacements (e.g., the second replacement in Figure 6) and, consequently, reduce their total expected number.

3.3 STRUCTURAL PROPERTIES

In this section, we provide several intuitive structural properties. More specifically, we establish the monotonicity of the total reward in both patient age and remaining capacity and show that the optimal policy is of control-limit type. The proofs are provided in Appendix B.1.

In Lemma 1, we prove the monotonicity of the maximum total expected reward $V(\ell, u)$ in the remaining battery capacity u. Lemma 1 demonstrates that for any given patient age, a battery with higher remaining capacity brings a greater expected reward for the patient. Because we proceed with the proof of Lemma 1 by induction on the remaining battery capacity u, we discretize this dimension of the state space as follows. The capacity increment, denoted by $\bar{\delta} \in \mathbb{R}_{++}$, is defined such that the remaining battery capacity at all of the intermediate states on any given sample path can be expressed as integer multiples of the capacity increment. To achieve this property, we assume that the initial battery capacity $\bar{u}$, the capacity consumed per period in the absence of any shocks δ, and the capacity consumed per charge δ_c can be set to integer multiples of the capacity increment, and define the capacity increment by

$$\bar{\delta} = \max\{\hat{\delta} \in \mathbb{R}_{++} : \frac{\delta}{\hat{\delta}} \in \mathbb{Z}_{++}, \frac{\delta_c}{\hat{\delta}} \in \mathbb{Z}_{++}, \frac{\bar{u}}{\hat{\delta}} \in \mathbb{Z}_{++}\}. \tag{3.5}$$

Lemma 1. *For any fixed patient age ℓ, the total reward $V(\ell, u)$ is non-decreasing in $u \geq 0$.*

In the same vein as Lemma 1, Corollary 1 establishes the monotonicity of the expected reward obtained upon the action "wait" in the remaining battery capacity, u.

Corollary 1. *For any fixed patient age ℓ, $C(\ell, u)$ is non-decreasing in $u \geq 0$.*

Lemma 2 establishes the monotonicity of the maximum total expected reward $V(\ell, u)$ in patient age ℓ. Lemma 2 implies that for any given remaining battery capacity, under the optimal policy, younger patients earn a greater expected reward.

Lemma 2. *For any fixed remaining battery capacity u, the total reward $V(\ell, u)$ is non-increasing in $\ell \geq 0$.*

Analogous to Lemma 2, Corollary 2 establishes the monotonicity of the reward obtained upon the actions "replace" and "wait," i.e., $R(\ell)$ and $C(\ell, u)$, respectively, in patient age ℓ. Corollary 2 implies that for any given remaining battery capacity and action, younger patients earn a greater expected reward.

Corollary 2. *For any fixed remaining battery capacity u, $C(\ell, u)$ and $R(\ell)$ are non-increasing in $\ell \geq 0$.*

Theorem 1 establishes that for any fixed patient age ℓ, the optimal policy is of control-limit type, i.e., there is a battery capacity $u^*(\ell)$ at and above which it is optimal to continue with the current generator and below which it is optimal to replace the generator. Let $a^*(\ell, u)$ denote the optimal action in state (ℓ, u) which is either to "replace" the generator or to "wait." Denote the former action by '1' and the latter by '0.' Hence,

Theorem 1. *For any fixed patient age ℓ, there exists a battery capacity $u^*(\ell)$ such that*

$$a^*(\ell, u) = \begin{cases} 0, & \text{if } u \geq u^*(\ell), \\ 1, & \text{otherwise.} \end{cases} \tag{3.6}$$

As established in Theorem 1, and seen in Figure 6, the optimal policy is of control-limit type in the remaining battery capacity u. Although the example policy in Figure 6 is of control-limit type in patient age ℓ as well, nontrivial problem instances exist in which this property is violated.

Lemma 3, and consequently Corollary 3, establish that for any given patient age ℓ and remaining capacity u, the maximum total reward and the reward obtained upon a decision, either "replace" or "wait," is less if the surgeries are riskier, i.e., the probability of replacement induced death is higher.

Lemma 3. *Let $V^1(\ell, u)$ and $V^2(\ell, u)$ be two problem instances given by equation (3.2) for which $\alpha_\Delta(\ell)$ equals $\alpha^1_\Delta(\ell)$ and $\alpha^2_\Delta(\ell)$, respectively. If $\alpha^2_\Delta(\ell) \geq \alpha^1_\Delta(\ell)$ $\forall \ell \leq \bar{\ell}$, then for any given state (ℓ,u), $V^1(\ell, u) \geq V^2(\ell, u)$.*

Corollary 3. *Let $R^i(\ell)$ and $C^i(\ell,u)$ denote reward instances given by equations (3.3) and (3.4) for which $\alpha_\Delta(\ell)$ equals $\alpha^1_\Delta(\ell)$ and $\alpha^2_\Delta(\ell)$ when $i=1$ and $i=2$, respectively. If $\alpha^2_\Delta(\ell) \geq \alpha^1_\Delta(\ell)\ \forall \ell \leq \bar{\ell}$, then for any given state (ℓ,u), $R^1(\ell) \geq R^2(\ell)$ and $C^1(\ell,u) \geq C^2(\ell,u)$.*

In the same vein as Lemma 3 and Corollary 3, Lemma 4 and Corollary 4 establish that for any given patient age ℓ and remaining capacity u, the maximum total reward and the reward obtained upon a decision, either "replace" or "wait," is less if the number of charges demanded per period is stochastically larger.

Lemma 4. *Let $V^1(\ell,u)$ and $V^2(\ell,u)$ be two problem instances given by equation (3.2) for which random variables D^1 and D^2 denote the number of charges demanded per period, respectively. If $D^2 \succeq D^1$, i.e., D^2 is stochastically larger than D^1, then for any given state (ℓ,u), $V^1(\ell,u) \geq V^2(\ell,u)$.*

Corollary 4. *Let $R^i(\ell)$ and $C^i(\ell,u)$ denote reward instances given by equations (3.3) and (3.4) for which D equals D^1 and D^2 when $i=1$ and $i=2$, respectively. If $D^2 \succeq D^1$, then for any given state (ℓ,u), $R^1(\ell) \geq R^2(\ell)$ and $C^1(\ell,u) \geq C^2(\ell,u)$.*

Finally, analogous to Lemmas 3-4 and Corollaries 3-4, Lemma 5 and Corollary 5 establish that for any given patient age ℓ and remaining capacity u, the maximum total reward and the reward obtained upon a decision, either "replace" or "wait," is less if the patient is more pacer-dependent, i.e., the rate of battery consumption in the absence of charges is higher.

Lemma 5. *Let $V^1(\ell,u)$ and $V^2(\ell,u)$ be two problem instances given by equation (3.2) for which δ equals δ^1 and δ^2, respectively. If $\delta^2 \geq \delta^1$, then for any given state (ℓ,u), $V^1(\ell,u) \geq V^2(\ell,u)$.*

Corollary 5. *Let $R^i(\ell)$ and $C^i(\ell,u)$ denote reward instances given by equations (3.3) and (3.4) for which δ equals δ^1 and δ^2 when $i=1$ and $i=2$, respectively. If $\delta^2 \geq \delta^1$, then for any given state (ℓ,u), $R^1(\ell) \geq R^2(\ell)$ and $C^1(\ell,u) \geq C^2(\ell,u)$.*

3.4 MODEL CALIBRATION AND EXPERIMENTAL DESIGN

In this section, to calibrate the mathematical model formulated in Section 3.2, we use values from the literature when available and estimate the remaining parameters using clinical data. Also, to facilitate the analysis on the effects of the patient-specific parameters

Table 7: Experimental-design factors and their corresponding levels. For "low," "all" and "high" distributions refer to Table 8.

Factor	Unit	No. of levels	Levels
$\bar{u}$	Ah	6	0.91, 0.96, 1.01, 1.06, 1.11, 1.16
δ	Ah	4	0.00265, 0.00301, 0.00464, 0.00565
$\underline{\ell}$	weeks	11	1560, 1820, 2080, 2340, 2600, 2860, 3120, 3380, 3640, 3900, 4160
$\alpha_\Delta(\ell)$	-	5	0.005, 0.01, 0.015, 0.02, 0.025
$p_D(d)$	-	3	low, all, high

on the optimal policy in Section 3.5, we design a computational study. In the remainder of the chapter, we set the decision periods equal to one week in length and hence let the ℓ dimension of the state space be expressed in weekly increments.

Table 7 summarizes the factors of the experiment and their corresponding levels that are estimated in Sections 3.4.1 and 3.4.2. We use this designed experiment to compare the results obtained under the optimal policy and current practice in Section 3.5.

3.4.1 Parameters Estimated from Existing Literature

Based on the existing literature, device manuals (e.g., Medtronic 2012c) and expert opinion, we estimate the values of parameters $\bar{u}$, $\underline{\ell}$, $\lambda(\ell)$, $\alpha_\Delta(\ell)$ and δ_c as follows.

Initial useful battery capacity, $\bar{u}$. Battery capacity, measured in ampere hours (Ah), is the amount of energy in the battery available for sensing (i.e., monitoring the patient's rhythm), pacing, and delivering charges. However, the battery capacity is not

Table 8: The estimated distribution of charges per week for patients with rates below ("low") or above ("high") the median rate of demanding charges. Distribution "all," previously given in Table 6, is the estimated distribution of charges per week for all patients.

d	Class	0	1	2	3	4	5	6	7
$p_D(d)$	low	0.964241	0.035687	0.000069	0.000003	0	0	0	0
	all	0.953759	0.045199	0.000817	0.000154	0.000044	0.000021	0.000005	0.000001
	high	0.943762	0.054270	0.001530	0.000299	0.000086	0.000041	0.000009	0.000003

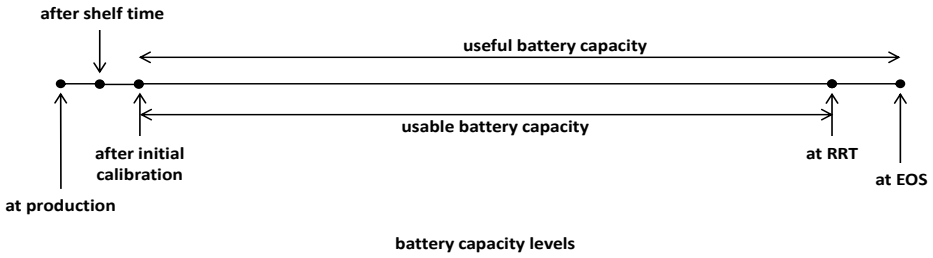


Figure 7: A schematic battery capacity diagram.

consumable in its entirety. ICDs typically experience a pre-implantation shelf time during which the battery is somewhat depleted (SECURA manual, Medtronic 2012c); the average shelf time is on the order of five months. Also, immediately after implantation, the ICD is typically tested to ensure proper functioning, during which the battery is further depleted. Furthermore, when the battery capacity becomes excessively low, i.e., when EOS is reached, the device loses its ability to perform certain functions. Therefore, we define the "useful" battery capacity, $\bar{u}$, to be the amount of energy stored in the battery after implantation, but before device functionality is affected. Figure 7 shows a schematic battery capacity diagram. In the remainder of this chapter, for simplicity, we refer to the useful battery capacity as battery capacity.

The initial battery capacity varies by device family, mainly due to differences in battery size and technology. The typical initial battery capacity for ICDs is on the order of 1.04 Ah, consisting of the usable battery capacity, 0.91 Ah, and the battery capacity remaining at RRT, 0.13 Ah (see Section 3.5.1). To account for the differences among various device families, we consider six values in the range of 0.91 to 1.16 Ah, i.e., $\bar{u} \in \{0.91, 0.96, 1.01, 1.06, 1.11, 1.16\}$.

Patient age at the time of initial implantation, $\underline{\ell}$; and the probability of surviving the competing risks of death, $\lambda(\ell)$. In most clinical studies, the mean age at first ICD implantation is between 55 and 68 years (Lee et al. 2010, 2007, Remmelts et al. 2009). Therefore, to capture a wide range of adult patients, we consider values of $\underline{\ell}$ between 1560 weeks (30 years) and 4160 weeks (80 years), i.e., $\underline{\ell} \in \{1560, 1820, \ldots, 4160\}$.

The values of $\lambda(\ell)$ are obtained from the United States total population life table provided by Arias (2011), adjusted across all ages for the excess rate of mortality for patients

with ICD devices. We estimate this excess rate of mortality by feeding a point estimate of the compound annual mortality rate of patients wearing ICD devices, i.e., 5.8% for patients of age 60 as reported by Bardy et al. 2005, to the DEALE method (Beck et al. 1982). The resulting excess rate of mortality is 0.012 per year. As an example, consider patients of ages 60 to 61. From the life table provided by Arias (2011), the probability of dying between ages 60 to 61 is approximately 0.0091. Hence, the probability of surviving the competing risks of death between ages 60 and 61 for patients with ICD devices is

$$\lambda(\ell) = \sqrt[52]{(1 - (0.0091 + 0.012))} = 0.999590, \tag{3.7}$$

where ℓ varies between 60×52 and $60 \times 52 + 51$ weeks, i.e., $\ell = 60 \times 52, 60 \times 52 + 1, \cdots, 60 \times 52 + 51$ weeks. (For simplicity we let the number of weeks in a year be exactly 52.)

Probability of replacement induced death, $\alpha_\Delta(\ell)$. After a generator replacement, significant complications may occur, e.g., infection, pulmonary edema (Krahn et al. 2011). There is also a positive likelihood that the patient dies as a result of a generator replacement surgery. Krahn et al. (2011) deem complications that require hospitalization, parenteral therapy or surgical intervention as "major" and the rest as "minor." In their study of 1,081 patients, 2.6% suffered from major complications. At 45 days, major complications originating from direct mechanical effects of surgery were associated with a 4.4% mortality. At 180 days, this number increased to 8.7%. In contrast, for those patients who did not experience these major complications, the mortality at 45 and 180 days, is 0.66% and 1.8% respectively. Therefore, at 45 days, we estimate the likelihood of major, recoverable complications and replacement induced death to be

$$0.026 \times (1 - 0.044) = 0.0249 \tag{3.8}$$

and

$$0.026 \times 0.044 + (1 - 0.026) \times 0.0066 = 0.0076, \tag{3.9}$$

respectively. At 180 days, the former decreases to

$$0.026 \times (1 - 0.087) = 0.0237 \tag{3.10}$$

while the latter increases to

$$0.026 \times 0.087 + (1 - 0.026) \times 0.018 = 0.0198. \tag{3.11}$$

Intuitively, the probability of replacement induced death increases in the age of the patient, resulting in more risky, less favorable ICD generator replacement outcomes as the patient ages. Unfortunately, as pointed out by Krahn et al. (2011), there is a relative paucity of data when it comes to the complication rate and risk factors associated with ICD generator replacement, as opposed to initial ICD implantation. Therefore, in our experimental design we let $\alpha_\Delta(\ell)$ be constant in ℓ, i.e., $\alpha_\Delta(\ell) = \alpha_\Delta$. However, to account for the effects of various comorbidities, we let α_Δ assume values in a range wider than that obtained from the point estimates of α_Δ in equations (3.9) and (3.11). More specifically, we consider $\alpha_\Delta \in \{0.005, 0.01, 0.015, 0.02, 0.025\}$.

Capacity consumed per charge, δ_c. When shock therapy is demanded, the ICD battery charges the capacitor to a high energy level within a few seconds, after which the capacitor rapidly delivers the charge(s) as a shock(s) to the patient. The default therapy, i.e., full energy charge, in most ICDs is fixed at 30 Joules (Medtronic 2012a, Medtronic 2012b) and it is reasonable to assume that the amount of battery capacity consumed by a full energy charge is fixed. According to subject matter experts, the capacity consumed per charge is consistent across most ICDs at 0.008053 Ah, i.e.,

$$\delta_c = 0.008053 \text{ Ah}. \tag{3.12}$$

3.4.2 Parameters Estimated from Data

We use clinical data for estimating the remaining parameters. The dataset is provided by Medtronic, one of the world's largest medical device companies and developer of the nation's leading remote monitoring service for cardiac devices, Medtronic CareLink® Network. ICDs manufactured by Medtronic may use the CareLink® Network to securely transmit information about the patient and the device to clinicians for monitoring. The dataset includes 17,958 transmissions from 1,633 University of Pittsburgh Medical Center (UPMC) patients from September, 2004 to January, 2012. On average, the dataset includes approximately 11 transmissions per patient. Each transmission includes statistics on the therapies that the device has delivered, i.e., atrial and ventricular pacing percentages, cumulative and average capacitor charge times, as well as information about the device itself, i.e., the average amount of current drained from the battery per hour, or "average current drain." The capacity depletion due to initial programming that occurs shortly after implantation is included in the

Table 9: Average current drains and estimates of the capacity consumed per week in the absence of any charges after categorizing patients based on atrial and ventricular pacing percentages.

Ventricular pace	Atrial pace	Current drain(μA)	δ(Ah)
$\leq$70%	$\leq$70%	15.80	0.00265
	$>$ 70%	17.89	0.00301
$>$70%	$\leq$70%	27.63	0.00464
	$>$ 70%	33.66	0.00565

first transmission of each patient; to avoid any bias these records may introduce, we either remove them or account for their effect in other ways when appropriate as described below.

Capacity consumed per period in the absence of any charges, δ. An ICD continuously monitors/senses the patient's heart rhythm and usually also functions as a pacer to maintain a proper rhythm. The associated continuous battery depletion is a function of the patient's sensing and pacing currents. According to expert opinion, the sensing current drawn for monitoring the patient's rhythm is constant at approximately 10 micro amperes (μA) and the pacing current varies as a function of the percentage of time the patient is paced. Hence, to categorize patients into groups according to the rate at which their generators are depleted in the absence of any charges, we use a threshold of 70% in both atrial and ventricular percent pacing. We refer to a patient who is consistently paced more than 70% of the time in both the atrium and ventricle as "pacer-dependent." Table 9 reports the average current drains and the values of δ estimated from the dataset for the resulting four clinically meaningful patient categories. More specifically, the third column of Table 9 shows the average current drains obtained from the dataset based on the 70% thresholds in both atrial and ventricular percent pacing. Finally, using the average current drains in the third column, the last column of Table 9 reports the estimates for the capacity consumed per week (168 hours) in the absence of any charges, δ. The dataset used to obtain the values in Table 9 is cleansed of the first recorded transmission of each patient, resulting in 16,325 transmissions from 1,539 patients.

Distribution of charges per period, $p_D(d)$. In Section 3.2, we assume that the patient dies if a needed charge is not delivered. However, not all charges correspond to "appropriate" shocks that if not delivered, may cause the patient's death. That is, it is possible for ICDs to misinterpret cardiac/noncardiac events and deliver inappropriate therapies (Van Welsenes et al. 2011). Although delivering inappropriate shocks deplete the ICD battery, not delivering

them does not cause death. Unfortunately, due to a lack of data, we have no reliable way to differentiate between appropriate and inappropriate charges and hence assume that all charges in the dataset are appropriate.

Furthermore, some charges are due to "reformations." To maintain adequately quick charge times, the capacitor is periodically "reformed" by charging the capacitor to its maximum voltage and allowing the charge to dissipate without delivering a shock to the patient. Although capacitor reformations help preserve the low charge time by maintaining the capacitor, they also deplete the battery. For simplicity of the model, we do not explicitly model reformations; however, we implicitly consider their depletion effect by estimating the distribution of charges using the dataset, which includes all types of charges.

Estimating the weekly distribution of charges is not straightforward as the dataset does not include the weekly number of charges delivered. Using average and cumulative charge times, we first estimate the number of charges delivered between every pair of consecutive transmissions. Next, we calculate the expected number of weeks between every pair of consecutive transmissions, from which we may derive the weekly distribution of charges.

Let $n \in \mathbb{Z}_+$ denote the number of weeks between two consecutive transmissions from a device and $m \in \mathbb{Z}_+$ denote the number of charges delivered in that interval as reported in the dataset. To estimate the weekly distribution of charges, we assume that charges and weeks are indistinguishable and all m charges are equally likely to occur in any of the n weeks. Therefore, for any combination of m and n, we may estimate the expected number of weeks with exactly $i \in \mathbb{Z}_+$ charges. Let the random variable W_i denote the number of weeks in which $i \in \mathbb{Z}_+$ charges occur. Therefore, (Johnson and Kotz (1977), page 114)

$$\mathbb{E}[W_i] = \begin{cases} 1, & \text{if } n = 1 \text{ and } m = i, \\ n \cdot \binom{m}{i} \left(\frac{1}{n}\right)^i \left(1 - \frac{1}{n}\right)^{m-i}, & \text{otherwise.} \end{cases} \tag{3.13}$$

The total number of weeks with i charges is obtained by summing the expected values of the number of weeks with i charges, $\mathbb{E}[W_i]$s, across all transmissions. Finally, the weekly distribution of charges is obtained by normalizing the total number of weeks with i charges.

Before performing these calculations, we first cleanse the dataset of those transmissions with critical missing values and repeat transmissions. We consider repeat transmissions to be those transmissions that occurred shortly (less than half a week) after the previous transmission(s) and carry no information, i.e., transmissions with the value zero for both the

integer number of weeks, n, and the integer number of charges, m. If, however, a transmission occurs shortly after the previous one and does carry a piece of information, i.e., at least one charge occurs between the two transmissions, or $m > 0$, we do not consider the second transmission to be a repeat and set its n value to one. The dataset after cleansing includes 12,640 transmissions from 1,505 patients. Finally, Table 8 gives the estimated distribution of charges for all patients ("all"). For practical purposes, we truncate the distribution at 7 charges and re-normalize.

The best criterion for categorizing patients into classes with significantly different distributions of charges is their "indication of implantation," which is either primary or secondary prevention. Primary prevention corresponds to implanting the device to avoid the first-time occurrence of any life-threatening arrhythmia, whereas secondary prevention corresponds to implanting the device to prevent arrhythmias that have already occurred from happening again. Van Welsenes et al. (2011) show that patients who receive ICDs for secondary prevention have a substantially higher propensity for appropriate shocks in the long-run than patients who receive ICDs for primary prevention. Unfortunately, the indication of implantation is not included in our dataset. Instead, to somewhat imitate the effect of categorizing patients into two groups based on the indication of implantation, we categorize the patients in our dataset into two classes based on how their rate of demanding charges compares with the median rate of 0.039682 charges per week. As a result, 747 out of 1,505 patient are categorized as having a charge rate below the median. Table 8 displays the estimated distribution of charges for the two resulting classes of patients ("low" and "high"). Table 8 also displays the distribution of charges per week for all patients ("all") considered simultaneously. Note that, as seen in Table 8, the number of charges for patients in "high," "all" and "low" are stochastically ordered, with the number of charges per week for patients in "high" being the largest.

3.5 COMPUTATIONAL STUDY

In this section, we first compare the performance of the replacement policy currently recommended by manufacturers to that of the optimal policy obtained via equation (3.2). Secondly, we conduct sensitivity analysis on the estimated parameters to investigate their effect on the optimal replacement threshold.

3.5.1 Policy Comparison

Expected number of replacements. Before performing the policy comparisons, we first introduce an additional metric, namely the total expected number of replacements. To obtain the total expected number of replacements under a given policy, $N(\ell, u)$, a recursive approach is used. Under a given policy, let $a(\ell, u)$ be the action taken in state (ℓ, u) which is either to "replace" the generator or to "wait." As in Section 3.3, we let the former action be denoted by '1' and the latter by '0.' Hence,

$$N(\ell,u) = \begin{cases} 0, & \text{if } \ell \geq \bar{\ell} \text{ or } u \leq 0, \\ 1 + \lambda(\ell) \cdot N(\ell+1, \bar{u}) \cdot (1 - \alpha_\Delta(\ell)), & \text{if } a(\ell,u) = 1, \\ \sum_{d=0}^{g(u)} \lambda(\ell) \cdot N(\ell+1, u - \delta - d \cdot \delta_c) \cdot p_D(d), & \text{if } a(\ell,u) = 0. \end{cases} \tag{3.14}$$

Equation (3.14) follows from the fact that if $\ell \geq \bar{\ell}$ or $u \leq 0$, the problem terminates and the number of additional replacements is zero. Because replacements are assumed to take one period to complete, under the replacement action the expected number of additional replacements is equal to one plus the expected number of replacements starting from state $(\ell + 1, \bar{u})$ weighted by the probability of surviving to the next period. For any state (ℓ, u) in which the action taken is to wait, the expected number of additional replacements is equal to the weighted sum of the expected number of replacements starting from states $(\ell + 1, u - \delta - d \cdot \delta_c)$, $d = 0, 1, \ldots, g(u)$.

Benchmark policy. Throughout the remainder of the manuscript, we refer to the replacement policy currently advised by manufacturers as the benchmark policy. As discussed in Section 3.1, manufacturers recommend that ICDs be replaced when they reach RRT. Let the remaining battery capacity at RRT be denoted by $\tilde{u}$. Based on communication with a major manufacturer,

$$\tilde{u} = 0.13 \text{ Ah}. \tag{3.15}$$

Note that the value given by equation (3.15) is consistent with the value suggested by the data and the clinical manuals (Medtronic 2012c), as follows. Based on this literature, the amount of battery capacity that separates RRT and EOS is defined as three months of constant pacing and six full-energy charges. Let $\hat{\delta}$ denote the capacity consumed per week excluding any charges for a 100% pacer-dependent patient, our best estimate of which is

$\hat{\delta} = 0.00565$ Ah (Table 9). Also, from equation (3.12), $\delta_c = 0.008053$ Ah. Therefore, a data-driven estimate for $\tilde{u}$, is given by

$$\tilde{u} \;=\; \frac{52}{4} \cdot \hat{\delta} + 6 \cdot \delta_c = \frac{52}{4} \times 0.00565 + 6 \times 0.008053 = 0.121768 \text{ Ah}. \tag{3.16}$$

For our analysis, we use $\tilde{u} = 0.13$ Ah.

Let $a_{\tilde{u}}(\ell, u)$ denote the action advised under the benchmark policy for patient age ℓ and remaining battery capacity u, i.e.,

$$a_{\tilde{u}}(\ell, u) = \begin{cases} 0, & \text{if } u \geq \tilde{u}, \\ 1, & \text{otherwise} \end{cases} \tag{3.17}$$

and let the total expected reward under the benchmark policy starting from state (ℓ, u) be given by

$$V_{\tilde{u}}(\ell, u) \;=\; \begin{cases} C(\ell, u), & \text{if } a_{\tilde{u}}(\ell, u) = 0, \\ R(\ell), & \text{if } a_{\tilde{u}}(\ell, u) = 1. \end{cases} \tag{3.18}$$

Finally, let $N_{\tilde{u}}(\ell, u)$ denote the expected number of replacements under the benchmark policy starting from state (ℓ, u), obtained from (3.14) with $N_{\tilde{u}}(\ell, u) = N(\ell, u)$ and $a(\ell, u) = a_{\tilde{u}}(\ell, u)$.

Optimal policy. To solve for the optimal policy we execute the backward induction algorithm using equation (3.2) starting from state $(\bar{\ell}, 0)$ (see Puterman (1994), page 92). Recall that patient age, ℓ, is expressed in weekly increments. We discretize remaining battery capacity, u, using $\bar{\delta}$ in equation (3.5) for any given δ and obtain the expected number of replacements under the optimal policy, $N^*(\ell, u)$, using the recursive approach presented in (3.14). That is, $N^*(\ell, u)$ is obtained from (3.14) with $N^*(\ell, u) = N(\ell, u)$ and $a(\ell, u) = a^*(\ell, u)$.

Furthermore, to eliminate undesirable end of horizon effects involved in obtaining the optimal policy, we artificially extend the maximum patient life beyond that reported in the Centers for Disease Control and Prevention (CDC) tables and truncate appropriately as follows. First, note that the probability of surviving the competing risks of death for patients of ages 99 and 100, provided by Arias (2011), are 0.698775 and 1, respectively, hence resulting a maximum reachable age of $\bar{\ell} = 5200$ weeks (100 years). Unfortunately, these parameter settings induce noticeably irregular behavior of the optimal policy close to the end of the horizon that is difficult to implement. Letting the optimal policy when the maximum reachable age is $\bar{\ell}$ be denoted by $\pi^*(\bar{\ell})$, we extrapolate the patient survival curve from the

competing risks of death up to 120 years (6240 weeks), obtain $\pi^*(6240)$ and then truncate at 100 years of age (see Figure 8). Let $\pi^*(6240, 5200)$ denote the resulting truncated policy. Table 10 reports the total expected reward and the total expected number of replacements across all patients types for three age groups under policies $\pi^*(5200)$ and $\pi^*(6240, 5200)$, assuming a maximum reachable age of 100 for all patients. As seen in Table 10, the difference between the values obtained under these two policies is negligible; the maximum difference between the total reward across all patient categories is 0.0011 weeks. Therefore, $\pi^*(6240, 5200)$ essentially performs the same as the "optimal" policy. In the remainder of the chapter, we refer to $\pi^*(6240, 5200)$ as optimal and use the same approach to obtain and evaluate the benchmark policy up to 100 years of age.

Discussion. Next, we compare the results obtained under the optimal and benchmark policies for the computational study designed in Section 3.4. First, however, we illustrate the difference between the replacement thresholds under the optimal and benchmark policies for the example in Figure 6. Figure 8 displays the threshold under the optimal and benchmark policies. According to both policies, the ICD generator should be replaced once the battery capacity falls below a threshold. However, the value of the thresholds are significantly different between the two policies. Also, while the optimal replacement threshold becomes less conservative, i.e., advises "late" replacements, as the patient ages, the benchmark replacement threshold remains constant.

Table 11 reports the summary of results for patients who undergo initial implantation at age 30-40, 41-60, 61-80. Specifically, Table 11 reports the increase in the total expected lifetime and the (percentage) decrease in the expected number of replacements under the optimal policy versus the benchmark policy across all patient types for the three age groups. From this table, the total expected lifetime may be extended by up to 40.6 weeks (0.78 years) under the optimal policy. The expected number of replacements may decrease by up to 19%.

Finally, in the remainder of this section, we present more elaborate results for a few patient categories using two detailed tables and provide general observations regarding the patient categories that benefit the most from the optimal policy. Table 12 reports the total expected reward and the total expected number of replacements for the optimal policy when the patient age at the time of initial implantation, $\underline{\ell}$, is 50, 60 or 70 years and the initial battery capacity is 1.06 Ah. Table 12 also presents the differences between the total reward and the total expected number of replacements under the optimal and the benchmark policies. In this table, the rewards and number of replacements are given for all combinations

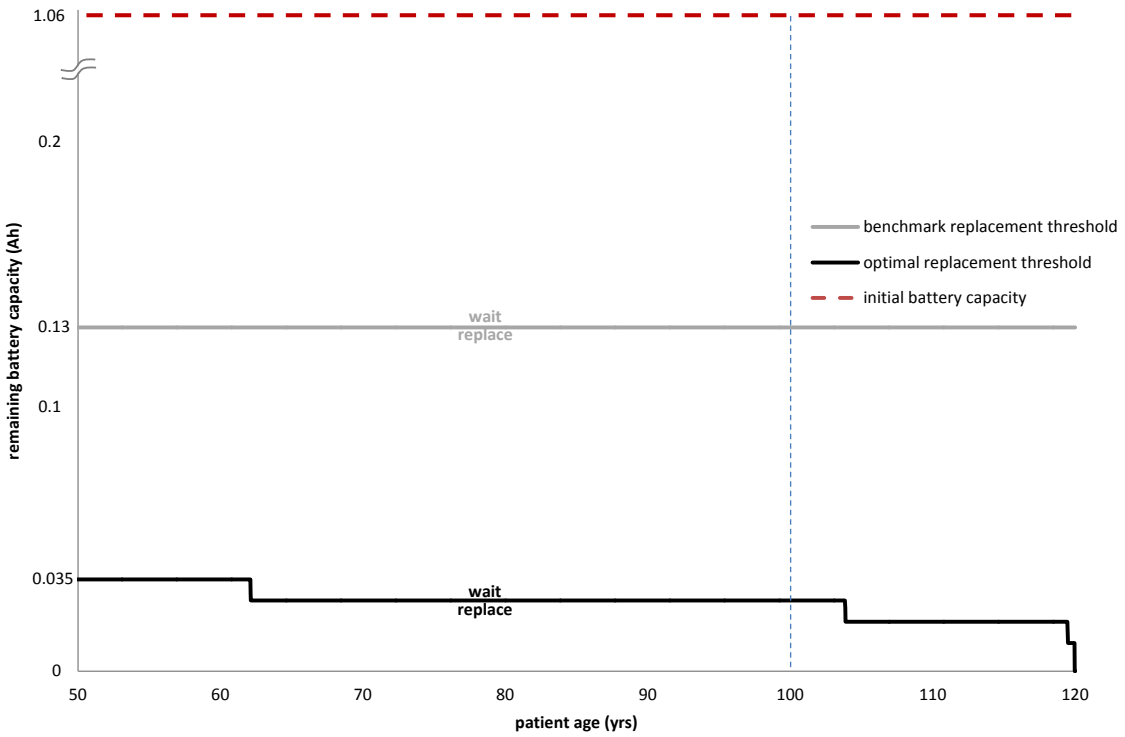


Figure 8: Optimal replacement policy versus benchmark policy for $\bar{u} = 1.06$ Ah, $\underline{\ell} = 2600$ weeks (50 years), $\alpha_\Delta = 0.02$, $\delta = 0.00265$ Ah, $\delta_c = 0.008053$ Ah and the distribution of charges given by Table 6.

Table 10: Comparison between the total reward and the total expected number of replacements across all patient types in the given age groups under $\pi^*(5200)$ and $\pi^*(6240, 5200)$.

Policies	Patient age at initial implantation	Difference in total reward (wks)			Difference in expected number of replacements		
		Min	Mean	Max	Min	Mean	Max
$\pi^*(5200)$ vs. $\pi^*(6240, 5200)$	30-40 years	0	3.3×10^{-5}	3.0×10^{-4}	0	2.2×10^{-4}	1.3×10^{-3}
	41-60 years	0	4.6×10^{-5}	4.8×10^{-4}	0	2.9×10^{-4}	2.5×10^{-3}
	61-80 years	0	8.7×10^{-5}	1.1×10^{-3}	0	5.5×10^{-4}	6.2×10^{-3}

Table 11: Results under the optimal policy versus benchmark policy across all patient types in the given age groups.

Optimal policy vs. current practice	Patient age at initial implantation					
	30-40 years		41-60 years		61-80 years	
	Min	Max	Min	Max	Min	Max
Increase in the total reward (wks)	1.8	40.6	0.7	25.6	0.1	9.6
Decrease in the expected number of replacements	0.36	1.58	0.23	1.25	0.10	0.76
Percentage decrease in the expected number of replacements	8%	14%	8%	15%	8%	19%

of pacer dependency levels, two levels ("low" and "high") of the distribution of charges and three levels of the probability of replacement induced death. Table 13 is similar to Table 12, except that the patient age at the time of initial implantation is fixed at 60 years and the initial battery capacity, $\bar{u}$, assumes values in $\{0.91, 0.96, 1.01, 1.06, 1.11, 1.16\}$.

Consider a patient (corresponding to the row in bold type in Table 12) who first undergoes ICD implantation at the age of 60 and receives a device with an initial battery capacity of 1.06 Ah. Suppose this patient is paced less than or equal to 70% in the ventricle, but more than 70% in the atrium and demands charges below the median rate. Also, let the probability of replacement induced death for this patient assume its smallest value, i.e., 0.005. As shown in Table 12, under the optimal policy this patient lives on average 990.1 weeks (19.04 years) and requires 2.65 generator replacements. Following the optimal policy, as opposed to the benchmark policy, increases the patient's expected remaining lifetime by 1.2 weeks. Although this increase in the expected remaining lifetime may seem modest, under the optimal policy the expected number of replacements decreases by 0.37 replacements, or 12%. The significance of this observation lies in the fact that the decrease in the number of replacements, and consequently their associated cost, is achieved without compromising clinical outcomes.

The significant decrease in the expected number of replacements is consistent across the experimental design. From Table 12, for patients who first undergo ICD implantation at ages 50, 60 or 70 and receive devices with an initial battery capacity of 1.06 Ah, the expected

Table 12: The optimal and benchmark policy comparison when the patient age at the time of initial implantation is 50, 60 or 70 years (equivalent to 2600, 3120 and 3640 weeks, respectively) and the initial battery capacity is 1.06 Ah. For "low" and "high" distributions refer to Table 8. V-pace and A-pace represent the ventricular pace and atrial pace, respectively.

Pacer dependency	Distribution of charges, $p_D(d)$	Probability of replacement induced death, α_Δ	Optimal reward (wks), $V(\underline{\ell}, 1.06)$			Increase in the total reward (wks)			Expected number of replacements under the optimal policy, $N^*(\underline{\ell}, 1.06)$			Decrease in the expected number of replacements			Percentage decrease in the expected number of replacements		
			$\underline{\ell}=2600$	$\underline{\ell}=3120$	$\underline{\ell}=3640$	$\underline{\ell}=2600$	$\underline{\ell}=3120$	$\underline{\ell}=3640$	$\underline{\ell}=2600$	$\underline{\ell}=3120$	$\underline{\ell}=3640$	$\underline{\ell}=2600$	$\underline{\ell}=3120$	$\underline{\ell}=3640$	$\underline{\ell}=2600$	$\underline{\ell}=3120$	$\underline{\ell}=3640$
V-pace and A-pace are both ≤ 70%; δ = 0.00265 Ah	low	0.005	1295.4	991.3	689.2	1.8	1.0	0.5	3.15	2.29	1.46	0.43	0.33	0.22	12%	13%	13%
		0.015	1271.8	978.2	683.5	5.1	3.1	1.5	3.1	2.26	1.44	0.41	0.33	0.22	12%	13%	13%
		0.025	1248.8	965.4	677.8	8.5	5.1	2.6	3.02	2.22	1.42	0.42	0.33	0.22	12%	13%	14%
	high	0.005	1294.1	990.4	688.8	1.4	0.8	0.4	3.46	2.54	1.62	0.37	0.27	0.2	10%	10%	11%
		0.015	1268.0	975.9	682.3	4.3	2.6	1.3	3.36	2.48	1.59	0.38	0.29	0.21	10%	10%	12%
		0.025	1242.7	961.8	676.0	7.3	4.4	2.2	3.3	2.45	1.57	0.36	0.28	0.21	10%	10%	12%
V-pace ≤ 70%, but A-pace > 70%; δ = 0.00301 Ah	low	0.005	**1293.5**	**990.1**	**688.6**	**2.0**	**1.2**	**0.6**	**3.61**	**2.65**	**1.69**	**0.48**	**0.37**	**0.26**	**12%**	**12%**	**13%**
		0.015	1266.2	974.9	681.8	5.8	3.4	1.7	3.54	2.61	1.67	0.46	0.36	0.26	12%	12%	14%
		0.025	1239.8	960.0	675.1	9.5	5.7	2.9	3.44	2.55	1.65	0.47	0.37	0.27	12%	13%	14%
	high	0.005	1292.1	989.3	688.2	1.6	0.9	0.5	3.93	2.9	1.87	0.4	0.3	0.21	9%	10%	10%
		0.015	1262.3	972.6	680.7	4.8	2.9	1.5	3.81	2.83	1.84	0.42	0.32	0.22	10%	10%	11%
		0.025	1233.6	956.3	673.2	8.1	4.9	2.5	3.73	2.78	1.82	0.4	0.31	0.22	10%	10%	11%
V-pace > 70%, but A-pace ≤ 70%; δ = 0.00464 Ah	low	0.005	1285.4	985.3	686.3	2.9	1.7	0.9	5.55	4.14	2.74	0.69	0.53	0.37	11%	11%	12%
		0.015	1242.9	961.0	674.8	8.3	5.0	2.5	5.34	4.01	2.68	0.69	0.54	0.38	11%	12%	13%
		0.025	1202.5	937.5	663.7	13.5	8.2	4.2	5.17	3.92	2.64	0.64	0.51	0.37	11%	12%	12%
	high	0.005	1283.8	984.4	685.8	2.3	1.4	0.7	5.92	4.43	2.93	0.58	0.44	0.31	9%	9%	10%
		0.015	1238.6	958.4	673.5	6.9	4.2	2.1	5.67	4.28	2.86	0.58	0.45	0.33	9%	10%	10%
		0.025	1195.7	933.4	661.6	11.2	6.9	3.6	5.45	4.14	2.79	0.57	0.46	0.34	9%	10%	11%
V-pace and A-pace are both > 70%; δ = 0.00565 Ah	low	0.005	1280.2	982.2	684.7	3.4	2.0	1.0	6.8	5.1	3.41	0.82	0.64	0.44	11%	11%	12%
		0.015	1228.1	952.1	670.3	9.8	5.9	3.0	6.48	4.91	3.31	0.8	0.64	0.45	11%	11%	12%
		0.025	1179.2	923.4	656.5	15.7	9.6	5.0	6.23	4.77	3.25	0.73	0.6	0.43	11%	11%	12%
	high	0.005	1278.5	981.2	684.2	2.7	1.6	0.8	7.19	5.4	3.62	0.67	0.51	0.36	9%	9%	9%
		0.015	1223.6	949.4	669.0	8.1	4.9	2.5	6.84	5.19	3.52	0.66	0.52	0.38	9%	9%	10%
		0.025	1172.3	919.1	654.3	13.1	8.1	4.2	6.51	5	3.42	0.66	0.53	0.39	9%	10%	10%

Table 13: The optimal and benchmark policy comparison when the initial battery capacity, $\bar{u}$, assumes values in $\{0.91, 0.96, 1.01, 1.06, 1.11, 1.16\}$ and the patient age at the time of initial implantation is 60 years (3120 weeks). For "low" and "high" distributions refer to Table 8. V-pace and A-pace represent the ventricular pace and atrial pace, respectively.

Pacer dependency	Distribution of charges, $p_D(d)$	Probability of replacement induced death, α_λ	Optimal reward (wks), $V(3120, \bar{u})$			Increase in the total reward (wks)			Expected number of replacements under the optimal policy, $N^*(3120, \bar{u})$			Decrease in the expected number of replacements			Percentage decrease in the expected number of replacements		
			Min	Mean	Max	Min	Mean	Max	Min	Mean	Max	Min	Mean	Max	Min	Mean	Max
V-pace and A-pace are both ≤ 70%; δ = 0.00265 Ah	low	0.005	989.8	990.9	992.0	0.9	1.1	1.4	2.07	2.39	2.76	0.26	0.35	0.45	11%	13%	14%
		0.015	973.8	977.3	980.3	2.5	3.3	4.2	2.05	2.36	2.71	0.26	0.35	0.45	11%	13%	14%
		0.025	958.3	963.9	968.8	4.2	5.5	7.0	2.02	2.31	2.65	0.27	0.35	0.45	12%	13%	15%
	high	0.005	988.8	990.1	991.2	0.7	0.9	1.2	2.28	2.64	3.06	0.24	0.3	0.39	9%	10%	11%
		0.015	971.0	974.9	978.3	2.1	2.8	3.6	2.24	2.58	2.98	0.24	0.32	0.41	10%	11%	12%
		0.025	953.9	960.2	965.6	3.6	4.7	6.1	2.21	2.55	2.93	0.24	0.31	0.4	10%	11%	12%
V-pace ≤ 70%, but A-pace > 70%; δ = 0.00301 Ah	low	0.005	988.5	989.9	991.0	1.0	1.3	1.6	2.36	2.73	3.16	0.3	0.39	0.5	11%	12%	14%
		0.015	970.1	974.1	977.5	2.8	3.7	4.7	2.33	2.69	3.1	0.3	0.39	0.49	11%	12%	14%
		0.025	952.3	958.7	964.3	4.7	6.1	7.9	2.29	2.63	3.03	0.31	0.39	0.5	12%	13%	14%
	high	0.005	987.5	989.0	990.3	0.8	1.0	1.3	2.59	3	3.47	0.25	0.33	0.43	9%	10%	11%
		0.015	967.3	971.7	975.4	2.4	3.1	4.0	2.54	2.92	3.37	0.26	0.35	0.45	9%	11%	12%
		0.025	947.7	954.8	961.0	4.0	5.2	6.7	2.5	2.87	3.3	0.26	0.34	0.43	9%	10%	12%
V-pace > 70%, but A-pace ≤ 70%; δ = 0.00464 Ah	low	0.005	982.8	984.8	986.6	1.4	1.8	2.4	3.74	4.3	4.94	0.44	0.57	0.74	10%	12%	13%
		0.015	953.6	959.5	964.6	4.1	5.4	6.9	3.64	4.16	4.76	0.45	0.58	0.74	11%	12%	13%
		0.025	925.8	935.2	943.4	6.8	8.8	11.2	3.56	4.06	4.63	0.42	0.55	0.69	11%	12%	13%
	high	0.005	981.6	983.8	985.8	1.1	1.5	1.9	4	4.6	5.29	0.36	0.47	0.61	8%	9%	10%
		0.015	950.4	956.8	962.3	3.4	4.5	5.8	3.88	4.44	5.08	0.37	0.49	0.62	9%	10%	11%
		0.025	920.8	930.9	939.7	5.6	7.4	9.6	3.78	4.29	4.88	0.37	0.49	0.63	9%	10%	11%
V-pace and A-pace are both > 70%; δ = 0.00565 Ah	low	0.005	979.3	981.7	983.8	1.7	2.2	2.8	4.62	5.27	6.02	0.52	0.68	0.87	10%	11%	13%
		0.015	943.7	950.6	956.5	4.9	6.4	8.1	4.47	5.07	5.75	0.53	0.67	0.85	11%	12%	13%
		0.025	910.1	920.9	930.4	8.0	10.3	13.0	4.35	4.92	5.56	0.5	0.63	0.79	10%	11%	12%
	high	0.005	978.0	980.6	982.9	1.3	1.7	2.2	4.89	5.59	6.39	0.43	0.56	0.72	8%	9%	10%
		0.015	940.4	947.7	954.1	4.1	5.3	6.8	4.72	5.36	6.09	0.44	0.57	0.72	8%	9%	11%
		0.025	905.0	916.5	926.6	6.7	8.7	11.1	4.55	5.14	5.82	0.45	0.57	0.72	9%	10%	11%

number of replacements decreases by 9% to 14% under the optimal policy. This range is nearly consistent across all initial capacities. From Table 12, for a patient who first receives a device with an initial battery capacity of 1.06 Ah at age 60 (corresponding to the column in bold type), the expected number of replacements decreases by 9% to 13% under the optimal policy. As seen in Table 13, which reports the results for patients who first undergo ICD implantation at the age of 60, this range only slightly widens to 8% to 15% when the initial battery capacity assumes a wide range of values from 0.91 to 1.16 Ah.

Obviously, while all patients benefit from implementing the optimal generator replacement policy, some categories of patients see more dramatic impacts than others. For instance (Table 12), for a given set of characteristics, the younger the patient at implementation, the longer the lifetime extension under the optimal policy. Also, the less prone to demanding charges or the more likely to die as a result of replacement surgery, the greater the lifetime extension under the optimal policy; this observation is mainly due to the fact that the benchmark policy is excessively conservative for such patients. As shown in Table 11, some patients' expected lifetimes may be extended by up to 40.6 weeks (0.78 years) under the optimal policy. Specifically, this maximum is achieved for those patients who undergo initial implantation at age 30, receive ICD generators with an initial battery capacity of 0.91 Ah, are paced more than 70% in both atrium and ventricle, demand charges below the median rate and carry the highest surgical risks. Also, as shown in Table 11, some patients may avoid as many as 1.6 replacement surgeries in expectation by following the optimal policy. These patients have the same characteristics as those for which the maximum lifetime extension is achieved, except for the fact that they carry the lowest surgical risks rather than the highest. Generally, the expected lifetime extension (the expected number of avoided surgeries) is more pronounced in younger patients who receive generators with smaller initial battery capacities, are more pacer dependent, demand fewer charges and are prone to high (respectively, low) surgical risks. Finally, as shown in Table 11, under the optimal policy, the decrease in the expected number of replacements in between 8% and 19% across all patient types. Generally, patients who undergo initial implantation at younger ages experience a larger reduction in the expected number of replacement surgeries than older patients; however, the percentage decrease in the expected number of replacements is greater for those patients who undergo initial implantation at older ages. For example, the patients with the highest percentage decrease in the expected number of replacements, i.e., 19%, are those who undergo initial implantation at age 80, receive ICD generators with an initial battery

Table 14: The parameter settings for Figures 9a-9c. For "low" distribution refer to Table 8.

Figure	Parameter	$\bar{u}$ (Ah)	$\underline{\ell}$ (wks)	$\bar{\ell}$ (wks)	δ	δ_c	α_Δ	$p_D(d)$
9a	α_Δ	1.16	1560 (30 yrs)	5200 (100 yrs)	0.00301	0.008053	-	low
9b	$p_D(d)$	1.16	1560 (30 yrs)	5200 (100 yrs)	0.00301	0.008053	0.01	-
9c	δ	1.16	1560 (30 yrs)	5200 (100 yrs)	-	0.008053	0.01	low

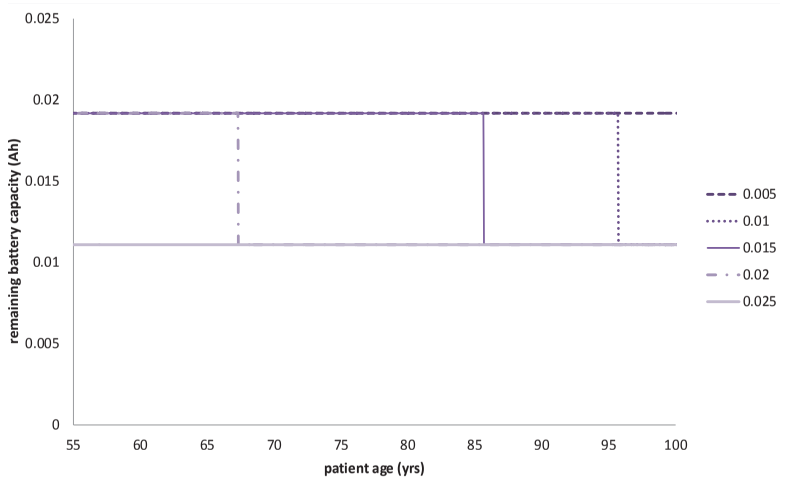
capacity of 1.06 Ah, are paced less than 70% in both atrium and ventricle, demand charges below the median rate and carry the average surgical risk of 0.015.

The results suggest that patients who demand fewer charges (i.e., receive the device for primary prevention) consistently benefit more from following the optimal policy. This observation is particularly promising because these patients constitute 50%-80% of new ICD patients every year (Proclemer et al. 2009), because clinical trials have shown that these patients benefit the most from receiving ICDs, and because the prevalence of this type of patient is expected to rise in years to come (Seidl and Senges 2003).

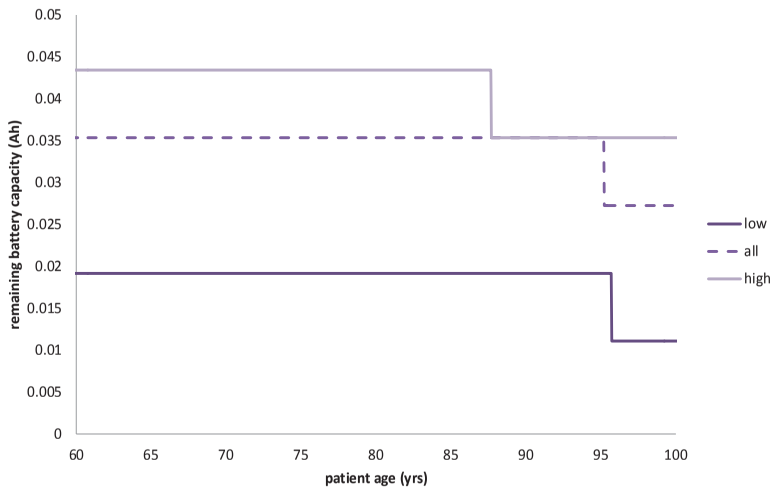
3.5.2 Sensitivity Analysis

In this section, we investigate the effects of changes in the estimated parameters on the optimal policy, the total expected reward and the total expected number of replacements under the optimal policy.

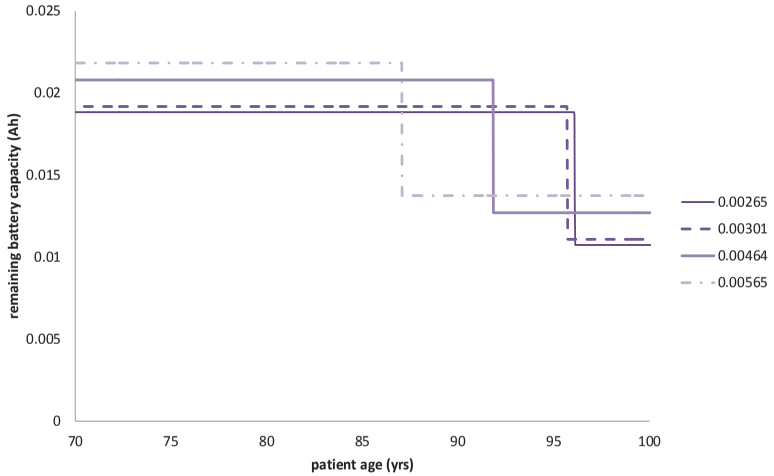
Probability of replacement induced death, α_Δ. Figure 9a portrays the optimal policy for five problem instances stratified across the probability of replacement induced death, α_Δ, with the other parameter settings as given in Table 14. In these example policies, given any fixed patient age ℓ and remaining battery capacity u, if it is optimal to replace the generator for any given probability of replacement induced death, it is also optimal to replace the generator when replacements are less risky, i.e., when the probability of replacement induced death is smaller. Table 15 lists the total expected reward and the total expected number of replacements obtained under the optimal replacement thresholds in Figure 9a. Consistent with Lemma 3, the optimal reward decreases as the likelihood of replacement induced death increases.



(a) replacement induced death



(b) weekly distribution of charges



(c) capacity consumed per period in the absence of any charges

Figure 9: The optimal replacement thresholds for patient categories stratified across (a) α_Δ, (b) $p_D(d)$ and (c) δ. The parameter settings are given by Table 14. None of the thresholds change below the minimum age reported.

Table 15: The optimal total reward and the optimal expected number of replacements across different α_Δ values where $\bar{u} = 1.16$ Ah, $\underline{\ell} = 1560$ weeks (30 years), $\delta = 0.00301$ Ah, $\delta_c = 0.008053$ Ah and the patient's rate of demanding charges is below the median rate (see Table 8).

Probability of replacement induced death, α_Δ	Optimal reward (wks), $V(1560, 1.16)$	Expected number of replacements under the optimal policy, $N^*(1560, 1.16)$
0.005	1867.8	4.89
0.01	1840.3	4.82
0.015	1813.2	4.75
0.02	1786.7	4.68
0.025	1760.9	4.59

Table 16: The optimal total reward and the optimal expected number of replacements across different distributions of charges per period, $p_D(d)$, where $\bar{u} = 1.16$ Ah, $\underline{\ell} = 1560$ weeks (30 years), $\delta = 0.00301$, $\delta_c = 0.008053$ Ah and $\alpha_\Delta = 0.01$. For "low," "all" and "high" distributions refer to Table 8.

Distribution of charges, $p_D(d)$	Optimal reward (wks), $V(1560, 1.16)$	Expected number of replacements under the optimal policy, $N^*(1560, 1.16)$
low	1840.3	4.82
all	1837.1	5.04
high	1835.1	5.22

Table 17: The optimal total reward and the optimal expected number of replacements across different types of pacer dependencies (δ values) where $\bar{u} = 1.16$ Ah, $\underline{\ell} = 1560$ weeks (30 years), $\delta_c = 0.008053$ Ah, $\alpha_\Delta = 0.01$ and the patient's rate of demanding charges is below the median rate (see Table 8).

Pacer dependency	Optimal reward (wks), $V(1560, 1.16)$	Expected number of replacements under the optimal policy, $N^*(1560, 1.16)$
V-pace and A-pace are both ≤ 70%; δ = 0.00265 Ah	1846.9	4.28
V-pace ≤ 70%, but A-pace > 70%; δ = 0.00301 Ah	1840.3	4.82
V-pace > 70%, but A-pace ≤ 70%; δ = 0.00464 Ah	1809.7	7.30
V-pace and A-pace are both > 70%; δ = 0.00565 Ah	1790.5	8.83

Distribution of charges per period, $p_D(d)$. Figure 9b portrays the optimal policy for three problem instances stratified across the distribution of charges per period, $p_D(d)$, with the other parameter settings as given in Table 14. Figure 9b illustrates that optimal replacement threshold becomes more conservative as the number of charges per period stochastically increases. In other words, for any fixed patient age ℓ and remaining battery capacity u, if it is optimal to replace the generator for a given distribution of charges $p_D(d)$, it is also optimal to replace the generator when the number of charges is stochastically larger. Also, similar to the results demonstrated for α_Δ, Table 16 reports a decrease in the optimal reward as the number of charges stochastically increases, which is consistent with Lemma 4.

Capacity consumed per period in the absence of any charges, δ. Figure 9c portrays the optimal policy for four problem instances stratified across the capacity consumed per period in the absence of any charges, δ, with the other parameter settings as given in Table 14. Figure 9c illustrates that, in general, the thresholds for more pacer-dependent patients are more conservative. However, in contrast to Figures 9a-9b, Figure 9c demonstrates that the relationship between the optimal replacement thresholds is not necessarily monotonic in the capacity consumption rate. That is, although it might be optimal to replace the genera-

tor given a certain rate of capacity consumption in the absence of charges for a fixed patient age and remaining battery capacity, it is not necessarily optimal to do so under a higher consumption rate, and vice versa. This property is mainly due to end of horizon effects.

Finally, Table 17 reports the total reward under the optimal replacement thresholds in Figure 9c. In this table, consistent with Lemma 5, the total reward decreases as the capacity consumption rate in the absence of charges increases. Table 17 also reports the expected number of replacements under the optimal policies in Figure 9c. From Table 17, under the optimal policy, the most pacer-dependent patient with V-pace and A-pace both $> 70\%$ ($\delta = 0.00565$) on average requires almost twice as many generator replacement surgeries as the least pacer-dependent patient with V-pace and A-pace both $\leq 70\%$ ($\delta = 0.00265$). Therefore, the capacity consumed per period in the absence of any charges, δ, is one of the most important factors in the decision making process, and consequently, the expected number of generator replacements that a patient requires.

3.6 CONCLUSION

In this chapter, we consider the important problem of timing ICD generator replacements to optimally balance the trade-off between prematurely exposing the patient to the risks of replacement and allowing for the possibility that the device is unable to deliver therapy when needed. In current practice, replacements are performed rather conservatively and are not tailored to individuals based on their personal characteristics. The MDP model analyzed here, however, determines patient-specific optimal replacement policies under the objective of maximizing the patient's expected lifetime.

That is, in contrast to the current one-size-fits-all replacement policy, which is a function of remaining battery capacity only, we obtain patient-specific optimal replacement thresholds, which are functions of the remaining battery capacity, patient age and other factors, e.g., pacer dependency and propensity for shocks. Based on clinical data, we conduct a large scale computational study to compare total expected lifetime and total expected number of replacements under the optimal policy and current practice. For every patient category, we obtain a threshold-type policy that is easy to implement; the policy is of threshold-type in the remaining battery capacity typically with one or two replacement thresholds in

patient age. Our results suggest that following the optimal policy decreases the expected number of replacements while achieving the same or greater expected lifetime. Across all patient types, the expected number of replacements (and consequently their associated cost of approximately $24,000 each) decreases by a minimum of 8% under the optimal policy. Also (Table 11), for patients with certain characteristics, following the optimal policy can be of significant benefit, e.g., the expected lifetime (the expected number of replacement surgeries) may be extended by 40.6 weeks (decreased by 19%) under the optimal policy.

4.0 OPTIMAL PLANNING OF LIFE-DEPLETING MAINTENANCE ACTIVITIES

4.1 INTRODUCTION

Consider a system with a known, deterministic initial lifetime $L < \infty$ that generates reward at a decreasing, average rate of $r(t) > 0$, where t is the virtual age (as defined by Kijima et al. (1988)) of the system. Preventive maintenance (PM) may be performed to adjust the system's virtual age back to zero (i.e., "perfect" maintenance), but at some "cost." We consider the case in which this PM cost corresponds to a reduction in the system's remaining lifetime.

Initially, in Section 4.2, we consider the deterministic case in which the system is not prone to failures. In this case, we assume a fixed PM interval $\tau > 0$ is used throughout the system's lifetime. That is, given an initial virtual age of 0, maintenance is performed periodically at time $\tau, 2\tau, 3\tau, \ldots, n\tau$, until the remaining system life does not allow for any additional maintenance, i.e., $L - n\big(\tau + f(\tau)\big) < \tau + f(\tau)$, where $f(\tau) > 0$ is the amount by which PM depletes the system lifetime. The objective is to select τ such that the total reward earned over the lifetime of the system is maximized, where the reward earned over a period of length τ, starting from a virtual age of t, is given by $R(t, \tau) = \int_t^{t+\tau} r(u)\,\mathrm{d}u$. In Section 4.3, we consider failure-prone systems subject to either perfect or imperfect maintenance, upon which the system's virtual age is set back to either zero or some non-negative value, respectively. The resulting stochastic dynamic program models incorporate lifetime-depleting preventive and reactive maintenance to adaptively determine when PM should be performed.

This problem setting is motivated in part by the practice of remotely monitoring battery-powered devices that are difficult to service and/or impossible to recharge, e.g., implanted medical devices (Darce July, 2010, Yekeh Yazdandoost and Kohno 2009) or sensors (Akyildiz et al. 2002). Such devices periodically transmit information about their condition and

performance to a remote data center. Hence, an interesting trade-off exists between battery longevity and transmission frequency. That is, more frequent transmissions result in a shorter battery life, but more timely data.

For example, consider an implanted cardiac device, e.g., a pacemaker or cardiac defibrillator. The lithium iodine batteries used in these devices exhibit stable voltage, resulting in predictable initial useful lifetimes (Mallela et al. 2004) given a set of patient characteristics. Data logging, however, can constitute a serious drain on battery life (Mallela et al. 2004). On the other hand, the more frequently the device remotely transmits data to clinicians, the more "protection" it provides for the patient. In this context, transmissions correspond to "maintenance actions" as they allow for device/patient inspections and possible adjustments. Some advanced systems transmit data daily; however, for other systems, daily transmission has a high impact on battery longevity, and hence weekly or bi-weekly intervals are typically used (Jung et al. 2008). Similarly, "failures" correspond to "adverse events" experienced by the patient due to device malfunction or a change in health condition (e.g., syncope, inappropriate shock).

Wireless sensor networks serve as another motivating application. One of the main constraints in these networks is the limited, typically irreplaceable power sources of the sensors (Akyildiz et al. 2002). Hence, a trade-off exists between achieving high quality service of the network and conserving power to prolong the lifetime of the network. Again, "maintenance actions" correspond to data transmissions. The more frequent the data transmissions, the more timely the decisions can be made; hence, the "reward rate" decreases in the time since the last transmission. In this context, "failures" correspond to sudden changes in the system (e.g., fatigue cracking in a building or an airframe) being monitored by the sensors.

Admittedly, in both contexts, the approach taken herein is myopic in that it does not consider the cost of device replacement, but rather maximizes the reward generated by the device currently in operation. Although beyond the scope of this work, the generalization could be handled by assigning a cost to replacement and taking a renewal reward approach. Such an approach would seek the transmission interval that maximizes the ratio of the total reward generated by the current device (less the replacement cost) to the replacement time induced by the transmission interval selected.

The majority of the existing maintenance optimization literature considers infinite horizon formulations and models the cost of performing maintenance as either a literal, economic cost or as downtime during which the system does not age, or both. In contrast, we model

the "cost" of performing PM as a depletion of the remaining, finite system lifetime, which can be equivalently viewed as a finite horizon formulation with non-instantaneous PM – a combination examined by relatively few (Dedopoulos and Smeers 1998, Jayabalan and Chaudhuri 1992, Singh et al.).

Singh et al. consider a finite horizon maintenance and production planning problem for a non-failure-prone system, but make decisions based on machine condition, which deteriorates according to a discrete time Markov chain, as opposed to (continuous) virtual age. The objective is to maximize total expected profit while meeting a known demand, subject to machine-condition-dependent production yield (analogous to our age-dependent reward rate). In contrast to the models considered here, however, the duration of each maintenance activity is assumed to take exactly one period regardless of the amount of time that has elapsed since the last maintenance activity was performed.

Dedopoulos and Smeers (1998) and Jayabalan and Chaudhuri (1992) both consider cost minimizing, non-instantaneous PM planning problems for failure-prone systems over finite horizons. In these models, however, reactive maintenance is assumed to be instantaneous and corresponds to a minimal repair (i.e., no change in virtual age), in which case all decisions can be made *a priori*. In contrast, the models in Section 4.3 consider reactive maintenance that depletes the system's remaining lifetime and alters the virtual age to either zero (in Section 4.3.1) or possibly a non-negative value (in Section 4.3.2), in which case decisions must be made adaptively.

Although our main contribution is the consideration of life-depleting (or time consuming) PM in a finite horizon setting, the literature that examines instantaneous PM planning as a function of virtual age over a finite horizon is also relevant. Chun (1992) and Nakagawa and Mizutani (2009), for example, determine the optimal number of periodic PMs for a failure prone system over a finite warranty period. They require that every time interval, including the interval following the last PM prior to the warranty's expiration, be of equal length. Jack and Dagpunar (1994) consider the same problem, but relax this requirement (as do we). Dagpunar and Jack (1994) generalize further by allowing the amount by which each PM reduces the virtual age to be a decision variable. Boland (1982), Boland and Proschan (1982), and Popova et al. (2010) consider the same finite-horizon, periodic maintenance planning problem as Jack and Dagpunar (1994) do, but with renewing PMs and different cost structures. Moghaddam and Usher (2010) consider a similar problem as Nakagawa and Mizutani (2009) do, but with periodic decisions as to whether to perform an imperfect PM,

perfect PM (replacement) or nothing. Lastly, Yeh et al. (2009), who consider a problem similar to Chun (1992), claim that the cost of PM includes downtime cost, however the dynamics of their model assume that PM is instantaneous.

We make the following assumptions throughout the remainder of the chapter:
A1: For $t \in [0, L]$, $r(t) > 0$ is differentiable and strictly decreasing, i.e., $r'(t) < 0$.
A2: For $\tau \in [0, L]$, $f(\tau) > 0$ is twice differentiable, nondecreasing, and convex, i.e., $f'(\tau) \geq 0$, $f''(\tau) \geq 0$. Additionally, let $f'(0) = 0$.
A3: $L > f(0)$.

The intuition behind **A1** follows from the fact that the greater the virtual age, the poorer the performance of the device and therefore the smaller the reward rate. In terms of **A2**, nondecreasing $f(\tau)$ reflects the fact that the longer the maintenance interval, the greater the burden of decreasing the virtual age. Additionally, because the greater the maintenance interval the more data there are to transmit, a convex $f(\tau)$ reflects the fact that the energy required to transmit data is typically convex in the data quantity; we also assume that the rate of increase is initially zero (Sengul et al. 2008). Assumption **A3** ensures that a non-trivial solution exists.

The remainder of the chapter is organized as follows. In Section 4.2, we consider the case in which the system is not subject to failure and preventive maintenance is perfect, i.e., the system's virtual age is renewed after each PM. Section 4.3 generalizes to the case in which the system is subject to random failures, which are both economically costly and lifetime-depleting, and maintenance activities may be imperfect. Lastly, we conclude in Section 4.4. All proofs are included in Appendix B.2.

4.2 PERFECT MAINTENANCE FOR FAILURE-FREE SYSTEMS

In this section, we assume that PM resets the virtual age of the system to zero. For a given feasible maintenance interval, τ, i.e., an interval that satisfies

$$\tau \leq L - f(\tau), \tag{4.1}$$

the total number of PMs performed, $n(\tau)$, is given by

$$n(\tau) = \begin{cases} \frac{L}{\tau + f(\tau)} - 1, & \text{if } \frac{L}{\tau + f(\tau)} \in \mathbb{Z}_+, \\ \left\lfloor \frac{L}{\tau + f(\tau)} \right\rfloor, & \text{otherwise.} \end{cases} \tag{4.2}$$

Hence, the remaining lifetime after the last PM is equal to $L - n(\tau) \cdot (\tau + f(\tau))$. Equation (4.2) assumes that for any given τ, we perform the maximum number of PMs possible unless the final PM would result in a remaining lifetime of zero. For example, if $L = 100, \tau = 3$ and $f(3) = 2$, then only 19 PMs are performed. Furthermore, from equation (4.2), $n(0)$ is the maximum number of PMs possible, which we denote by

$$n_{max} \equiv n(0). \tag{4.3}$$

Figure 10 illustrates the problem dynamics for the perfect maintenance case. Initially, as illustrated in Figure 10a, both the actual age and the virtual age of the system is zero, the reward rate is $r(0)$, and the remaining lifetime is L. By assumption **A1**, as time passes, the reward rate decreases. At time τ, the first perfect PM is performed which resets the virtual age of the system back to zero. However, this PM also depletes the remaining lifetime by $f(\tau)$. Therefore, after the first PM, the remaining lifetime is $L - 1 \cdot (\tau + f(\tau))$. The total reward obtained between time zero and time τ is $R(0, \tau)$. The PMs are performed periodically at times $2\tau, 3\tau, \ldots, n(\tau)$, when the remaining lifetime is such that another PM is not possible. Hence, as shown in Figure 10b, the last interval is of size $L - n(\tau) \cdot (\tau + f(\tau))$, in which the reward $R(0, L - n(\tau) \cdot (\tau + f(\tau)))$ is earned.

The overall goal is to maximize the total reward earned over the system's lifetime. This objective can be expressed as

$$\max_{\tau > 0} \left\{ n(\tau) R(0, \tau) + R(0, L - n(\tau) \cdot (\tau + f(\tau))) \right\}, \tag{4.4}$$

which is discontinuous and neither concave nor convex. Note that by (4.2), any feasible $n \in \mathbb{Z}_+$ must satisfy

$$0 \leq n \leq n_{max}. \tag{4.5}$$

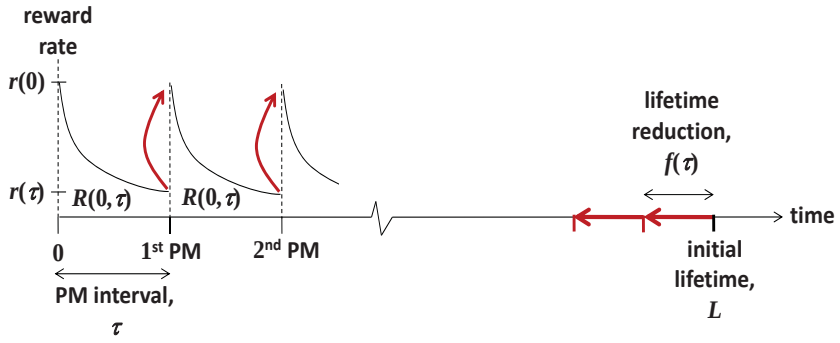
Furthermore, given a feasible non-zero $n \in \mathbb{Z}_+$, the corresponding maintenance interval, $\tau > 0$, must satisfy

$$\frac{L}{n+1} - f(\tau) \leq \tau < \frac{L}{n} - f(\tau). \tag{4.6}$$

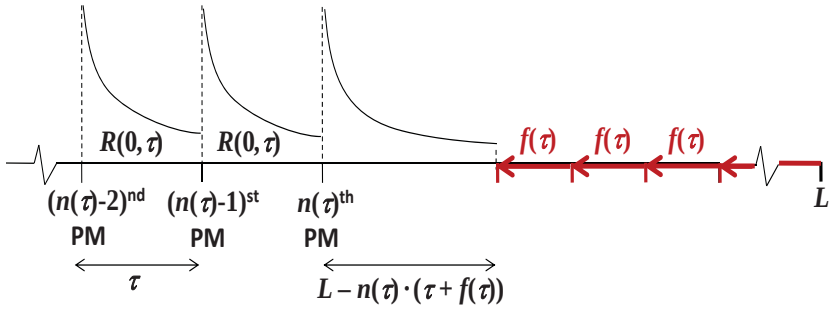
To facilitate further analysis, define the continuous function $V(\cdot, \cdot)$ for any pair (τ, n) as follows

$$V(\tau, n) = nR(0, \tau) + R\big(0, L - n \cdot (\tau + f(\tau))\big). \tag{4.7}$$

When $n \in [1, n_{max}] \cap \mathbb{Z}_+$ and τ is given by (4.6), or when $n = 0$, equation (4.7) provides the total reward for a feasible solution to the problem given by (4.4)-(4.6). Note that for any



(a)



(b)

Figure 10: Illustration of the problem dynamics under perfect maintenance and no failures at (a) the beginning of the system's lifetime and (b) the end of the system's lifetime.

given feasible interval length, τ, the number of PMs, n, is uniquely determined; however, for any given feasible non-zero n, any τ that satisfies (4.6) gives a feasible interval length. For this reason, the total reward function, given by equation (4.7), is expressed as a function of both τ and n, i.e., $V(\tau, n)$. In Theorem 2, we establish a simple solution procedure that exploits the underlying structure of the problem. Prior to presenting Theorem 2, however, we present three technical lemmas.

Define $\bar{n}_{max} = \frac{L}{f(0)}$, which serves as an upper bound for n_{max} as $n_{max} < \bar{n}_{max}$. Also, let $\bar{\tau}_n$ be the solution to $\tau = \frac{L}{n} - f(\tau)$ when solved for τ. Note that for any fixed $n \in (0, \bar{n}_{max})$, a unique $\bar{\tau}_n$ exists and satisfies $0 < \bar{\tau}_n \leq \frac{L}{n} - f(0)$ due to equation (4.3) as well as assumptions **A2** and **A3**.

First, Lemma 6 establishes the concavity of the function $V(\tau, n)$ in the interval length, τ, for any fixed $n \in (0, \bar{n}_{max})$. Subsequently, we use this result to show that the total reward function $V(\tau, n)$ can be locally maximized for any fixed, positive integer n.

Lemma 6. *For any fixed $n \in (0, \bar{n}_{max}) \subset \mathbb{R}_+$ the function $V(\tau, n)$ is strictly concave in τ, $\tau \in (0, \bar{\tau}_n) \subset \mathbb{R}_+$.*

Lemma 6 implies that for any fixed $n \in (0, \bar{n}_{max})$, the maximum of $V(\tau, n)$ over $\tau \in (0, \bar{\tau}_n)$ exists if the following equation is solvable for some $\tau \in (0, \bar{\tau}_n)$:

$$\frac{\partial V(\tau, n)}{\partial \tau} = n \cdot \Big(r(\tau) - \big(1 + f'(\tau)\big)\, r\big(L - n \cdot (\tau + f(\tau))\big) \Big) = 0. \tag{4.8}$$

For a given $n \in (0, \bar{n}_{max})$, let τ_n be the solution to (4.8) if it is solvable for τ, i.e.,

$$r(\tau_n) = r(L - n \cdot (\tau_n + f(\tau_n)))\big(1 + f'(\tau_n)\big). \tag{4.9}$$

Next, Lemma 7 establishes that (4.8) is indeed solvable under assumptions **A1-A3**.

Lemma 7. *For any fixed $n \in (0, \bar{n}_{max}) \subset \mathbb{R}_+$ there exists a unique $\tau_n \in (0, \bar{\tau}_n) \subset \mathbb{R}_+$ such that $\tau_n = \arg\max_{\tau} \{V(\tau, n) \mid \tau \in (0, \bar{\tau}_n)\}$.*

Note, however, that for a fixed $n \in [1, n_{max}] \cap \mathbb{Z}_+$, τ_n maximizes the total reward given by (4.4) only if τ_n satisfies (4.6). If (4.6) does not hold, then it can be formally shown that the optimal interval is equal to the solution of $\tau = \frac{L}{n+1} - f(\tau)$ when solved for τ. We discuss the situation in which (4.6) does not hold in more detail in Section 4.2.2.

Next lemma, Lemma 8, establishes the concavity of $V(\tau_n, n)$ in n, $n \in (0, \bar{n}_{max}) \subset \mathbb{R}_+$.

Lemma 8. *The function $V(\tau_n, n)$ is concave in n, $n \in (0, \bar{n}_{max}) \subset \mathbb{R}_+$.*

By Lemma 8 and equation (4.9), the maximum of $V(\tau_n, n)$ over $n \in [1, n_{max}] \subset \mathbb{R}_+$ is attained either at $n = 1$, or at $n = n_{max}$, or at some point in $(1, n_{max}) \subset \mathbb{R}_+$ that satisfies

$$\frac{\partial V(\tau_n, n)}{\partial n} = \int_0^{\tau_n} r(t)\,\mathrm{d}t - \frac{r(\tau_n)}{1 + f'(\tau_n)}\big(\tau_n + f(\tau_n)\big) = 0. \tag{4.10}$$

Let $\tilde{n}$ be the solution to (4.10) if it is solvable for n.

Finally, let the optimal maintenance interval for the problem given by (4.4)-(4.6) be denoted by τ^* and the corresponding number of PMs by n^*. Also, without loss of generality, let

$$\tau_0 \equiv L \tag{4.11}$$

and $V(\tau_0, 0) = R(0, L)$. Theorem 2 establishes conditions under which we can solve for the optimal maintenance interval τ^*, by

(i) solving equations (4.9) and (4.10) simultaneously to obtain $\tilde{n} \in \mathbb{R}_{++}$;

(ii)obtaining $\tau_{\lfloor \tilde{n} \rfloor}$, if $\lfloor \tilde{n} \rfloor \in (1, n_{max})$, and $\tau_{\lceil \tilde{n} \rceil}$, if $\lceil \tilde{n} \rceil \in (1, n_{max})$, using equation (4.9); and

(iii) setting n^* equal to the value from $\{0, 1, \{\lfloor \tilde{n} \rfloor, \lceil \tilde{n} \rceil\} \cap (1, n_{max}), n_{max}\}$ that results in the greater total reward in (4.7).

Theorem 2. *If τ_n satisfies (4.6) for all $n \in [1, n_{max}] \cap \mathbb{Z}_+$, then $\tau^* = \tau_{n^*}$, where*

$$n^* = \underset{n \in \{0,1,\{\lfloor \tilde{n} \rfloor, \lceil \tilde{n} \rceil\} \cap (1, n_{max}), n_{max}\}}{\arg\max} V(\tau_n, n). \tag{4.12}$$

For this solution procedure to be valid, however, τ_n must satisfy (4.6) for all $n \in [1, n_{max}] \cap \mathbb{Z}_+$. In the following subsection we perform a more detailed analysis of one special case under which these conditions hold.

Lastly, Proposition 1 establishes a technical property of τ_n, $n \in (0, \bar{n}_{max})$, that is necessary for our further discussion in Section 4.2.2. Namely, Proposition 1 implies that for any fixed number of PMs $n \in [1, n_{max}] \cap \mathbb{Z}_+$, the last maintenance interval, i.e., the $(n+1)^{\text{st}}$ interval, is at least as long as the first n intervals.

Proposition 1. *For a fixed $n \in (0, \bar{n}_{max})$*

$$L - n \cdot (\tau_n + f(\tau_n)) \geq \tau_n.$$

4.2.1 Constant Maintenance Cost

Consider the special case in which the amount of life depletion is independent of the length of the maintenance interval, i.e.,

$$f(\tau) = \Delta \quad \forall \tau \in \mathbb{R}_{++}, \tag{4.13}$$

where $\Delta > 0$. A simple example of this case may arise when the amount of data transmitted is predetermined, e.g., a sensor or implanted cardiac device transmits a snapshot of the patient/device's most recent status, as opposed to an entire history collected since the last transmission. Note that because constant $f(\tau)$ satisfies assumptions **A2** and **A3**, Lemmas 6, 7 and 8 as well as Proposition 1 hold.

Next, Proposition 2 provides closed form expressions for τ_n, the optimal maintenance interval length for any fixed n, as well as for $\tilde{n}$, the (non-integer) optimal number of PMs. As a result of Proposition 2, it is clear that τ_n satisfies (4.6) for all $n \in [1, n_{max}] \cap \mathbb{Z}_+$; hence, Theorem 2 applies to this special case. Furthermore, under a constant amount of life depletion, the optimal total reward is achieved when the last interval is of the same length as the rest, i.e., all maintenance intervals are of equal length. This result is similar in spirit to analogous results obtained by Belyi et al. (2009), Boland (1982) and Boland and Proschan (1982).

Proposition 2. *If $f(\tau)$ is given by (4.13), then*

(i) $\tau_n = \frac{L - n\Delta}{n+1}$ *for all* $n \in (0, \bar{n}_{max})$,
(ii) τ_n *satisfies (4.6) for all* $n \in [1, n_{max}] \cap \mathbb{Z}_+$, *and*
(iii) the solution of (4.10) satisfies

$$\tilde{n} = \frac{(L + \Delta)\, r(\tau_{\tilde{n}})}{\int_0^{\tau_{\tilde{n}}} r(t)\, \mathrm{d}t} - 1.$$

Recall that for any fixed number of PMs, the interval length that maximizes the total reward is chosen from a range of feasible interval lengths, and hence, there is a possibility of miscalculation of this interval length by a decision maker. Proposition 3 provides a bound on the amount of total reward loss that a decision maker may incur by choosing a sub-optimal interval length, e.g., due to parameter misspecification, for any given positive number of PMs.

Proposition 3. *Suppose $f(\tau)$ is given by (4.13). For any positive number of PMs, n,*

$$\max_{\frac{L}{n+1}-\Delta\leq\tau<\frac{L}{n}-\Delta}\{V(\tau_n,n)-V(\tau,n)\}\leq\max\left\{\frac{n\Delta}{n+1}\cdot\left(r\left(\frac{L}{n+1}-\Delta\right)-r\left(\frac{L}{n+1}\right)\right),\right.$$
$$\left.\frac{L-n\Delta}{(n+1)}\cdot\left(r(0)-r\left(\frac{L}{n}-\Delta\right)\right)\right\}. \tag{4.14}$$

For the case in which the maintenance cost is constant and the reward function is linear, i.e.,

$$r(t)=-at+b>0 \qquad a,b>0,\ \forall t\in[0,L], \tag{4.15}$$

Corollaries 6 and 7 (to Propositions 2 and 3, respectively), provide closed form expressions for $\tilde{n}$ and the upper bound established in Proposition 3.

Corollary 6. *Suppose $f(\tau)$ and $r(t)$ are given by (4.13) and (4.15), respectively. Then the solution to (4.10) is given by*

$$\tilde{n}=\frac{a(L+\Delta)}{\sqrt{a\Delta(2b+a\Delta)}}-1. \tag{4.16}$$

Corollary 7. *Suppose $f(\tau)$ and $r(t)$ are given by (4.13) and (4.15), respectively. For any positive number of PMs, n,*

$$\max_{\frac{L}{n+1}-\Delta\leq\tau<\frac{L}{n}-\Delta}\{V(\tau_n,n)-V(\tau,n)\}=\begin{cases}\frac{an\Delta^2}{2(1+n)}, & \text{if } \frac{L}{2}\leq n\Delta,\\ \frac{a(L-n\Delta)^2}{2n(1+n)}, & \text{otherwise.}\end{cases} \tag{4.17}$$

Corollary 7 formally establishes the intuitive fact that when the reward function is linear, the maximum penalty associated with performing maintenance at a sub-optimal interval length is linear in the slope of the reward function, a. Also from Corollary 7, the maximum penalty for choosing a sub-optimal interval length is quadratic in the maintenance "cost," Δ. Therefore, given any predetermined number of PMs, it is important to perform the PMs near their optimal times for large values of Δ.

Next, we present a numerical example that illustrates the results established in this section. Let $a=0.5$, $b=30$, $\Delta=5$ and $L=50$. Figure 11 provides a plot of the total reward function. As mentioned at the beginning of Section 4.2, the function is discontinuous and neither concave nor convex. However, as established in Lemma 6 and illustrated in Figure 11, $V(\tau,n)$ is concave in τ for each feasible n. Maximizing the function for a given n (as in equation (4.8)) yields τ_n, the optimal maintenance interval length for the given n. In Figure 11, the

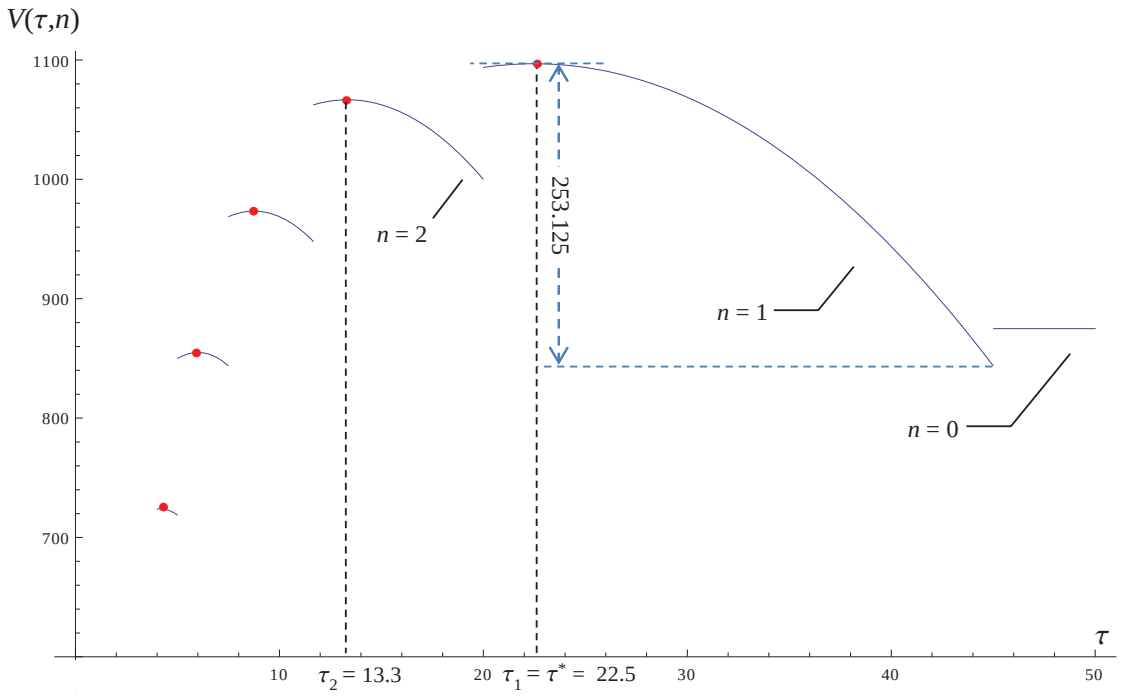


Figure 11: Total reward versus maintenance interval length for linear reward rate of $r(t) = -0.5t + 30$, $L = 50$ and $f(\tau) = 5\ \forall\tau$.

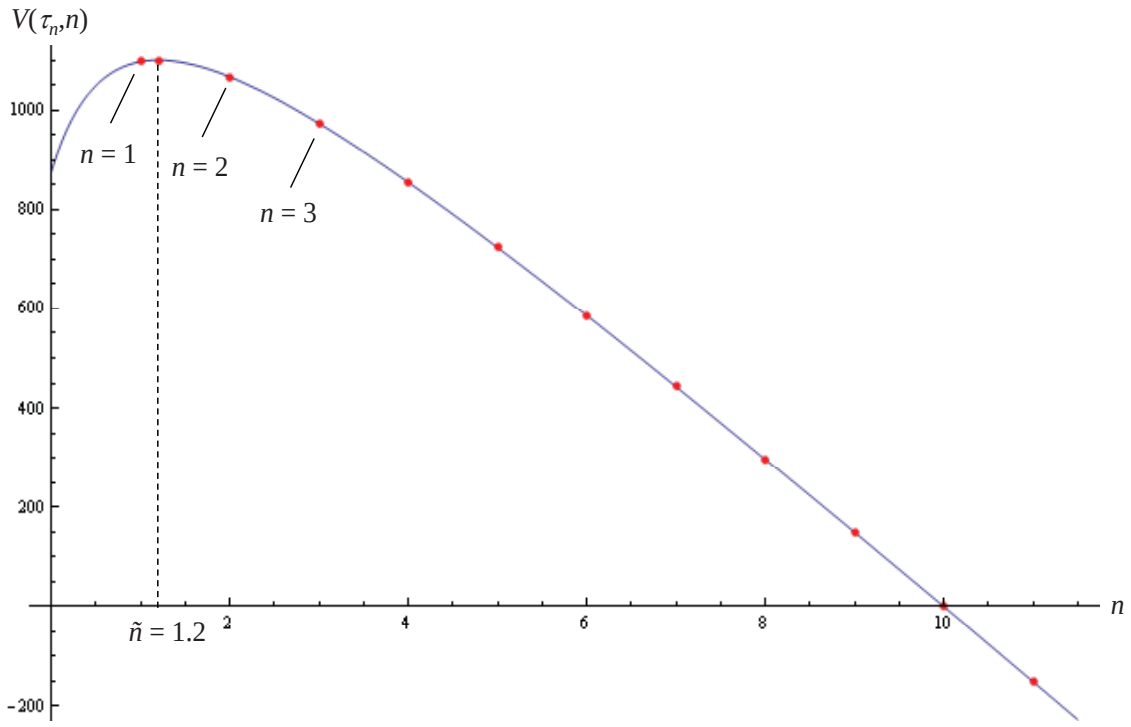


Figure 12: Total reward versus number of PMs for linear reward rate of $r(t) = -0.5t + 30$, $L = 50$ and $f(\tau) = 5\ \forall \tau$.

points $(\tau_n, V(\tau_n, n))$ are indicated by bold dots. Furthermore, as established in Lemma 8 and illustrated in Figure 12, $V(\tau_n, n)$ is concave in n. However, only the integral points are feasible solutions. In Figure 12, the non-integer maximum point and the points $(n, V(\tau_n, n))$ at integral values of n are indicated by bold dots. To solve for the optimal policy, we substitute a, b, Δ and L into equation (4.16) which yields $\tilde{n} = 1.2$, and hence, by Proposition 2, $\tau_{\lfloor \tilde{n} \rfloor} = \tau_1 = 22.5$ and $\tau_{\lceil \tilde{n} \rceil} = \tau_2 = 13.33$. Using equation (4.7), we see that $V(\tau_1, 1) = 1096.88 > V(\tau_2, 2) = 1066.67 > V(L, 0) = 875$, hence, by equation (4.12), $n^* = 1$ and $\tau^* = 22.5$. That is, in this example, chosen simply to illustrate the solution procedure, PM is performed only once at time 22.5. From equation (4.17), the maximum total reward loss associated with performing maintenance at a feasible time different from 22.5 is bounded above by 253.13.

4.2.2 An Ill-behaved Case

If τ_n does not satisfy (4.6) for at least one $n \in [1, n_{max}] \cap \mathbb{Z}_+$, then Theorem 2 does not hold and finding the optimal maintenance interval length τ^* is no longer straightforward. We illustrate this situation with a numerical example. Figure 13 provides a plot of the total reward function for the same scenario depicted in Figure 11, but with $f(\tau)$ redefined to be the quadratic function $\frac{\tau^2}{4} + 0.5$. The points $(\tau_n, V(\tau_n, n))$, $n = 1, 2, 3$, are indicated by bold dots; the solid portions of the curves satisfy (4.6) and the dashed portions do not. Note that $\tau_n, n = 1, 2, 3$ (and others) do not satisfy (4.6). Hence, the solution procedure established in Theorem 2 cannot be applied to obtain the optimal interval length τ^*, and a different approach must be used.

Let $\underline{\tau}_n$ be the solution of equation $\tau = \frac{L}{n+1} - f(\tau)$ when solved for τ. Note that $\underline{\tau}_n$ exists for any integer n such that $0 < n \leq n_{max} - 1$ due to assumptions **A2** and **A3**. Proposition 4 establishes that this solution maximizes the total reward if the solution to (4.9) falls outside the interval given by (4.6).

Proposition 4. *For any fixed $n \in [1, n_{max}] \cap \mathbb{Z}_+$, if τ_n does not satisfy (4.6), then the maximum total reward is attained at $\underline{\tau}_n$.*

As a result, to determine the overall optimal interval length τ^*, we can compare the total reward function values for each feasible n at its corresponding optimal interval length which is either τ_n (if (4.6) holds) or $\underline{\tau}_n$ (if (4.6) does not hold) and report the one which yields the greatest total reward function value. In the example illustrated in Figure 13, it is optimal

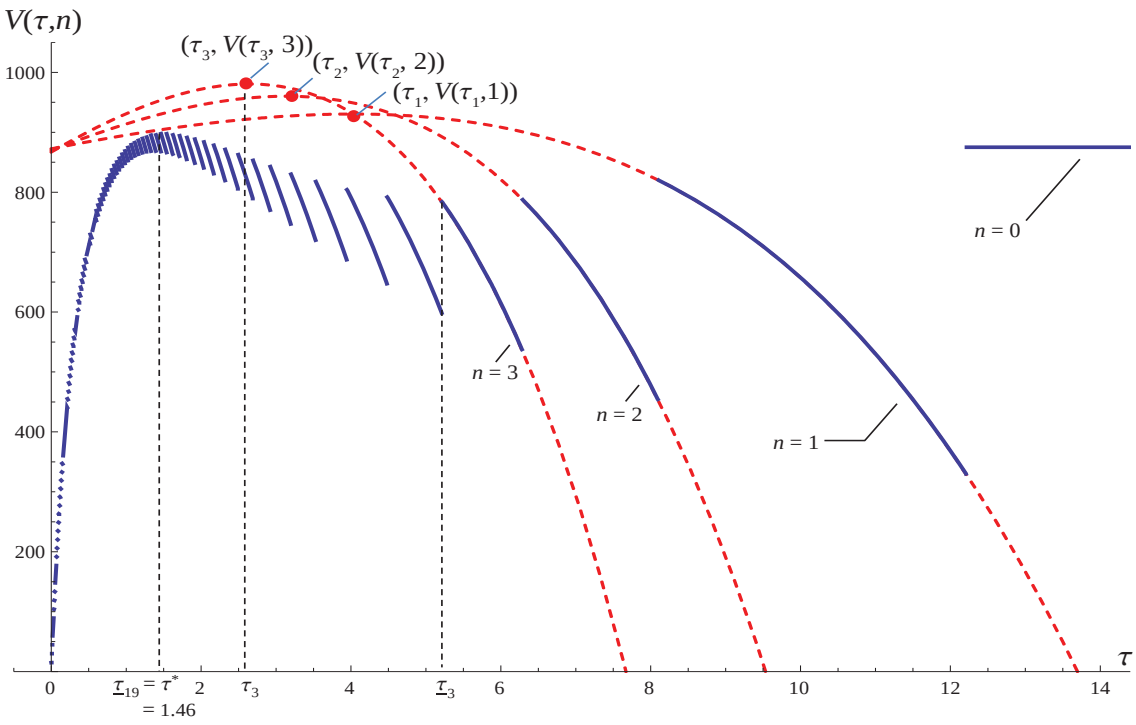


Figure 13: Total reward versus maintenance interval length for linear reward rate of $r(t) = -0.5t + 30$, $L = 50$ and $f(\tau) = \frac{\tau^2}{4} + 0.5$.

to perform $n^* = 19$ PMs spaced $\tau^* = \underline{\tau}_{19} = 1.46$ time units apart. The optimal total reward is $V(\tau^*, n^*) = V(\underline{\tau}_{19}, 19) = 897.79 > V(L, 0) = 875.0$.

4.2.3 Computational Examples

In this section, we more deeply explore how changes in the form of the reward and lifetime depletion functions affect the optimal policy. More specifically, we let the reward function, $r(t)$, and the lifetime depletion function, $f(\tau)$, assume various forms (Figure 14) and compute the total reward and the optimal interval length for each combination. Table 18 summarizes these combinations and the corresponding results.

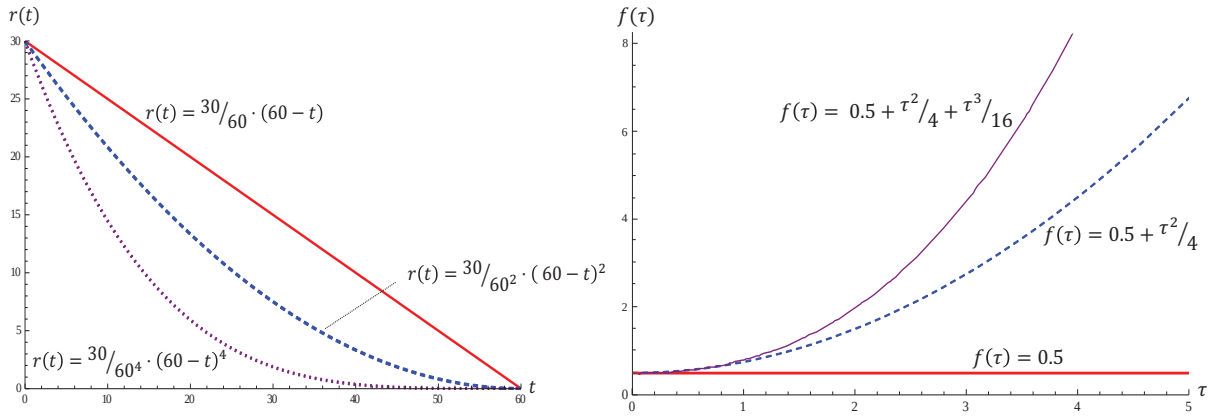
First, consider the effect of the form of $r(t)$ on the maximum total reward and the optimal interval length. The results in Table 18 indicate that as the total reward in the absence of any PMs (i.e., the area beneath the curves in Figure 14a) decreases: (i) the maximum total reward decreases and (ii) the PMs are to be performed with at least the same (or greater) frequency. For instance, when $f(\tau) = 0.5$, the optimal number of PMs increases from 6 to 8 and then to 11 across the three reward functions depicted in Figure 14a.

Next, consider the effect of the form of $f(\tau)$ on the maximum total reward and the optimal interval length. As the PMs grow more "costly," i.e., deplete a greater amount of battery lifetime for any given interval length, the maximum total reward decreases. Also, as the rate of growth of the lifetime depletion function increases, the optimal number of PMs increases sharply to maintain a short interval length and reduce PM costs. For instance, when $r(t) = \frac{30}{60} \cdot (60 - t)$, the optimal number of PMs increases from 6 to 19 and then to 22 across the three lifetime depletion functions depicted in Figure 14b.

As seen in Table 18, the increase in the optimal number of PMs across the three reward functions depends on the form of the lifetime depletion function, i.e., the increase is less pronounced as $f(\tau)$ grows faster in τ. This observation is due to the fact that when $f(\tau)$ is independent of the interval length, i.e., is constant, the rate of decrease of $r(t)$ is the only factor that affects the optimal number of PMs. However, as the rate of growth of $f(\tau)$ increases, the effect of $f(\tau)$ on the optimal number of PMs becomes more pronounced and dwarfs the effect of $r(t)$ on n^*.

Table 18: The maximum total reward and the optimal interval length across all combinations of the reward and lifetime depletion functions plotted in Figure 14 for $L = 50$.

$r(t)$	$f(\tau)$	τ^*	n^*	$V(\tau^*, n^*)$
$30/60 \cdot (60 - t)$	0.5	6.71	6	1331.11
	$0.5 + \tau^2/4$	1.46	19	897.79
	$0.5 + \tau^2/4 + \tau^3/16$	1.2	22	850.16
$30/60^2 \cdot (60 - t)^2$	0.5	5.11	8	1265.78
	$0.5 + \tau^2/4$	1.46	19	886.26
	$0.5 + \tau^2/4 + \tau^3/16$	1.15	23	841.53
$30/60^4 \cdot (60 - t)^4$	0.5	3.71	11	1179.87
	$0.5 + \tau^2/4$	1.33	21	864.95
	$0.5 + \tau^2/4 + \tau^3/16$	1.11	24	824.99



(a) (b)

Figure 14: (a) Reward functions, $r(t)$; (b) lifetime depletion functions, $f(\tau)$.

4.3 FAILURE PRONE SYSTEMS

In this section, we investigate the case in which the system is prone to failures, which require immediate reactive maintenance. First, we assume that maintenance (both preventive and reactive) is perfect. Second, we generalize to the case of imperfect, and possibly damaging, maintenance. For both cases we assume that the lifetime depletion function is constant and given by Δ.

Here, because the virtual age may be altered at any time due to a random failure, decisions are made adaptively rather than *a priori*. We assume that a decision is made at the beginning of each time period and implemented at the end of the period. Let the state of the process be given by $s = (t, \alpha) \in S$ where t is the remaining system lifetime, α is the virtual age, and $S = \{0, 1, 2, \ldots, L\} \times \{0, 1, 2, \ldots, L\}$. For $t \leq \Delta$, the only possible decision is to 'do nothing.' For $t > \Delta$, the possible decisions are to either 'perform PM' at the end of the period or 'do nothing.' The overall objective is to maximize the total reward obtained over the system's lifetime. Let $V^*(t, \alpha)$ denote the maximum total reward obtained starting from virtual age α with remaining lifetime t. Clearly,

$$V^*(0, \alpha) = 0 \quad \forall \alpha \geq 0. \tag{4.18}$$

Let the random variable Y with p.m.f. p_Y and c.d.f. F_Y denote the time to failure starting from virtual age zero. Also, let $h_Y(\alpha)$ denote the probability of failure in the next period given a current virtual age of α, i.e.,

$$h_Y(\alpha) = \frac{p_Y(\alpha + 1)}{1 - F_Y(\alpha)}. \tag{4.19}$$

Reactive maintenance (RM) is mandatory upon failure, costs c units of reward and depletes the remaining system lifetime by Δ. PMs, in contrast, are free, although they also deplete the remaining system lifetime by Δ. Finally, for ease of notation, let $R(\alpha) \equiv R(0, \alpha)$.

In our formulation, we assume both failures and PM occur at the end of the period. However, we assume that the former (if occurring) occurs before the latter. Hence, if the system fails at the end of a period, the extra charge of c units is imposed even if PM is already scheduled. We also make the following additional assumption in the remainder of this section:

A4: The random variable Y has increasing failure rate (IFR), i.e., $h_Y(\alpha)$ is nondecreasing in α.

4.3.1 Perfect Maintenance

In this section, the virtual age of the system is renewed to zero after every maintenance activity, both preventive and reactive. Therefore, because 'do nothing' is the only possible decision when $t \leq \Delta$, the maximum total reward starting from (t, α) is simply

$$V^*(t,\alpha) \;=\; R(\alpha+1) - R(\alpha) + h_Y(\alpha)\cdot\big(0-c\big) + \big(1-h_Y(\alpha)\big)\cdot V^*(t-1,\alpha+1). \quad (4.20)$$

For $t \geq \Delta + 1$,

$$\begin{aligned} V^*(t,\alpha) \;=\;& R(\alpha+1) - R(\alpha) + h_Y(\alpha)\cdot\big(V^*(t-\Delta-1,0) - c\big) \\ & + \big(1-h_Y(\alpha)\big)\cdot \max\left\{ \begin{array}{ll} V^*(t-\Delta-1,0) & \text{(perform PM)}, \\ V^*(t-1,\alpha+1) & \text{(do nothing)} \end{array} \right\}. \end{aligned} \quad (4.21)$$

Finally, given that the initial virtual age of the system is zero, the optimal total reward is given by $V^*(L,0)$.

Lemma 9 establishes that, under no additional conditions, for a given remaining lifetime, the maximum total reward is nonincreasing in the virtual age. The same is not necessarily true, however, for the behavior of the total reward function in the remaining lifetime for any fixed virtual age. For instance, when $r(t) = -t + 1100$, $L = 1000$, $\Delta = 30$, $c = 10000$ and $F_Y(y) = 1 - e^{-(\frac{y}{200})^{1.5}}$, under the optimal policy $V^*(0,930) = 0$, $V^*(15,930) = 23.63$ and $V^*(30,930) = -128.91$. In Lemma 10, we present a sufficient condition under which $V^*(t,\alpha)$ is monotone in t for any fixed $\alpha \in [0, L]$. The intuition behind the condition, (4.22), is simply that in order to have a monotone total reward in the remaining lifetime for any fixed virtual age, the reward obtained in the next period should be no less than the expected loss due to a possible random failure during that period.

Lemma 9. *For any fixed $t \in [0, L]$, $V^*(t,\alpha)$ is nonincreasing in α, $\alpha \in [0, L-t]$.*

Lemma 10. *If*

$$R(L) - R(L-1) \geq c \cdot h_Y(L-1), \quad (4.22)$$

then for any fixed $\alpha \in [0, L]$, $V^*(t,\alpha)$ is nondecreasing in t, $t \in [0, L-\alpha]$.

Theorem 3 establishes that the optimal policy is of threshold type in the virtual age, i.e., for every t there is a virtual age $\alpha^*(t)$ at and below which it is optimal to do nothing and above which it is optimal to perform PM. Note that the proof of Theorem 3 relies only on Lemma 9. Let $a^*(t, \alpha)$ denote the optimal decision at remaining lifetime t and virtual age α, where '0' corresponds to 'do nothing' and '1' corresponds to 'perform PM.'

Theorem 3. *For any system remaining lifetime t, there exists a virtual age $\alpha^*(t)$ such that*

$$a^*(t, \alpha) = \begin{cases} 0, & \text{if } \alpha \leq \alpha^*(t), \\ 1, & \text{otherwise.} \end{cases} \tag{4.23}$$

Figure 15 presents the optimal policy for a failure prone system with $r(t) = -t + 1100$, $L = 1000$, $\Delta = 30$, $c = 500$ and $F_Y(y) = 1 - e^{-(\frac{y}{400})^3}$. Note that because PMs are perfect, any given remaining system lifetime states with virtual ages greater than $L - t$ are unreachable and hence excluded. For this problem instance, the failure rate is relatively low, $\mathbb{E}[Y]$ is approximately 357.2 and performing PM optimally results in a 4.3% greater total expected reward than performing only reactive maintenance. The optimal PM threshold indicates the virtual age at and below which it is optimal to do nothing and above which it is optimal to perform PM for any given remaining system lifetime, as established in Theorem 3.

The optimal PM threshold in Figure 15 has a noticeably irregular shape. Consider the two failure free sample paths, I, in light grey, and II, in dark grey. Starting from state $(1000, 0)$, along sample path I the virtual age increases and t decreases until PM is scheduled in state $(763, 237)$. After performing this PM, the virtual age becomes zero, however, $\Delta = 30$ units of lifetime is lost, rendering the process in state $(733, 0)$, and the process continues. Sample path I indicates that starting from state $(L, 0)$, in the absence of any failures, it is optimal to perform three PMs. However, as indicated by sample path II, if the system's initial lifetime is 825, it is optimal to perform PM only twice in the absence of any failures. This difference between the optimal number of PMs is due to the saw-shaped form of the optimal PM threshold.

Figures 16 and 17 illustrate how the optimal policy is affected by the parameter Δ and the c.d.f. of Y, F_Y, respectively. Figures 16a and 16b present the optimal policy for the same scenario as in Figure 15 with $\Delta = 60$ and $\Delta = 30$, respectively. As expected, a smaller value of Δ results in a greater number of states in which PM is optimal.

Figures 17a and 17b compare the optimal policies for four problem instances. In both figures, $r(t) = -t + 1100$, $L = 1000$ and the random time to failure Y has c.d.f. $F_Y(y) =$

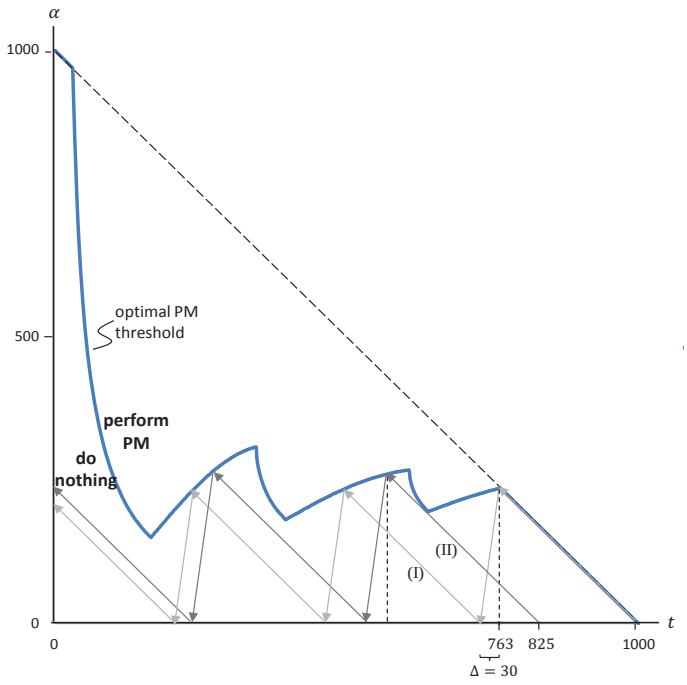
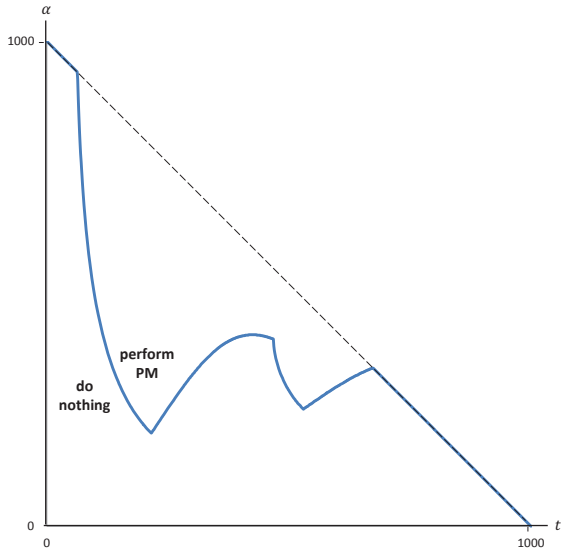
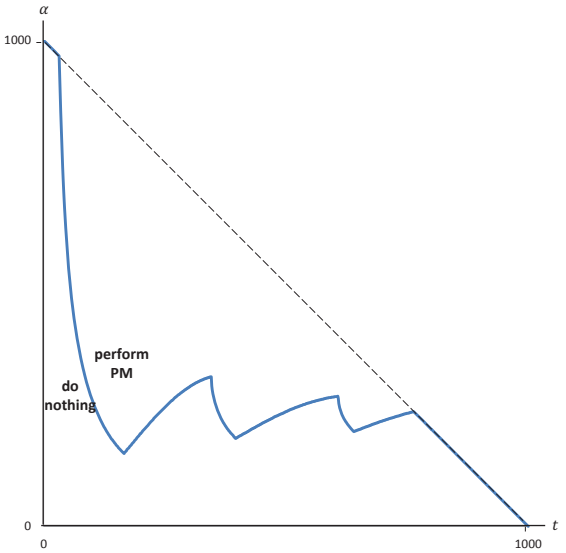


Figure 15: The optimal PM threshold for a problem instance with $r(t) = -t + 1100$, $L = 1000$, $\Delta = 30$, $c = 500$ and $F_Y(y) = 1 - e^{-(\frac{y}{400})^3}$. I and II are two failure free sample paths starting from states $(1000, 0)$ and $(825, 0)$, respectively.

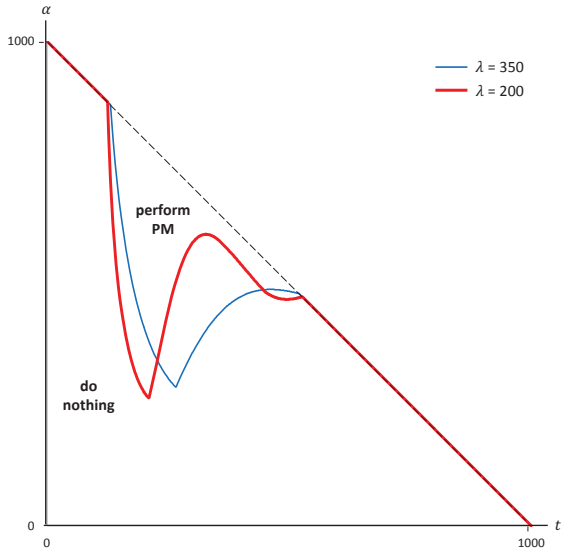


(a) Greater life depletion per PM: $\Delta = 60$

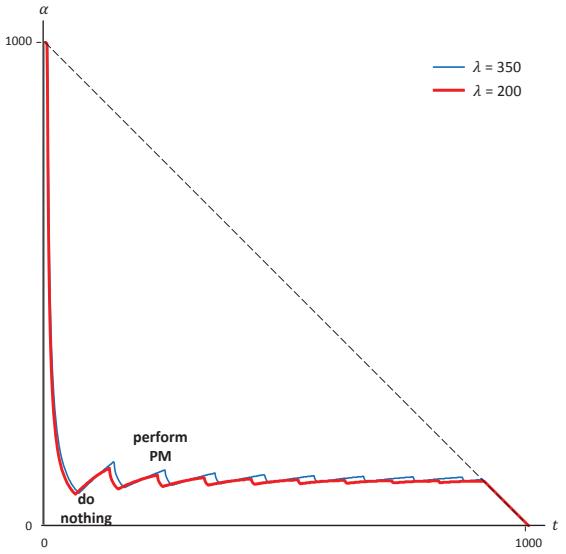


(b) Lesser life depletion per PM: $\Delta = 30$

Figure 16: The optimal PM thresholds for two problem instances with $r(t) = -t + 1100$, $L = 1000$, $c = 500$ and $F_Y(y) = 1 - e^{-(\frac{y}{400})^3}$.



(a) for two λ values when $\Delta = 120$ and $c = 500$



(b) for two λ values when $\Delta = 5$ and $c = 4000$

Figure 17: The optimal PM thresholds for four problem instances with $r(t) = -t + 1100$, $L = 1000$ and $F_Y(y) = 1 - e^{-(\frac{y}{\lambda})^2}$.

$1 - e^{-(\frac{y}{\lambda})^2}$, with $\lambda = 200$ and $\lambda = 350$. In Figure 17a, $\Delta = 120$ and $c = 500$, whereas in Figure 17b, $\Delta = 5$ and $c = 4000$. Clearly, the system is less prone to failure when the expected time to failure is higher, i.e., when λ is larger. As expected, and seen in Figure 17a, when the economic cost of RM (i.e., the value of c) is relatively small compared to the lifetime depletion of PMs and RMs (i.e., the value of Δ), it is optimal to wait longer before performing PM thereby relying on RMs to renew the virtual age of the system to zero. However, as seen in Figure 17b, when the value of c is relatively large compared to the value of Δ, PM is performed sooner. Also, as seen in Figure 17a, for the majority of the values of t, the optimal PM threshold when $\lambda = 350$ falls below the optimal PM threshold when $\lambda = 200$. This observation is due to the fact that when $\lambda = 350$, the system is less prone to failure and performing PMs more frequently is the only way of maintaining a high reward rate.

4.3.2 Imperfect Maintenance

In this section, we consider the case in which maintenance does not necessarily reset the system's virtual age to zero. As explained by Pham and Wang (1996), performing maintenance sometimes renders the system in a worse condition than it was in prior to the maintenance action, typically due to human error. In the context of the implanted cardiac device follow-up care example mentioned in Section 4.1, imperfect maintenance may occur due to misinterpretation of the transmitted data by technicians/nurses.

Let the random variables X_p and X_r, with p.m.f.s p_{X_p} and p_{X_r} and c.d.f.s F_{X_p} and F_{X_r}, denote the virtual age of the system after preventive and reactive maintenance, respectively. We assume that the virtual age after a maintenance action is always less than the maximum remaining system lifetime, L, i.e., $F_{X_p}(L-1) = F_{X_r}(L-1) = 1$. We also assume that RM is immediately performed whenever the virtual age reaches L and the resulting remaining lifetime is positive, i.e.,

$$V^*(t, L) = \begin{cases} 0, & \text{if } t \leq \Delta, \\ \sum_{x=0}^{L-1} V^*(t - \Delta - 1, x) \cdot p_{X_r}(x) - c, & \text{otherwise.} \end{cases} \tag{4.24}$$

Because 'do nothing' is the only possible action when $t \leq \Delta$, the maximum total reward starting from state (t, α) remains the same as in the perfect maintenance scenario and is

given by equation (4.20). In contrast to the perfect maintenance scenario, for $t \geq \Delta + 1$ we now have

$$V^*(t,\alpha) = R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot \left(\sum_{x=0}^{L-1} V^*(t-\Delta-1,x) \cdot p_{X_r}(x) - c \right) + \big(1 - h_Y(\alpha)\big) \cdot \max \left\{ \begin{array}{ll} \sum_{x=0}^{L-1} V^*(t-\Delta-1,x) \cdot p_{X_p}(x) & \text{(perform PM)}, \\ V^*(t-1,\alpha+1) & \text{(do nothing)} \end{array} \right\}. \quad (4.25)$$

Finally, given that the initial virtual age of the system is zero, the optimal total reward is given by $V^*(L,0)$.

Figure 18 presents an example optimal policy for a failure-prone system subject to imperfect preventive and reactive maintenance with $r(t) = -t + 1100$, $L = 1000$, $c = 60$, $\Delta = 120$, $F_Y(y) = 1 - e^{-(\frac{y}{250})^2}$ and $p_{X_p}(x)$ and $p_{X_r}(x)$ given by Table 19. Clearly, this optimal policy is not of threshold type. Also, note that as opposed to the perfect maintenance scenario, here, under imperfect, possibly damaging maintenance, some of the states in $\{(t,\alpha) \in S : \alpha > L - t\}$ are reachable. For instance, if the system is preventively maintained at $t = 980$ in the absence of any prior RMs, the system may transit to state $(980 - 120 - 1, 990) = (859, 990)$ with probability 0.07.

Now, let the random variable X with p.m.f. p_X and c.d.f. F_X denote the virtual age of the system after any maintenance activity, i.e., either preventive or reactive maintenance. Analogous to Lemmas 9 and 10, Lemma 11 establishes the monotonicity of the total reward function $V^*(t,\alpha)$ in both t and α under the sufficient condition given by equation (4.22). In contrast to Lemma 9, Lemma 11 requires condition (4.22) for establishing the monotonicity of the total reward function in α, mainly because of the additional boundary condition given by equation (4.24). Furthermore, Theorem 4, which is analogous to Theorem 3, establishes that for any fixed system remaining lifetime t, the optimal policy is of control-limit type in $\alpha < L$. (Recall that at $\alpha = L$, RM is instantaneously initiated.)

Lemma 11. *Let the random variable X denote the virtual age of the system after both preventive and reactive maintenance. If equation (4.22) holds, then*

(i) $V^*(t,\alpha)$ is nonincreasing in α,

(ii) $V^*(t,\alpha)$ is nondecreasing in t.

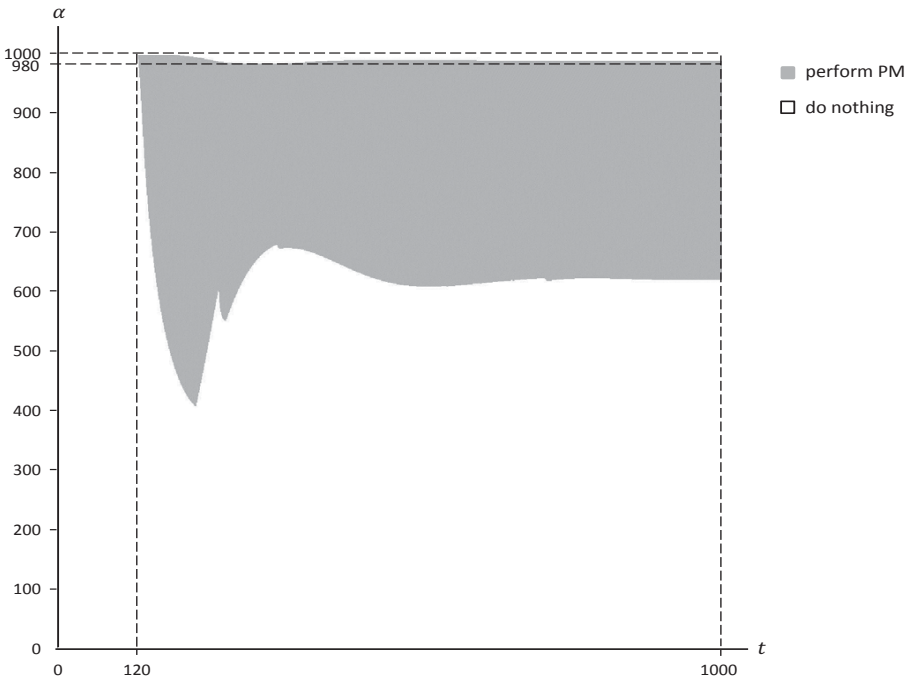


Figure 18: The shaded area indicates $(t, \alpha) \in S$ for which the optimal action is to perform PM when $r(t) = -t + 1100$, $L = 1000$, $c = 60$, $\Delta = 120$, $F_Y(y) = 1 - e^{-(\frac{y}{250})^2}$ and $p_{X_p}(x)$ and $p_{X_r}(x)$ are given by Table 19.

Table 19: Probability distribution of the virtual age after preventive maintenance and reactive maintenance.

X	0	50	100	150	990
$p_{X_p}(x)$	0.7	0.08	0.08	0.07	0.07
$p_{X_r}(x)$	0.68	0.27	0.03	0.02	0.00

Theorem 4. *Let the random variable X denote the virtual age of the system after both preventive and reactive maintenance. If equation (4.22) holds, then for any system remaining lifetime t, there exists a virtual age $\alpha^*(t)$ such that for all $\alpha < L$,*

$$a^*(t,\alpha) = \begin{cases} 0, & \text{if } \alpha \leq \alpha^*(t), \\ 1, & \text{otherwise.} \end{cases} \tag{4.26}$$

Lastly, Lemma 12 establishes that for any given system remaining lifetime t and virtual age α, the maximum total reward is less if the virtual age of the system after maintenance is stochastically larger.

Lemma 12. *Let $V^1(t,\alpha)$ and $V^2(t,\alpha)$ be two problem instances given by (4.20),(4.24)-(4.25) for which the random variable X^i denotes the virtual age of the system after both preventive and reactive maintenance for $i = 1, 2$. If $X^2 \succeq X^1$, i.e., X^2 is stochastically larger than X^1, then for any given state (t,α), $V^1(t,\alpha) \geq V^2(t,\alpha)$.*

Figure 19 presents the optimal PM threshold for three problem instances (referred to as problems I-III) with $r(t) = -t + 1100$, $L = 1000$, $\Delta = 50$, $c = 4000$, $F_Y(y) = 1 - e^{-(\frac{y}{350})^2}$ and different maintenance outcomes: in I, both PM and RM are perfect, in II, PM is perfect and RM is imperfect, and in III, PM and RM have identical, imperfect outcomes. Table 19 provides the probability distribution of the virtual age after RM for problems II and III. For illustrative purposes, the unreachable states are not excluded from Figure 19. Consistent with Theorem 4, the optimal policy for problem III is of threshold type. As shown in Figure 19, the optimal PM threshold for problem II is lower than that for I because RMs are imperfect in problem II, whereas in problem I, they are perfect. Therefore, it is optimal to perform PMs more frequently in II. In problem III, PMs are imperfect. Therefore, among the three problem instances, performing PM is clearly least beneficial in problem III, hence the highest optimal PM threshold. In terms of the total reward, problems I-III generate $822,188$, $815,031$ and $807,853$ in units of reward starting from state (1000,0), respectively. This decrease in the reward from problem I, with perfect PM and RM, to problem III, with imperfect, but identical PM and RM outcomes, is consistent with Lemma 12.

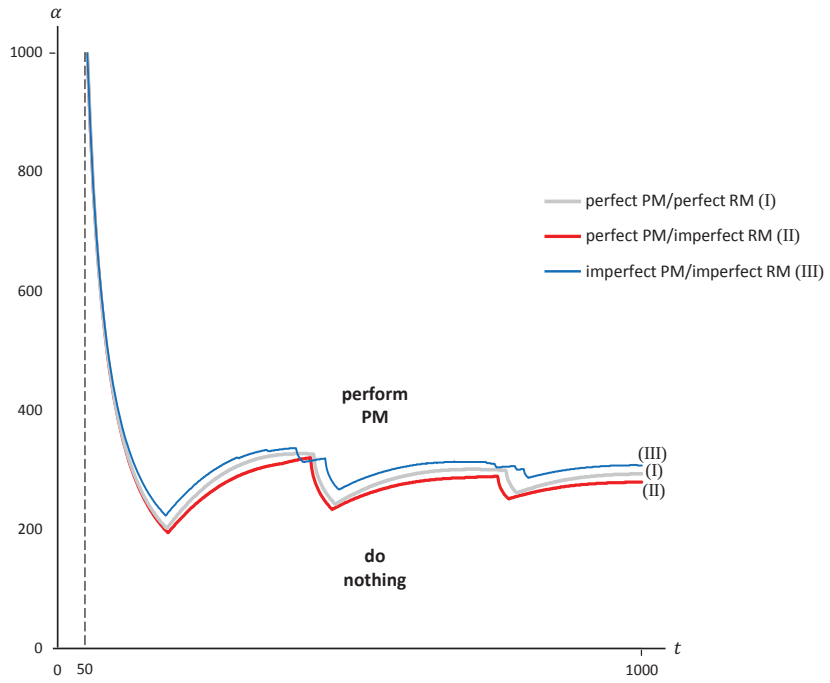


Figure 19: The optimal PM threshold for three problem instances with $r(t) = -t + 1100$, $L = 1000$, $\Delta = 50$, $c = 4000$ and $F_Y(y) = 1 - e^{-(\frac{y}{350})^2}$ where $p_{X_r}(x)$ is given by Table 19.

4.4 CONCLUSION

In this chapter, we consider a system with a deterministic initial lifetime that generates reward at a decreasing rate as its virtual age increases. Maintenance can be performed to decrease the system's virtual age, and hence, increase the reward rate. However, maintenance shortens the remaining lifetime of the system. Given this trade-off, we analyze the lifetime-reward-maximizing maintenance policies under various maintenance scenarios. This problem is motivated in part by the practice of remotely monitoring battery-powered devices that periodically transmit information about their condition and performance to a remote data center, e.g., implanted cardiac devices. In this application, the more frequent the transmissions, the more timely the collected data, but the greater the reduction in battery longevity.

First, we consider non-failure-prone systems and develop a solution procedure to obtain the reward-maximizing maintenance interval under the assumption that maintenance restores the virtual age to zero. In this setting, we also derive closed form results for the special case of constant maintenance life depletion. Next, we investigate failure prone systems under both perfect and imperfect maintenance where failures not only incur an economic cost, but also shorten the system's lifetime. We formulate stochastic dynamic programs under both perfect and imperfect maintenance, prove the monotonicity of the total reward in both the system's virtual age and the remaining lifetime (under certain conditions) and establish a structural property of the optimal maintenance policy.

5.0 CONCLUSIONS AND FUTURE RESEARCH

In this dissertation, we address three problems concerning follow-up care for patients with CIEDs. This work is particularly timely given the lack of clinical guidelines for management of patients with implanted cardiac devices, despite the aging population and the ever growing number of these patients. There is a tremendous need for clinicians to justify their actions and to be able to make challenging treatment choices based on particular patient characteristics; however, mostly due to large policy spaces, traditional clinical approaches are not viable to provide such solutions. Here, we use a host of mathematical methodologies and powerful optimization techniques to develop customized treatment policies that provide patients with better quality of care. The resulting policies, which are easy to implement, can decrease the burden on the healthcare system by reducing the number of surgeries, in-office visits, and so on, without compromising the patients' well-being.

This work contributes to the operations research and clinical literature in novel and important ways. In Chapter 2, we develop MDP models to determine patient-specific CIED lead abandon/extract policies for four major types of CIEDs as a function of patient age and the age of every implanted lead. We carefully calibrate these models and present insightful numerical results, including comparisons to heuristic policies that are commonly used in practice. We observe that under the optimal policy, the abandon/extract decision for each failed lead does not depend on the exact ages of all implanted leads; this decision only depends on the lead's age, patient age, lead's age rank among the lead ages, the total number of implanted leads and, in the case of multi-chamber devices, the age of the working lead(s). Hence, the optimal policy is easy to implement. Additionally, we show that in comparison to the commonly used heuristic policies, following the optimal policy can extend an average patient's expected lifetime by up to 1.2 years and decrease the likelihood of device related death by up to 94%. Note that by using MDPs, we may only compare the expected values (e.g., the expected lifetime of patients) under various policies. Hence, in the future, we

may build simulation models to measure the variability between the results under different policies and possibly introduce new metrics that are not easy to measure using MDPs.

Chapter 3 presents a MDP model to optimally time the otherwise conservatively performed ICD generator replacement surgeries with the objective of maximizing the patient's expected lifetime. We carefully calibrate this model using clinical data and expert opinion to obtain results tailored for given individuals. Our large computational study shows that following the optimal policy both extends the patient expected lifetime and decreases the total expected number of replacements. Under the optimal policy, patient expected lifetime may be extended by up to 40.6 weeks (0.78 years). Additionally, patients undergoing initial implantation at age 30-40, 41-60, and 61-80 experience an approximate decrease in the total expected number of replacements of 8-14%, 8-15% and 8-19%, respectively, while achieving the same or greater expected lifetime.

Finally, in Chapter 4, inspired by the practice of remote monitoring of CIEDs, we build mathematical models to examine the trade-off between battery longevity and the frequency of life-depleting, remote follow-ups of cardiac devices in a finite horizon setting. These stylized models capture novel battery life considerations and yet are compact and amenable to structural analysis. In future research, these models may serve as a basis for a more clinically relevant investigation of the problem based on clinical data.

APPENDIX A

EXTENDED DISCUSSION FOR CHAPTER 2

A.1 DUAL-CHAMBER DEVICES WITH IDENTICAL LEADS: MODEL FORMULATION

Similar to Sections 2.2.1 and 2.2.2.1, let the random variable X with p.m.f. p_X, c.d.f. F_X and survival function $\bar{F}_X$ denote the time to failure for a new lead. We also assume that all leads survive up to specified maximum age, $\bar{\ell}$, with some positive probability. Lastly, for $t = \overline{T}$, the maximum total expected reward is given by equation (2.16).

Decision epoch due to infection. For $t < \overline{T}$, first consider the case in which $\theta = 0$. Here, the total expected reward $\nu_t(n)$ is given by equation (2.17), where

$$\begin{aligned}\varphi_i(t,n) &= p_X(n)^{\mathbb{1}_{\{i\in\{1,2\}\}}+2\cdot\mathbb{1}_{\{i\in\{0\}\}}}\cdot\bar{F}_X(n)^{\mathbb{1}_{\{i\in\{1,2\}\}}} \\ &\quad\cdot\Bigg(r_t(n)+\sum_{m=1}^{n-1}\rho(m)\cdot V_{t+m}(\ell'(m),w,0) \\ &\quad+\eta(n)\cdot\gamma\cdot V_{t+n}(\ell'(n),\mathbb{1}_{\{i\in\{1,2\}\}},1)\Bigg), \quad i\in\{0,1,2\} \qquad \text{(A.1)}\\ \varphi_\Delta(t,n) &= \bar{F}_X(n-1)^2\cdot\left(r_t(n)+\sum_{m=1}^{n-1}\rho(m)\cdot V_{t+m}(\ell'(m),w,0)\right). \qquad \text{(A.2)}\end{aligned}$$

Equations (A.1)-(A.2) are analogous to equation (2.18). Note that in (A.1)-(A.2), because the current leads are of the same age and type at patient age $t+n$, without loss of generality, we assume the lead with the smaller index continues working; hence, when $i = 2$, $w = 1$ in the last expression in equation (A.1). Finally, for $t < \overline{T}$, the maximum total expected reward at a decision epoch with $\theta = 0$ is given by equation (2.19).

Decision epoch due to failure. Next, for $t < \overline{T}$, consider the case in which $\theta = 1$. We redefine $\ell''(a,m)$ from Section 2.2.2.1 to denote the lead age vector m years after a transition from state $s_t = (\ell, w, 1)$ under action a, i.e., $\ell''(a,m) = [(\ell''_{(1)}, \ell''_{(2)}), \ldots, \ell''_{(L)}]$, where $\ell''_{(1)}$ and $\ell''_{(2)}$ denote the ages of the current P leads at patient age $t+m$, when ordered non-increasingly, and $\ell''_{(i)}$, $i \in \{3, \ldots, L\}$, denotes the age of the i^{th} oldest, previously abandoned lead, if present, and assumes the value -1, otherwise. Hence, the vector $\ell''(a,m)$ is as given in Section 2.2.2.1, with the exception that its two first components are now ordered non-increasingly. For example, let $\bar{\ell} = 40$ and consider a decision epoch at which the process is in state $s_{60} = ([(8,3),5,4,-1],2,1)$, i.e., $\ell_{(1)} = 8$, $\ell_{(2)} = 3$, $\ell_{(3)} = 5$, $\ell_{(4)} = 4$, $\ell_{(5)} = -1$, $w = 2$ and $\theta = 1$. Because the only working lead is the younger, current P lead, $a \subseteq \{1,3,4\}$. Now, suppose action $a = \{3\}$ is taken and the newly implanted lead fails 3 years later. Therefore, from equation (2.20), the first two components of $\ell''(a,m)$ are 3 and 6 and from equation (2.21), $\psi\{[(8,3),5,4,-1],\{3\},3\} = \{11,7\}$; hence, at the next decision epoch the process is in state $s_{63} = ([(6,3),11,7,-1],\cdot,\cdot)$, i.e., $\ell''_{(1)} = 6$, $\ell''_{(2)} = 3$, $\ell''_{(3)} = 11$, $\ell''_{(4)} = 7$, $\ell''_{(5)} = -1$.

The total expected reward $u_t(\ell, w, a, n)$ is given by equation (2.22), where for $w = 0$, $v_i(t,\ell,w,a,n)$, $i \in \{1,\ldots,4\}$, is given by a set of equations similar to (A.1)-(A.2), in which $\ell'(m)$ and $\ell'(n)$ are substituted with $\ell''(a,m)$ and $\ell''(a,n)$, respectively, and for $w > 0$,

$$
\begin{aligned}
v_i(t,\ell,w,a,n) &= \Pr(X = \ell_{(w)} + n | X > \ell_{(w)})^{\mathbb{1}_{\{i\in\{0,2\}\}}} \cdot p_X(n)^{\mathbb{1}_{\{i\in\{0,1\}\}}} \\
&\quad \cdot \Pr(X > \ell_{(w)} + n | X > \ell_{(w)})^{\mathbb{1}_{\{i\in\{1\}\}}} \cdot \bar{F}_X(n)^{\mathbb{1}_{\{i\in\{2\}\}}} \\
&\quad \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \\
&\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a,n), i, 1) \Bigg), \qquad i \in \{0,1,2\} \qquad \text{(A.3)} \\
v_\Delta(t,\ell,w,a,n) &= \Pr(X > \ell_{(w)} + n - 1 | X > \ell_{(w)}) \cdot \bar{F}_X(n-1) \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \Bigg). \qquad \text{(A.4)}
\end{aligned}
$$

Equations (A.3)-(A.4) are analogous to equation (2.23). Therefore, when $\theta = 1$, the maximum total expected reward is given by equation (2.24).

A.2 CRT-D DEVICES: MODEL FORMULATION

Similar to Section 2.2.2.1, let the random variable X_j, $j = 1, 2$, with p.m.f. p_{X_j}, c.d.f. F_{X_j} and survival function $\bar{F}_{X_j}$ denote the time to failure for a new P lead and a new D lead, respectively, and assume that all leads survive up to a specified maximum age, $\bar{\ell}$, with some positive probability. Additionally, we let $\mu((\ell, w, \theta), a)$ be given by equation (2.15), where $\phi(w, \theta)$ is given by equation (2.27). We redefine $V_t(\ell, w, \theta)$ to denote the maximum total expected reward starting from state $s_t = (\ell, w, \theta)$. Clearly, $V_{\overline{T}}(\ell, w, \theta) = 0$.

Decision epoch due to infection. For $t = \overline{T}$, first consider the case in which $\theta = 0$. Redefine $\ell'(m)$ to denote the lead age vector m years after an infection for a CRT-D device, i.e., $\ell'(m) = [(m, m, m), -1, -1]$. Also, redefine $\nu_t(n)$ to denote the total expected reward obtained starting from state $s_t = (\ell, w, 0)$, conditional on surviving the infection and the requisite lead procedures, weighted by the likelihood of the next lead failure occurring in n periods, i.e.,

$$\nu_t(n) = \begin{cases} \sum_{i \in \{\bar{3}, \ldots, 3\}} \varphi_i(t, n), & \text{if } n < \overline{T} - t, \\ \varphi_\Delta(t, n), & \text{if } n = \overline{T} - t, \end{cases} \tag{A.5}$$

where

$$\begin{aligned} \varphi_i(t, n) = {} & \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{2}, 1\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{1}, 0, 2, 3\}\}}} \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{1}, 2\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{2}, 0, 1, 3\}\}}} \\ & \cdot \bar{F}_{X_2}(n)^{\mathbb{1}_{\{i \in \{\bar{2}, \bar{1}, 3\}\}}} \cdot p_{X_2}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, 0, 1, 2\}\}}} \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), w, 0) \\ & + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell'(n), \mathbb{1}_{\{i \in 1, 2\}} + \bar{2} \cdot \mathbb{1}_{\{i \in \bar{2}, \bar{1}\}} + i \cdot \mathbb{1}_{\{i \in \bar{3}, 0, 3\}}, 1) \Bigg), \\ & i \in \{\bar{3}, \ldots, 3\} \end{aligned} \tag{A.6}$$

$$\varphi_\Delta(t, n) = \bar{F}_{X_1}(n-1)^2 \cdot \bar{F}_{X_2}(n-1) \cdot \left(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell'(m), w, 0) \right). \tag{A.7}$$

Equations (A.6)-(A.7) are analogues to equations (2.18) and (A.1)-(A.2). More specifically, equation (A.6) corresponds to the total expected reward obtained when $w = i$ at patient age $t + n$, with the exception that $w = 1$ when $i = 2$ and $w = \bar{2}$ when $i = \bar{1}$. The reason is that, without loss of generality, we assume if exactly one of the current P leads fail at $t + n$ while

the leads are of the same age, the one with the smaller index continues working. Therefore, for $t < \overline{T}$, the maximum total expected reward at a decision epoch with $\theta = 0$ is given by

$$V_t(\ell, w, 0) = \mu((\ell, w, 0), \bar{a}(\ell)) \cdot \sum_{n=1}^{\overline{T}-t} \nu_t(n), \quad \forall w \in W. \tag{A.8}$$

Decision epoch due to failure. Next, for $t < \overline{T}$, consider the case in which $\theta = 1$. We redefine $\ell''(a, m)$ from Section 2.2.2 to denote the lead age vector m years after a transition from state $s_t = (\ell, w, 1)$ under action a, i.e., $\ell''(a, m) = [(\ell''_{(1)}, \ell''_{(2)}, \ell''_{(3)}), \ldots, \ell''_{(L)}]$, where $\ell''_{(1)}$ and $\ell''_{(2)}$ denote the ages of the current P leads at patient age $t + m$, when ordered non-increasingly, $\ell''_{(3)}$ denotes the age of the current D lead, and $\ell''_{(i)}$, $i \in \{4, \ldots, L\}$, denotes the age of the i^{th} oldest, previously abandoned lead, if present, and assumes the value -1, otherwise. For $j = 1, 2$, let

$$\hat{\ell}''_{(j)} = \begin{cases} m, & \text{if } w = 0, \text{ or } w \in \{1, 2, 3\} \text{ and } j \neq w, \text{ or } w \in \{\bar{3}, \bar{2}, \bar{1}\} \text{ and } \bar{j} = w, \\ \ell_{(j)} + m, & \text{otherwise.} \end{cases} \tag{A.9}$$

Also, we have

$$\ell''_{(3)} = \begin{cases} m, & \text{if } w = \bar{3}, 0, 1, 2, \\ \ell_{(j)} + m, & \text{otherwise.} \end{cases} \tag{A.10}$$

Lastly, we modify the set $\psi(\ell, a, m, w)$ to be

$$\psi(\ell, a, m, w) = \Big\{ \min\{\ell_{(i)} + m, \bar{\ell}\} : 1 \leq i \leq L, i \notin a, \ell_i \neq -1, i \neq w, \bar{i} = w \text{ or } w = 0 \Big\}. \tag{A.11}$$

Hence, the first two components of vector $\ell''(a, m)$ are given by equation (A.9), where the components $\hat{\ell}''_{(1)}$ and $\hat{\ell}''_{(2)}$ are ordered non-increasingly, the third component of vector $\ell''(a, m)$ is given by equation (A.10), and its remaining components are given by the non-increasingly ordered members of the set $\psi(\ell, a, m, w)$, with the unfilled components set to -1. For example, let $\bar{\ell} = 40$ and consider a decision epoch at which the process is in state $s_{60} = ([(6, 3, 4), 9, -1], \bar{1}, 1)$, i.e., $\ell_{(1)} = 6$, $\ell_{(2)} = 3$, $\ell_{(3)} = 4$, $\ell_{(4)} = 9$, $\ell_{(5)} = -1$, $w = \bar{1}$ and $\theta = 1$. Because the only working leads are the younger, current P lead and the current D lead, $a \subseteq \{1, 4\}$. Now, suppose action $a = \emptyset$ is taken and the newly implanted P lead fails 5 years later. Therefore, from equation (A.9), $\hat{\ell}''_{(1)} = 5$, $\hat{\ell}''_{(2)} = 8$, from equation (A.10), $\ell''_{(3)} = 9$, and from equation (A.11), $\psi([(6, 3, 4), 9, -1], \emptyset, 3) = \{11, 14\}$;

hence, at the next decision epoch the process is in state $s_{65} = ([(8,5,9),14,11],\cdot,\cdot)$, i.e., $\ell''_{(1)} = 8$, $\ell''_{(2)} = 5$, $\ell''_{(3)} = 9$, $\ell''_{(4)} = 14$, $\ell''_{(5)} = 11$.

Now, we redefine $u_t(\ell, w, a, n)$ to denote the total expected reward obtained starting from state $s_t = (\ell, w, 1)$ under action a, conditional on the next lead failure occurring in n periods and weighted by its likelihood, i.e.,

$$u_t(\ell, w, a, n) = \begin{cases} \sum_{i\in\{\bar{3},\ldots,3\}} v_i(\ell, w, a, n), & \text{if } n < \overline{T} - t, \\ v_\Delta(\ell, w, a, n). & \text{if } n = \overline{T} - t, \end{cases} \tag{A.12}$$

If $w = \bar{3}$, the only working leads are the current P leads; hence

$$\begin{aligned} v_i(\ell, \bar{3}, a, n) &= \Pr(X_1 > \ell_{(1)} + n | X_1 > \ell_{(1)})^{\mathbb{1}_{\{i\in\{\bar{3},\bar{2},1\}\}}} \\ &\quad \cdot \Pr(X_1 = \ell_{(1)} + n | X_1 > \ell_{(1)})^{\mathbb{1}_{\{i\in\{\bar{1},0,2,3\}\}}} \\ &\quad \cdot \Pr(X_1 > \ell_{(2)} + n | X_1 > \ell_{(2)})^{\mathbb{1}_{\{i\in\{\bar{3},\bar{1},2\}\}}} \\ &\quad \cdot \Pr(X_1 = \ell_{(2)} + n | X_1 > \ell_{(2)})^{\mathbb{1}_{\{i\in\{\bar{2},0,1,3\}\}}} \\ &\quad \cdot \bar{F}_{X_2}(n)^{\mathbb{1}_{\{i\in\{\bar{2},\bar{1},3\}\}}} \cdot p_{X_2}(n)^{\mathbb{1}_{\{i\in\{\bar{3},0,1,2\}\}}} \\ &\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \\ &\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a,n), i, 1) \Bigg), \quad i \in \{\bar{3}, \ldots, 3\} \end{aligned} \tag{A.13}$$

$$\begin{aligned} v_\Delta(\ell, \bar{3}, a, n) &= \Pr(X_1 > \ell_{(1)} + n - 1 | X_1 > \ell_{(1)}) \cdot \Pr(X_1 > \ell_{(2)} + n - 1 | X_1 > \ell_{(2)}) \\ &\quad \cdot \bar{F}_{X_2}(n-1) \cdot \left(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \right). \end{aligned} \tag{A.14}$$

Analogous to equation (A.6), equation (A.13) corresponds to the total expected reward obtained when $w = i$ at patient age $t+n$. Equation (A.14) is also analogous to equation (A.7).

The total expected reward $u_t(\ell, w, a, n)$ for $w \in \{\bar{2}, \bar{1}, 0, 1, 2, 3\}$ is given by the same logic. If $w = \bar{2}$, the older, current P lead and the current D lead are working; hence,

$$\begin{aligned}
\upsilon_i(\ell, \bar{2}, a, n) &= \Pr(X_1 > \ell_{(1)} + n | X_1 > \ell_{(1)})^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{2}, 1\}\}}} \\
&\quad \cdot \Pr(X_1 = \ell_{(1)} + n | X_1 > \ell_{(1)})^{\mathbb{1}_{\{i \in \{\bar{1}, 0, 2, 3\}\}}} \\
&\quad \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{1}, 2\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{2}, 0, 1, 3\}\}}} \\
&\quad \cdot \Pr(X_2 > \ell_{(3)} + n | X_2 > \ell_{(3)})^{\mathbb{1}_{\{i \in \{\bar{2}, \bar{1}, 3\}\}}} \\
&\quad \cdot \Pr(X_2 = \ell_{(3)} + n | X_2 > \ell_{(3)})^{\mathbb{1}_{\{i \in \{\bar{3}, 0, 1, 2\}\}}} \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), w, 0) \\
&\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a, n), i, 1) \Bigg), \quad i \in \{\bar{3}, \ldots, 3\} \qquad \text{(A.15)} \\
\upsilon_\Delta(\ell, \bar{2}, a, n) &= \Pr(X_1 > \ell_{(1)} + n - 1 | X_1 > \ell_{(1)}) \cdot \bar{F}_{X_1}(n-1) \\
&\quad \cdot \Pr(X_2 > \ell_{(3)} + n - 1 | X_2 > \ell_{(3)}) \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), w, 0) \Bigg). \qquad \text{(A.16)}
\end{aligned}$$

Analogously, if $w = \bar{1}$, the younger, current P lead and the current D lead are working; hence, $\upsilon_i(\ell, \bar{1}, a, n)$ and $\upsilon_4(\ell, \bar{1}, a, n)$ are given by equations (A.15) and (A.16) in which '$\ell_{(1)}$' is replaced with '$\ell_{(2)}$.' If $w = 1, 2$, the only working lead is the older and the younger current P lead, respectively; hence

$$\begin{aligned}
\upsilon_i(\ell, w, a, n) &= \Pr(X_1 > \ell_{(w)} + n | X_1 > \ell_{(w)})^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{2}, 1\}\}}} \\
&\quad \cdot \Pr(X_1 = \ell_{(w)} + n | X_1 > \ell_{(w)})^{\mathbb{1}_{\{i \in \{\bar{1}, 0, 2, 3\}\}}} \\
&\quad \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, \bar{1}, 2\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i \in \{\bar{2}, 0, 1, 3\}\}}} \cdot \bar{F}_{X_2}(n)^{\mathbb{1}_{\{i \in \{\bar{2}, \bar{1}, 3\}\}}} \cdot p_{X_2}(n)^{\mathbb{1}_{\{i \in \{\bar{3}, 0, 1, 2\}\}}} \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), w, 0) \\
&\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a, n), i, 1) \Bigg), \quad i \in \{\bar{3}, \ldots, 3\} \qquad \text{(A.17)} \\
\upsilon_\Delta(\ell, w, a, n) &= \Pr(X_1 > \ell_{(w)} + n - 1 | X_1 > \ell_{(w)}) \cdot \bar{F}_{X_1}(n-1) \cdot \bar{F}_{X_2}(n-1) \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a, m), w, 0) \Bigg). \qquad \text{(A.18)}
\end{aligned}$$

If $w = 0$, all the leads are failed; hence,

$$\begin{aligned}
\upsilon_i(\ell,0,a,n) &= \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{3},\bar{2},1\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i\in\{0,3\}\}}} \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{3}\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{2},0,1,3\}\}}} \\
&\quad \cdot \bar{F}_{X_2}(n)^{\mathbb{1}_{\{i\in\{\bar{2},3\}\}}} \cdot p_{X_2}(n)^{\mathbb{1}_{\{i\in\{\bar{3},0,1\}\}}} \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \\
&\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a,n), i, 1) \Bigg), \quad i \in \{\bar{3},\bar{2},0,1,3\} \qquad \text{(A.19)} \\
\upsilon_2(\ell,0,a,n) &= \upsilon_1(\ell,0,a,n) \qquad \text{(A.20)} \\
\upsilon_{\bar{1}}(\ell,0,a,n) &= \upsilon_{\bar{2}}(\ell,0,a,n) \qquad \text{(A.21)} \\
\upsilon_\Delta(\ell,0,a,n) &= \bar{F}_{X_1}(n-1)^2 \cdot \bar{F}_{X_2}(n-1) \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \Bigg). \qquad \text{(A.22)}
\end{aligned}$$

Equations (A.19)-(A.22) are similar in structure to equations (A.6)-(A.7). Lastly, if $w = 3$, the only working lead is the current D lead; hence

$$\begin{aligned}
\upsilon_i(\ell,3,a,n) &= \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{3},\bar{2},1\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i\in\{0,3\}\}}} \cdot \bar{F}_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{3}\}\}}} \cdot p_{X_1}(n)^{\mathbb{1}_{\{i\in\{\bar{2},0,1,3\}\}}} \\
&\quad \cdot \Pr(X_2 > \ell_{(w)} + n | X_2 > \ell_{(3)})^{\mathbb{1}_{\{i\in\{\bar{2},3\}\}}} \cdot \Pr(X_2 = \ell_{(3)} + n | X_2 > \ell_{(3)})^{\mathbb{1}_{\{i\in\{\bar{3},0,1\}\}}} \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \\
&\quad + \eta(n) \cdot \gamma \cdot V_{t+n}(\ell''(a.n), i, 1) \Bigg), \quad i \in \{\bar{3},\bar{2},0,1,3\} \qquad \text{(A.23)} \\
\upsilon_2(\ell,3,a,n) &= \upsilon_1(\ell,3,a,n) \qquad \text{(A.24)} \\
\upsilon_{\bar{1}}(\ell,3,a,n) &= \upsilon_{\bar{2}}(\ell,3,a,n) \qquad \text{(A.25)} \\
\upsilon_\Delta(\ell,3,a,n) &= \bar{F}_{X_1}(n-1)^2 \cdot \Pr(X_2 > \ell_{(3)} + n - 1 | X_2 > \ell_{(3)}) \\
&\quad \cdot \Bigg(r_t(n) + \sum_{m=1}^{n-1} \rho(m) \cdot V_{t+m}(\ell''(a,m), w, 0) \Bigg). \qquad \text{(A.26)}
\end{aligned}$$

Therefore, when $\theta = 1$, the maximum total expected reward is given by (2.24), where $\mu((\ell,w,1),a)$ is updated as defined earlier in this section and $V(\ell''(a,0),w,0)$ is given by equation (A.8).

A.3 MODEL CALIBRATION

Probability of surviving the competing risks of death, $\lambda(\ell)$. From Saxon et al. (2010), patients on average receive ICD devices at age 66 and their one- and five-year survival probabilities are 92% and 68%, respectively. By applying the DEALE method to these values, the former survival probability results in an excess rate of mortality of 0.028, whereas the latter yields 0.022. Hence, we use their midpoint, i.e., 0.025, as the excess rate of mortality for patients with ICD devices, regardless of their age at initial implantation. Applying the same method to CRT-D data yields an excess rate of mortality of 0.075.

Distribution of the time to failure of a new lead, $p_X(x)$ (or $p_{X_1}(x)$) and $p_{X_2}(x)$. As discussed in Section 2.4, to obtain $p_X(x)$, we fit a Gompertz distribution (Cox and Oakes 1984) to the appended data and discretize to obtain a p.m.f., $p_{\tilde{X}}(x)$, which we then adjust so that it exhibits constant hazard after age $\underline{\ell}$. More specifically, we solve the following convex optimization problem that guarantees the probability distribution $p_X(x)$ (i) is "smooth," (ii) has a mean as close as possible to the mean of the p.m.f. and (iii) has constant hazard after $\underline{\ell}$:

$$\min_{p_X, h_X, c} \left(\sum_{i=1}^{\bar{\ell}} i \cdot p_X(i) - \sum_{i=1}^{\bar{\ell}} i \cdot p_{\tilde{X}}(i) \right)^2 \tag{A.27a}$$

subject to

$$\sum_{i=1}^{\bar{\ell}} p_X(i) = 1, \tag{A.27b}$$

$$h_X(i) = \frac{p_X(i)}{\bar{F}_X(i-1)} = c, \qquad i = \underline{\ell}, \underline{\ell}+1, \ldots, \bar{\ell}-1, \tag{A.27c}$$

$$h_X(\bar{\ell}) = \frac{p_X(\bar{\ell})}{\bar{F}_X(\bar{\ell}-1)} = 1, \tag{A.27d}$$

$$h_X(i) = \frac{p_X(i)}{\bar{F}_X(i-1)} \leq \frac{p_X(i+1)}{\bar{F}_X(i)}, \qquad i = 1, 2, \ldots, \underline{\ell}-1, \tag{A.27e}$$

$$|p_X(i) - p_{\tilde{X}}(i)| \leq \epsilon_1, \qquad i = 1, 2, \ldots, 8, \tag{A.27f}$$

$$p_X(i) - p_X(i-1) \leq \epsilon_2, \qquad i = 9, \ldots, \underline{\ell}, \tag{A.27g}$$

$$p_X(i) \geq 0,\ h_X(i) \geq 0, \qquad i = 1, 2, \ldots, \underline{\ell}-1, \tag{A.27h}$$

$$c \geq 0. \tag{A.27i}$$

Table 20: Estimated hazard function for both pacemaker and ICD leads for all values of ω.

(a) pacemaker lead

Lead age (yrs)	Estimated hazard function when $\omega = 0.45$	$\omega = 0.5$	$\omega = 0.55$
0	0	0	0
1	0.005980	0.006197	0.006456
2	0.006341	0.006597	0.006898
3	0.006817	0.007114	0.007454
4	0.007444	0.007783	0.008158
5	0.008276	0.008651	0.009053
6	0.009380	0.009779	0.010190
7	0.010849	0.011247	0.011638
8	0.012806	0.013160	0.013483
9	0.023678	0.024070	0.024432
10	0.035217	0.035662	0.036078
11	0.047868	0.048387	0.048876
12	0.062212	0.062833	0.063423
13	0.079067	0.079835	0.080568
14	0.099675	0.099492	0.091316
15	0.108319	0.099492	0.091316
16-68	0.108324	0.099492	0.091317
69	1	1	1

(b) ICD lead

Lead age (yrs)	Estimated hazard function when $\omega = 0.4$	$\omega = 0.45$	$\omega = 0.5$
0	0	0	0
1	0.030700	0.032162	0.033672
2	0.032678	0.033800	0.034924
3	0.034808	0.035541	0.036239
4	0.037104	0.037395	0.037624
5	0.039584	0.039371	0.039082
6	0.042265	0.041480	0.040622
7	0.045168	0.043736	0.042251
8	0.048320	0.046069	0.043754
9	0.063774	0.060759	0.052099
10	0.073465	0.063082	0.052099
11	0.073465	0.063082	0.052099
12	0.073465	0.063082	0.052099
13	0.073465	0.063082	0.052099
14	0.073465	0.063082	0.052099
15	0.073465	0.063082	0.052099
16-68	0.073465	0.063082	0.052099
69	1	1	1

The objective function minimizes the difference between the means of $\tilde{X}$ and X. Constraint (A.27b) guarantees that p_X is a discrete probability distribution. Constraints (A.27c) and (A.27d) ensure the constant hazard property after age $\underline{\ell}$ and certain lead failure at age $\bar{\ell}$, respectively. Constraint (A.27e) enforces the increasing failure rate property before age ℓ. Constraint (A.27f) ensures the estimated distribution closely follows $p_{\tilde{X}}(x)$ in the first 8 years, for which published data are readily available. Constraint (A.27g) ensures a smooth distribution after the first 8 years by limiting the magnitude of variation in the estimated probabilities from one year to another. Finally, we let $\epsilon_1 = 0.005$ and $\epsilon_2 = 0.01$ and solve the model given by (A.27) using GAMS/Baron (BARON version 9.0.6. Built: LNX Sat May 22 23:10:41 EDT 2010, with GAMS Rev 235 LEX-LEI 23.5.1 x86_64/Linux). Table 20 provides the estimated hazard functions.

We obtain the values of the decision variables by up to eight significant digits. To ensure that the constant hazard property after $\underline{\ell}$ is not compromised due to possible precision errors, we use the values of variables $h_X(i)$, $i = 1, \ldots, \bar{\ell}$, and c to estimate the values of $p_X(i)$, $i = 1, \ldots, \bar{\ell}$, when needed. It is worth mentioning that the estimated and the software-generated optimal solution values of $p_X(i)$, $i = 1, \ldots, \bar{\ell}$, match by up to seven significant digits.

Table 21: Estimated probability of death following lead extraction, $\beta_{-1}(\ell)$.

Lead age, ℓ (yrs)	Probability of death following lead extraction, $\boldsymbol{\beta_{-1}(\ell)}$		
	low	average	high
0	0.001555	0.002066	0.002577
1	0.001821	0.002332	0.002843
2	0.002116	0.002627	0.003138
3	0.002440	0.002951	0.003462
4	0.002798	0.003309	0.003820
5	0.003190	0.003701	0.004212
6	0.003619	0.004130	0.004641
7	0.004089	0.004600	0.005111
8	0.004601	0.005112	0.005623
9	0.005158	0.005669	0.006180
10	0.005764	0.006275	0.006786
11	0.006420	0.006931	0.007442
12	0.007130	0.007641	0.008152
13	0.007897	0.008408	0.008919
14	0.008723	0.009234	0.009745
15	0.009612	0.010123	0.010634
16+	0.010566	0.011077	0.011588

Probability of death following extraction of a lead of age ℓ, $\beta_{-1}(\ell)$. Recall that Table 3 summarizes the published data on lead extraction procedure-induced mortality. In this table, the mean lead dwell time is the reported mean lead implant duration in each study. Note that in Table 3, to obtain the number of deceased patients, we consider all procedure-induced deaths during the perioperative period, from admission to recovery, plus a short term follow-up whenever data is available. We exclude infection-induced mortality when the indication of death is given. Finally, the observed mortality following lead extraction is given by the ratio of the number of reported deaths to the number of extracted leads.

The number of reported deaths in Table 3 are obtained as follows. Byrd et al. (1999) report one instance of death in 2,338 patients undergoing lead extraction. In a study by Epstein et al. (1999), using the three comparably safe and effective methods of lead extraction, four, one and two out of, respectively, 248, 177, 438 patients died during the perioperative period. At one month follow-up, complications associated with lead extraction had resulted in death in three additional patients in the first group and four additional patients in the third group, resulting the final death tally of seven, one and six as reported in Table 3. In a study by Kennergren (1999), no mortality is reported during the somewhat short mean hospital stay of three days. Wilkoff et al. (1999) report one case of mortality out of 153 patients. Byrd et al. (2002) report 13 in-hospital deaths in 1,684 patients who underwent lead extraction. In this study, 10 additional patients died in the following 69 ± 66 days. However, because of the somewhat long mean follow-up length and the unspecified indication of death, we use 13 as the number of procedure-induced deaths. Saad et al. (2003), Roux et al. (2007) and Bongiorni et al. (2008) report one, one and three cases of death, respectively. No in-hospital death was reported by Jones IV et al. (2008). In a study by Agarwal et al. (2009), only one case of death is observed. In a study by Kennergren et al. (2009), 592 patients underwent 647 extraction procedures, resulting in the death of three; however, one death is excluded from Table 3 as it was caused by infection. Finally, in a study by Wazni et al. (2010), out of 1,449 patients, 27 died during the hospitalization, out of which only four were specified as lead extraction procedure-induced.

As discussed in Section 2.4, to estimate $\beta_{-1}(\ell)$, we fit a Gompertz function to the observed probability of death reported in Table 3, which we then shift by $\pm 10\%$ of its mid-range value to obtain two additional estimates for $\beta_{-1}(\ell)$. Table 21 reports the estimated probability of death following lead extraction for the three resulting functions.

Probability of surviving infection, δ. Sohail et al. (2007a) report seven out of 189 patients with infected pacemaker or ICD devices died during hospitalization and two additional patients died following a three month follow-up, partially due to the mismanagement of the infection. In this study, 40 patients were lost to follow-up. Considering that two out of 142 patients died in a three month period after the infection occurred, we estimate the total number of deaths from direct or indirect consequences of the infection to be ten out of 189 patients, i.e., almost 5%. Hence, a point estimate for the probability of surviving infection is on the order of 95%.

Because the total number of extracted leads and the mean lead dwell time is not given in the study by Sohail et al. (2007a), we use Table 3 to obtain a point estimate for the average ratio of extracted leads to patients. First, note that although the number of extracted leads in the study by Saad et al. (2003) is reported as 161 in Table 3, the total number of leads removed in this study is 262. (The number 161 is the size of a subgroup of leads to which the analysis in the study by Saad et al. (2003) is restricted.) An estimated ratio of extracted leads to patients from the studies reported in Table 3 is as follows:

$$\frac{1}{14}\cdot\left(\frac{3,540}{2,338}+\frac{413}{248}+\frac{201}{177}+\frac{671}{438}+\frac{179}{149}+\frac{244}{153}+\frac{2,561}{1,684}+\frac{262}{161}+\frac{270}{175}+\frac{2,065}{1,193}\right.$$
$$\left.+\frac{975}{498}+\frac{456}{212}+\frac{1,032}{592}+\frac{2,405}{1,449}\right)\simeq 1.6. \tag{A.28}$$

APPENDIX B

PROOFS

B.1 PROOFS FOR CHAPTER 3

Proof of Lemma 1. Clearly, the lemma holds for patient age $\ell = \bar{\ell}$. For $\ell < \bar{\ell}$, the proof follows by induction on u. We discretize the state space in the u dimension using $\bar{\delta}$ given by equation (3.5). Therefore, for any fixed patient age $\ell < \bar{\ell}$ and remaining battery capacity $u = \bar{\delta}$, by equations (3.2)-(3.5), we have

$$\begin{aligned} V(\ell, \bar{\delta}) &= \max\{R(\ell), C(\ell, \bar{\delta})\} \\ &= \max\Bigg\{1 + (1 - \alpha_\Delta(\ell)) \cdot \lambda(\ell) \cdot V(\ell + 1, \bar{u}), \\ &\qquad 1 + \sum_{d=0}^{g(\bar{\delta})} \lambda(\ell) \cdot V(\ell + 1, \bar{\delta} - \delta - d \cdot \delta_c) \cdot p_D(d)\Bigg\} \\ &\geq 0. \end{aligned} \tag{B.1}$$

Hence, $V(\ell, \bar{\delta}) \geq V(\ell, 0) = 0$.

Now, suppose for any given $\ell < \bar{\ell}$ and $u = \bar{\delta}, 2\bar{\delta}, \ldots, (k-1)\bar{\delta}$ we have

$$V(\ell, u + \bar{\delta}) \geq V(\ell, u). \tag{B.2}$$

Next, we show that $V(\ell, u + \bar{\delta}) \geq V(\ell, u)$ for $u = k\bar{\delta}$.

From equations (3.2), (3.3) and (3.4), for any fixed patient age $\ell < \bar{\ell}$ and remaining battery capacity $u = k\bar{\delta}$, we have

$$\begin{aligned} V(\ell, k\bar{\delta} + \bar{\delta}) &= \max\{R(\ell), C(\ell, (k+1)\bar{\delta})\} \\ &= \max\left\{R(\ell), 1 + \sum_{d=0}^{g((k+1)\bar{\delta})} \lambda(\ell) \cdot V(\ell+1, (k+1)\bar{\delta} - \delta - d \cdot \delta_c) \cdot p_D(d)\right\} \quad \text{(B.3)} \\ &\geq \max\left\{R(\ell), 1 + \sum_{d=0}^{g(k\bar{\delta})} \lambda(\ell) \cdot V(\ell+1, k\bar{\delta} - \delta - d \cdot \delta_c) \cdot p_D(d)\right\} \quad \text{(B.4)} \\ &= \max\left\{R(\ell), C(\ell, k\bar{\delta})\right\} \\ &= V(\ell, k\bar{\delta}). \quad \text{(B.5)} \end{aligned}$$

Inequality (B.4) follows from equation (3.2), equation (B.2), the induction hypothesis, and the fact that $g(u)$, given by equation (3.1), is non-decreasing in u. Therefore, the result follows.

□

Proof of Corollary 1. The result follows from Lemma 1 and the fact that $g(u)$, given by equation (3.1), is non-decreasing in u. □

Proof of Lemma 2. Clearly, from equation (3.2), the lemma holds for battery capacity $u \leq 0$. For any battery capacity $u > 0$ and patient age $\ell = \bar{\ell}$, we have

$$V(\bar{\ell}, u) = 0. \quad \text{(B.6)}$$

Also, for any fixed remaining battery capacity $u > 0$ and patient age $\ell = \bar{\ell} - 1$, by (3.2), we have

$$V(\bar{\ell} - 1, u) = \max\{R(\bar{\ell} - 1), C(\bar{\ell} - 1, u)\} = 1. \quad \text{(B.7)}$$

Hence, $V(\bar{\ell} - 1, u) \geq V(\bar{\ell}, u)$.

Now suppose for any fixed remaining battery capacity $u > 0$ we have

$$V(\ell, u) \geq V(\ell + 1, u) \quad \text{(B.8)}$$

where $\ell = \bar{\ell} - 2, \bar{\ell} - 3, \ldots, k$ and $k > \underline{\ell}$. Next, we show $V(\ell, u) \geq V(\ell + 1, u)$ for $\ell = k - 1$.

From equations (3.2), (3.3) and (3.4), for any fixed remaining battery capacity $u > 0$ and patient age $\ell = k - 1$ we have

$$\begin{aligned} V(k-1,u) &= \max\{R(k-1), C(k-1,u)\} \\ &= \max\Bigg\{1 + (1-\alpha_\Delta(k-1)) \cdot \lambda(k-1) \cdot V(k,\bar{u}), \\ &\qquad 1 + \sum_{d=0}^{g(u)} \lambda(k-1) \cdot V(k, u-\delta-d\cdot\delta_c) \cdot p_D(d)\Bigg\} \\ &\geq \max\Bigg\{1 + (1-\alpha_\Delta(k)) \cdot \lambda(k) \cdot V(k+1,\bar{u}), \\ &\qquad 1 + \sum_{d=0}^{g(u)} \lambda(k) \cdot V(k+1, u-\delta-d\cdot\delta_c) \cdot p_D(d)\Bigg\} \qquad \text{(B.9)} \\ &= \max\{R(k), C(k,u)\}, \qquad \text{(B.10)} \end{aligned}$$

where equation (B.9) follows from equation (3.2), equation (B.8), the induction hypothesis, and the assumptions that $\lambda(\ell)$ and $\alpha_\Delta(\ell)$ are non-increasing and non-decreasing in ℓ, respectively. Hence, the result follows. □

Proof of Corollary 2. The result follows from Lemma 2 and the assumptions that $\lambda(\ell)$ and $\alpha_\Delta(\ell)$ are non-increasing and non-decreasing in ℓ, respectively. □

Proof of Theorem 1. From equation (3.3), for any fixed patient age ℓ, $R(\ell)$ is constant in u. Also, by Corollary 1, for any fixed patient age ℓ, $C(\ell,u)$ is non-decreasing in u. Since by equation (3.2), $V(\ell,u)$ is given as the maximum of $R(\ell)$ and $C(\ell,u)$, the result follows. □

Proof of Lemma 3. Let $C^i(\ell,u)$ and $R^i(\ell)$ denote the reward obtained if the decision is to "wait" or "replace," respectively, where $\alpha_\Delta(\ell) = \alpha^i_\Delta(\ell)$. Let

$$\alpha^2_\Delta(\ell) \;\geq\; \alpha^1_\Delta(\ell), \forall \ell \leq \bar{\ell}. \qquad \text{(B.11)}$$

Clearly, from equation (3.2), the lemma holds for battery capacity $u \leq 0$. For battery capacity $u > 0$, the proof follows using an induction on ℓ.

For any given $u > 0$ and $\ell = \bar{\ell} - 1$, from equation (3.2) we have,

$$V^i(\bar{\ell}-1,u) = 1 \quad i = 1,2. \qquad \text{(B.12)}$$

Hence, $V^1(\bar{\ell}-1,u) = V^2(\bar{\ell}-1,u)$.

Suppose, for $\ell = \bar{\ell} - 2, \bar{\ell} - 3, \ldots, k$ and any given $u > 0$, we have

$$V^2(\ell, u) \leq V^1(\ell, u). \tag{B.13}$$

Therefore, for any given $u > 0$ and $\ell = k - 1$, from equation (3.2) we have

$$\begin{aligned}
V^2(k-1,u) &= \max\{R^2(k-1), C^2(k-1,u)\} \\
&= \max\Bigg\{1 + (1 - \alpha^2_\Delta(k-1)) \cdot \lambda(k-1) \cdot V^2(k, \bar{u}), \\
&\qquad 1 + \sum_{d=0}^{g(u)} \lambda(k-1) \cdot V^2(k, u - \delta - d \cdot \delta_c) \cdot p_D(d)\Bigg\} \\
&\leq \max\Bigg\{1 + (1 - \alpha^1_\Delta(k-1)) \cdot \lambda(k-1) \cdot V^1(k, \bar{u}), \\
&\qquad 1 + \sum_{d=0}^{g(u)} \lambda(k-1) \cdot V^1(k, u - \delta - d \cdot \delta_c) \cdot p_D(d)\Bigg\} \qquad \text{(B.14)} \\
&= \max\{R^1(k-1), C^1(k-1,u)\} \\
&= V^1(k-1,u), \qquad \text{(B.15)}
\end{aligned}$$

where equation (B.14) follows by equations (3.2) and (B.11) and the induction hypothesis, equation (B.13). Therefore, the result follows. □

Proof of Corollary 3. The result follows from Lemma 3 and equation (B.11). □

Proof of Lemma 4. The proof is completed similar to the proof of Lemma 3, when using Lemma 1 and Lemma 4.7.2 on page 106, Puterman (1994). □

Proof of Corollary 4. The result follows from Lemmas 1 and 4 as well as Lemma 4.7.2 on page 106, Puterman (1994). □

Proof of Lemma 5. The proof is completed similar to the proof of Lemma 3, when using Lemma 1 and equation (3.1). □

Proof of Corollary 5. The result follows from Lemmas 1 and 5 and equation (3.1). □

B.2 PROOFS FOR CHAPTER 4

Proof of Lemma 6. Differentiating $V(\tau, n)$ twice yields

$$\begin{aligned}\frac{\partial^2 V(\tau,n)}{\partial \tau^2} &= n\, r'(\tau) + n^2\, r'\big(L - n\cdot(\tau + f(\tau))\big)(1+f'(\tau))^2 \\ &\quad -n\, r\big(L - n\cdot(\tau+f(\tau))\big) f''(\tau) \\ &< 0, \end{aligned} \tag{B.16}$$

where (B.16) follows from **A1** and **A2**. □

Proof of Lemma 7. For a fixed $n \in (0, \bar{n}_{max})$, consider the function

$$\rho(\tau) = \big(1 + f'(\tau)\big) r(L - n\cdot(\tau + f(\tau))).$$

By assumptions **A1**-**A3**, $\rho(0) = r(L - nf(0)) < r(0)$. Similarly,

$$\rho(\bar{\tau}_n) = (1 + f'(\bar{\tau}_n))\, r(0) \geq r(0) > r(\bar{\tau}_n).$$

Because the functions $\rho(\tau)$ and $r(\tau)$ are continuous for $\tau \in [0, \bar{\tau}_n]$, τ_n exists and $0 < \tau_n < \bar{\tau}_n$. Uniqueness follows because $r(\tau)$ is strictly decreasing and $\rho(\tau)$ is increasing. Lemma 6 with (4.8) and (4.9) implies that τ_n maximizes $V(\tau, n)$ over $\tau \in (0, \bar{\tau}_n)$ for any fixed $n \in (0, \bar{n}_{max})$. □

Proof of Lemma 8. Define

$$g(n,\tau) = r(\tau) - \big(1 + f'(\tau)\big)\, r\big(L - n\cdot(\tau + f(\tau))\big),$$

where $(n,\tau) \in \{(n,\tau) \in \mathbb{R}^2_+ \mid n \in (0, \bar{n}_{max}),\ \tau \in (0, \bar{\tau}_n)\}$. By Lemma 7, for any fixed $n \in (0, \bar{n}_{max})$, $g(n, \tau_n) = 0$. Note that $\frac{\partial g(n,\tau)}{\partial \tau}|_{\tau=\tau_n} < 0$ and hence, it is always non-zero. Therefore, by the Implicit Function Theorem, τ_n is a continuously differentiable function of n (see Knapp (2005), page 155). Equation (4.9) implies that $\frac{\partial \tau_n}{\partial n} \leq 0$, i.e., τ_n is decreasing in n, since otherwise, due to assumptions **A1** and **A2**, equation (4.9) would be violated as its left-hand-side would decrease while its right-hand-side would increase. Differentiating $V(\tau_n, n)$ twice yields

$$\begin{aligned}\frac{\partial^2 V(\tau_n,n)}{\partial n^2} &= -\frac{\big(\tau_n + f(\tau_n)\big)}{1+f'(\tau_n)} \cdot \frac{\partial \tau_n}{\partial n} \cdot \Big(r'(\tau_n) - f''(\tau_n)\cdot r\big(L - n\cdot(\tau_n + f(\tau_n))\big)\Big) \\ &\leq 0, \end{aligned} \tag{B.17}$$

which follows by **A1** and **A2** and the fact that $\frac{\partial \tau_n}{\partial n} \leq 0$. □

Proof of Theorem 2. The proof directly follows from Lemmas 6 and 8 as well as the definition of $\tilde{n}$. □

Proof of Proposition 1. The result follows from equation (4.9) and assumptions **A1** and **A2.** □

Proof of Proposition 2. (i) From equation (4.9) and assumption **A1**

$$\tau_n = L - n \cdot (\tau_n + \Delta). \tag{B.18}$$

Therefore, the optimal interval is

$$\tau_n = \frac{L - n\Delta}{n+1}. \tag{B.19}$$

(ii) Consider a fixed $n \in [1, n_{max}] \cap \mathbb{Z}_+$. Then

$$\frac{L}{n+1} - \Delta \leq \frac{L}{n+1} - \frac{n\Delta}{n+1} < \frac{L}{n} - \Delta.$$

(iii) Substituting (B.19) into equation (4.10) yields

$$\begin{aligned} \int_0^{\tau_n} r(t)\,\mathrm{d}t &= (\tau_n + \Delta) r(\tau_n) \\ &= \left(\frac{L+\Delta}{n+1}\right) r(\tau_n), \end{aligned} \tag{B.20}$$

and hence

$$\tilde{n} = \frac{(L+\Delta)\, r(\tau_{\tilde{n}})}{\int_0^{\tau_{\tilde{n}}} r(t)\,\mathrm{d}t} - 1. \tag{B.21}$$

□

Proof of Proposition 3. From Proposition 2, for any feasible non-zero $n \in \mathbb{Z}$, the optimal maintenance interval τ_n is given by equation (B.19) and satisfies equation (4.6). Also, by Lemma 6, $V(\tau, n)$ is strictly concave in τ. As a result, the total lost reward attains its maximum at one of the endpoints in (4.6). Therefore,

$$\begin{aligned}
&\max_{\frac{L}{n+1}-\Delta \le \tau < \frac{L}{n}-\Delta} \{V(\tau_n, n) - V(\tau, n)\} = \\
&\max\left\{V\left(\frac{L-n\Delta}{n+1}, n\right) - V\left(\frac{L}{n+1} - \Delta, n\right), V\left(\frac{L-n\Delta}{n+1}, n\right) - V\left(\frac{L}{n} - \Delta, n\right)\right\} \quad \text{(B.22)} \\
&\le \max\left\{\max_{\frac{L}{n+1}-\Delta \le \tau \le \frac{L-n\Delta}{n+1}} \left|\frac{\partial V(\tau, n)}{\partial \tau}\right| \cdot \left(\left(\frac{L-n\Delta}{n+1}\right) - \left(\frac{L}{n+1} - \Delta\right)\right),\right. \\
&\left.\max_{\frac{L-n\Delta}{n+1} \le \tau < \frac{L}{n}-\Delta} \left|\frac{\partial V(\tau, n)}{\partial \tau}\right| \cdot \left(\left(\frac{L}{n} - \Delta\right) - \left(\frac{L-n\Delta}{n+1}\right)\right)\right\} \\
&= \max\left\{\max_{\frac{L}{n+1}-\Delta \le \tau \le \frac{L-n\Delta}{n+1}} |n \cdot (r(\tau) - r(L - n \cdot (\tau + \Delta)))| \cdot \left(\frac{\Delta}{n+1}\right),\right. \\
&\left.\max_{\frac{L-n\Delta}{n+1} \le \tau < \frac{L}{n}-\Delta} |n \cdot (r(\tau) - r(L - n \cdot (\tau + \Delta)))| \cdot \left(\frac{L-n\Delta}{n(n+1)}\right)\right\} \\
&= \max\left\{n \cdot \left(r\left(\frac{L}{n+1} - \Delta\right) - r\left(\frac{L}{n+1}\right)\right) \cdot \frac{\Delta}{n+1},\right. \\
&\left. n \cdot \left|r\left(\frac{L}{n} - \Delta\right) - r(0)\right| \cdot \frac{L-n\Delta}{n(n+1)}\right\} \\
&= \max\left\{\frac{n\Delta}{n+1} \cdot \left(r\left(\frac{L}{n+1} - \Delta\right) - r\left(\frac{L}{n+1}\right)\right),\right. \\
&\left.\frac{L-n\Delta}{(n+1)} \cdot \left(r(0) - r\left(\frac{L}{n} - \Delta\right)\right)\right\}. \quad \text{(B.23)}
\end{aligned}$$

Hence, the result follows. □

Proof of Corollary 7. The result follows from equations (4.15) and (B.22). □

Proof of Proposition 4. Lemma 7 and Proposition 1 imply that $\frac{L}{n} - f(\tau_n) \ge \frac{(n+1)\tau_n}{n} > \tau_n$; thus, if for $\tau = \tau_n$ condition (4.6) does not hold, then $\tau_n < \frac{L}{n+1} - f(\tau_n)$. Furthermore, $n < n_{max}$ because $\tau_n > 0$ (Lemma 7) and $\frac{L}{n_{max}+1} - f(\tau_{n_{max}}) \le \frac{L}{n_{max}+1} - f(0) \le 0$, where the last inequality follows from the definition of n_{max}. Therefore, $0 < n \le n_{max} - 1$, in which case $\underline{\tau}_n$ exists. Moreover, $\underline{\tau}_n > \tau_n$ due to assumption **A2** and the fact that (4.6) does not

hold. Finally, because Lemma 6 still holds, $V(\tau, n)$ is concave in τ and the optimal total reward for the given n is attained at $\underline{\tau}_n$. □

Proof of Lemma 9. First, we prove by induction that the result holds for $t \leq \Delta$. For $t = 0$, by (4.18),

$$V^*(0, \alpha) = 0 \geq V^*(0, \alpha + 1) = 0 \quad \forall \alpha \geq 0. \tag{B.24}$$

Now, suppose for $t = 1, 2, \ldots, \bar{t} - 1$, where $0 < \bar{t} - 1 < \Delta$,

$$V^*(t, \alpha) \geq V^*(t, \alpha + 1) \quad \forall \alpha \geq 0. \tag{B.25}$$

For $t = \bar{t}$ we have,

$$\begin{aligned} V^*(\bar{t}, \alpha) &= \big(R(\alpha + 1) - R(\alpha)\big) + h_Y(\alpha) \cdot \big(0 - c\big) + \big(1 - h_Y(\alpha)\big) \cdot V^*(\bar{t} - 1, \alpha + 1) \\ &\geq \big(R(\alpha + 2) - R(\alpha + 1)\big) + h_Y(\alpha + 1) \cdot \big(0 - c\big) \\ &\quad + \big(1 - h_Y(\alpha + 1)\big) \cdot V^*(\bar{t} - 1, \alpha + 2) \qquad \text{(B.26)} \\ &= V^*(\bar{t}, \alpha + 1), \qquad \text{(B.27)} \end{aligned}$$

where (B.26) follows from **A1**, **A4** and the induction hypothesis (B.25). Therefore, the reward function is monotone in α for $t \leq \Delta$, i.e., for $t = 0, 1, \ldots, \Delta$,

$$V^*(t, \alpha) \geq V^*(t, \alpha + 1) \quad \forall \alpha \geq 0. \tag{B.28}$$

Next, we complete the proof by establishing the monotonicity of the function in α for $\Delta + 1 \leq t \leq L$. As before, we proceed by induction. By (4.21), for $t = \Delta + 1$ we have

$$\begin{aligned} V^*(\Delta + 1, \alpha) &= \big(R(\alpha + 1) - R(\alpha)\big) + h_Y(\alpha) \cdot (V^*(0, 0) - c) \\ &\quad + (1 - h_Y(\alpha)) \cdot \max\{V^*(0, 0), V^*(\Delta, \alpha + 1)\} \\ &\geq \big(R(\alpha + 2) - R(\alpha + 1)\big) + h_Y(\alpha + 1) \cdot (V^*(0, 0) - c) \\ &\quad + (1 - h_Y(\alpha + 1)) \cdot \max\{V^*(0, 0), V^*(\Delta, \alpha + 2)\} \qquad \text{(B.29)} \\ &= V^*(\Delta + 1, \alpha + 1), \qquad \text{(B.30)} \end{aligned}$$

where (B.29) follows from **A1**, **A4** and (B.28). Suppose for $t = \Delta + 2, \Delta + 3, \ldots, \bar{t} - 1$, where $\Delta + 1 < \bar{t} - 1 < L$, we have

$$V^*(t, \alpha) \geq V^*(t, \alpha + 1) \quad \forall \alpha \geq 0, \tag{B.31}$$

and consider $V^*(\bar{t}, \alpha)$. First, let

$$V^*(\bar{t} - 1 - \Delta, 0) = \vartheta, \tag{B.32}$$

$$V^*(\bar{t} - 1, \alpha + 1) = \iota, \tag{B.33}$$

$$\text{and } V^*(\bar{t} - 1, \alpha + 2) = \kappa, \tag{B.34}$$

and note that by (B.31),

$$\iota \geq \kappa. \tag{B.35}$$

Therefore, for $t = \bar{t}$,

$$V^*(\bar{t}, \alpha) = \big(R(\alpha + 1) - R(\alpha)\big) + h_Y(\alpha) \cdot (\vartheta - c) + (1 - h_Y(\alpha)) \cdot \max\{\vartheta, \iota\} \tag{B.36}$$

and

$$\begin{aligned} V^*(\bar{t}, \alpha + 1) &= \big(R(\alpha + 2) - R(\alpha + 1)\big) + h_Y(\alpha + 1) \cdot (\vartheta - c) \\ &\quad + (1 - h_Y(\alpha + 1)) \cdot \max\{\vartheta, \kappa\}. \end{aligned} \tag{B.37}$$

The relation between (B.36) and (B.37) can be established using the three possible relations between (B.32), (B.33) and (B.34):
(i) $\vartheta \geq \iota$. By (B.35), $\vartheta \geq \iota \geq \kappa$. Hence,

$$\begin{aligned} V^*(\bar{t}, \alpha) &= \big(R(\alpha + 1) - R(\alpha)\big) + h_Y(\alpha) \cdot (\vartheta - c) + (1 - h_Y(\alpha)) \cdot \vartheta \\ &= \big(R(\alpha + 1) - R(\alpha)\big) + h_Y(\alpha) \cdot (-c) + \vartheta \\ &\geq \big(R(\alpha + 2) - R(\alpha + 1)\big) + h_Y(\alpha + 1) \cdot (-c) + \vartheta \qquad \text{(B.38)} \\ &= \big(R(\alpha + 2) - R(\alpha + 1)\big) + h_Y(\alpha + 1) \cdot (\vartheta - c) + (1 - h_Y(\alpha + 1)) \cdot \vartheta \\ &= V^*(\bar{t}, \alpha + 1), \qquad \text{(B.39)} \end{aligned}$$

where (B.38) follows from **A1** and **A4**.
(ii) $\vartheta \leq \iota$ and $\vartheta \leq \kappa$. By (B.35),

$$\iota \geq \kappa \geq \vartheta. \tag{B.40}$$

Hence,

$$\begin{aligned} V^*(\bar{t},\alpha) &= \big(R(\alpha+1)-R(\alpha)\big)+h_Y(\alpha)\cdot(\vartheta-c)+(1-h_Y(\alpha))\cdot\iota \\ &\geq \big(R(\alpha+1)-R(\alpha)\big)+h_Y(\alpha)\cdot(\vartheta-c)+(1-h_Y(\alpha))\cdot\kappa \qquad \text{(B.41)} \\ &= \big(R(\alpha+1)-R(\alpha)\big)+h_Y(\alpha)\cdot(-c)+\kappa+h_Y(\alpha)\cdot(\vartheta-\kappa) \\ &\geq \big(R(\alpha+2)-R(\alpha+1)\big)+h_Y(\alpha+1)\cdot(-c)+\kappa+h_Y(\alpha+1)\cdot(\vartheta-\kappa) \qquad \text{(B.42)} \\ &= \big(R(\alpha+2)-R(\alpha+1)\big)+h_Y(\alpha+1)\cdot(\vartheta-c)+(1-h_Y(\alpha+1))\cdot\kappa \\ &= V^*(\bar{t},\alpha+1), \qquad \text{(B.43)} \end{aligned}$$

where (B.41) follows from (B.40) and (B.42) follows from **A1**, **A4** and (B.40).
(*iii*) $\vartheta \leq \iota$ and $\vartheta \geq \kappa$. By (B.35),

$$\iota \geq \vartheta \geq \kappa. \qquad \text{(B.44)}$$

Hence,

$$\begin{aligned} V^*(\bar{t},\alpha) &= \big(R(\alpha+1)-R(\alpha)\big)+h_Y(\alpha)\cdot(\vartheta-c)+(1-h_Y(\alpha))\cdot\iota \\ &= \big(R(\alpha+1)-R(\alpha)\big)+h_Y(\alpha)\cdot(-c)+(1-h_Y(\alpha))\cdot(\iota-\vartheta)+\vartheta \\ &\geq \big(R(\alpha+2)-R(\alpha+1)\big)+h_Y(\alpha+1)\cdot(-c)+\vartheta \qquad \text{(B.45)} \\ &= \big(R(\alpha+2)-R(\alpha+1)\big)+h_Y(\alpha+1)\cdot(\vartheta-c)+(1-h_Y(\alpha+1))\cdot\vartheta \\ &= V^*(\bar{t},\alpha+1), \qquad \text{(B.46)} \end{aligned}$$

where (B.45) follows from **A1**, **A4** and (B.44).
Hence, $V^*(\bar{t},\alpha) \geq V^*(\bar{t},\alpha+1)\ \forall\alpha \geq 0$, which implies that $V^*(t,\alpha)$ is nonincreasing in α for $t \geq \Delta+1$ and the result follows. □

Proof of Lemma 10. First, we establish the monotonicity of the reward function in t for $t \leq \Delta$. Next, we show that for every virtual age, the reward function is greater at $t=\Delta+1$ than at $t=\Delta$. Finally, by proving the monotonicity of the reward function in $t \geq \Delta+1$, the result follows.

Note that by **A1** and **A4**, $R(\alpha)-R(\alpha-1)$ and $h_Y(\alpha)$ are decreasing and nondecreasing in α, respectively. Hence, by (4.22), for all $\alpha = 1,2,\ldots,L-1$,

$$R(\alpha)-R(\alpha-1) \geq c\cdot h_Y(\alpha-1). \qquad \text{(B.47)}$$

First, consider the case where $t \leq \Delta$. When $t = 1$, by (4.20),

$$\begin{aligned} V^*(1,\alpha) &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (0-c) + (1-h_Y(\alpha)) \cdot V^*(0,\alpha+1) \\ &= R(\alpha+1) - R(\alpha) - c \cdot h_Y(\alpha) \qquad \text{(B.48)} \\ &\geq V^*(0,\alpha) = 0, \qquad \text{(B.49)} \end{aligned}$$

where (B.48) follows from (4.18) and (B.49) follows from (B.47).
Now, suppose for $t = 2, 3, \ldots, \bar{t}-1$, where $1 < \bar{t} - 1 < \Delta$, we have

$$V^*(t-1,\alpha) \leq V^*(t,\alpha) \ \forall \alpha \geq 0. \qquad \text{(B.50)}$$

For $t = \bar{t}$ we obtain

$$\begin{aligned} V^*(\bar{t},\alpha) &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (0-c) + (1-h_Y(\alpha)) \cdot V^*(\bar{t}-1,\alpha+1) \\ &\geq R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (0-c) + (1-h_Y(\alpha)) \cdot V^*(\bar{t}-2,\alpha+1) \qquad \text{(B.51)} \\ &= V^*(\bar{t}-1,\alpha), \qquad \text{(B.52)} \end{aligned}$$

where (B.51) follows from the induction hypothesis given by (B.50). Therefore, the reward function is monotone in $t \leq \Delta$.

Next, we show that $V^*(\Delta+1,\alpha) \geq V^*(\Delta,\alpha)$. When $t = \Delta+1$, by equation (4.21) we have

$$\begin{aligned} V^*(\Delta+1,\alpha) &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (V^*(0,0) - c) \\ &\quad + (1-h_Y(\alpha)) \cdot \max\{V^*(0,0), V^*(\Delta,\alpha+1)\} \\ &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (0-c) + (1-h_Y(\alpha)) \cdot V^*(\Delta,\alpha+1) \\ &\geq R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (0-c) + (1-h_Y(\alpha)) \cdot V^*(\Delta-1,\alpha+1) \qquad \text{(B.53)} \\ &= V^*(\Delta,\alpha), \qquad \text{(B.54)} \end{aligned}$$

where (B.53) follows from the monotonicity of $V^*(t,\alpha)$ in $t \leq \Delta$ and (B.54) follows from equation (4.20). Hence, for $t = 1, 2, \ldots, \Delta+1$,

$$V^*(t-1,\alpha) \leq V^*(t,\alpha) \ \forall \alpha \geq 0. \qquad \text{(B.55)}$$

Now consider the case where $t \geq \Delta + 1$. By (4.21), for $t = \Delta + 2$ we have

$$\begin{aligned} V^*(\Delta+2,\alpha) &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (V^*(1,0) - c) \\ &\quad + (1 - h_Y(\alpha)) \cdot \max\{V^*(1,0), V^*(\Delta+1,\alpha+1)\} \\ &\geq R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (V^*(0,0) - c) \\ &\quad + (1 - h_Y(\alpha)) \cdot \max\{V^*(0,0), V^*(\Delta,\alpha+1)\} \qquad \text{(B.56)} \\ &= V^*(\Delta+1,\alpha), \qquad \text{(B.57)} \end{aligned}$$

where (B.56) follows by (B.55). Suppose for $t = \Delta+3, \Delta+4, \ldots, \bar{t}-1$, where $\Delta+2 < \bar{t}-1 < L$, we have

$$V^*(t-1,\alpha) \leq V^*(t,\alpha) \ \forall \alpha \geq 0. \qquad \text{(B.58)}$$

For $t = \bar{t}$ we have,

$$\begin{aligned} V^*(\bar{t},\alpha) &= R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (V^*(\bar{t}-1-\Delta,0) - c) \\ &\quad + (1 - h_Y(\alpha)) \cdot \max\{V^*(\bar{t}-1-\Delta,0), V^*(\bar{t}-1,\alpha+1)\} \\ &\geq R(\alpha+1) - R(\alpha) + h_Y(\alpha) \cdot (V^*(\bar{t}-2-\Delta,0) - c) \\ &\quad + (1 - h_Y(\alpha)) \cdot \max\{V^*(\bar{t}-2-\Delta,0), V^*(\bar{t}-2,\alpha+1)\} \qquad \text{(B.59)} \\ &= V^*(\bar{t}-1,\alpha), \qquad \text{(B.60)} \end{aligned}$$

where (B.59) follows from the monotonicity of the reward function in $t \leq \Delta + 1$ and the induction hypothesis given by (B.58). Therefore, the reward function is also monotone in $t \geq \Delta + 1$ for any fixed $\alpha \in [0, L]$ and the result follows.

□

Proof of Theorem 3. If $t \leq \Delta$, performing PM is not an option, hence the result follows. For $t \geq \Delta + 1$, suppose $a^*(t, \alpha') = 1$, i.e.,

$$V^*(t-1-\Delta,0) \geq V^*(t-1,\alpha'+1), \qquad \text{(B.61)}$$

using equation (4.21). Recall that by Lemma 9, $V^*(t,\alpha)$ is nonincreasing in α for all $t \in [0, L]$. Hence,

$$V^*(t-1-\Delta,0) \geq V^*(t-1,\alpha'+2). \qquad \text{(B.62)}$$

Therefore, from equation (4.21), at $\alpha = \alpha' + 1$ we have

$$a^*(t,\alpha'+1) = 1. \qquad \text{(B.63)}$$

Therefore, the result follows. □

Proof of Lemma 11. (i) The proof is similar to the proof of Lemma 9. We only need the sufficient condition given by equation (4.22) to show that for $t \leq \Delta + 1$,

$$\begin{aligned} V^*(t, L-1) &= R(L) - R(L-1) + h_Y(L-1) \cdot (0-c) + (1 - h_Y(L-1)) \cdot V^*(t-1, L) \\ &= R(L) - R(L-1) + h_Y(L-1) \cdot (0-c) \qquad \text{(B.64)} \\ &\geq V^*(t, L) = 0, \qquad \text{(B.65)} \end{aligned}$$

where equation (B.64) follows from equation (4.24). The rest of the proof is completed when for $t \geq \Delta + 1$, we modify equation (B.32) to

$$\sum_{x=0}^{L-1} V^*(t - \Delta - 1, x) \cdot p_X(x) = \vartheta. \qquad \text{(B.66)}$$

(ii) The proof of is similar to the proof of Lemma 10.

□

Proof of Theorem 4. The proof is similar to the proof of Theorem 3 and uses Lemma 11.

□

Proof of Lemma 12. The proof is completed by induction on t, when using Lemma 11 and Lemma 4.7.2 on page 106, Puterman (1994). □

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