Referral, Appropriateness and Eligibility of Implantable Cardioverter Defibrillator Therapy in Alberta

by

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ABSTRACT

Background: Sudden cardiac death (SCD) is responsible for 50% of all cardiovascular deaths and is primarily due to rapid, life-threatening heart rhythm abnormalities. Multiple large, randomized clinical trials have demonstrated that implantable cardioverter defibrillator (ICD) therapy reduces morbidity and mortality in patients with heart failure and an impaired ejection fraction at risk for SCD or patients who have suffered a life-threatening ventricular arrhythmia. Although guidelines exist to help identify patients who may benefit from device therapy, sparse data exists evaluating the referral, appropriateness and eligibility of ICD therapy in clinical practice.

Aims: This thesis has three main aims: (i) to evaluate referring physician's knowledge regarding indications for primary prevention ICD and to identify potential barriers for referral (Project 1), (ii) to evaluate adherence to guideline recommendations and appropriate use criteria for patients who underwent ICD therapy and to identify reasons for non-evidence based implants (Project 2) and (iii) to determine the rates of ICD eligibility and utilization among patients seen in heart function clinic and to identify reasons for non-implantation (Project 3). The work performed for this thesis was part of a quality improvement initiative performed by the Arrhythmia Working Group of the Alberta Health Services Cardiovascular and Stroke Strategic Clinical Network.

Methods/Results:

Project 1: A web-based survey consisting of demographics, practice characteristics, case scenarios regarding indications for a primary prevention ICD and a list of potential barriers for referral was administered to Internists, Cardiologists and Cardiology Residents in Alberta. The survey response rate was 14%. Among respondents, 55% were Internists, 32% Cardiologists and 13% Cardiology Residents. Overall, 34% of physicians provided answers concordant with

guidelines. In multivariable analysis, predictors of complete guideline concordance were being a Cardiologist (odd ratio (OR) 5.9, confidence interval (CI) 2.1-16.4, p=0.001) and Cardiology Resident (OR 6.7, CI 1.7-27.3, p=0.007). The most common barrier for referral for Internists was lack of confidence in knowledge of guideline recommendations; while Cardiologists reported concerns about cost-effectiveness and Cardiology Residents were most concerned with inappropriate shocks.

Project 2: A retrospective review of ICD procedures from January 1st, 2015-December 31st, 2016 in Alberta was performed. Implants were classified as Class I/IIa/IIb/III according to 2008 ACC/AHA/HRS ICD guidelines and 2012 ACCF/AHA/HRS Focused Update, yes/no according to 2013 Canadian Cardiovascular Society(CCS) cardiac resynchronization therapy(CRT) guidelines and 'appropriate'/'maybe appropriate'/'rarely appropriate' according to 2013 AUC. There were 1300 ICD procedures over the 2-years. Among all implants, 0.3% of primary prevention, 0.7% of secondary prevention implants and 0.2% of generator replacements were non-evidence based. Among CRT implants, 11% were inconsistent with CCS recommendations. When applying AUC, 92% of implants were classified 'appropriate' and 4% did not meet a recommendation. For both guideline recommendations and AUC, overlapping reasons for non-adherence existed, including QRS width <120ms (n=3), LVEF >0.35 (n=2) and recent myocardial infarction (n=1). The AUC had no existing criteria in 3% (n=41) of procedures.

Project 3: A retrospective chart review of consecutive patients seen at two heart function clinics in Edmonton and Calgary from 2012-2015 was performed to determine device eligibility by collecting demographics, clinical indications, comorbidities and to identify reasons for non-implantation. A total of 1294 patients were seen in HF clinic. Yearly rates of device eligibility and utilization ranged from 32-52% and 19-56%, respectively. When a documented reason for

non-implantation existed, yearly utilization rates increased to 36-64%. Independent predictors of non-implantation were age>75 years (OR 1.80, 1.23-2.63), LVEF≤0.35 (OR 4.69, 2.74-8.04), kidney disease (OR 1.71, 1.04-2.80) and cancer (OR 2.56, 1.23-5.34). Almost half of the time (46%), there was no documented reason for non-implantation among eligible patients.

Conclusions: These data suggest: (i) knowledge regarding indications for primary prevention ICD is limited and varies among referring physicians, with Cardiologist and Cardiology Residents most familiar with ICD indications. Overall barriers for referral included cost of ICD therapy, lack of confidence in knowledge of ICD guidelines and risk of inappropriate shocks, (ii) that a formal process of specialist evaluation, eligibility reminders on device requisitions and peer-review consensus resulted in less than 1% of non-evidence-based ICD procedures and (iii) that less than half of eligible patients receive an ICD and reasons for non-implant are often missing. This thesis may help to inform future initiatives that can lead to efficient and effective delivery of ICD therapy.

Preface

This thesis is the original work by Rochelle Bernier. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Assessing Barriers to ICD Referral Pro00058148 June 22, 2016 (Project 1), A Population Based Study of Adherence to Appropriate Use Criteria and Guideline Recommendations for Implantable Cardioverter Defibrillators Pro00069363 December 12, 2016 (Project 2), Complex Device Eligibility in HF Pro00063905 February 22, 2017 (Project 3). The research conducted for this thesis forms part of a provincial wide research collaboration performed by the Arrhythmia Working Group of the Alberta Health Services Cardiovascular and Stroke Strategic Clinical Network Electrophysiology Expert Working Group, led by Dr. Roopinder K Sandhu at the University of Alberta and funded by the PERFORM grant. The data collection, analysis and manuscripts are my original work.

Project 1

Assessing Physician Knowledge Regarding Indications for a Primary Prevention Implantable Defibrillator and Potential Barriers for Referral was written collaboration with Raj SR, Tran D, Reyes L, Sauve M, Sumner GL, Exner DV, Sandhu RK and was published in the *Journal of Cardiovascular Electrophysiology.* I was responsible for the data collection, analysis and writing of the manuscript.

Editorial

Gaps in Physician Knowledge are Associated with Under-Referral for Evidence-Based Implantable Cardioverter Defibrillator Therapy: *How Can We Improve Care?* was written by Dr. Andrea Russo and published in the *Journal of Cardiovascular Electrophysiology*

as an editorial of the manuscript 'Assessing Physician Knowledge Regarding Indications for a Primary Prevention Implantable Defibrillator and Potential Barriers for Referral'.

Project 2

A Population-based Study of Adherence to Guideline Recommendations and Appropriate Use Criteria for Implantable Cardioverter Defibrillators has been submitted and is being considered for publication at *Circulation: Cardiovascular Quality and Outcomes.* It was written in collaboration with Raj SR, Reyes L, Lockwood E, Gulamhusein S, Williams R, Valtuille L, Sivakumaran S, Hruczkowski T, Kimber S, Exner DV and Sandhu RK. I was responsible for the data collection, analysis and writing of the manuscript.

Project 3

A Population-Based Study of Complex Device Eligibility, Utilization and Reasons for Non-Implantation in Patients at Heart Function Clinics is an ongoing project done in collaboration with Jessica Ng, Dat Tran, Dr. Evan Lockwood, Lucy Reyes, Karen Cowan, Dr. Justin Ezekowitz, Dr. Derek V Exner, Dr Satish R Raj and Dr Roopinder K Sandhu and is awaiting abstract submission to the American Heart Association Scientific Sessions and manuscript publication of this project is anticipated.

Acknowledgements

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Introduction

Sudden cardiac death (SCD) is the leading cause of cardiovascular mortality and is responsible for approximately 50% of all cardiovascular deaths. [1] Several large, randomized clinical trials have demonstrated that implantable cardioverter defibrillator (ICD) therapy reduces morbidity and mortality in patients with heart failure and impaired ejection fraction [2-6] and among patients who have suffered a life threatening ventricular arrhythmia.[7-11] However, sparse data exists assessing the referral, appropriateness and eligibility of ICD therapy in clinical practice.

An important factor leading to ICD under-utilization [12-14] is high rates of non-referral [14, 15] to a device specialist and this may, in part, be explained by gaps in physician knowledge regarding ICD indications. Studies have found that physicians who are commonly involved in referral are familiar with ICD indications ranging from 15% [16]-66%. [15] Primary care physicians were found to be less familiar with guideline recommendations when compared to Cardiologists.[15-19]

It is unclear how recognition of eligible, high-risk patients actually translates into referrals and subsequent ICD implants. Several, single center retrospective reports [20, 21] have shown, in a mix of inpatient and outpatient populations that 15% [20] -87% [21] of eligible patients receive an ICD. Among centers with low ICD implants common reasons included patient preference and patient's not being medically optimized.[20]

Once a patient is eligible, is the ICD implant evidence-based? Data from the United States National Cardiovascular Data Registry has found that approximately 15%[22]-20% [23] of primary prevention ICD therapy among Medicare beneficiaries are non-evidence based. However, the registry self-reports, which may lead to misclassification, is comprised of only primary prevention ICD therapy and is not contemporary. A possible explanation for the high

rate rates of non-adherence is the presence of clinical scenarios that warrant ICD but where data is lacking and consequently no guideline exists.

An improved understanding of how device guideline recommendations translate into real world practice is needed given the expanded use of device therapy and current healthcare resource restraints. In this context, the aims of this thesis are: (i) to evaluate referring physician's knowledge regarding indications for primary prevention ICD and to identify potential barriers for referral (**Project 1**), (ii) to evaluate adherence to guideline recommendations and appropriate use criteria for patients who underwent ICD therapy and to identify reasons for non-evidence based implants (**Project 2**) and (iii) to determine the rates of ICD eligibility and utilization among patients seen in heart function clinic and to identify reasons for non-implantation (**Project 3**).

Project 1

Assessing Physician Knowledge Regarding Indications for a Primary Prevention Implantable Defibrillator and Potential Barriers for Referral

ABSTRACT

Background: Although there is clear evidence to demonstrate that primary prevention implantable defibrillators (ICDs) reduce mortality in high-risk patients, ICDs are under-utilized. Limited data exists assessing referring physicians' knowledge about guideline indications and attitudes towards ICDs, which may influence decision for referral.

Methods and Results: The Arrhythmia Working Group from the Alberta Cardiovascular and Stroke Strategic Clinical Network developed a web-based survey consisting of case scenarios regarding primary prevention ICD indications and a list of barriers for referral to aid in the design of a complex device care pathway. We invited referring physicians to participate in the survey including Internists and Cardiologists and Cardiology Residents. The survey was completed by 109 of 799 (response rate=14%) of physicians. Of those, 55% were Internists, 32% Cardiologists and 13% Cardiology Residents. The majority of physicians were male (62%), practicing in a University Hospital (66%). Overall, complete guideline-concordant answers were provided by 34% of physicians. In multivariable analysis, predictors of complete guideline concordance were being a Cardiologist (odd ratio (OR) 5.9, confidence interval (CI) 2.1-16.4, p=0.001) and Cardiology Resident (OR 6.7, CI 1.7-27.3, p=0.007). The most common barrier for referral for Internists was lack of confidence in knowledge of guideline recommendations; while Cardiologists reported concerns about cost-effectiveness and Cardiology Residents were most concerned with inappropriate shocks.

Conclusion: Knowledge regarding indications for primary prevention ICD is limited and varies significantly amongst referring physicians. The barriers for referral differ among physician groups and addressing these identified barriers may help to improve appropriate ICD utilization.

Introduction

Several large, randomized clinical trials have demonstrated that primary prevention implantable cardioverter defibrillator (ICD) therapy reduces mortality in patients with a low ejection fraction and heart failure at risk of sudden cardiac death (SCD). [1-4] In the last decade, recommendations for the use of primary prevention ICD therapy have remained relatively unchanged [5,6] with the exception of identifying patients who may also benefit from cardiac resynchronization pacing. Despite the guideline recommendations, population-based cohort studies demonstrate low rates of ICD utilization in eligible patients. [7-9] The high rates of non-referral [9,10] to a device specialist is an important factor leading to under-utilization and may, in part, originate from gaps in physician knowledge regarding indications. Given the growing heart failure population, [11-13] a better understanding of contemporary physician knowledge and attitudes regarding ICD therapy is needed to address existing treatment gaps. [14]

Studies assessing knowledge about indications for primary prevention ICD are sparse. [10,15-18] In a survey administered to a national sample of family physicians, Internal medicine specialists and Cardiologists in the United States, approximately two thirds of physicians provided answers concordant with primary prevention recommendations. [10] Awareness of guideline recommendations was much lower in Sweden, where only 15% of referring physicians recognized that a left ventricular ejection fraction (LVEF) ≤ 0.35, without a history of ventricular arrhythmias, was sufficient to implant a primary prevention ICD. [15] When knowledge amongst physician groups were compared [10,15-18], primary care physicians were found to be less familiar with ICD indications compared to Cardiologists. However even among cardiology specialists an estimated one third were unaware of recommendations.[16] Physician knowledge is an important

factor influencing decision for ICD referral, however little is known about other reasons for non-referral [19] and whether barriers differ among referring physicians.

The aims of this study were to determine knowledge regarding primary prevention ICD indications among referring physicians including Internists, Cardiologists and Cardiology Residents, to identify potential barriers for referral and to determine whether these barriers differ among physician groups.

Methods

Study Population

All Internists and Cardiologists with an active Alberta Medical Association membership and Cardiology Residents at the University of Alberta and University of Calgary training programs in 2016 were invited to participate in the study. We selected Cardiologists, Internists and Cardiology Residents because they represent physicians encountered in a typical device care pathway for patients with clinical features associated with device eligibility.

Survey Composition

As part of an initiative to deliver efficient and effective care, the Arrhythmia Working Group of the Alberta Health Services Cardiovascular and Stroke Strategic Clinical Network developed a brief web-based survey to inform the development of an ICD care pathway. The survey consisted of questions regarding baseline demographics and practice characteristics. It also included, five case scenarios regarding indications for a primary prevention ICD based on guideline recommendations [20-23] which physicians were instructed to select the best answer. The survey also consisted of questions regarding potential barriers for referral. Complete guideline concordance was assessed by correct responses to all case scenarios. The five case scenarios with all answer choices is shown in the Appendix.

Physicians were then asked to check all potential barriers they felt influenced their decision to refer including: system barriers (i.e. inability to get an appropriate consultant, inability to get appropriate investigations and concerns about cost-effectiveness) and physician barriers (i.e. uncertainty about ICD guidelines, concerns about surgical complications and concerns about inappropriate shocks). The working group focused on assessing knowledge regarding (i) LVEF cutoff, (ii) etiology of cardiomyopathy and timing of diagnosis (iii) use of guideline directed medical therapy (GDMT) in identifying patients eligible for primary prevention ICD therapy. It was felt that decisions regarding device type would be up to the device specialist.

Surveys were administered using the REDCap electronic data capture tools hosted by the Clinical Research Informatics Core at the University of Alberta. [24] The survey was administered from September 1st, 2015 to December 31st, 2015. Physicians were given up to three months to complete the survey with up to three email reminders. In a strategy to improve response rate, a $10.00 coffee gift card was provided to physicians upon survey completion. This study was approved by the Health Research Ethics Board at the University of Alberta (Pro00058148) and the Conjoint Human Research Ethics Board (REB152015; Calgary, Alberta). Informed consent was assumed if the subjects continued the survey after agreeing to the Ethics Board's consent language preceding the survey.

Outcomes

The primary outcome for this study was to determine the proportion of physicians who demonstrated complete ICD guideline-concordant answers. Secondary outcomes included identification of potential barriers for device referral, whether reasons for non-referral varied by

physician specialty, physician age and location of practice and to identify predictors of complete ICD guideline concordance.

Statistical Analysis

Descriptive statistics were reported as count and percentage. Correct responses in 5 case scenarios and barriers for ICD referral were calculated and compared across physician specialties, age groups and location of practice by Chi-Square tests. We used logistic regression to examine univariate and multivariable association between baseline characteristics with complete ICD guideline concordance. Variables associated with complete guideline concordance with a p-value < 0.1 in univariate analyses were added to the multivariable model. All analyses were conducted using Stata version 14 (Stata Corporation, College Station, Texas). Two-sided p-values < 0.05 were considered statistically significant.

Results

Baseline Characteristics

Baseline demographics are shown in Table 1.1. The survey was completed by 109 of 799 physicians (response rate 14%), of which 55% were Internists, 32% Cardiologists and 13% Cardiology Residents. Among physicians, 62% were male, 42% were < 40 years and 45% had $\geq$ 10 years of experience.

Table 1. 1 Baseline Characteristics

Characteristics	Cardiologists (n=35)	Internists (n=60)	Cardiology Residents (n=14)
Age (n)			
≤ 40	8, [23%]	25, [42%]	13, [93%]
41-50	12, [34%]	17, [28%]	1, [7%]
>50	15, [43%]	18, [30%]	-
Sex, Male (n)	31, [88%]	29, [48%]	7, [50%]
Location of Practice (n)			
University Hospital	31, [88%]	31, [52%]	13, [93%]
Community Hospital	4, [12%]	22, [36%]	-
Primary Care Network	-	7, [12%]	1, [7%]
Years of Practice (n)			
<1 year	3, [9%]	9, [15%]	14, [100%]
1-5 years	5, [14%]	14, [23%]	-
6-10 years	7, [20%]	8, [14%]	-
> 10 years	20, [57%]	29, [48%]	-

Knowledge of ICD Guidelines

Overall, 34% (n=37) of physicians provided correct answers to all case scenarios (Figure 1.1). Among these physicians, complete guideline-concordant answers differed significantly depending on specialty (Internists 15%, Cardiologists 57%, Residents 57%, p<0.001). In multivariable analysis, predictors of complete guideline-concordance were being a Cardiologist (odd ratio (OR) 5.9, confidence interval (CI) 2.1-16.4, p=0.001) and Cardiology Resident (OR 6.7, CI 1.7-27.3, p=0.007; Table 1.2).

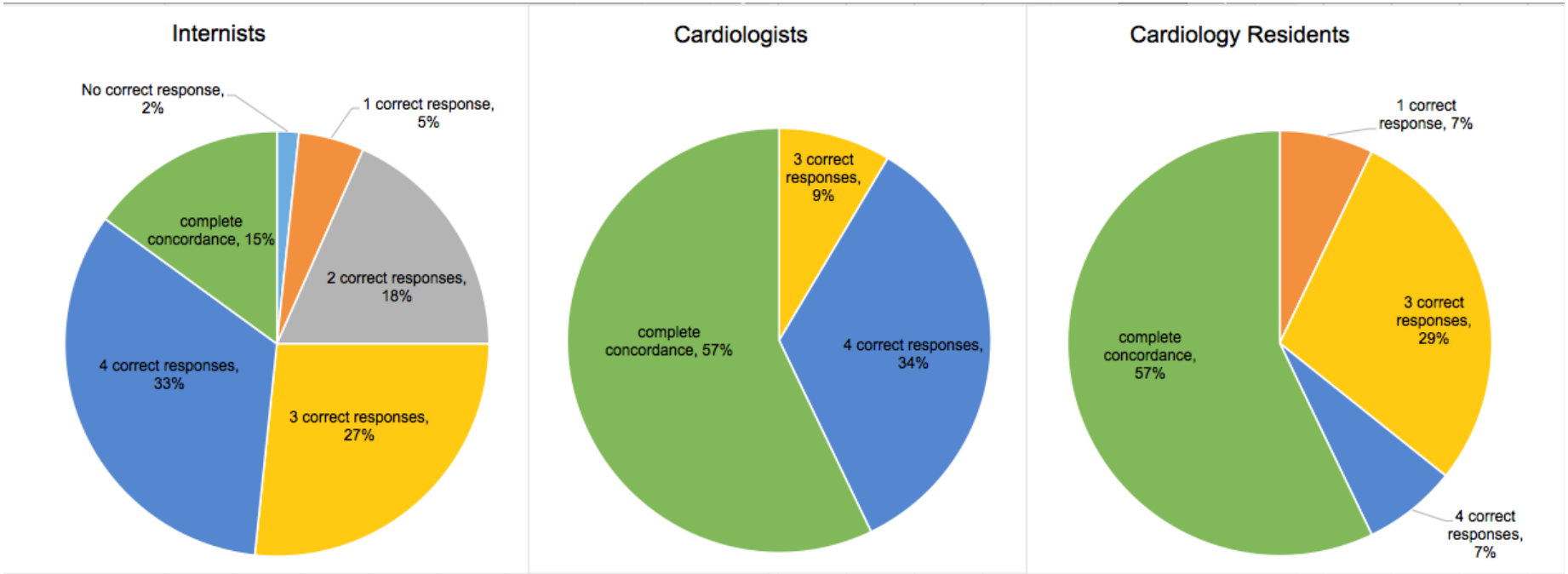

Figure 1. 1 Guideline concordant responses according to physician specialty.

Table 1. 2 Predictors of complete guideline concordance.

	Univariate model		Multivariable model	
Variable	**Odd Ratio (OR) (95% CI)**	**p**	**Odd Ratio (OR) (95% CI)**	**p**
Sex				
Female	Ref			
Male	1.79 (0.77-4.16)	0.178		
Age				
≤ 40 years	Ref			
41-50 years	1.52 (0.58-3.99)	0.391		
> 50 years	1.14 (0.43-2.97)	0.785		
Specialty training				
Internists	Ref		Ref	
Cardiologists	**7.56 (2.85-20.03)**	**<0.001**	**5.88 (2.11-16.37)**	**0.001**
Cardiology Residents	**7.56 (2.11-27.01)**	**0.002**	**6.74 (1.67-27.25)**	**0.007**
Location of practice				
University hospital	Ref		Ref	
Community hospital	0.32 (0.11-0.94)	0.038	0.68 (0.20-2.30)	0.534
Years of practice				
< 1 year	Ref			
1-5 years	0.30 (0.07-1.30)	0.107		
6-10 years	1.83 (0.51-6.61)	0.358		
> 10 years	0.78 (0.29-2.09)	0.615		

The distribution of correct answers for each case scenario according to physician groups is shown in Table 1.3. Correct answers for each case scenario ranged from 45%-88% for Internists, 77%-97% for Cardiologists and 72%-86% for Residents (S1). Both Internists and Cardiologists were least familiar with an ICD indication for a patient with non-ischemic cardiomyopathy, LVEF=0.32, New York Heart Association Class (NYHA) II, sinus rhythm with left bundle branch block (LBBB) 150ms on GDMT (case scenario 3). While Cardiology Residents were least familiar with ICD indication for a patient with ischemic cardiomyopathy, LVEF=0.27, NYHA I, sinus rhythm on GDMT (case scenario 5).

Table 1. 3 Distribution of correct responses to case scenarios according to physician group.

Expected Answer	Physician Specialties		
	Cardiologists	Internists	Cardiology Residents
Case Scenario 1	50 year-old discharged from hospital, 2 weeks post-acute myocardial infarction and a stent. Prior to discharge, an echocardiogram measured a LVEF of 20%. He was started on a low dose beta-blocker, ace-inhibitor, statin and anti-platelet agents. Today in clinic, he is asymptomatic with a blood pressure of 150/60 mmHg, heart rate of 100 bpm. ECG shows sinus rhythm (QRS 98ms). What is your next step?		
Optimize medical therapy and once stable doses are achieved wait 3 months and repeat echocardiogram.	**33 (94%)**	**53 (88%)**	**11 (79%)**
Case Scenario 2	65 year-old with past medical history significant for coronary bypass graft surgery 2 years ago, diabetes and hypertension. He has NYHA III on GDMT at optimal doses. LVEF is 29%, unchanged for the last 2 years. ECG shows sinus rhythm and LBBB (QRS 140ms). What is your next step?		
Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**31 (89%)**	**40 (67%)**	**12 (86%)**
Case Scenario 3	75 year-old with non-ischemic dilated cardiomyopathy and NYHA class II symptoms, LVEF was 25% one year ago and after optimizing GDMT; repeat LVEF is 32%. ECG shows sinus rhythm and LBBB (QRS 150ms). What is your next step?		
Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**27 (77%)**	**27 (45%)**	**12 (86%)**
Case Scenario 4	70 year-old with past medical history significant for ischemic cardiomyopathy, LVEF is 28% on GDMT, NYHA I and current smoker. ECG shows sinus rhythm and LBBB (QRS 150ms). Recently, he noted weight loss and a cough. Evaluation revealed metastatic lung cancer with a life expectancy of 9 months. What is your next step?		
No further cardiac management at this time.	**34 (97%)**	**50 (84%)**	**12 (86%)**
Case Scenario 5	55 year-old with ischemic cardiomyopathy, LVEF of 27% on GDMT. He exercises every day for 30 minutes without any symptoms and golf's 3 times per week in the summer. ECG shows sinus rhythm (QRS 88ms). What is your next step?		
Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**32 (91%)**	**28 (47%)**	**10 (72%)**

We also assessed the potential under-utilization and over-utilization of referrals for device therapy (Appendix). Among all physicians, the potential under-utilization of referral for device therapy occurred in 1% of responses for case scenario 1, 24% of responses for case 2, 39% of responses for case 3 and 36% of responses for case 5. The potential over-utilization of referral for device therapy occurred in 10% of responses for case scenario 1 and 12% of responses for case 4.

Barriers for Referral

Barriers for ICD referral according to physician group are shown in Figure 1.2. The most common barrier for referral was a lack of confidence in knowledge of the guideline recommendations for Internists (70%), cost-effectiveness for Cardiologists (54%) and inappropriate shocks for Residents (64%). Knowledge of ICD indications was the only reason that significantly differed between specialties ($p<0.001$).

We then evaluated whether perceived barriers for ICD referral differed by age groups and location of practice. Physicians < 40 years reported the most overall barriers (< 40 years; [n=105] vs. 41-50 years [n=51] and > 50 years [n=54], Figure 1.3). The most common barrier for physicians <40 years was confidence regarding knowledge of guidelines (58%), while concerns about ICD cost-effectiveness was most common for physicians between 41-50 (60%) and > 50 years (48%). Confidence in knowledge of ICD indications was the only barrier that differed according to physician age ($p =0.044$) and location of practice (Figure 1.4, $p=0.023$).

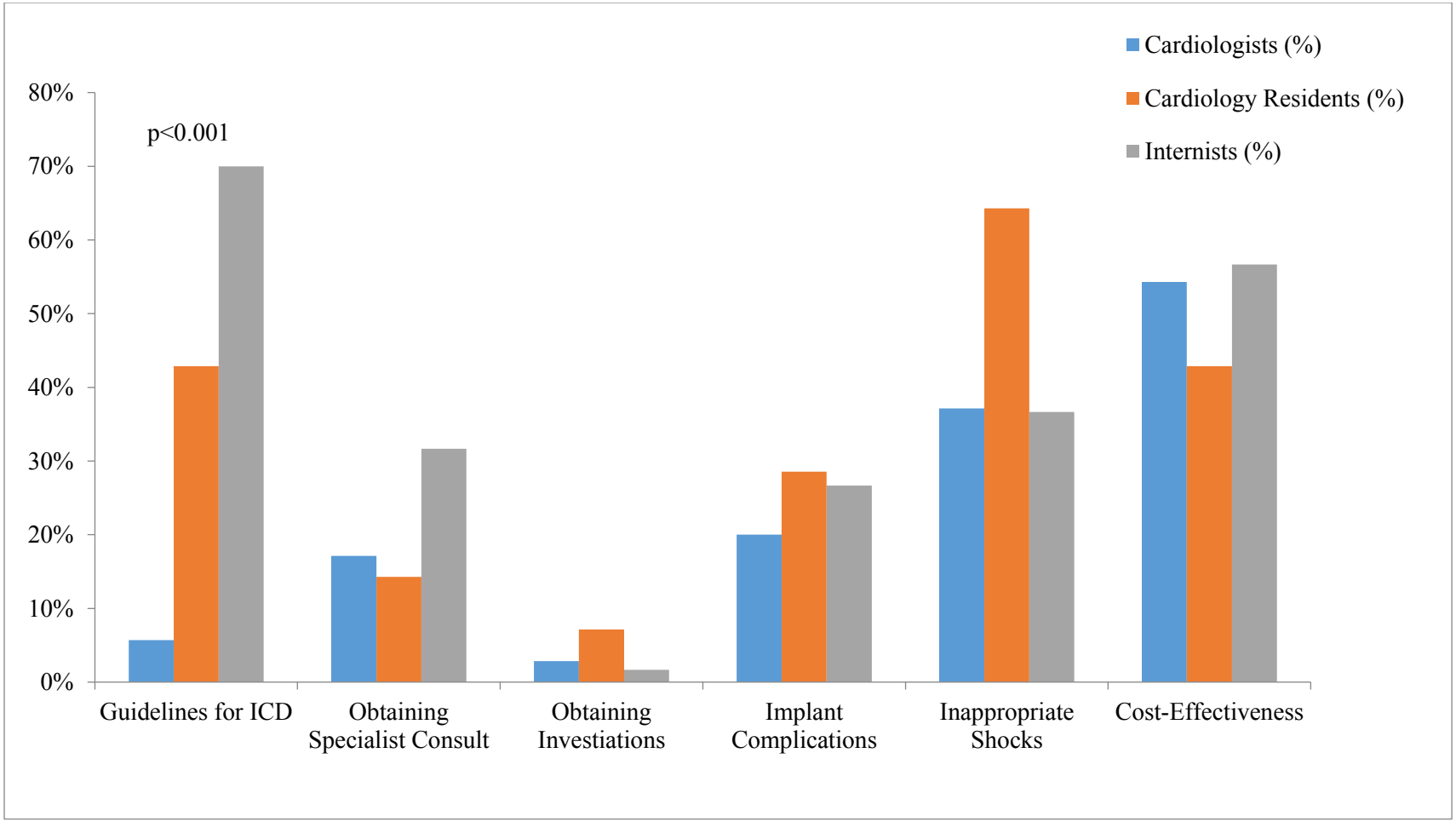

Figure 1. 2 Barriers for a primary prevention ICD referral according to physician specialty.

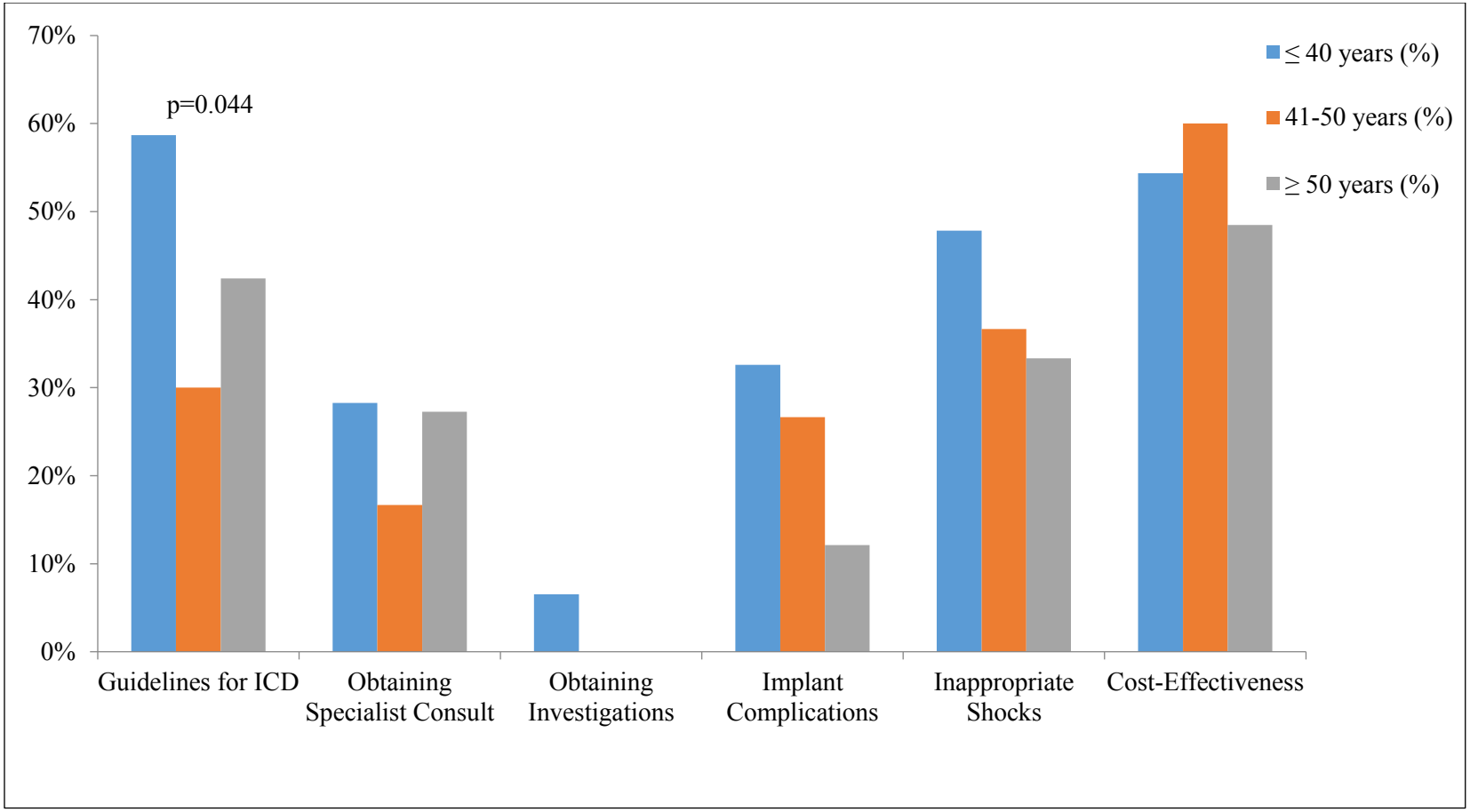

Figure 1. 3 Barriers for a primary prevention ICD referral according to physician age.

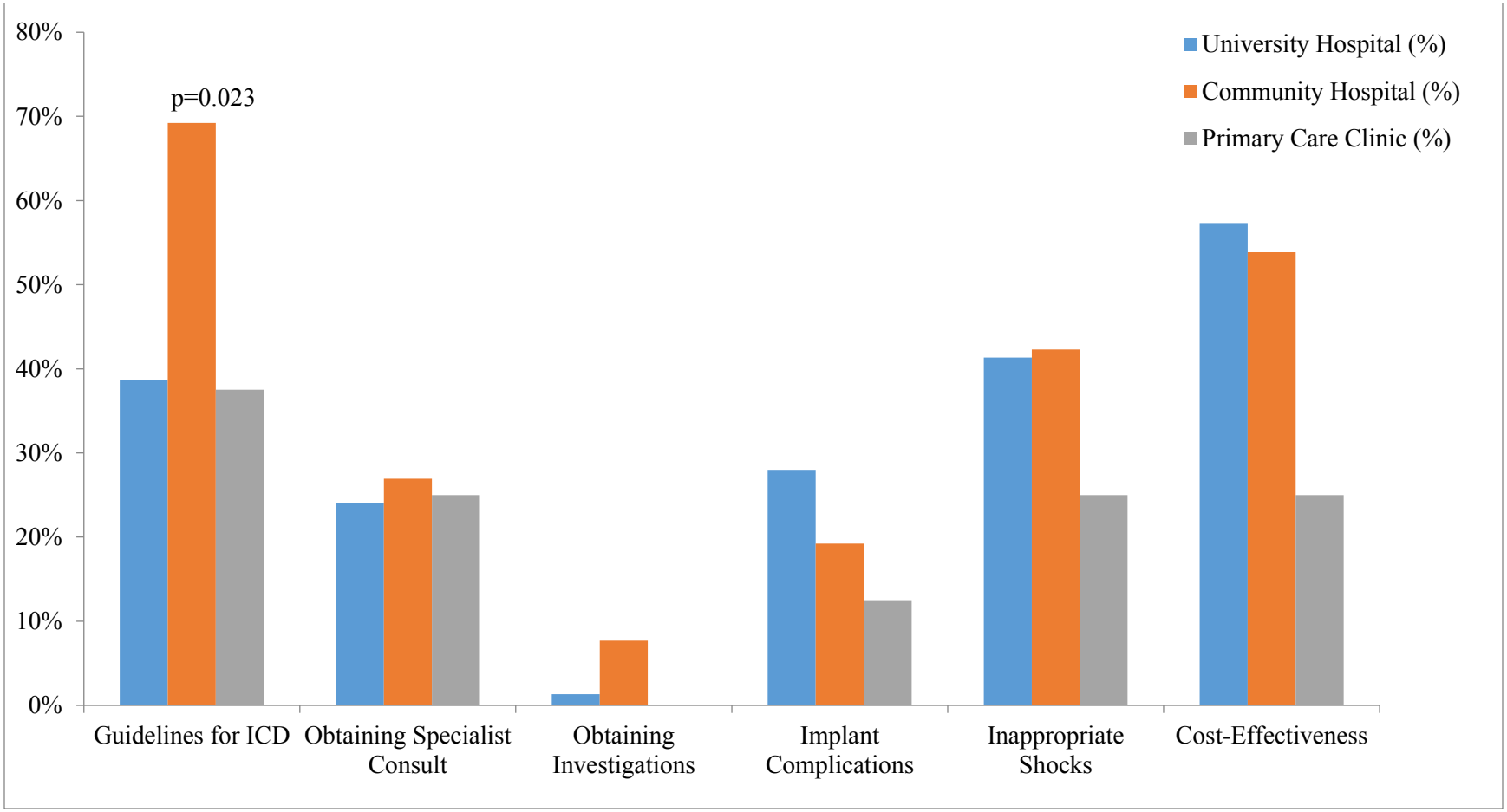

Figure 1. 4 Barriers for a primary prevention ICD referral according to location of practice.

Discussion

In this population-based study, we found that only a third of referring physicians were completely aware of the indications for a primary prevention ICD. Cardiologists had the most guideline-concordant responses while Internists were least familiar with current recommendations for primary prevention ICD therapy. The vast majority of Internists identified a lack of confidence in knowledge regarding guideline recommendations as the most frequent reason for non-referral. However, the most common barrier for referral was cost-effectiveness for Cardiologists and inappropriate shocks for Cardiology Residents. Regardless of the physician group, access to investigations or obtaining specialist evaluation was less likely to influence decision for referral.

The use of primary prevention ICD to improve survival in selected populations is well established. Despite limited new recommendations in primary prevention guidelines since 2008, awareness of guideline recommendations remains poor. [10,15-18] Similar to other studies from other countries, we found significant differences in knowledge amongst physicians in the referral pathway. [10,15,16] Amongst a Swedish cohort, 61% of Cardiologists were able to identify appropriate indications for ICD therapy while 13% of Internists and 2% of family practitioners were aware of recommendations. [15] In a study of physicians at both academic and community-based hospitals, knowledge regarding LVEF criteria for primary prevention ICD was higher amongst Cardiologists compared to primary care physicians. [16] Even amongst Cardiologists who are responsible for the referral to the device specialist, there is a considerable gap in knowledge. In a representative survey of American physicians, 25% of Cardiologists felt a LVEF > 0.40 was an appropriate cut-off for ICD implant, and 19% would refer within 40 days of myocardial

infarction. [10] We also report for the first time that the majority of Cardiology Residents are familiar with guideline recommendations for primary prevention ICD implantation.

Our study differs from prior assessments because it consisted entirely of case scenarios that not only required physicians to acknowledge information needed for assessment of ICD indication (LVEF criteria, etiology of cardiomyopathy, NYHA class, QRS configuration and duration) but also included other important factors to consider in the decision process. These factors included the optimization of GDMT, awareness of contraindications to ICD therapy i.e. life expectancy < one year and distinguishing between other guideline recommendations i.e. cardiac transplant guidelines. Ensuring a comprehensive understanding of guidelines is needed particularly as previous registry data had shown that almost a quarter of patients receive non-evidence based ICD implants. [25] We found that 89-97% of Cardiologists were able to correctly answer a particular case scenario with the exception of 33% who were less familiar with ICD indication for non-ischemic cardiomyopathy, NYHA II, LVEF 0.32, LBBB and QRS 150ms. It is possible that the low correct response rate to this case scenario may have been the result of not having CRT as part of the answer. However, the case describes key features of eligibility for a primary prevention device where referral to a specialist was appropriate. Our study also showed over 80% of Internists correctly identified the need to further optimize medical therapy prior to implant. They also recognized the lack of benefit in patients with short life span while they were less familiar with identifying Class I indications for ICD therapy. In addition, we report that the majority of Cardiology Residents provided guideline-concordant responses.

Prior studies report various physician barriers for ICD referral. [16,18] The self-perceived unawareness of guidelines has been a major reason for non-referral among family physicians [15] and was also reported as an important barrier in our study. This lack of confidence is important

as primary care physicians provide an essential role in the referral process as they encounter an overall larger segment of the population with high-risk SCD features. [26,27] However, this finding is unsurprising as primary care physicians, in general, manage a higher prevalence of chronic diseases in their practices [28,29] and having an adequate awareness of the many guidelines for various conditions is challenging. Having simplified interventions integrated into daily work flow is a potential solution to identifying eligible patients such as flags incorporated into electronic medical charting [30] or providing financial incentive to general practitioners who perform pulse palpation to increase the detection of atrial fibrillation. [31]

Our study found that a concern about the cost-effectiveness of primary prevention ICD therapy was the most common barrier for referral for Cardiologists and an important consideration for Internists. This finding is consistent with a New Zealand study that found 88% of Cardiologists and non-cardiologists managing heart failure believed cost influenced their decision-making. [18] We also found that cost was a major reason for non-referral among physicians across each age group and regardless of hospital or community practice setting. Several studies [32,33] have shown that primary prevention ICD is cost-effective; but these calculations require several assumptions and may be challenging to extrapolate to patients with varying comorbidity burden and subsequent lifespan. In Alberta, Canada ICD therapy has decreased by almost four times over the last seven years and a similar finding has occurred in other provinces (Alberta Health Services Correspondence).

Finding that risk of inappropriate shocks is a major barrier considered by Cardiology Residents is novel to our study. This was also a barrier in over a third of Internists and Cardiologists who may have encountered patients with emotional distress after suffering a shock. Minimizing shocks has been an important area of research in electrophysiology and several

clinical trials [34,35] have provided programming guidelines associated with up to a 77% reduction of inappropriate shocks. [34] Familiarity with the device programming for implants may help to address this barrier.

The barriers reported in this study provide valuable information for the development of quality assurance and knowledge translation initiatives. Overcoming these barriers may involve utilization of strategies such as workshops at scientific meetings involving referring physicians, formal talks, web-based educational sessions, reminders on electronic medical records and implementation of simple device care pathways. It is also important to inform the general public with increased awareness of SCD and to empower them to know key information such as ejection fraction as demonstrated in the 'know your EF campaign'. These knowledge translation efforts should be formally evaluated for effectiveness.

There are several limitations of our study that warrant discussion. First, the response rate for our study was low, although comparable to other survey-based studies. [16-18] Accordingly, our study may introduce selection bias with only physicians who are confident in the subject matter self-selected as participants. However, even among these respondents, there is evidence of knowledge gaps. Second, this is the first study to assess knowledge and attitudes of ICD therapy in Canada however, the study was conducted in one province and findings may not be generalizable to the whole country. Third, we did not address patient's knowledge and barriers of ICD therapy, which are integral parts of the decision-making process. Lastly, case scenario 3 did not include CRT as part of any of the answer choices and could have contributed to the low correct response rate.

Conclusions

We found knowledge about indications for primary prevention ICD therapy amongst physicians involved in the referral pathway is poor and varies significantly depending on physician specialty. Cardiologists and Cardiology residents are most familiar with indications when compared to Internists. Our study highlights several important barriers for ICD referral including cost of ICD therapy, lack of confidence in knowledge and the risk of inappropriate shocks. Enhanced knowledge translation efforts are needed to address barriers and improve utilization of this life-saving therapy.

Project 2

A Population-based Study of Adherence to Guideline Recommendations and Appropriate Use Criteria for Implantable Cardioverter Defibrillators

ABSTRACT

Background: Studies evaluating physician adherence to guideline recommendations for implantable cardioverter defibrillators (ICD) therapy are sparse and none exist for the application of appropriate use criteria (AUC) in clinical practice. We evaluated the proportion of patients who underwent an ICD implant (de novo, generator replacement, or upgrade) for primary or secondary prevention according to guideline recommendations and AUC and identified reasons for non-adherence.

Methods and Results: As part of a quality improvement initiative, a chart review of all ICD procedures was performed from January 1, 2015-December 31, 2016 in Alberta, Canada. Our device implant process includes evaluation by an electrophysiologist, completion of a device form including checkboxes pertaining to guideline recommendations and AUC fulfillment and peer-review consensus. Implants were classified as Class I/IIa/IIb/III according to 2008 ACC/AHA/HRS ICD guidelines and 2012 ACCF/AHA/HRS Focused Update, yes/no according to 2013 Canadian Cardiovascular Society (CCS) cardiac resynchronization therapy (CRT) guidelines and 'appropriate'/'maybe appropriate'/'rarely appropriate' according to 2013 AUC. There were 1300 ICD procedures over the 2 years, the mean age was 63.8±12.9 years; 79% were male; the mean ejection fraction was 0.32 ±0.13 and 69% of implants were for primary prevention. Among all implants, 0.3% of primary prevention, 0.7% of secondary prevention implants and 0.2% of generator replacements were non-evidence based. Among CRT implants, 11% were inconsistent with CCS recommendations. When applying AUC, 92% of implants were classified 'appropriate' and 4% did not meet a recommendation. Reasons for non-adherence to guideline recommendations included QRS width < 120msec (n=3), LVEF > 0.35 (n=2) and

recent myocardial infarction (n=1). The most common reason for non-adherence to AUC was the absence of criteria (3%, n=41).

Conclusion: In this population-based study, we found that a process of specialist evaluation, eligibility reminders on device form and a peer-review consensus resulted in < 1% of non-evidence based ICD procedures.

Introduction

The implantable cardioverter-defibrillator (ICD) is a well-established therapy to reduce mortality for patients who have suffered a life-threatening ventricular tachyarrhythmia or are at high risk for sudden cardiac death (SCD). Although specific guideline criteria exist regarding who would benefit from ICD therapy, data regarding adherence to recommendations in clinical practice are sparse. [1-4]

The majority of data[5-7] regarding adherence to the inclusion criteria from primary prevention ICD clinical trials [8-13] comes from the National Cardiovascular Data Registry (NCDR) almost 10 years ago, which found anywhere from 15%[7] to over 20%[5] of ICD therapy among Medicare beneficiaries is non-evidence based. The centers involved in the NCDR self-report and this may lead to measurement bias or misclassification; in addition, the registry is primarily comprised of a primary prevention indication for ICD therapy. A small retrospective study from two Veterans Affairs medical centers found 26% of patients no longer met an indication for a primary prevention ICD at the time of generator replacement based on improved left ventricular ejection $\geq$ 0.40 or absence of appropriate ICD therapy. [14] A possible explanation suggested for these high rates of non-adherence to trial-based guideline recommendations was the presence of clinical circumstances that warrant ICD but where data is lacking and consequently no guideline recommendation exists. In 2013, the Heart Rhythm Society and the American College of Cardiology Foundation along with several other specialty societies reviewed common clinical scenarios where ICD and cardiac resynchronization defibrillator therapy (CRT-D) are commonly considered and developed appropriate use criteria[2] however; the application of these criteria in a real-world setting is unknown.

Therefore, we sought to determine the proportion of patients receiving an ICD including cardiac resynchronization therapy (de novo, generator replacement or upgrade) for primary and secondary prevention according to guideline recommendations and appropriate use criteria (AUC) in a contemporary province-wide study with detailed chart review.

Methods

The Arrhythmia Expert Working Group of the Alberta Health Services Cardiovascular and Stroke Strategic Clinical Network reviews processes related to all electrophysiology procedures in the province to ensure effective and efficient healthcare delivery. As part of a quality improvement initiative, a review of all consecutive ICD implants (including CRT), generator changes and upgrades in Alberta, Canada from January 1, 2015 – December 31, 2016 was performed. The three ICD implanting centers in Alberta are the Mazankowski Alberta Heart Institute, the Royal Alexandra Hospital and the Foothills Medical Centre.

Prior to implant, patients were evaluated by an electrophysiologist or implanting cardiologist for eligibility and then a device form was completed. The ICD form collected demographics, comorbidities (including calculating the Charlson comorbidity score[15]), clinical indications (i.e. primary or secondary prevention), imaging, ECG and medication use. The ICD form also included a section where physicians checked the guideline recommendation and AUC fulfilled. All implants were classified as Class I/IIa/IIb/III according to the 2008 American College of Cardiology/ American Heart Association/Heart Rhythm Society (ACC/HRS/HRS) ICD guidelines[1] and the 2012 American College of Cardiology Foundation/ American Heart Association/ Heart Rhythm Society (ACCF/AHA/HRS) Focused Update[3], as 'yes' or 'no' according to the 2013 Canadian Cardiovascular Society (CCS) CRT guidelines [4] and as 'appropriate', 'maybe appropriate' and 'rarely appropriate' according to the 2013 AUC[2]. The

AUC were released two years prior to the start of the study, giving implanting physicians sufficient time to become familiar with the document. Differences between guideline recommendations and CCS CRT guidelines are shown in Table 2.1. A formal peer review process occurred for consensus decision prior to implant. A detailed medical chart review was performed to confirm accuracy of device form; complete any missing information and to identify reasons for non-adherence. The medical chart review occurred by trained personnel. This study was approved by the Health Research Ethics Boards at the University of Alberta (Pro00069363) and the Conjoint Human Research Ethics Board (REB; Calgary, Alberta).

Descriptive statistics and factors associated with non-adherence were reported as a count and percentage.

Table 2. 1 Differences between ACC guideline recommendations and CCS CRT guidelines.

Guideline Recommendations	**CCS CRT Guidelines**
Minimum QRS width of 120ms with LBBB	Minimum QRS width of 130ms with LBBB
Minimum NYHA Class I, LVEF <0.30	Minimum NYHA Class II, LVEF <0.35

Outcomes

The primary outcome for this study was to determine the proportion of patients receiving ICD therapy according to guideline recommendations and AUC. The secondary outcome was to identify reasons for non-adherence to guideline recommendations and AUC.

Results

Baseline Characteristics

Over the two year period, a total of 1344 ICD procedures were performed. Of these, 37 were excluded due to missing information and another 7 because they were part of a research protocol, leaving 1300 implants for our final analysis. Baseline characteristics are shown in Table 2.2. The mean age was 63.8±12.9 years; the majority were male (79%), with a mean left ventricular ejection fraction (LVEF) of 0.32±0.13 and a Charlson Comorbidity score of 2.94±2.65. A total of 58% of implants were de novo, 34% were for generator replacements and the remaining were upgrades. The most common reason for implant was for a primary prevention indication (69%). Among ICD recipients, 83% were on beta-blockers, 54% were on angiotensin converting enzyme-Inhibitors, 45% were on aspirin and 34% were on lipid lowering therapy.

Table 2. 2 Baseline Demographics

Characteristics	n (%)
Total Implants n=1300	
Age (mean)	63.8±12.8
Sex (male)	1027 (79%)
Charlson Comorbidity Index (mean)	2.94±2.65
QRS (mean)	135±41
LVEF (mean)	0.32±0.13
Primary Prevention	890 (68%)
History and Risk Factors	
Ischemic Cardiomyopathy	872 (67%)
NYHA II-III	754 (58%)
Previous CABG	128 (10%)
Previous PCI	80 (6%)
Previous MI	563 (43%)
Atrial Arrhythmias	254 (20%)
Procedure Type	
New Implant	761 (58%)
ICD	518 (68%)
CRT	243 (32%)
Generator Replacement	442 (33%)
ICD	227 (51%)
CRT	215 (49%)
Upgrade	97 (9%)
ICD	25 (26%)
CRT	72 (74%)
Device Type	
Single Chamber	326 (25%)
Dual Chamber	429 (33%)
Biventricular	530 (41%)
Subcutaneous	15 (1%)
Medications	
Ace-Inhibitor	701 (54%)
Beta-Blocker	1073 (83%)
Coumadin	280 (22%)
NOAC	193 (15%)
Lipid Lowering Therapy	439 (34%)
Aspirin	580 (45%)
Diuretic	367 (28%)

* LVEF= Left Ventricular Ejection Fraction; NYHA= New York Heat Association; CABG= Coronary Artery Bypass Grafting; PCI= Percutaneous Coronary Intervention; MI= Myocardial Infarction; ICD= Implantable Cardioverter Defibrillator; CRT= Cardiac Resynchronization Therapy; NOAC= Novel Oral Anti-Coagulant

Adherence to Guideline Recommendations and AUC

The proportion of patients undergoing various ICD procedures according to guideline recommendations and AUC is shown in Figure 2.1. Of the total procedures that were performed, 68% (n=884) were for a Class I indication, 32% (n=410) were for a Class IIa or IIb indication. A total of 6 of implants did not fit into the guideline recommendations. When evaluating adherence to AUC, the vast majority of ICD procedures classified as either 'appropriate' or 'maybe appropriate' (96%, n=1244) and no implants were classified as 'rarely appropriate'. The remaining 4% (n=56) did not fit into the AUC recommendations.

Among the implants performed for a primary prevention indication, only 0.3% (n=2) of new implants and 0.2% (n=1) of generator replacements did not meet a Class I, IIa or IIb indication, while all upgrades adhered to guideline recommendations. Among CRT implants, 10% (n=41) of procedures were inconsistent with CCS CRT guidelines. According to AUC, 4% (n=37) of ICD procedures for primary prevention did not fit into any existing criteria.

For secondary prevention procedures, 0.4% (n=2) of new implants and 4% (n=1) of upgrades did not meet a Class I, IIa or IIb indication. Among CRT implants, 17% (n=16) of procedures were inconsistent with CCS CRT guidelines. According to AUC, there were 5% (n=19) of secondary prevention procedures that did not fit into the AUC.

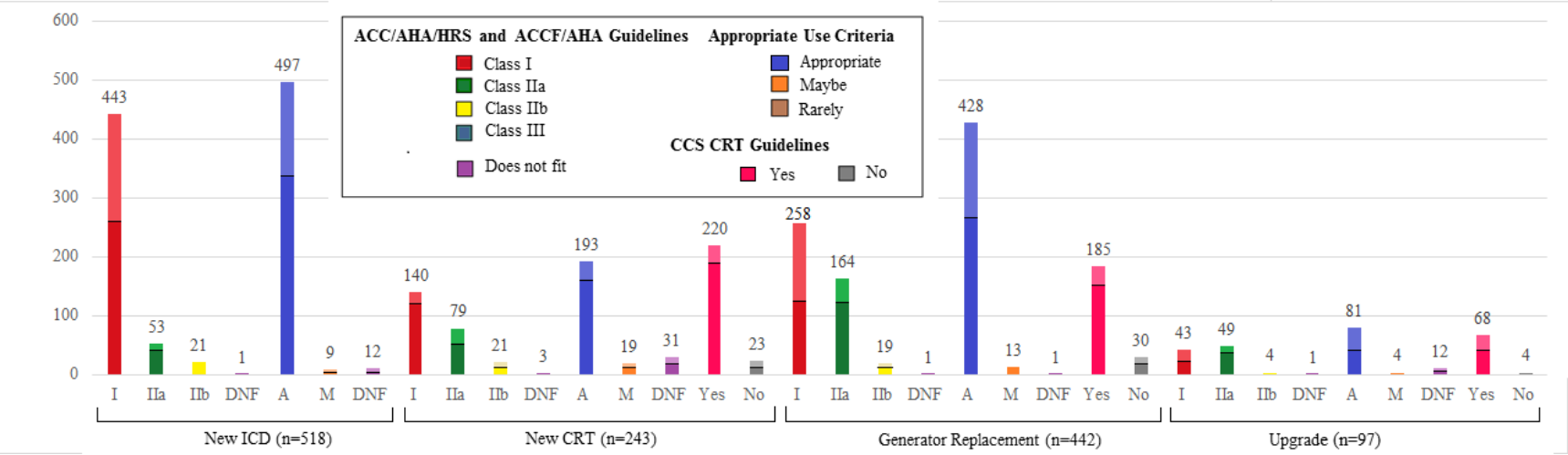

Figure 2. 1 Proportion of implants meeting guideline recommendations and appropriate use criteria according to various procedure types.

[1] The proportion of primary prevention and secondary prevention indications for device procedures is represented by darker shading and lighter shading, respectively.

Reasons for Non-Adherence to Guideline Recommendations, AUC and CCS guidelines

Among ICD procedures performed for non-adherence to guideline recommendations, 3 were for primary prevention: one patient had a new ICD implant with a recent myocardial infarction (MI), one patient had a new CRT implant with a QRS width <120msec and one patient had a CRT generator replacement with a QRS width < 120msec. There were 3 implants for secondary prevention that did not fit guideline recommendations; all were CRT implants (one patient with a LVEF >0.35, one patient was an upgrade with a LVEF >0.35 and one patient was new implant with a QRS width <120msec). Among CRT implants, 57 did not meet CCS CRT guidelines (Figure 2) because of NYHA Class I (63%, n=36), QRS width < 130msec (33%, n=19) or LVEF > 0.35 (4%, n=2). However 91% of CRT implants were indicated if only the 2008 ACC/AHA/HRS ICD guidelines were used. According to AUC, 56 implants did not fit criteria; 6 of these for overlapping reasons for non-adherence to guideline recommendations. There were 11 additional implants that did not fit the AUC because of recent MI or revascularization (MI >48 hours but < 40 days and revascularization < 3 months). Although, most implants that did not fit into the AUC occurred because no criteria existed for classification (70%, n=39). After excluding ICD procedures that had no existing AUC for classification, non-adherence decreased to 1% (n=17).

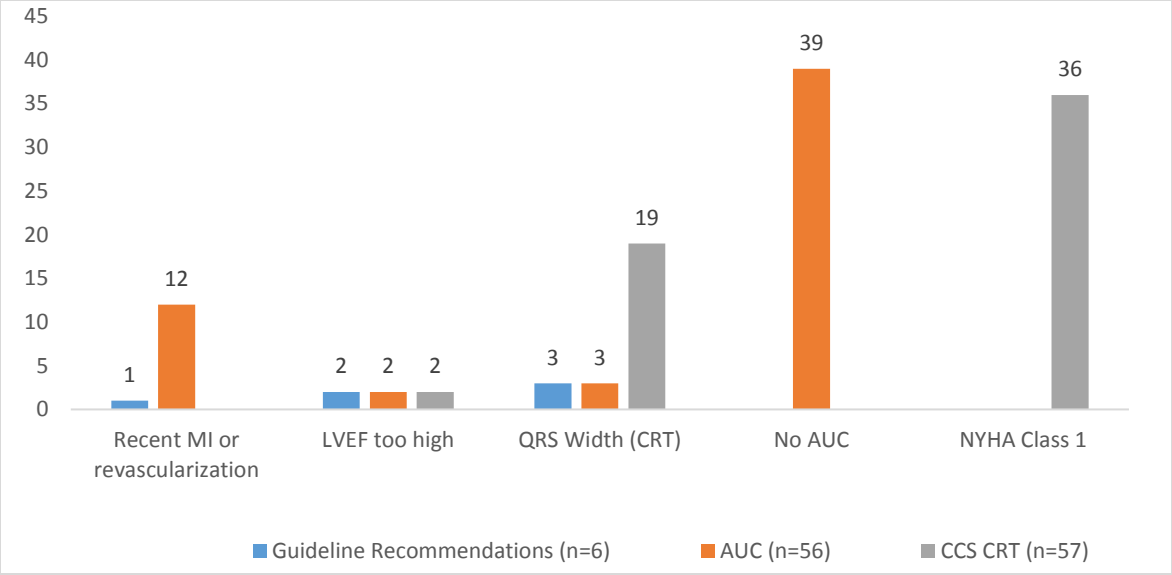

Figure 2. 2 Reasons for non-adherence to guideline recommendations and appropriate use criteria.

Discussion

In this population-based study of consecutive complex device implants, we found that less than 1% of all procedures performed were non-evidence based. We found 0.3% of primary prevention and 0.7% of secondary prevention ICD implants did not meet a guideline recommendation. When applying AUC, over 90% of procedures were classified correctly as 'appropriate'. For patients who did not meet guideline recommendations, half were CRT procedures performed for secondary prevention where LVEF >0.35 or QRS width < 120 msec) The most common reason for non-adherence to AUC, occurring in over two thirds of cases, was the absence of criteria for classification.

Guideline recommendations exist to help identify at risk patients, aid in decision-making and improve patient outcomes. Physician adherence to guidelines can also be used to assess healthcare delivery and inform reimbursement policy. In Canada, reimbursement for ICD therapy is not regulated to the same extent as US agencies, however, there is enormous pressure for cost-saving measures in a healthcare system with finite resources and certain provinces having implemented a cap for device implants. The NCDR was created in response to a mandate

by the Center for Medicaid and Medicare Services (CMS) to characterize patients receiving a primary prevention ICD for reimbursement purposes. Evaluation of this U.S. registry for class I guideline indications demonstrated as high as 22.5% of Medicare beneficiaries received an ICD that was non-evidence based. [5] We found only 0.3% of new, primary prevention implants did not meet Class I guideline recommendations. This is similar to another study performed during a federal audit of claims to the CMS of all de novo non-resynchronization ICD implants for primary prevention that found 1.3% of implants were not indicated with after detailed chart review from an initial 8.7%.[16].

A prior study of the Veterans Affairs Medical centers evaluating first-time, primary prevention generator replacements found that 26% of generator replacements no longer met guideline-derived indications. [14] In contrast, we report that only 0.2% of primary prevention generator replacements no longer met guideline recommendations. A possible explanation for this difference is that we included all generator replacements while the Veterans Affairs study included only first-time generator replacements. In our study, generator replacements accounted for a third of all ICD procedures yet at present, guidelines do not provide recommendation for replacement. However, the AUC does outline clinical scenarios where generator changes are appropriate. We found that over 99% of generator changes were consistent with the AUC. Given the growing heart failure population that would be eligible for ICD therapy[17-19] and the eventual need for future generator replacements balanced with studies demonstrating high risk of infection;[20-22] obtaining more data regarding indications for primary or secondary generator replacement are needed.

We also demonstrated that a third of ICD procedures fulfill a Class IIa or IIb recommendation, whereas the majority of adherence analyses focus on a Class I indications. [5-7,14]

Our study is also novel by assessing adherence to the newly published AUC for device implants. We found 96% of implants (including generator replacements and upgrades) were consistent with 'appropriate' or 'maybe appropriate' AUC criteria and no device procedures that would have been deemed 'rarely' appropriate.

Our study identified reasons for non-adherence to guideline recommendations and AUC. We found that an improved ejection fraction, improved NYHA Class and QRS width < 120ms were common reasons for non-adherence among CRT implants. This is expected because several studies have demonstrated that CRT therapy improves LVEF, the functional capacity and QRS width in patients. [23-25] Another reason non-adherence was recent MI or revascularization which is consistent with a study of non-evidence based implants that found devices implanted within 40 days of an MI or within 3 months of a revascularization were responsible for 40% of non-evidence based implants. [5] Large, randomized clinical trials have failed to demonstrate mortality benefit from early use of ICDs in post-MI patients, [26,27] however, in some cases, pacemakers are indicated in post-MI patients with low LVEF. The decision for immediate ICD implant is made to prevent multiple procedures in patients where LVEF may not improve.

There are several possible reasons to explain the low rate of non-adherence whether applying the guideline recommendations and AUC in our analysis including: (i) specialist evaluation for ICD eligibility. A study of non-evidence based implants demonstrated that the rate of adherence is significantly higher among electrophysiologists compared to other implanting physicians.[5], (ii) a device form that incorporated a checkbox reminder to classifying eligibility according to guideline recommendation and AUC and (iii) formal peer review meeting for discussion and consensus decision. It is unlikely that guideline recommendations and AUC will cover all clinical scenarios that arise when considering device therapy. In these complex cases, it

is important to make decisions that are individualized to the patient and that to utilize peer-review. However, when re-occurring clinical scenarios are identified, it is important to examine large databases for outcomes and to perform clinical trials to confirm indication for device therapy among these sub-groups.

There are several limitations of our study that warrant discussion. First, we did not compare our data to a non-peer reviewed implanting center. Despite, this comparison, our data suggest that simple strategies can produce consistency with guideline recommendations and AUC. Second, we did not capture appropriate therapies of device recipients. Third, our study was performed in one province and the findings may not be generalizable to the whole country. Lastly, our study did not assess the proportion of patients eligible for device therapy.

Conclusion

In this population-based study, we found that a formal process of specialist evaluation, reminders of eligibility incorporated into the device requisition and peer-review consensus was highly effective at achieving consistency with guideline recommendations and AUC. This care pathway can be easily implemented at other implanting centers. Future research is needed to address common clinical scenarios where no recommendation or appropriate use criteria exist.

Project 3
A Population-Based Study of Complex Device Eligibility, Utilization and Reasons for Non-Implantation in Patients at Heart Function Clinics

ABSTRACT

Background: Implantable cardioverter defibrillators (ICD) reduce morbidity and mortality in patients at risk for sudden cardiac death. Yet, data regarding device eligibility and utilization in a real-world setting remains sparse.

Aims: The primary aim of this study was to determine the rates of ICD eligibility and utilization among patients seen at heart function clinics. Secondary aims were to identify reasons for non-implantation among eligible patients and to determine significant predictors of non-implantation.

Methods: As part of a quality improvement initiative, we performed a retrospective review of consecutive patients seen at two heart function clinics in Alberta, Canada from 2012-2015. A detailed chart review was performed to collect demographics, clinical indications, comorbidities and to identify reasons for non-implantation. Eligibility was determined using the 2008 ACC/AHA/HRS ICD guidelines and the 2013 CCS CRT guidelines. Logistic regression was used (odd ratio, OR and 95% CI) to identify predictors of device non-implantation.

Results: Overall, 1294 patients were seen in HF clinic, the majority were male (67%), the median age was 69 (IQR 59-80) and the mean ejection fraction (EF) was 0.40 (SD $\pm$0.15). Over the follow-up period, 53% of patients were never eligible for device therapy based on EF criteria. Yearly rates of eligibility and utilization ranged from 32-52% and 19-56%, respectively. When a reason for non-implantation was accounted for, yearly utilization rates increased to 36-64%. Among eligible patients, independent predictors of device non-implantation were age >75 years (OR 1.80, 1.23-2.63), LVEF $\leq$0.35 (OR 4.69, 2.74-8.04), kidney disease (OR 1.71, 1.04-2.80) and cancer (OR 2.56, 1.23-5.34). Almost half of the time (46%), no clear documented reason for non-implantation was found. When a reason was documented, it was most commonly included patient preference (25%), technical reasons (19%) and medical reasons (10%).

Conclusions: In this population-based study, we found that less than half of eligible patients received an ICD and a reason for non-implant was often missing. Better screening and documentation is needed in order to improve ICD utilization.

Introduction

Several randomized clinical trials have demonstrated implantable cardioverter defibrillator (ICD) therapy reduces morbidity and mortality in patients with heart failure and a reduced ejection fraction, at risk for sudden cardiac death. [1-5] The results of these primary prevention ICD trials, have formed guideline recommendations to help physicians identify patients who would benefit from for this life-saving therapy. However, data regarding how guideline recommends translates into ICD eligibility and utilization in clinical practice is sparse. [9-11]

Prior observational studies[9-11] assessing ICD eligibility have found that the use of ICD therapy varies widely with approximately 20.5%[10] -57% [9] of patients seen in hospitals and outpatient heart function clinics are eligible and only 13%-87%[9-11] receive a primary prevention device. The higher rates of eligibility and utilization was from the one study that used chart-level data to identify at-risk population and documented reasons for non-implantation. [9] The most common reasons for not implanting a device in an otherwise eligible candidate include older age, [12-15] female sex[13,15,16] and reduced left ventricular ejection fraction (LVEF). [9] These prior works have been limited by small inpatient populations[10] or single-center studies [9-11] and the majority did not query medical charts for reasons for non-implantation which may not have captured a population of eligible patients.

Therefore, we aimed to determine rates of ICD eligibility and utilization using chart-level data in a province-wide study based on the 2008 American College of Cardiology/ American Heart Association/Heart Rhythm Society (ACC/HRS/HRS) ICD and cardiac resynchronization therapy (CRT) guidelines and the 2012 American College of Cardiology Foundation/ American Heart Association/ Heart Rhythm Society (ACCF/AHA/HRS) Focused Update. [6,7] We also

aimed to determine reasons for non-implantation and to identify significant predictors for device non-implantation among eligible patients.

Methods

Study Population

As part of a quality improvement initiative, the Arrhythmia Expert Working Group of the Alberta Health Services Cardiovascular and Stroke Strategic Clinical Network oversaw a retrospective review of all active patients at two tertiary heart function clinics in Alberta, Canada from 2012-2015 in order to ensure effective and efficient healthcare delivery. The composition of the study cohort varied each year depending on referrals, frequency of follow-up and patients leaving the clinic for various reasons (i.e. death or other reasons). Patient inclusion criteria included: age > 18 years, history of HF, etiology of cardiomyopathy; New York Heart Association (NYHA) functional class and left ventricular ejection (LVEF) documented within two years of enrollment into the study.

We used the REDCap electronic data capture tools hosted by the Clinical Research Informatics Core at the University of Alberta to electronically input patient characteristics. [17] This study was approved by the Health Research Ethics Board of the University of Alberta (Pro00063905) and the Conjoint Human Research Ethics Board (CHREB Calgary, Alberta)

Patients active as of January 1st of each year (2012-2015) were screened for a detailed review of device eligibility, utilization and documentation of reasons for non-adherence. Baseline demographics, clinical indications and comorbid disease were abstracted from the chart. A history of arrhythmias including atrial fibrillation (AF) or flutter (AFl) were confirmed by electrocardiogram. Assessments of LVEF were taken closest to the most recent clinic visit. LVEF measurement modalities included magnetic resonance imaging, echocardiogram and

multi-gated acquisition scan. Chart reviewers were independent of the heart function clinic physicians.

ICD Eligibility

Eligibility criteria were based from 2008 guideline recommendations for primary prevention ICD and CRT and the 2012 focused update.[6,7] Patients were considered "guideline eligible" if they met the following criteria; LVEF ≤0.35, NYHA Class I-III and an absence of either revascularization within 3 months or acute myocardial infarction within 40 days of determined device eligibility.

Reasons for non-implantation

Patients were stratified into "never guideline eligible" or "ever guideline eligible". Ever guideline eligible patients were further stratified into "device recipients" and "device non-recipients". Reasons for non-implantation were determined by reviewing physician letters, EP consults and nurses notes. Reasons for non-adherence included patient preference, medical reason (life expectancy < 1 year, poor quality of life, severe CKD or significant comorbidities), technical reason (not medically optimized, device attempted but failed or LVEF improved on subsequent tests) and other (other reason or not documented). Patients who were categorized as guideline eligible and had no documented reason for non-implantation were identified as "truly eligible".

Outcomes

The primary outcome for this study was to determine rates of ICD eligibility and utilization. Secondary outcomes were to identify reasons for non-implant and to determine significant predictors for device non-implantation in eligible patients.

Statistical Analysis

Baseline demographics were presented as a count, mean (standard deviation) or median (inter-quartile range). Characteristics were stratified into 'never guideline eligible' patients and 'ever guideline eligible' patients and then were further stratified into device recipients and device non-recipients. Device recipients and non-recipients were compared using Kruskal-Wallis tests for continuous variables and Chi squared tests for categorical variables. We used logistic regression to identify predictors of device non-implantation. The primary predictors were sex and age >75 years. We used the likelihood ratio test to examine the inclusion of additional independent variables such as ischemic cardiomyopathy, LVEF < 35%, and NYHA class. We also examined inclusion of patient comorbidities such as atrial fibrillation, hypertension, hyperlipidemia, acute myocardial infarction, diabetes, peripheral vascular disease, cerebrovascular disease, kidney disease, liver disease, cancer, and dementia. Except for the primary predictors, a variable remained in the final multivariate model if the likelihood ratio test was significant at a 5% level.

Results

Baseline Demographics

A total of 1935 patients were actively followed at the two Heart Function Clinics from 2012-2015. Of these, 641 were excluded due to missing information such as no NYHA Class or LVEF documented within 2 years of study enrollment (Figure 3.1). Of the final cohort (n=1294), 53% (n=691) of patients were never eligible for a device. Among guideline eligible patients, 40% (n=243) received a device during the study follow-up (Figure 3.1).

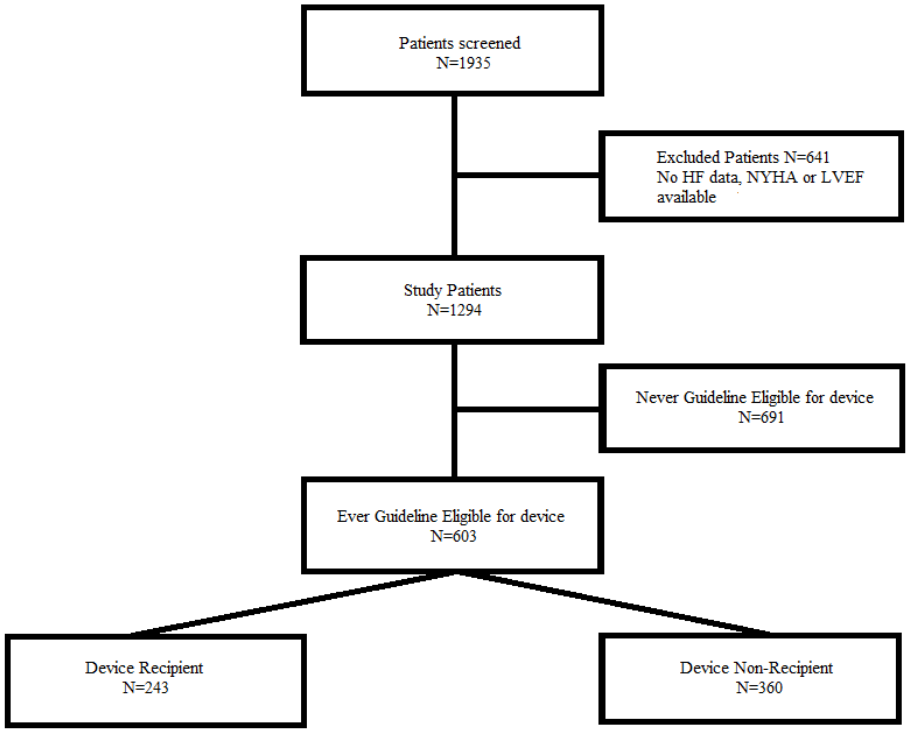

Figure 3. 1 Patient Flow Diagram

Baseline demographics are shown in Table 3.1. The median age of the population was 69 years (IQR 59-80), majority were male (67%), 35% of patients had ischemic cardiomyopathy and the mean LVEF was 0.40±0.147. Among eligible patients, device non-recipients were more likely to be older than 75 years (39% vs 24%, $p<0.001$), to have a lower LVEF (median 26.2 vs 28.3, $p=0.003$), and more likely to have had cancer (10.7% vs 4.1 %, $p=0.0003$) as well as less likely to have paroxysmal AF (22.8% vs 42.3%, $p=0.01$) when compared to device recipients (Table 1).

Table 3. 1 Baseline Demographics

Characteristic	All Patients	Never Guideline Eligible	Ever Guideline Eligible		P
			Device Recipients	Device Non-recipients	
Patients, N	1,294	691	243	403	
Age (y), median (IQR)	69 (59-80)	71 (59-81)	67 (59-75)	69 (60-81)	0.002
Age > 75 y, n (%)	458 (35.4)	256 (37.1)	59 (24.3)	157 (39)	<0.001
Sex: male, n (%)	868 (67.1)	412 (59.6)	183 (75.3)	304 (75.4)	0.971
Heart Failure Etiology, ischemic, n (%)	453 (35)	204 (29.5)	106 (43.6)	162 (40.2)	0.392
LVEF, mean (SD)	40.1 (14.7)	51.5 (8.5)	28.3 (10)	26.2 (6.3)	0.003
NYHA Class, n, (%)					
-I	363 (28.1)	237 (34.3)	51 (21)	87 (21.6)	0.212
-II	522 (40.3)	258 (37.3)	101 (41.6)	174 (43.2)	
-III	255 (19.7)	112 (16.2)	70 (28.8)	90 (22.3)	
-IV	12 (0.9)	3 (0.4)	4 (1.7)	6 (1.5)	
-Not reported	142 (11)	81 (11.7)	17 (7)	46 (11.4)	
Cardiovascular Comorbidities, n (%)					
Atrial Fibrillation	509 (39.3)	303 (43.9)	78 (32.1)	145 (36)	0.315
-Paroxysmal	143 (28.9)	85 (28.1)	33 (42.3)	33 (22.8)	0.010
-Persistent	282 (55.4)	166 (54.8)	36 (46.2)	87 (60)	
-Not reported	84 (16.5)	52 (17.2)	9 (11.5)	25 (17.2)	
Atrial Flutter	39 (3)	22 (3.2)	5 (2.1)	12 (3)	0.615
Hypertension	627 (48.5)	360 (52.1)	110 (45.3)	175 (43.4)	0.648
Hyperlipidemia	108 (8.4)	59 (8.5)	25 (10.3)	30 (7.4)	0.210
Myocardial Infarction	271 (20.9)	111 (16.1)	68 (28)	102 (25.3)	0.455
Cerebrovascular Disease	130 (10.1)	71 (10.3)	24 (9.9)	40 (9.9)	0.984
Diabetes	386 (29.8)	208 (30.1)	71 (29.2)	122 (30.3)	0.777
-Complicated	23 (6)	15 (7.2)	2 (2.8)	6 (4.9)	0.118
-Uncomplicated	278 (72)	143 (68.8)	60 (84.5)	87 (71.3)	
-Not reported	85 (22)	50 (24)	9 (12.7)	29 (23.8)	
Peripheral Vascular Disease	38 (2.9)	22 (3.2)	6 (2.5)	13 (3.2)	0.640
Other Comorbidities, n (%)					
Kidney Disease	224 (17.3)	121 (17.5)	30 (12.4)	81 (20.1)	0.011
-Mild	115 (51.3)	64 (52.9)	18 (60)	36 (44.4)	0.356
-Moderate-Severe	68 (30.4)	37 (30.6)	8 (26.7)	27 (33.3)	
-Not reported	41 (18.3)	20 (16.5)	4 (13.3)	18 (22.2)	
Liver Disease	3 (0.2)	1 (0.1)	0 (0)	2 (0.5)	0.530
Cancer	126 (9.7(	77 (11.1)	10 (4.1)	43 (10.7)	0.003

[4] IQR= Inter-quartile Range. SD= Standard Deviation, LVEF= Left Ventricular Ejection Fraction, NYHA= New York Heart Association

-Active	16 (12.7)	12 (15.6)	1 (10)	3 (7)	0.306
-Remission	92 (73)	56 (72.7)	9 (90)	31 (72.1)	
-Not reported	18 (14.3)	9 (11.7)	0 (0)	9 (20.9)	
Dementia	13 (1)	5 (0.7)	1 (0.4)	7 (1.7)	0.270

Device Eligibility and Utilization

Yearly rates of device eligibility and utilization are shown in Figure 3.2. Rates of device eligibility for 2012-2015 ranged from 32%-52% and device utilization among eligible patients ranged from 19%-56%. Yearly rates of device eligibility among 'truly eligible' patients ranged from 13%-46% and yearly utilization rates increased ranging from 36%-64% (Figure 3.3).

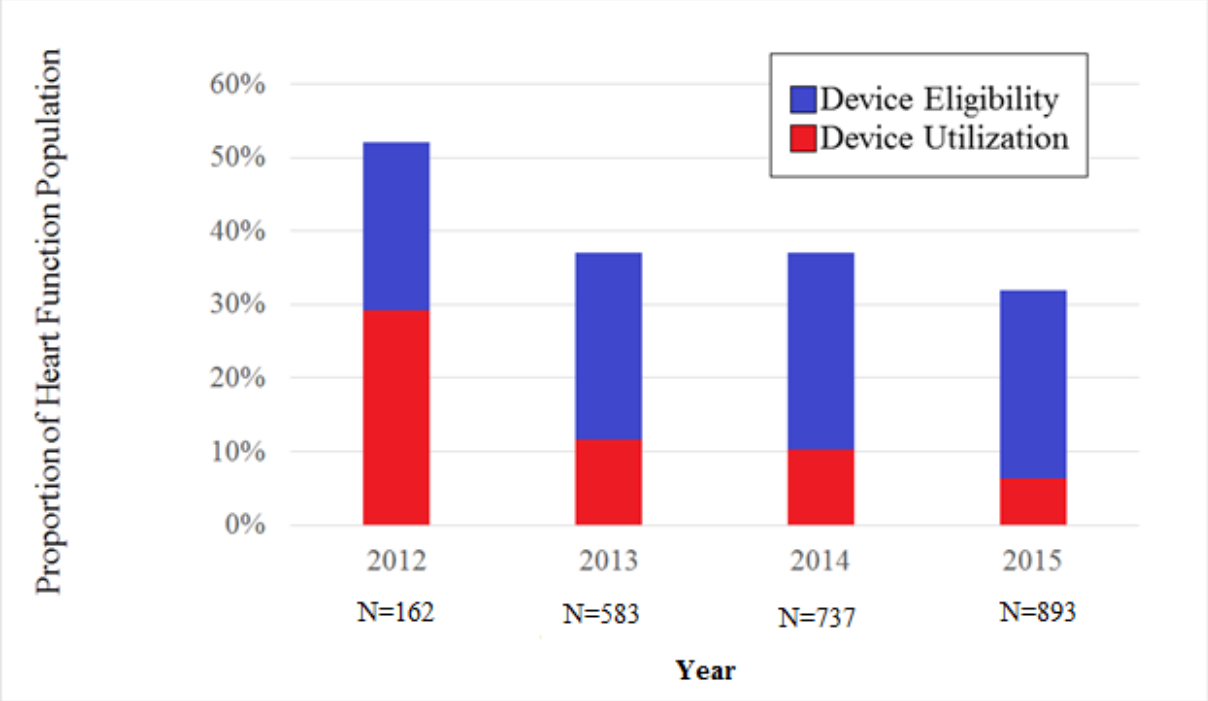

Figure 3. 2 Yearly rates of device eligibility and utilization among patients seen in heart function clinic.

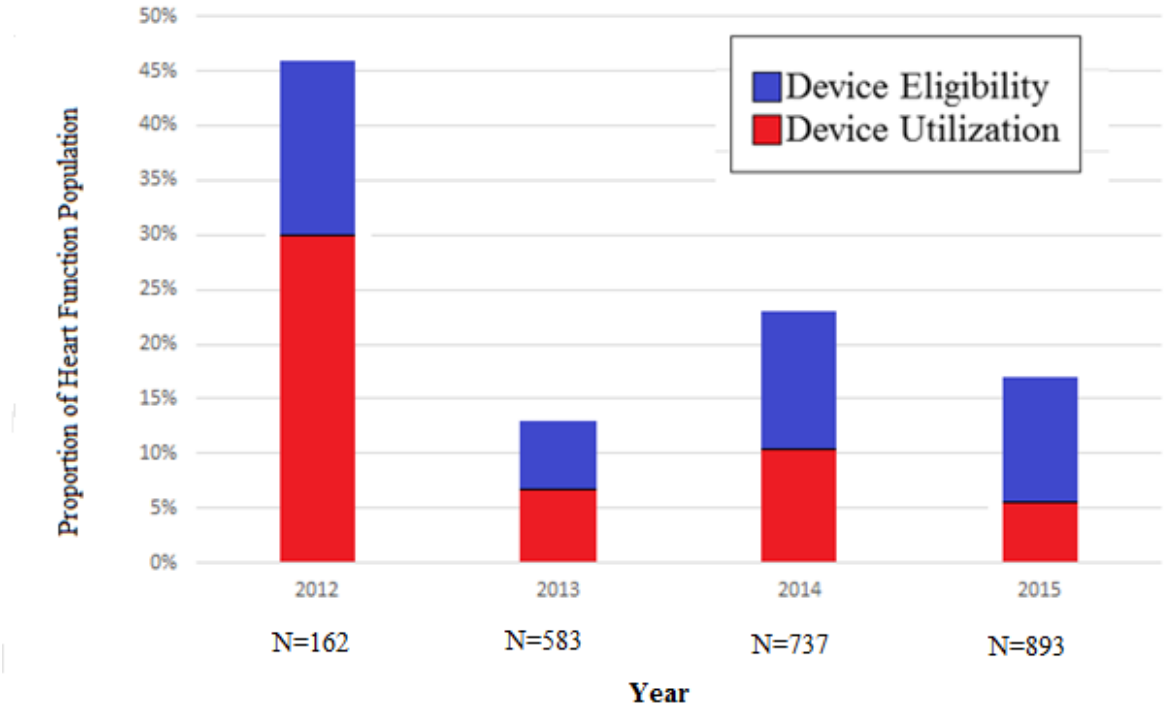

Figure 3. 3 Yearly rates device eligibility and utilization among truly eligible patients. Reasons for non-implantation

Documented reasons for non-implantation are shown in Figure 3.4. 'Patient preference' was the most commonly documented reason for non-implantation (25%), followed by 'technical reason' (19%) and 'medical reason' (10%). However, a documented reason for non-implantation was not found in 46% eligible patients.

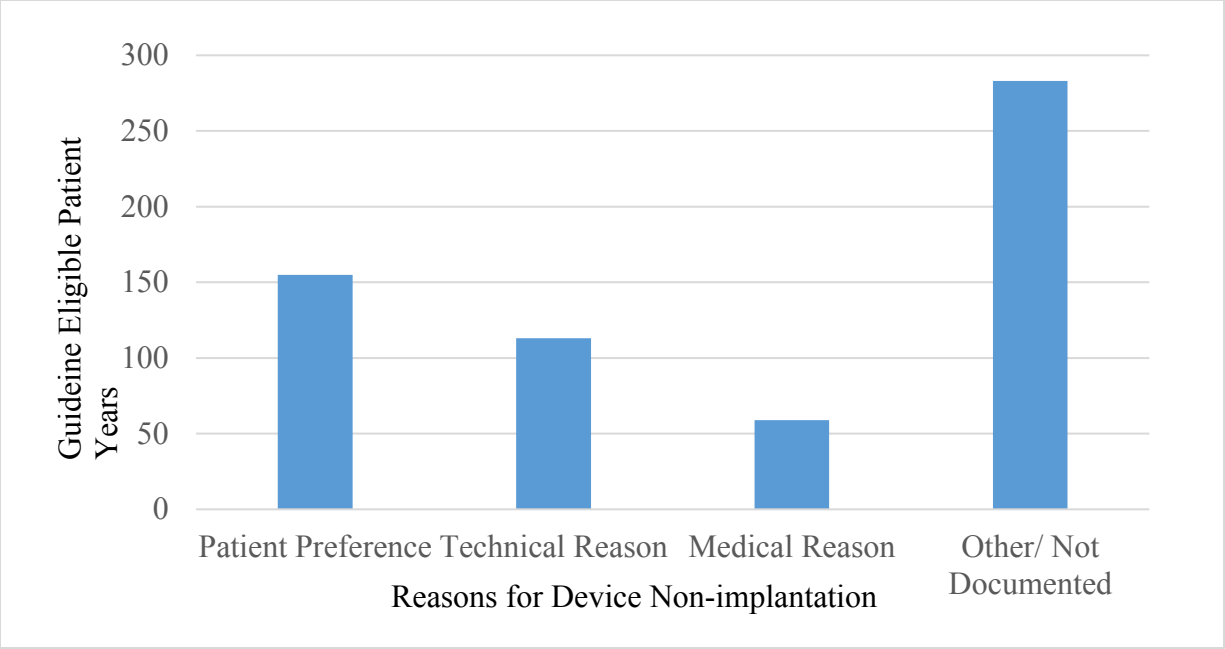

Figure 3. 4 Reasons for non-implantation among eligible patients.

Factors associated with non-implantation

Patient characteristics that were significantly associated with device non-implantation among all eligible patients is shown in Table 3.2. Ever guideline eligible patients were more likely to be older than 75 years (OR 1.80; 95% CI 1.23-2.63), have a reduced ejection fraction (OR 4.69; 95% CI 2.74-8.04), suffer from kidney disease (OR 1.71; 95% CI 1.04-2.80) and have a history of cancer (OR 2.56; 95% CI 1.23-5.34). Whereas 'truly eligible' patients were only more likely to be older than 75 years (OR 1.49; 95% CI 1.04-2.13) and have a history of cancer (OR 1.71; 95% CI 1.02-2.88).

Table 3. 2 Factors associated with non-implantation in 'ever guideline eligible' patients and 'truly eligible' patients.

	Ever guideline-eligible patients (n=646)		Ever truly eligible patients (n=619)	
Associated Factor	OR (95% CI)	P	OR (95% CI)	P
Age > 75 years	**1.80 (1.23-2.63)**	**0.002**	**1.49 (1.04-2.13)**	**0.027**
Female sex	0.96 (0.65-1.43)	0.855	0.95 (0.63-1.43)	0.807
LVEF < 35%	**4.69 (2.74-8.03)**	**<0.001**		
NYHA				
-I (ref.)	1	--		
-II	0.88 (0.56-1.37)	0.565		
-III	0.59 (0.36-0.98)	0.040		
-IV	0.88 (0.22-3.56)	0.855		
-Not reported	1.24 (0.61-2.54)	0.549		
Kidney Disease	**1.71 (1.04-2.80)**	**0.034**		
Cancer	**2.56 (1.23-5.34)**	**0.012**	**1.71 (1.02-2.88)**	**0.044**

Discussion

In this large, population-based study of complex device eligibility and utilization over a contemporary period, approximately only a third of eligible patients receive an ICD. When accounting for reasons for non-implantation, utilization rates increased to approximately half of patients. Although, the most common documented reason for non-implantation was 'patient preference', almost half of the time there was no documented reason for why a device was not implanted.

We found that rates of ICD utilization among guideline eligible patients were lower than previous reports. [9, 10,18] Even after accounting for reasons for non-implantation, utilization rates remained low at 36%-64% among 'truly eligible' patients. These differences are most likely due to study methodology. We excluded implants occurring before the study period, which provided a more accurate estimation of device utilization. Prior reports[9] included this sub-group of patients in their analysis which could have increased device utilization estimates. The significant under-

utilization of ICD therapy found in our study has been previously reported in other retrospective reviews.[11,14,19]

There were several reasons for non-implantation identified in our study, however almost half of the time, there was no documented reason for non-implantation among eligible patients. This is similar to a previous single-center, retrospective study in which 42% of the time a documented reason for non-implantation among eligible patients was not found [9] This highlights the need for quality improvement initiatives that are geared towards emphasizing complete and clearly documented medical records that consist of patient preferences, risks and contraindications. In addition, 'patient preference' was the most common documented reason for non-implantation among eligible patients. This is consistent with other studies that report 'patient preference' accounted for 17%[10] and 19%[9] of reasons for non-adherence among eligible patients. It is important to address patient barriers for device implantation in order to increase the utilization of this life-saving therapy.

In our study, we also found that older age, reduced ejection fraction and the presence of kidney disease and cancer were associated with device non-implantation among eligible patients. This is similar to other retrospective reviews that have also reported older age and reduced ejection as significant predictors for non-implantation. [9,10] In addition, the presence of significant comorbidities has been previously associated with device non-adherence. [11] Our study also reports that the presence of comorbidities such as kidney disease or cancer was associated with device non-implantation.

There are several initiatives known to improve adherence to device-based therapy. [20-23] The IMPROVE HF registry is quality improvement registry designed to evaluate the outpatient management of systolic heart failure and to assess the effect of various improvement

interventions such as education initiatives, reminder systems and quality reports. With use of the IMPROVE HF registry, ICD utilization increased dramatically from 50.1% to 77.5%.[22] The use of electronic screening tools have also shown to significantly improve appropriate ICD referrals.[23] However our data suggests that further initiatives are needed in order to improve device utilization among patients identified as guideline eligible such as electronic reminders of ICD eligibility incorporated into medical records.

There are limitations to our study that warrant discussion. First, the number of chart reviews in 2012 was lower than other study years and was due to limited use of electronic medical records at that time. This may have skewed the eligibility and utilization rates for that year. Second, this was a retrospective study where abstraction errors and variability in medical chart completeness pose a risk. However, in order to minimize this, we used a single medical chart reviewer and adhered to strict definitions of device eligibility. Third,, study was performed in one province and the results may not be generalizable to other areas and healthcare systems.

Conclusion

In this population-based study of complex device eligibility and utilization, we found that less than half of eligible patients received an ICD and a documented reason for non-implantation was often missing. Initiatives geared towards improving patient screening and medical chart documentation are needed in order to improve ICD utilization.

Overall Conclusions

This thesis provides several important findings. In Project 1, we found that knowledge regarding indications for primary prevention ICD therapy amongst referring physicians is poor and varies significantly depending on physician specialty, with Cardiologists and Cardiology Residents being most familiar with ICD indications. It also highlighted several important overall barriers for ICD referral including cost of ICD therapy, lack of confidence in knowledge and the risk of inappropriate shocks. When looking at appropriateness of device therapy in Project 2, we demonstrated that a process consisting of initial specialist evaluation, reminders of device eligibility incorporated into requisitions and peer-review consensus in resulted in less than 1% of ICD procedures being non-evidence based. The most common reason for non-adherence was no existing criteria for classification. The initial work done for Project 3 suggests that less than half of eligible patients receive an ICD and that a documented reason for non-implantation was often missing. The most common reasons for non-implant included patient preference, technical reasons (not medically optimized, device attempted but failed or LVEF improved on subsequent tests) and medical reasons (life expectancy < 1 year, poor quality of life, severe chronic kidney disease or significant comorbidities).

The poor knowledge of ICD therapy and lack of confidence in knowledge of ICD indications which was demonstrated in Project 1 may, in part, explain the low rates of ICD utilization found in Project 3. Future initiatives that may improve the delivery of ICD therapy based on the results from Project 1 and 3 include; knowledge translation efforts regarding ICD recommendations such as workshops at scientific meetings, formal talks and web-based educational sessions. As well as incorporating electronic reminders in medical records regarding device eligibility may improve ICD referral of high risk patients for specialist evaluation. The

device implant process studied in Project 2 could also be implemented in order to improve the appropriate utilization of this life-saving therapy.

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Appendix 1**.** Complete survey with responses distributed according to the physician specialty.

Case Scenarios	**Physician Specialties**		
	Cardiologists	Internists	Cardiology Residents
Case Scenario 1	You are seeing a 50 year-old patient discharged from hospital 2 weeks after an acute myocardial infarction and a drug-eluting stent to the circumflex artery. Prior to discharge, an echocardiogram measured a LVEF of 20%. He was started on a low dose beta-blocker, ace-inhibitor, statin and anti-platelet agents. Today in clinic, he is asymptomatic with a blood pressure of 150/60 mmHg, heart rate of 100 bpm. ECG shows sinus rhythm (QRS 98ms). What is your next step?		
A: Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	1 (3%)	3 (5%)	1 (7%)
B: Wait 1 month and refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	1 (3%)	3 (5%)	2 (14%)
C: Optimize medical therapy and once stable doses are achieved wait 3 months and repeat echocardiogram.	**33 (94%)**	**53 (88%)**	**11 (79%)**
D: No further cardiac management at this time.	0	1 (2%)	0
Case Scenario 2	You are seeing a 65 year-old patient with past medical history significant for coronary bypass graft surgery 2 years ago, diabetes and hypertension. He has NYHA III heart failure symptoms on GDMT at optimal doses. LVEF is 29%, which is unchanged for the last 2 years. ECG shows sinus rhythm and LBBB (QRS 140ms). What is your next step?		
A: Refer for cardiac transplant.	0	5 (8%)	2 (14%)
B: Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**31 (89%)**	**40 (67%)**	**12 (86%)**
C: Assess for ongoing ischemia with coronary angiogram.	4 (11%)	11 (18%)	0
D: No further cardiac management at this time.	0	4 (7%)	0
Case Scenario 3	You are seeing a 75 year-old female with non-ischemic dilated cardiomyopathy and NYHA class II symptoms, LVEF was 25% one year ago and after optimizing GDMT; repeat LVEF is 32%. ECG shows sinus rhythm with a LBBB (QRS 150ms). What is your next step?		
A: Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**27 (77%)**	**27 (45%)**	**12 (86%)**
B: Wait 9 months and repeat echocardiogram.	5 (14%)	13 (22%)	1 (7%)
C: Refer to Heart Function clinic to further titrate medications.	2 (6%)	10 (16.5%)	1 (7%)
D: No further cardiac management at this time.	1 (3%)	10 (16.5%)	0
Case Scenario 4	You are seeing a 70 year-old man with past medical history significant for ischemic cardiomyopathy, LVEF is 28% on GDMT, NYHA I and a current smoker. ECG shows sinus rhythm with a LBBB (QRS 150ms). Recently, he noted weight loss and a cough. Evaluation revealed metastatic lung cancer with a life expectancy of 9 months. What is your next step?		
A: Optimize medical therapy and once stable doses are achieved wait 3 months and repeat echocardiogram.	1 (3%)	8 (13%)	1 (7%)
B: Repeat echocardiogram in 9 months	0	2 (3%)	1 (7%)
C: Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	0	0	0
D: No further cardiac management at this time.	**34 (97%)**	**50 (84%)**	**12 (86%)**
Case Scenario 5	You are seeing a 55 year-old patient with ischemic cardiomyopathy, LVEF of 27% on GDMT. He exercises everyday for 30 minutes without any symptoms and golf's 3 times per week in the summer. ECG shows sinus rhythm (QRS 88ms). What is your next step?		
A: Refer to cardiac rehab.	1 (3%)	2 (3%)	1 (7%)
B: Refer to a Cardiac Electrophysiologist for consideration of a primary prevention ICD.	**32 (91%)**	**28 (47%)**	**10 (72%)**
C: Titrate medications further.	0	4 (7%)	1 (7%)
D: No further cardiac management at this time.	2 (6%)	26 (43%)	2 (14%)

BPM= Beats per minute, CS= Case Scenario, ECG = Electrocardiogram, GDMT= Guideline directed medical therapy, LBBB= Left bundle branch block, LVEF= Left ventricular ejection fraction, NYHA= New York Heart Association class