Pacemakertherapie voor bradycardie in België.

KCE reports 137A

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
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PACEMAKERTHERAPIE VOOR BRADYCARDIE IN BELGIE

KCE rapporten 137A

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VOORWOORD

De introductie van de pacemaker in de vijftiger jaren van de vorige eeuw geldt ongetwijfeld als een van de succesverhalen van de medische technologie. Het implanteren van een technisch apparaat in het menselijk lichaam was toen nog revolutionair en voor de patiënten bij wie een pacemaker werd ingeplant was het klinisch resultaat soms miraculeus. Een hartritme van amper 25 slagen per minuut werd meteen opgedreven tot 70 slagen per minuut, waardoor klachten van flauwvallen en hartfalen prompt verdwenen.

Tot halfweg de jaren 1970 werden in België tot 1000 pacemakers per jaar geïmplanteerd. Een kwarteeuw later waren de indicaties fors uitgebreid, en waren er dat tienmaal meer. Ons land is in Europa altijd bij de koplopers geweest wat betreft het aantal pacemaker-implantaties. Dit was de aanzet om in 1981 te starten met een nationaal register voor het verzamelen van implantatiegegevens omtrent pacemakers, en ook dat was toen pionierswerk. In dit verband ook heeft het RIZIV het KCE verzocht te peilen naar de huidige positie van België binnen Europa inzake het gebruik van pacemakers. Tevens werd gevraagd om na te gaan aan de hand van de gegevens uit het register van de Belgian Heart Rhythm Association (BeHRA), deze van de ziekteverzekeraars (Intermutualistisch Agentschap, IMA) en deze van de FOD Volksgezondheid, of de Belgische praktijk overeenkomt met wat voorgeschreven wordt in internationale praktijkrichtlijnen voor pacemakertherapie. Zoals vaak het geval is bij succesvolle technologieën, werd dit een oefening in het aftasten van de limieten van een indicatiegebied.

Een speciaal woord van dank willen we richten aan de experten van de eerder vermelde instellingen voor het ter beschikking stellen van hun gegevens.

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Samenvatting en aanbevelingen

INLEIDING

Meer dan 50 jaar geleden werd de pacemaker, of implanteerbare hartstimulator, in de geneeskundige praktijk geïntroduceerd ter behandeling van syncopes veroorzaakt door een extreem traag hartritme (bradycardie) wegens totaal hartblok. De klinische verbetering die hierdoor meteen optrad, was bijna miraculeus.

In de loop van de tijd werd het gebruik van pacemakers uitgebreid tot andere types van bradycardie, zoals die welke zich kan voordoen bij sinusknoopziekte of bij voorkamerfibrillatie. Deze bradycardietypes vormen een heterogene mix van aandoeningen met verschillende graden van ernst en een reeks uiteenlopende symptomen, gaande van recidiverende syncopes tot duizeligheid. Soms veroorzaken ze zelfs helemaal geen symptomen. Jammer genoeg werd de klinische doeltreffendheid van pacemakertherapie bij deze aandoeningen nooit in goede wetenschappelijke studies onderzocht. Toch vormden ze geleidelijk aan de voornaamste redenen voor een pacemaker-implantatie.

Reeds geruime tijd wordt bezorgdheid geuit over het hoge aantal pacemaker implantaties dat in België plaatsvindt in vergelijking met andere Europese landen. Het doel van dit rapport is om de huidige pacemakerpraktijk voor het behandelen van bradycardie in België te beschrijven en deze te vergelijken met de praktijkaanbevelingen uit wetenschappelijke richtlijnen en met de pacemakerpraktijk in andere Europese landen.

KLINISCHE ACHTERGROND

De implantatie van een pacemaker heeft tot doel de klachten te voorkomen die veroorzaakt worden door een abnormaal laag hartritme of “bradycardie”. Een plots optredend tijdelijk bewustzijnsverlies of “syncope” is het meest dramatische symptoom van bradycardie. Minder ernstige symptomen die verband kunnen houden met bradycardie zijn onder meer duizeligheid, vermoeidheid en kortademigheid. Een pacemaker is in staat om het hartritme van een persoon bij wie hij werd ingeplant voortdurend te controleren. Als het hartritme onder een vooraf bepaalde drempel zakt, stuurt het apparaat een prikkel naar het hart waardoor het samentrekt. Pacemakertherapie is de enige doeltreffende behandeling van bradycardie. Pacemakers ontworpen voor het behandelen van bradycardie staan bekend als “bradycardie” of “conventionele” pacemakers, om ze te onderscheiden van een nieuw type pacemaker dat wordt gebruikt ter behandeling van hartfalen. Deze laatste staat bekend onder de naam cardiale resynchronisatietherapie (CRT) maar valt buiten het opzet van dit rapport.

Bradycardie wordt veroorzaakt door een stoornis in het geleidingsweefsel van het hart dat zorgt voor het ontstaan en de voortplanting van de elektrische prikkel die de hartspier doet samentrekken Een vertraging in de geleiding van die prikkel kan zich voordoen in de voorkamer(s) van het hart (waardoor sinusknoopziekte ontstaat), of in de overgangszone tussen de voorkamers en de kamers (wat leidt tot verschillende graden van hartblok of tot een traag ventriculair antwoord in geval van voorkamerfibrillatie). Geleidingsstoornissen ontstaan doorgaans als gevolg van een leeftijdsgebonden degeneratie van het geleidingsweefsel van het hart. Afhankelijk van de ernst ervan kan de bradycardie die hierdoor ontstaat onopgemerkt blijven, of leiden tot een min of meer belangrijke vertraging van het hartritme en eventueel tot de hierboven vermelde symptomen.

PACEMAKERTECHNOLOGIE

Een pacemaker is een apparaatje met een batterij dat verbonden is met het hart door middel van een of twee draden, de zogenaamde elektrodes (of 'leads'). Het apparaat wordt onder plaatselijke verdoving vlak onder de huid geïmplanteerd, gewoonlijk beneden het rechter- of linkersleutelbeen. De elektrodes worden onder radioscopische controle langs een ader opgeschoven tot in het hart.

De meeste moderne pacemakers moeten 5 tot 9 jaar na de eerste (of primo) implantatie worden vervangen. De levensduur van de elektrode is langer, en wanneer een pacemaker wordt vervangen omdat de batterij uitgeput is, kunnen de oorspronkelijke elektrodes meestal behouden blijven en gewoon aangesloten worden op het nieuwe apparaat.

ORGANISATIE VAN DE PACEMAKERPRAKTIJK IN BELGIE

In 1999 werden zogenaamde "zorgprogramma's" ingevoerd door de Belgische federale regering. Ze omschrijven organisatorische aspecten van een aantal ziekenhuisdiensten waaronder geriatrie, pediatrie, oncologie, reproductieve gezondheid en cardiologie. In dit rapport worden de verschillende zorgprogramma's die betrekking hebben op cardiologie "cardiaal zorgprogramma" of CZP genoemd. Bijna alle acute ziekenhuizen hebben een CZP "A" certificering die niet-invasieve klinische cardiologie toelaat. Ziekenhuizen met een CZP "P" zijn erkend voor het toepassen van pacemakertherapie. CZP "B" verwijst naar de vergunning om invasieve procedures uit te voeren, terwijl CZP "E" verwijst naar de kwalificatie om elektrofysiologische interventies te doen.

Belgische ziekenhuizen die standaard hartzorg leveren (CZP "A") hebben doorgaans ook een CZP "P" kwalificatie. Een ziekenhuis met een CZP "P" is verplicht om een formeel samenwerkingsakkoord te sluiten met een ziekenhuis dat zowel over een CZP "B" als "E" beschikt. De wetgeving met betrekking tot CZP "P" vermeldt ook een aantal kwaliteitsnormen waaraan moet worden voldaan. Voor pacemaker-implantaties met andere indicaties dan totaal hartblok of dan voorkamerfibrillatie met pauzes van meer dan 2,5 seconden, moet deskundig advies worden ingewonnen van een elektrofysioloog die verbonden is aan een CZP "E". Bij Koninklijk Besluit moet een zorgprogramma verplicht onderworpen worden aan een interne en een externe kwaliteitsbeoordeling. Deze laatste opdracht werd toevertrouwd aan het College van Geneesheren. In het geval van het CZP "P" is dit het College van Geneesheren – Cardiale pathologie – Afdeling Pacing en Elektrofysiologie. In de praktijk werd deze verplichting echter nooit afgedwongen en ziekenhuizen werden er alleen toe aangemoedigd om gegevens te bezorgen aan het pacemakerregister van de Belgian Heart Rhythm Association (BeHRA). Deze gegevens worden traditioneel overgenomen en geannoteerd in het jaarrapport van de Colleges van Geneesheren.

KLINISCHE RICHTLIJNEN VOOR PACEMAKERTHERAPIE

De eerste klinische richtlijn over pacemakertherapie werd in 1974 uitgevaardigd door de US Pacemaker Study Group. Sindsdien werden verschillende updates gepubliceerd door cardiologische verenigingen in de VS. De meest recente update gebeurde in 2008. De enige richtlijn die ooit door de European Society of Cardiology werd gepubliceerd verscheen in 2007.

Er werden nooit goede wetenschappelijke klinische studies uitgevoerd om de klinische doeltreffendheid van pacemakertherapie aan te tonen. De klinische pacemaker praktijk berust grotendeels op expert opinie, gebaseerd op ervaring en consensus. Geen enkele van de aanbevelingen van de European Society of Cardiology over het gebruik van pacemakers heeft een niveau van bewijskracht graad A (d.w.z. wetenschappelijk ondersteund door meerdere gerandomiseerde gecontroleerde onderzoeken of meta-analyse). Op een totaal van 40 aanbevelingen zijn er slechts 12 die worden ondersteund door studies met een niveau van bewijskracht B, terwijl het in die gevallen dan doorgaans nog gaat om zeldzame pacemaker indicaties. De resterende 28 aanbevelingen, die betrekking hebben op de meest courante pacemaker indicaties, zijn louter gebaseerd op expert opinie (niveau C).

In het algemeen wordt aanvaard dat de implantatie van een pacemaker geïndiceerd is bij patiënten met (1) een gedocumenteerde bradycardie (2) die aanleiding geeft tot symptomen en (3) waarbij het verband tussen deze bradycardie en de symptomen vaststaat. De wetenschappelijk best onderbouwde indicatie voor pacemakertherapie is voor de behandeling van symptomatisch totaal hartblok. Voor deze aandoening is reeds lang aangetoond dat de behandeling met een pacemaker de symptomen doet verdwijnen en de overleving verlengt. Er is indirect bewijs van een gunstig symptomatisch effect van pacemakertherapie bij voorkamerfibrillatie met traag ventriculair antwoord en bij sinusknoopziekte met lange pauzes indien ze gecompliceerd worden door ernstige klachten. Voor asymptomatische voorkamerfibrillatie met traag ventriculair antwoord is de klinische doeltreffendheid echter onzeker en de richtlijnen voor pacemakertherapie zijn hieromtrent niet eenduidig.

TOEPASSING VAN PACEMAKERRICHTLIJNEN IN BELGIE

De evaluatie van de toepassing van de pacemakerrichtlijnen in de klinische praktijk kan worden benaderd uitgaande van de databank van de BeHRA, of op basis van administratieve gegevens ingezameld door de ziekenfondsen of door de Federale Overheidsdienst Volksgezondheid.

HET BELGISCHE PACEMAKERREGISTER

De BeHRA pacemakerdatabank is een register met gegevens van bijna 117.600 pacemaker-implantaties die plaatsvonden tijdens de periode 1993-2007. Uit een vergelijking met de gegevens van de ziekenfondsen blijkt dat het register ongeveer 80% van alle terugbetaalde implantaties in België omvat. Doordat het register op vrijwillige basis is gestoeld, is de bruikbaarheid ervan voor een formele kwalitatieve en kwantitatieve beoordeling van de Belgische praktijk eerder beperkt. Bovendien zou zo'n beoordeling slechts mogelijk worden mits een gedegen doorlichting en een herziening van de databankstructuur (variabelen en definities), zodat er gevalideerde kwaliteitsindicatoren kunnen worden uit afgeleid.

Het is de bedoeling dat het RIZIV vanaf 2011 een webapplicatie aanbiedt voor de registratie van pacemakervoorschriften. Deze zal het huidige BeHRA-register vervangen. De registratie zal verplicht zijn en gekoppeld worden aan de terugbetaling van de toestellen.

BELGISCHE ADMINISTRATIEVE GEGEVENS OVER PACEMAKERPRAKTIJK

De gegevens over alle pacemaker-gerelateerde procedures tussen 2002 en 2007 werden verkregen van het Intermutualistisch Agentschap (IMA) en van de eraan gekoppelde Minimale Klinische Gegevens en Minimale Facturatie Gegevens (MKG/MFG). In 2007 bedroeg het totaal aantal pacemakers dat in België werd geïmplanteerd 10.914 of 10,3 implantaties per 10.000 inwoners. Daarvan waren er 7.487 eerste implantaties, d.w.z. 7,1 per 10.000 inwoners. De gemiddelde leeftijd van patiënten bij hun eerste implantatie steeg lichtjes gedurende de periode 2002 tot 2007 en bedroeg in 2007 75,2 jaar voor mannen en 78,1 jaar voor vrouwen. In dat zelfde jaar was 85% van alle mannen met een eerste implantatie ouder dan 65 jaar; bij vrouwen was dit 92%.

Er zijn aanzienlijke verschillen in het relatief aantal implantaties tussen de 43 Belgische arrondissementen. Zo varieert het primo implantatiecijfer van 4,2 per 10.000 inwoners in Moeskroen tot 12,3 in Veurne. Binnen België houdt deze variatie in implantatiecijfers duidelijk verband met lokale demografische en socio-economische factoren: een hoog aandeel van een oudere en mannelijke populatie, lage inkomensniveaus en lage percentages vreemdelingen gaan samen met hoge implantatiecijfers. Na standaardisatie voor deze factoren verdwijnen de verschillen in primo implantatiecijfers tussen de arrondissementen bijna volledig.

In 2007 bedroeg de gemiddelde terugbetaling €4.419 voor een pacemaker en €571 per electrode. Sinds 2002 is de gemiddelde terugbetaling gedaald met 11,1% voor pacemakers en met 3,9% voor electrodes. Van 2002 tot 2007 bedroeg de gemiddelde jaarlijkse terugbetaling met betrekking tot pacemakers en electrodes zo'n 60 miljoen euro.

Vergeleken met de gegevens van de ziekenfondsen telde BeHRA 20,6% minder pacemaker-implantaties in 2007, maar het percentage primo implantaties versus vervangingen en de verdeling over leeftijd en geslacht zijn zeer vergelijkbaar. Een erg groot verschil tussen de twee databanken komt echter naar voren bij de vergelijking van de meest frequent gemelde indicaties: in 2006 had 43% van alle gevallen in het BeHRA-register betrekking op sinusknoopziekte, terwijl dit in de MKG/MFG data slechts 32% was. Het percentage totaal hartblok is ook hoger bij BeHRA (22 %) dan bij MKG/MFG (18%). Geen van beide databanken werd echter ooit formeel doorgelicht en het valt dus onmogelijk te zeggen welke van de twee in dit opzicht de meest nauwkeurige gegevens bevat.

INTERNATIONALE PACEMAKERREGISTERS

Net zoals in België worden de meeste buitenlandse registers beheerd door verenigingen van cardiologen en zijn ze gestoeld op vrijwillige deelname. Zodoende hebben ze allemaal in meer of mindere mate te kampen met onvolledige registratie.

De meest betrouwbare bron voor de vergelijking van het aantal pacemaker-implantaties tussen verschillende landen zijn de verkoopcijfers van Eucomed, de Europese koepelorganisatie van de medische hulpmiddelenindustrie. Jammer genoeg bevatten deze gegevens alleen het totaal aantal pacemakers dat per land wordt verkocht en geven ze geen klinische patiënteninformatie. De verkoop van pacemakers steeg in West-Europa geleidelijk aan van 8,3 per 10.000 inwoners in 2004 tot 9,1 per 10.000 in 2008 (+9%). Deze tendens is vrij algemeen. De hoogste aantallen worden aangetroffen in Duitsland (12,0), gevolgd door België (11,3) en Italië (10,3). Het totale implantatiecijfer in België gedurende de jaren 2004 tot en met 2008 lag 20 tot 26% hoger dan het West-Europese gemiddelde.

Voor geen van de landen is het aantal pacemakers dat medisch verantwoord is per miljoen inwoners gekend. Anderzijds zijn er geen aanduidingen voor een verschil in prevalentie van bradycardie-veroorzakende aandoeningen tussen West-Europese landen. Bovendien kunnen demografische en structurele factoren, zoals een hoog percentage ouderen, hoge gezondheidsuitgaven of een hoog BBP per capita, slechts een klein deel van de totale variatie tussen de implantatiepercentages per land verklaren. De aanzienlijke internationale verschillen in pacemaker-implantatie percentages blijven dus grotendeels onverklaard.

CONCLUSIES

Er zijn twee belangrijke redenen waarom we geen eenduidig antwoord kunnen geven op de vraag of de Belgische pacemakerpraktijk klinisch gerechtvaardigd is:

- De klinische richtlijnen voor pacemakertherapie bij patiënten met bradycardie zijn voornamelijk gebaseerd op expert opinie en niet op stevige wetenschappelijke bewijzen.
- Omdat het *de facto* gebaseerd is op vrijwillige deelname, blijft het BeHRA-register onvermijdelijk onvolledig, zowel met betrekking tot het aantal implantaties dat wordt gemeld, als wat betreft de klinische indicaties die deze implantaties rechtvaardigen. Deze laatste beperking geldt ook voor de gegevens die afkomstig zijn van het MKG/MFG. Geen van deze databanken geeft een betrouwbare identificatie van de klinische redenen voor pacemaker-implantaties en daarom kunnen ze niet worden gebruikt om te beoordelen in welke mate de internationale pacemakerrichtlijnen door de Belgische cardiologen worden gevolgd.

De aangekondigde internetgebaseerde applicatie voor pacemaker-implantaties biedt de kans om de registratie te optimaliseren. Deze verplichte registratie kan ook bijdragen tot een verbetering van de kwaliteit van de geleverde zorg door het registreren en bewaken van de technische aspecten van de interventie (positionering van de pacemakerelektrodes, röntgenstralenbelasting, complicaties) en van bepaalde follow-up gegevens (bijvoorbeeld de performantie van het apparaat en van de elektrodes). De implementatie en de kwaliteitscontrole van de registratie berust bij Koninklijk Besluit bij het College van Geneesheren.

In België variëren de vastgestelde primo implantatiepercentages aanzienlijk. Deze variatie hangt sterk samen met regionale verschillen in de demografische structuur van de populatie en de socio-economische kenmerken ervan zoals inkomen en het percentage vreemdelingen. Binnen de hierboven vermelde beperkingen laten de gegevens ook zien dat in Belgische arrondissementen met een lager primo implantatiepercentage er een hoger percentage implantaties gebeurt omwille van totaal hartblok, die de best onderbouwde indicatie is voor pacemakertherapie.

Door de onvolledigheid van de registraties en het feit dat de gegevens van verzekeraars niet publiek beschikbaar zijn op internationaal niveau, moet men uitgaan van verkoopgegevens van fabrikanten (Eucomed) om het aantal pacemakers dat in een bepaald land werd geïmplanteerd, te schatten. Samen met Duitsland en Italië heeft België het hoogste verkoopcijfer voor pacemakers per 10.000 inwoners in Europa, met cijfers die tot meer dan 25% boven het West-Europese gemiddelde liggen. De redenen voor de verschillen die doorheen Europa worden vastgesteld, blijven onduidelijk.

AANBEVELINGEN[a]

- Het opstarten van de internetgebaseerde applicatie voor de registratie van pacemaker-implantaties, zoals ze door het RIZIV tegen 2011 gepland is, zou moeten aangegrepen worden om de huidige BeHRA-databank om te vormen tot een instrument voor ondersteuning en evaluatie van de pacemaker-praktijk in België:
  - De verplichte deelname aan de registratie moet afgedwongen worden en moet worden gekoppeld aan de terugbetaling van de implantaten zoals voorgesteld door het RIZIV.
  - De keuze en de definitie van de te registreren variabelen moet herzien worden. Er moeten kwaliteitsindicatoren opgesteld worden, afgeleid uit deze gegevens, volgens een vooraf bepaald analyseprotocol. Dit is een taak voor het College van Geneesheren.
  - De registratieprocedure dient onderworpen te worden aan een regelmatige kwaliteitscontrole.
- Er moet werk gemaakt worden van de evaluatie van de kwaliteit van de klinische pacemakerpraktijk. Deze evaluatie kan onder meer gebaseerd zijn op de geregistreerde gegevens en dient te worden gesuperviseerd door het College van Geneesheren dat hiertoe bij Koninklijk Besluit de opdracht kreeg.
- Veelbelovende technologieën die reeds uit de experimentele fase zijn maar die niet worden ondersteund door goed wetenschappelijk onderzoek, zouden slechts restrictief mogen terugbetaald worden, terwijl ondertussen bijkomend bewijsmateriaal gegenereerd wordt. De latere uitbreiding van de terugbetaling tot nieuwe indicaties, of de verlenging van de terugbetaling, moet stapsgewijze gebeuren, en alleen nadat relevant ondersteunend wetenschappelijk bewijs werd gevonden.

Onderzoeksagenda

- Gerandomiseerde klinische studies (RCT's) zijn nodig om de klinische doeltreffendheid van pacemakertherapie aan te tonen in de indicaties waar hun impact op de gezondheid van de patiënt momenteel niet duidelijk is. Dit geldt voor bepaalde gevallen van voorkamerfibrillatie met traag ventriculair antwoord, sinusknoopziekte of lagere graden van hartblok, vooral bij patiënten die slechts milde symptomen vertonen of bij wie het verband tussen bradycardie en symptomen onzeker is.

a De beleidsaanbevelingen vallen onder de volledige en exclusieve verantwoordelijkheid van het KCE.

Scientific summary

GLOSSARY

2AVB	second degree atrioventricular block
3AVB	third degree atrioventricular block
ACC	American College of Cardiology
ACC#n	recommendations number n in the ACC 2008 GLs on cardiac pacing as shown in appendix
AF	Atrial fibrillation
AHA	American Heart Association
AMI	Acute Myocardial Infarction
AVB	atrioventricular block
AVN	atrioventricular node
BBB	bundle branch block
BeHRA	Belgian Heart Rhythm Association
BPEG	British Pacing and Electrophysiology Group
BWGCPE	Belgian Working Group of Cardiac Pacing and Electophysiology
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CCOHTA	Canadian Coordinating Office for Health Technology Assessment
CCP	Cardiac care program
CHB	Complete Heart Block
CHD	Coronary Heart Disease
CRD	Centre for Reviews and Dissemination
CRT	Cardiac Resynchronisation Therapy
CRT-D	Cardiac Resynchronisation Therapy in combination with an implanted defibrillator
CRT-P	Cardiac Resynchronisation Therapy in combination with an anti-bradycardia pacemaker
CVD	Cardiovascular Disease
DIPR	Dutch ICD and Pacemaker Registry
ECG	Electrocardiogram
EHRA	European Heart Rhythm Association
EHS	Euro Heart Survey
EPS	Electrophysiological Study
ESC	European Society of Cardiology
European PM CARD	European Pacemaker Patient Identification Card
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GL	Guideline
HAS	Haute Autorité de Santé
HTA	Health Technology Assessment
IAPM	International Association of Prostheses Manufacturers
ICER	Incremental Cost-Effectiveness Ratio
ICPES	International Cardiac Pacing and Electrophysiology Society
IHD	Ischemic Heart Disease
INAHTA	International Network of Agencies for Health Technology Assessment
LAH	left anterior hemiblock
LBBB	left bundle branch block
LVEF	Left Ventricular Ejection Fraction
MI	Myocardial Infarction
NASPE	North American Society of Pacing and Electrophysiology

NBG	NASPE/BPEG Generic
NHS	National Health Service
NHSEED	National Health Service Economic Evaluation Database
NICE	National Institute for Health and Clinical excellence
NIHDI	National Institute for Health and Disability Insurance (=RIZIV/INAMI)
NSR	normal sinus rhythm
NYHA	New York Heart Association
PM	Pacemaker
QALY	Quality Adjusted Life Year
RBBB	right bundle branch block
RCT	Randomized Controlled Trial
RIZIV/INAMI	National Institute for Health and Disability Insurance (Rijksinstituut voor Ziekte- en Invaliditeitsverzekering/National d'Assurance Maladie-Invalidité) (=NIHDI)
SND	Sinus node disease
SPRN	Stichting Pacemaker Registratie Nederland
SR	Systematic Review
SSS	Sick sinus syndrome = sinus node disease
TCI	Technical Council for Implants (=TRI/CTI)
TCT	Technical Cel (Technische Cel / Cellule Technique)
TRI/CTI	Technical Council for Implants (Technische Raad voor Implantaten/Conseil Technique des Implants) (=TCI)

1 SCOPE

The purpose of this Good Clinical Practice (GCP) report is to describe pacemaker (PM) therapy for treating bradycardia in adults in Belgium in both qualitative and quantitative terms. It aims to compare Belgian practice with recommendations formulated in scientific guidelines and with clinical pacing practice in other European countries. The report should enable the KCE to formulate recommendations to the federal health authorities to improve the quality and efficiency of conventional cardiac pacing in Belgium.

The main research questions are:

1. What are the clinical indications for permanent pacing according to international guidelines? Is Belgian practice in accordance with these guidelines?
2. How does clinical pacemaker practice in Belgium quantitatively compare with other European countries?
3. To what extent the data of the pacemaker register of the Belgian Heart Rhythm Association (BeHRA) correspond to those obtained from health insurers and administrative hospital-based clinical data?

2 CLINICAL BACKGROUND

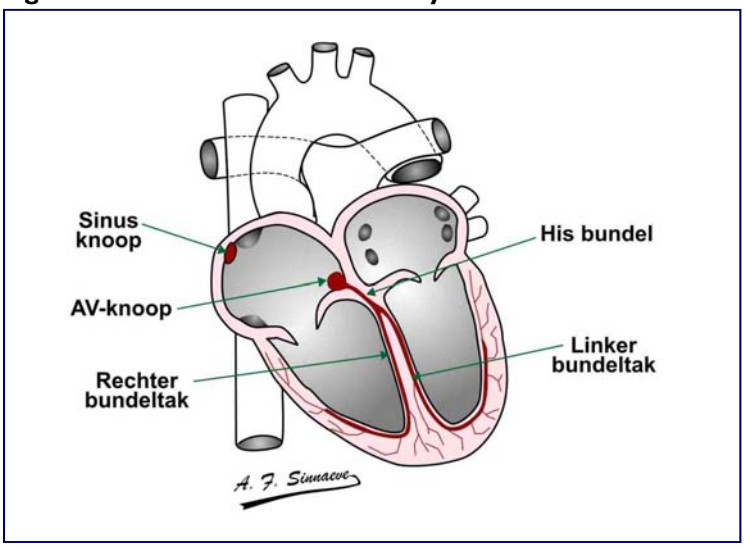
Pacemaker (PM) therapy is related to the prevention of symptoms induced by an inappropriately slow heart rate or "bradycardia". The PM is able to continuously monitor the heart rate of an individual in whom such a device has been implanted. If a predefined low heart rate is detected, it sends an impulse to the heart stimulating its contraction. This impulse is repetitively delivered at a given frequency as long as the patient's own heart rhythm has not regained the lower limit. PM therapy is the only known effective treatment for chronic symptomatic bradycardia. PMs intended to treat bradycardia further in this report are denoted as "conventional" or "bradycardia" PMs, to distinguish them from a new type of PMs, used for the treatment of heart failure. The latter pacing mode is known as cardiac resynchronisation therapy (CRT) which is beyond the scope of the present report.

2.1 BRADYCARDIA

Bradycardia is defined as a lower than normal heart rate at a given physiologic condition. Normally, the heart rate is determined by a natural pacemaker, residing within the sino-atrial node (SAN), a structure that is lying within the wall of the right atrium. This rhythm is defined as "sinus rhythm". Other cells or structures within the heart may function as a natural pacemaker as well if the inherent SAN rate falls below a certain level. The SAN may also become dominated by a faster rate originating in other areas of the heart, leading to abnormal fast heart rates or tachy-arrhythmias. These may find their origin within the atria (e.g. atrial fibrillation), the atrioventricular junction or the ventricles (e.g. ventricular tachycardia).

Once an impulse leaves the SAN, it traverses the atrium and the atrioventricular node (AVN) to the conduction system in the ventricles, and further to the myocardial cells, that are thus stimulated to contract. Both the SAN and the AVN are significantly influenced by autonomous tone. This leads to an increase of the heart rate during exercise or to a decrease during sleep. In adults, the normal sinus rate under basal conditions is 60 to 100 beats/min. The heart rate normally increases during exercise. Failure to do so has been termed "chronotropic incompetence". There is a wide variation of heart rate among individuals, and rates below 60 beats/min do not necessarily indicate pathologic states. For example, trained athletes often exhibit resting rates below 50 beats/min. Elderly individuals may also show marked sinus bradycardia at rest.[1] According to the European guidelines for cardiac pacing, bradycardia is deemed "exaggerated" if the heart rate falls below 40 beats per minute.[2]

Figure 1: The cardiac conduction system



Courtesy R. Stroobandt, Hartcentrum, UZ Gent. Sinus knoop: sino-atrial node (SAN); AV-knoop: atrioventricular node; Rechter bundeltak: right bundle branch; Linker bundeltak: left bundle branch.

Within certain limits, a slow heart rate may remain unnoticed because of compensatory physiologic mechanisms that lead to an increase in the stroke volume of the heart. Otherwise, bradycardia may give rise to syncope or other less striking or atypical symptoms such as dizziness, lightheadedness, fatigue or weakness. In the latter, the relation between the symptoms and a documented bradycardia may be less certain, and interventions directed solely to the bradycardia may prove to be ineffective.[3]

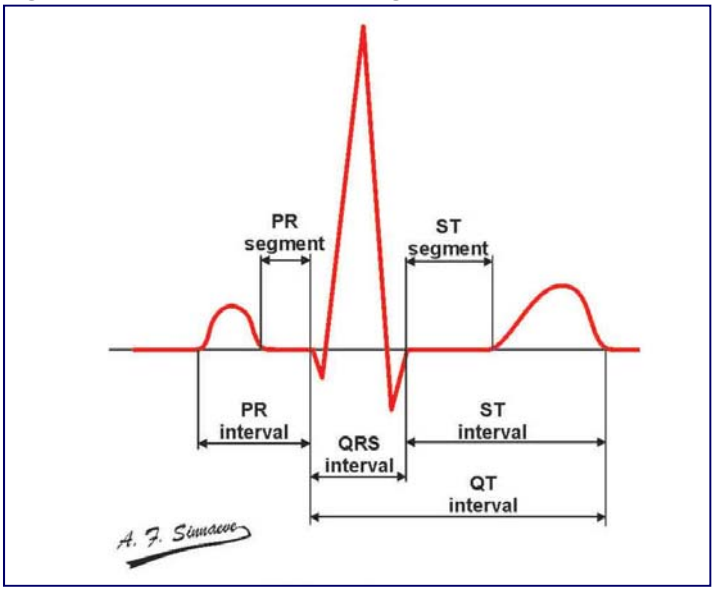
Bradycardia may be induced by several pathologic conditions, but apart from drug induced bradycardia, it is most often caused by an age-dependent degeneration of conductive tissues in the heart.[1] When this tissue degeneration is located within the SAN it will lead to an impairment of impulse initiation and is known as sick sinus syndrome (SSS) or sinus node disease. If it is located within the conduction system of the heart, it leads to an abnormal delay of impulse propagation and is called atrioventricular block (AVB). Further in the present report, we refer to SSS and AVB as "bradycardia provoking diseases". AVB also includes slow atrial fibrillation as will be discussed later on.

2.1.1 Conduction disturbances

In pathologic conditions, the propagation of the cardiac impulse originating from the SAN may be delayed on its way to the myocardial cell where it initiates contraction (Figure 1). This is called "atrioventricular block" or "AV-block" (AVB). The delay of the impulse propagation can be more or less pronounced, giving rise to different grades of AVB. In its most severe form, impulse propagation can be completely blocked, a condition known as complete or third degree AVB.

The degree of conduction delay can be inferred from the electrocardiogram (ECG). The PR-interval on the ECG represents the conduction time of the impulse from the SAN through the atrium, the AVN and the ventricular conduction system, to the myocardial cells where it induces ventricular contraction (Figure 2).

Figure 2: Normal electrocardiogram



Courtesy R. Stroobandt, Hartcentrum, UZ Gent.

In first degree atrioventricular block (1AVB), there is only an abnormal prolongation of the PR interval, and every impulse from the atrium is conducted to the ventricles. It represents a slowing of the impulse propagation over the AVN, but by itself does not lead to bradycardia. In second-degree atrioventricular block (2AVB) not every impulse originating from the atria is conducted to the ventricles. Several patterns of 2AVB are observed. "Mobitz type I" or "Wenckebach block" is diagnosed when the ECG shows a progressive increase in the PR interval until a P wave fails to conduct to the ventricle.

In "Mobitz type II", there is a stable PP interval with no prolongation of the PR interval before an abrupt conduction failure of a P wave. When 2 or more consecutive P waves are blocked, 2AVB is designated "advanced".[4] In third-degree atrioventricular block (3AVB), also often referred to as "complete heart block (CHB)" no conduction at all takes place from atrium to the ventricles. Atrial activity and ventricular activity become independent of each other. Contraction will then be initiated by a so called "escape rhythm" that spontaneously originates within the ventricle, mostly at a very slow rate (20 to 40 beats per minute).

Impulse propagation can also be delayed in subsections of the ventricular conduction system, leading to bundle branch block. The latter does however not lead to bradycardia, but as time goes by, bundle branch blocks may lead to AVB.

AVB is most often caused by an age related degeneration of the conduction system. In the 1950s, AVB was generally assumed to be ischemic in origin, but pathologic studies later on made it apparent that ischemic heart disease was an uncommon cause. Therefore, in the 1960s, "isolated disease of the conduction system" or "primary heart block" were introduced for patients with 3AVB.[5] AVB can also result from the destruction of conductive tissue caused by myocardial infarction, infiltrative heart disease or more rarely by infectious disease. Conduction disturbances can also be drug induced and in these cases, they may be reversible.[1] 3AVB rarely occurs as a congenital anomaly. The occurrence of symptoms due to 3AVB depends on the severity of the accompanying bradycardia. In 3AVB, the residual heart rhythm is always very slow (20-40/min) or can even lead to cardiac arrest. In 2AVB, bradycardia may be less pronounced and even remain unnoticed. In some patients 2AVB heralds progression of conduction disease towards 3AVB.

Symptoms definitely attributable to an irreversible bradycardia are treated with permanent pacing.[3] Before the advent of PM technology, prognosis of symptomatic 3AVB was ominous. 50% of patients died within the first year following its development, whereas 75-90% died within 5 years.[6, 7] The immediate clinical improvement of a patient presenting with 3AVB and treated with a PM is almost miraculous. After PM implantation, one-year survival of patients with 3AVB was 80 to 93% whereas 5 year survival was 50 to 65%.[8] Consensus has emerged that 3AVB represents a definite indication for permanent pacemaker implantation, even in asymptomatic patients.[3, 8] Otherwise, permanent pacing is very rarely indicated in asymptomatic patients.[3]

2.1.2 Sick sinus syndrome

Sick sinus syndrome (SSS), also referred to as "sinus node disease" or "sino-atrial node dysfunction", includes a broad spectrum of arrhythmias, ranging from the usually benign sinus bradycardia to sinus arrest (i.e. a prolonged inactivity of the natural pacemaker, giving rise to a brief cardiac arrest). It also includes the so-called "bradycardia-tachycardia syndrome" that is characterised by episodes of sinus bradycardia, alternated with bouts of atrial tachycardias.[2] Chronotropic incompetence, i.e. the inadequate increase of heart rate during exercise, is also part of the syndrome. Most cases of SSS occur in the elderly[8] and are due to an idiopathic degeneration of atrial tissue, or are secondary to pharmacologic agents.[1] If the resulting bradycardia is severe enough, it may lead to symptoms due to the impaired blood supply to the brain.

In the late 1960s, the era when permanent cardiac pacing emerged, the concept of SSS was recognised as a clinical entity. No studies have been performed to compare the outcome of patients with SSS that were treated with and without PM therapy. Data from registers indicate that PM implantation for SSS does not reduce mortality, even in patients with symptoms. It is generally accepted that PM therapy is effective in patients with incapacitating symptoms, in whom it is documented that the bradycardia is directly responsible for the clinical manifestations. Several authors claim that patients who are only mildly symptomatic should not receive a PM.[3, 4, 8-10]

2.1.3 Atrial fibrillation

Atrial fibrillation (AF) is an arrhythmia characterised by a very fast atrial activation, typically associated with tachycardia. The condition can occur intermittently or remain chronic. It is the most common arrhythmia in clinical practice. The prevalence of AF is age-dependent and is present in 10% of octogenarians.[11] Patients with AF have large variations in their heart rate and many of them require drug therapy to slow down heart rate. Some patients with AF may develop symptomatic bradycardia due to a degeneration of the heart's conduction system, but bradycardia may also result from the drugs that are required to prevent episodic tachycardia. Asymptomatic ventricular pauses occur often in chronic AF. In one study of asymptomatic patients two thirds had pauses longer than 2 seconds, and 20% had pauses longer than 3 seconds. These authors concluded that daytime pauses of up to 2.8 seconds and nocturnal pauses of up to 4 seconds during AF may not require cardiac pacing unless they coincide with symptoms.[12] Some authors argue that it is wise to consider isolated, asymptomatic pauses during AF as benign.[3] Others feel that a ventricular pause of 3 seconds or more represents a definite indication for permanent pacing.[8] In its most recent guideline update, the ACC/AHA considers a prolonged pause in the setting of AF (greater than 5 seconds) to be caused by advanced 2AVB. The ACC/AHA recommends permanent pacing in asymptomatic patients with chronic AF and pauses of at least 5 seconds while awake.[4]

2.2 SYNCOPE

Syncope is defined as a "transient loss of consciousness, due to a transient global cerebral hypo-perfusion, characterised by rapid onset, short duration, and spontaneous complete recovery".[13] It represents the most dramatic symptom of bradycardia and can be elicited by different pathological processes. Three major types of syncope are distinguished: (1) Reflex or neurally-mediated syncope, (2) syncope due to orthostatic hypotension and (3) cardiac syncope. Reflex syncope refers to a group of conditions in which normally useful cardiovascular reflexes become intermittently inappropriate in response to a trigger, resulting in vasodilatation and/or bradycardia and a loss of consciousness.[13] It can be triggered by stimuli in a variety of conditions such as emotional stress, cough, urination, or following a meal. It can also occur after stimulation of the carotid sinus ("carotid sinus syncope"). In orthostatic hypotension, there is an abnormal decrease in blood pressure upon standing, caused by a chronically impaired autonomic nervous system leading to a deficient vasoconstriction. Upon standing, blood pressure falls and syncope or pre-syncope occurs. In cardiac syncope, cerebral blood flow is impaired due to brady- or tachy-arrhythmias, or consequential to a variety of some structural diseases affecting the heart. Patients presenting with (recurrent) syncope or near-syncope pose a clinical challenge to identify the underlying pathology because of the short lasting nature of symptoms (a matter of seconds). Further neurologic and cardiologic examinations are often needed to confirm or dismiss a postulated mechanism. Ambulatory or in-hospital long term ECG monitoring, invasive testing (electrophysiologic testing - EPS), tilt table testing and sometimes implantable recording devices may be needed to pinpoint bradycardia as the reason for the syncope. It is beyond the scope of the present report to further discuss these techniques.

2.3 PACEMAKER TECHNOLOGY

2.3.1 Device description

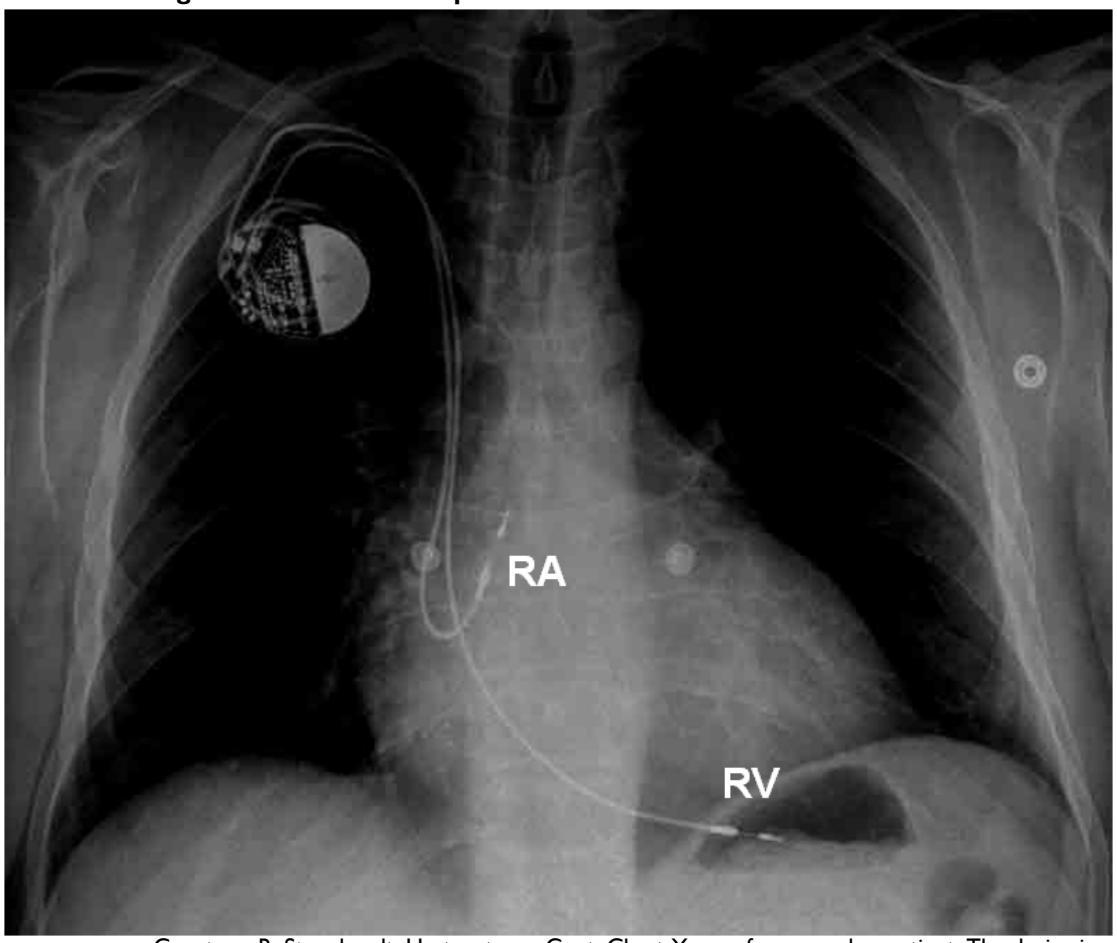
A pacemaker (PM) is an electronic device, powered from an internal battery, that is connected to the heart with one or more insulated electric wires, denoted leads or electrodes. The device is implanted subcutaneously, generally under local anesthesia, usually below the right or left clavicle. The lead(s) are advanced through a vein to the inner surface of the heart's right atrium and/or right ventricle, using fluoroscopic guiding. The technique has been developed in the 1950s, and since 1959 transvenous pacing, requiring only minor surgery, has become the standard procedure. The leads that are introduced into the heart can be actively fixated to its inner surface by means of a screw at the tip of the lead, but sometimes there is only a passive fixation by means of barbs protruding from the tip of the lead.

Pacemakers may be either "single-chamber" or "dual-chamber" depending on whether or not both the right atrium and/or the right ventricle are involved. The PM is able to detect ("sense") the heart rate and is programmed to stimulate ("pace") the heart via the leads when the patient's heart rate falls below a pre-specified rate. The choice of the type of PM depends on the exact nature of the bradycardia. Once a PM has been implanted, several parameters can be changed noninvasively by using an external programmer that communicates with the PM by means of magnetic coupling via a wand placed on the patient's skin above the device.

Most modern PMs have to be replaced 5 to 9 years after the first (or primo) implantation. The service life of the leads is longer, and when a PM is replaced because of battery depletion, the original leads can most often be left in place and simply be plugged into the new PM device.

Six PM manufacturers are represented on the Belgian market: Biotronik, Boston Scientific, Medico BMED, Medtronic, Sorin Biomedica, and St Jude Medical.

Figure 3: Dual chamber pacemaker



Courtesy R. Stroobandt, Hartcentrum, Gent. Chest X-ray of a pacemaker patient. The device is situated below the right clavicle (left upper corner of the picture) and is connected to two wires that lead to the right atrium (RA) and right ventricle (RV).

The NBG (NASPE/BPEG Generic) code is a 5-position-descriptor of implantable cardiac electronic devices defined by the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) in order to describe different pacing modes (Table 1). The different positions of the code indicate which cardiac chamber is being sensed and/or paced, the response that is initiated if a sensed event occurs, whether the device is programmable and whether or not it has anti-tachyarrhythmia features. In the fourth position, O (none) indicates that the device has no programmable parameters but this is nowadays no longer encountered. C (communicating) tells that the PM is capable of transmitting and/or receiving data for informational or programming purposes. Most if not all devices currently manufactured have a communicating ability. P (simple programmable) usually indicates that the PM is limited to 3 or fewer programmable parameters. Most PMs are however multi-programmable (M), indicating that the device can be programmed in more than 3 parameters such as rate, output and mode. The rate responsiveness (R) in the fourth position indicates whether the device is capable to adapt its stimulating rate during periods of physical activity 0

Table 1: NBG codes for Pacing Modes

Chamber(s) being paced	Chamber(s) being sensed	Mode(s) of Response	Programmablility of rate modulation	Antitachyarrhythmia functions
O=None	O=None	O=None	O=None	O=None
V= Ventricle	V=Ventricle	T=Triggered	R=Rate Modulated	D=Dual (P&S)
A=Atrium	A=Atrium	I=Inhibited	C=Communicating	P=Paced
D=Dual (A and V)	D=Dual (A and V)	D=Dual (inhibited and triggered)	M=Multiprogrammable	S=Shocks
			P=Simple Programmable	

Source: KCE.

The most frequently used pacing modes are VVI-R-O (or simply VVI) and DDD-R-O (or simply DDD). In a VVI pacemaker, the device stimulates the ventricle when the patient's heart rate falls below a preset threshold, and in case a ventricular event is sensed, it inhibits the ventricular output. A DDD pacemaker is able to stimulate both the right atrium and the right ventricle. An atrial sensed event can trigger the ventricular channel to pace. The notion "physiological pacing" indicates pacing modes that most closely mimic normal cardiac physiology, especially in terms of AV synchrony, and mostly refers to DDD pacing.[14]

2.3.2 Clinical benefit

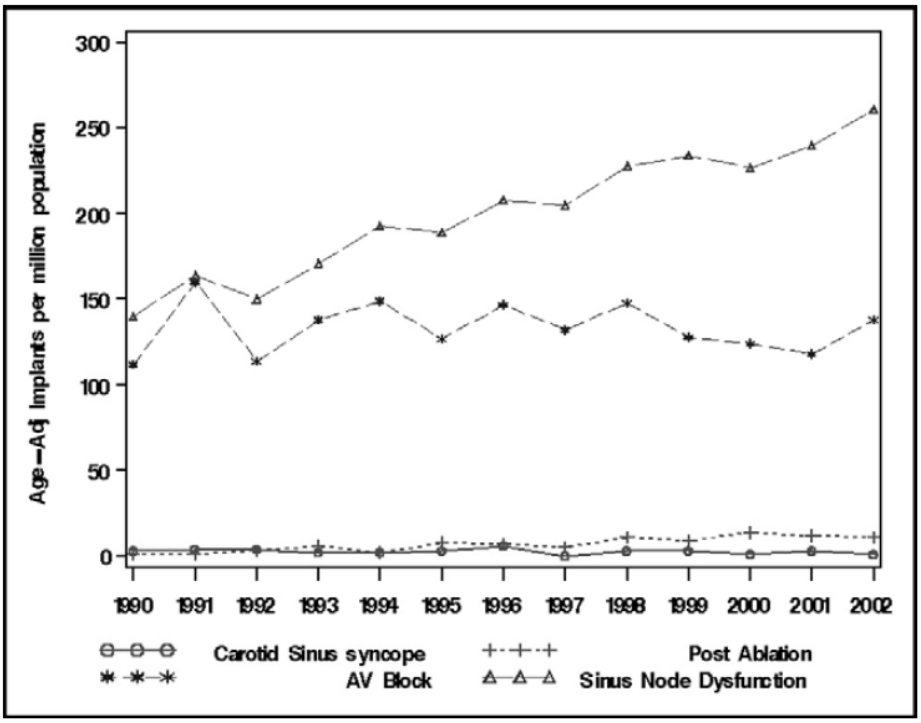
The clinical effectiveness of PM therapy is discussed in more detail in Chapter 3 (Scientific evidence supporting the use of PMs). Cardiac pacing is the only known effective long-term treatment for symptomatic bradycardia.[15] In the late 1950s, the clinical benefit of PM therapy in patients with symptomatic 3AVB became evident right from the start. Due to the large effect size there was no need for randomised trials to prove its effectiveness.[16] Later on, the use of PM therapy was expanded towards other types of bradycardia, such as SSS and AF. These arrhythmias represent a heterogeneous mix of conditions, characterised by different grades of severity and a variety of symptoms, ranging from recurrent syncope to lightheadedness. No clinical trials have ever been performed to clearly define the clinical effectiveness of PM therapy in these conditions. International recommendations are mostly based on expert opinion. For some indications, such as SSS with prolonged ventricular pauses complicated by recurrent syncope, circumstantial evidence indicates a clear symptomatic benefit. However for conditions such as slow AF and lower grades of AV block, especially in patients who are not, or only mildly symptomatic, the usefulness of pacing is less clear.

In the 1990s and early 2000s, randomised trials of PM therapy have been performed, but these were only comparing the clinical effectiveness of different modes of pacing (e.g. single versus dual chamber pacing) and they were not addressing PM therapy in itself. In 2005, a technology appraisal has been published by NICE on the use of dual-chamber PMs.[17] It concluded that dual-chamber pacing is generally preferred to VVI pacing, except in patients with chronic AF or in patients with SSS in whom, after full evaluation, there is no evidence of impaired AV conduction. A Cochrane review of 2004 on the subject found that pooled data from parallel studies showed a statistically non-significant preference for physiologic pacing for the prevention of stroke, heart failure and mortality, and a statistically significant beneficial effect regarding the prevention of AF. Pooled data from crossover studies showed a statistically significant trend towards DDD pacing being more favorable in terms of exercise capacity.[14]

In the 1980s and 1990s, there was a steady increase in the number of PM implants in most countries. From 2003-2004 on, this increase became less pronounced.[16] The increase has been ascribed to the ageing of the population, the increasing number of surviving PM recipients that need a replacement, and an increase in clinical indications. In the Netherlands, it has been shown that during the period 1984-1997, the increase of the number of primo implantations was higher than what one would expect from the increasing age of the population.[7] In a US study, an age standardised increase in the use of PMs from 1990 through 2002 was found.

Based on administrative hospital data, this increase was attributed to a higher number of SSS diagnoses leading to PM implantation, the number of PM implants for 3AVB remaining constant (Figure 4).[18]

Figure 4: Temporal trends in age-adjusted PM implantations in US, 1990-2002



Source: Birnie et al.[18]: Age–adjusted temporal trends: PM implantation rates stratified by electrocardiographic pacing indication.

During the late 1990s, a new pacing modality has been developed for the treatment of heart failure. With this therapy, the aim of pacing is not to prevent bradycardia but to synchronise the contraction of the ventricles of the heart to improve cardiac output. This pacing mode is known as "cardiac resynchronisation therapy" or "CRT". The technology can be used in combination with a conventional pacemaker where it is called a "CRT-P", or in combination with an implantable defibrillator where it is called a "CRT-D". The topic of CRT pacing is beyond the scope of the present report.

2.3.3 Clinical harm

Consequential to its invasive nature, PM implantation can lead to surgical complications such as wound infection and wound hematoma. Very rarely, complications can arise by perforating the vascular structures through which the leads are advanced, leading to pneumothorax, hemothorax, or perforation of the heart and pericardial effusion. These complications all occur in less than 1% of primo implantations.[19, 20] Very rarely, they lead to death. In the annual report of the German PM register, death due to the PM procedure is reported in 0.07 to 0.06% of primo implantations.[19]

In some patients, dislocation of the tip of the PM lead occurs, leading to an inability to stimulate the heart. This most often occurs within the first weeks after implantation and affects more atrial then ventricular leads. The incidence of early displacements is 1% in VVI pacemakers and 5.2% in DDD pacemakers (3.8% of the cases affecting atrial leads and 1.4% ventricular leads).[21] In those cases, a re-intervention for repositioning of the electrode is needed. Pacemaker problems can also occur later after the implantation. These include lead failure, infection and generator failure. According to the Danish register, PM infection occurs in up to 0.6% of implants.[20] Most modern PMs have an expected longevity of 5 to 9 years.[15]

It is not fully clear how many PMs in Belgium have been prematurely replaced as a consequence of a manufacturer's recall action. From 2001 through 2007, there were 11 recorded Field Safety Corrective Actions (FSCA) in Belgium. An FSCA is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. Of these 11 FSCAs, one was an informative action and the other 10 constitute a "recall" action that could potentially have led to prophylactic explantations. Over the above-mentioned time period, the latter type of FSCA affected at least 7,437 devices in Belgium and resulted in at least 311 confirmed prophylactic explantations, not including the effectively affected devices that were among the reported provoking incidents. Further details on PM recalls and vigilance are discussed in the appendix to this report.

PM therapy can also lead to heart failure and atrial fibrillation. This has been shown in patients with SSS and normal baseline QRS duration and is attributed to ventricular desynchronisation imposed by right ventricular apical pacing.[22]

2.3.4 Device reimbursement

The reimbursement tariffs of PM devices and leads that are applicable in Belgium are described in art. 35 of the NIHDI reimbursement nomenclature. The 2010 tariffs are listed in Table 2. In the appendix to this report, a more extensive list of the NIHDI reimbursement codes relevant to PM therapy is provided.

Table 2: 2010 NIHDI device reimbursement tariffs (€)

	NOMENCLATURE CODE	€
PM LEAD - unipolar	685731/685742	571,15
PM LEAD - bipolar	685753/685764	571,15
PM LEAD - myocardial	685775/685786	571,15
PM LEAD - single-pass	685790/685801	777,72
SINGLE CHAMBER PM	684530/684541 684375/684386	3230,00
DUAL CHAMBER PM		4104,00
CRT-P		4544,00

Key points

- **A low heart rate or "bradycardia" (< 40 heart beats per minute) can lead to symptoms due to an inadequate blood flow to the brain. Bradycardia can be short-lasting (seconds or minutes) and nevertheless lead to symptoms. Syncope is the most typical symptom of severe bradycardia. Other less specific symptoms such as near-syncope lightheadedness or dizziness may also be caused by bradycardia.**
- **Severe bradycardia is due to an age-dependent degeneration of the conductive tissue of the heart, leading to varying degrees of atrioventricular block (AVB), slow atrial fibrillation (AF) or sick sinus syndrome (SSS).**
- **Bradycardia can also be induced by certain pharmacological agents that are often used in cardiac patients (beta-blockers, digitalis, anti-arrhythmic drugs, …).**
- **Permanent cardiac pacing is the only known effective treatment for chronic symptomatic bradycardia.**
- **In patients with complete heart block, pacemaker therapy alleviates symptoms and prolongs life.**
- **In sick sinus syndrome and slow atrial fibrillation PM therapy is useful for the treatment for incapacitating symptoms such as syncope, but patients who are only mildly symptomatic should, according to experts, not receive a PM.**
- **In most countries an age-standardised increase in the number of pacemakers implanted has been documented.**

2.4 ORGANISATION OF PACING PRACTICE IN BELGIUM

2.4.1 Cardiac care programs

In 1999, so-called "care programs" ("zorgprogramma's", "programmes de soins") have been installed by the Belgian federal government. They are related to a variety of hospital services such as geriatrics, pediatrics, oncology, reproductive health and cardiology. Further in this report, the latter will be referred to as "cardiac care program (CCP)". Several distinct CCPs have been defined: A, B, P, E, T, and C (Table 3). CCP "T", relating to heart- and lung transplantation, and CCP "C" relating to congenital heart disease, are beyond the scope of the present report. Virtually all acute hospitals can have a CCP "A" certification allowing for clinical cardiology without limitations as far as non-invasive diagnosis or non-invasive treatment are concerned. To obtain a higher level of CCP a hospital needs to adhere to a number of qualitative and quantitative criteria. CCP "B" relates to the license to perform invasive coronary diagnosis (B1), percutaneous treatment of coronary disease (B2) and cardiac surgery (B3). Hospitals with a CCP "P" (P=pacemaker) are accredited to provide PM therapy. In order to obtain a CCP "E" (electrophysiology) qualification, a hospital must have a CCP "B" and a CCP "P" accreditation in addition to a number of quantitative requirements, amongst others subject to a minimum number of electrophysiology procedures and the number of cardiologists affiliated with the hospital.

Table 3: Cardiac Care Programs in Belgium

CARDIAC CARE PROGRAMS (CCP)		
A		basic clinical cardiology
B	B1	invasive coronary diagnosis
	B2	percutaneous treatment of coronary disease
	B3	cardiac surgery
P		PM therapy
E		electrophysiology
T		heart- and lung transplantation
C		congenital heart disease

Most if not all Belgian hospitals providing standard cardiac care (CCP "A") are qualified as CCP "P" as well. It is mandatory for a hospital with a CCP "P" to have a formal cooperation statement with a hospital that has both CCP "B" and "E" qualifications. The legislation related to CCP "P" also mentions a number of quality standards to be fulfilled. For PM implants with indications other than 3AVB or slow AF with pauses longer than 2.5 seconds, expert advice from an electrophysiologist affiliated with a CCP "E" has to be obtained and registered.

By Royal Decree, all care programs must be submitted to an internal and an external quality appraisal, the latter to be organised and controlled by the College of Physicians. More specifically, the responsibility for the quality control of the CCP "P" lies with the College of Physicians – Cardiac Pathology - Section Pacing and Electrophysiology. In practice however, this obligation has never been enforced, and hospitals have only been encouraged to contribute data to the Belgian Heart Rhythm Association (BeHRA) pacemaker register, whose register data are copied within the activity reports of the College of Physicians.

2.4.2 Implantation reimbursement

In appendix (9.5) to this report, a list of the NIHDI reimbursement codes of PM related devices and medical procedures is provided. Physician's fees for implantation and replacement of PMs and PM leads are applicable to both cardiologists and surgeons. The list also includes the reimbursement codes connected to the follow-up of PMs ("System integrity check"). The latter are available to cardiologists only.

Article 35 of the NIHDI reimbursement nomenclature lists a number of additional requirements needed to obtain a reimbursement of the PM and its accessories. They refer to the need of the hospital to dispose of a CCP "P" accreditation and a number of formal prescription rules. Reimbursement requires a standardised prescription form (depicted in appendix) representing details of the PM and the leads that have been implanted, together with coded information on clinical and electrocardiographic characteristics of the patient that justify the implantation. The prescription form has to be signed by 2 cardiologists (or 1 cardiologist and 1 internist) and sent to the patient's health insurer. Each hospital must also proclaim to the NIHDI the cardiologist that is responsible for the clinical PM activity.

Under these conditions, cardiologists working in a CCP A hospital are entitled to perform PM implants in patients presenting with strictly described clinical indications: *"(1) complete heart block and (2) SSS and/or AF with ventricular pauses of more than 2.5 seconds with symptoms of syncope, and/or bradycardia with a heart rate lower than 30 beats per minute"*. In other conditions, the CCP-A cardiologists are legally obliged to ask and register the advice of an electrophysiologist who is connected to a CCP-E hospital.

The PM prescription form mimics the "European Pacemaker Patient Identification Card" (further referred to as the "European PM ID Card"). A copy of it is depicted in the appendix to the present report. It was first designed in 1978, jointly by the International Association of Prostheses Manufacturers (IAPM) and the European Working Group on Cardiac Pacing (EWGCP).[23] The Card is filled in by the implanting physician at the time of the implantation. It is added as a reference to the patient's hospital file, and is used by the manufacturer to design a personalised "Patient PM Card" that is sent to the patient and contains essential data of his or her PM.

By law, implantation centers (CCP "P") must engage in a peer review of their PM related clinical practice. In that context a duplicate of the PM prescription form is sent to the Belgian Heart Rhythm Association (BeHRA).

A PM replacement can be reimbursed not earlier than five years after the previous implantation, except for some specific indications (e.g. in case of infection, in children,…), subject to the acceptance by the insurer. Yearly, the insurers have to provide a detailed summary file of all the PMs that have been reimbursed to the NIHDI.

By January 2011, a web-based application is planned to be introduced for the prescription and the registration of PM implantation on-line: the "E-care QERMID@Pacemakers". It is a strictly secured computer application that has a limited accessibility for the attending physician and well-defined administrative personnel (hospital pharmacist, insurers, e-health platform). This application is intended to become mandatory in 2011 and will be linked to the reimbursement of the device.

2.4.3 Belgian Heart Rhythm Association (BeHRA)

The Belgian Heart Rhythm Association (BeHRA), formerly the Belgian Working Group on Cardiac Pacing and Electrophysiology (BWGCPE), is a working group of the Belgian Society of Cardiology, established in 1980. On its website (www.behra.be) it proclaims that it "aims to promote scientific activity and good clinical practice by encouraging discussions and meetings." From 1981 onwards, the BWGCPE started with a systematic registration of clinical PM activity in Belgium under the impulse of H. Ector and R. Van den Oever.[8] In 1984, a comprehensive analysis of the Belgian data was performed by H. Ector in his doctoral thesis.[8] The BeHRA yearly summarises the clinical pacing activity in Belgium based on the forms provided by its members. Hospitals receive a yearly aggregated overview of the Belgian clinical pacing activity. The BeHRA has provided the KCE with data from their database. These will be discussed in detail in a further chapter.

Key points

- **Belgian hospitals providing standard cardiac care (cardiac care program A) deliver pacemaker therapy (cardiac care program P) as well.**
- **The reimbursement of a pacemaker requires a standardised prescription form that represents details of the PM, together with coded information on the clinical and electrocardiographical characteristics of the patient justifying the implantation.**
- **By law, pacemaker implantation centers must engage in a peer review of their clinical practice. In that context a duplicate of the PM prescription form is sent to the Belgian Heart Rhythm Association (BeHRA).**
- **Since 1981, the BeHRA registers clinical PM activity in Belgium and sends a yearly report to its members.**

3 SCIENTIFIC EVIDENCE SUPPORTING THE USE OF PACEMAKERS

In the present Good Clinical Practice report, the clinical effectiveness of PM therapy has been derived from clinical guidelines, published in scientific literature. It was beyond the scope of the report to perform a systematic review of the literature on PM effectiveness.

3.1 LITERATURE SOURCES

Clinical guidelines (GLs) for cardiac pacing were searched in Medline (via Pubmed), EMBASE, the National Guideline Clearinghouse and the Guideline International network (GIN). In addition, the websites of the European (ESC), the US (ACC/AHA) and the Belgian (BeHRA) cardiologic societies were consulted. No date limits were applied.

The following search strings were used:[24]

- PubMed: (guideline[pt] OR practice guideline[pt] OR "Guidelines as Topic"[Mesh] OR recommendation*[ti] OR standard*[ti] OR guideline*[ti]) AND ("Pacemaker, Artificial"[Mesh])
- EMBASE: 'practice guideline'/exp AND 'artificial heart pacemaker'/exp
- National Guideline Clearinghouse: 'pacemaker'
- GIN: pacemaker

During the initial search, it soon became evident that chronic AF was only marginally discussed in the PM GLs, although this condition can give rise to symptomatic bradycardia, thus representing an indication for cardiac pacing. Therefore, as a second step an additional search for GLs on AF was performed.

3.2 RESULTS OF LITERATURE SEARCH

Based on title and abstract, dedicated pacing guidelines were identified. GLs related to pacing in children, those limited to CRT pacing in heart failure, and reports strictly limited to modes of pacing, PM programming or PM leads were excluded. GLs published before the year 2000 were only taken into consideration for their historical meaning. The first formal pacing GLs we could identify were those emerging from the US Pacemaker Study Group, issued in 1974.[25, 26] The most recent US GL has been published in 2008 and represents an update of previous ones, issued in 2002, 1998, 1991, 1984 and 1974 respectively. Several GLs, originating from national pacemaker societies have been published, mostly based on the by then most recently available US document and often written in the local language. In 2000, a GL originating from a Belgian researcher was published.[27] It represents a narrative update of the 1998 ACC/AHA GLs.[28] The one and only GL issued by the ESC has been published in 2007.[2] In this way, our literature search resulted in two major GLs that were strictly related to cardiac pacing (Table 4):

1. The ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac abnormalities. Further in this report, it is referred to "US GL".
2. The 2007 ESC guidelines for cardiac pacing and cardiac resynchronization therapy. Further in the present report, it is referred to as "European GL".

A summary of these guidelines, representing the current state-of-the-art in pacing practice, will be presented further on. Because the present report is essentially related to the PM practice in Belgium since 2002, the recommendations formulated in the recently published guidelines will be compared with those issued previously. In addition, relevant topics about AF, originating from specific guidelines, will also be taken into consideration. This report does not consider pacing in paediatrics, in congenital heart disease or other uncommon indications for PM therapy such as hypertrophic obstructive cardiomyopathy.

Table 4: Review of guidelines on conventional cardiac pacing

	PACING GLs	ATRIAL FIBRILLATION GLs
North America & NZ	2008: AHA/ACC/HRS, Epstein et al.[4]	2006: ACC/AHA Füster et al. In collaboration with ESC.[29]
		2008: ICSI.[30]
		2005: New Zealand.[31]
Europe	2007: ESC, Vardas et al.[2]	2007/2008: HAS.[32]
		Cfr. 2006 AHA/ACC.[29]
		2006: NICE.[33]

Source: KCE.

3.3 GUIDELINES FOR CARDIAC PACING

The European 2007 GL for cardiac pacing constitutes the first ever GL issued by the ESC.[2] The US 2008[4] GL represents the most recent of a consecutive series of US pacing GLs, the oldest one published in 1974.[25, 26]

The results of a critical appraisal of these GLs is presented in the appendix.

Recommendations formulated in the European 2007 and the US 2008 GLs are copied in the appendix to the present report.[2, 4]

3.3.1 European guideline on cardiac pacing

The European GL, issued by the ESC, formulates 40 recommendations on bradycardia pacing (we excluded recommendations on the mode of pacing).[2] Besides pacing in bradycardia, it also considers PM therapy in patients with heart failure (cardiac resynchronisation therapy or CRT) that is however beyond the scope of this report. Each recommendation is assigned a level of evidence and a class of recommendation as explained in Table 5.

Table 5: Classes of recommendation and levels of evidence in the European guideline

Classes of recommendation	
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, and effective
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy
ClassIIb	Usefulness/efficacy is less well established by evidence/opinion
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective and in some cases may be harmful
Levels of Evidence	
Level A	Data derived from multiple randomized clinical trials or meta-analyses
Level B	Data derived from a single randomized clinical trial or large non-randomized studies
Level C	Consensus of opinion of the experts and/or small studies, retrospective studies, and registries

Source: Vardas et al.[2]

None of the European recommendations reaches a "level of evidence A". Only 12 recommendations (30%) are supported with a level B evidence, whereas the remainder (70%) are essentially based on expert opinion. Of the 12 "level B" recommendations, 5 are related to uncommon pacing indications (acute myocardial infarction, muscular dystrophy) and 5 are recommendations against pacing (class III). The remaining 2 "level B" recommendations are related to unexplained syncope and have been attributed a class IIaB recommendation, indicating that "Weight of evidence/opinion is in favour of usefulness/efficacy". This indicates that clinical practice of PM therapy mainly rests on expert opinion and consensus. The most solid scientific evidence for the clinical effectiveness of PM therapy is for patients with 3AVB. For this condition non-randomised studies demonstrate that permanent pacing improves survival, especially in symptomatic patients who experienced episodes of syncope.

Whereas "syncope" is a well-defined symptom, other potential manifestations of bradycardia are more vague, yet may be considered as valid symptoms for justifying PM therapy. These include dizziness, fatigue, dyspnoea, reduced exercise capacity, cognitive impairment and chronotropic incompetence. Of 40 recommendations in this GL, 10 require syncope as the presenting symptom in order to qualify for PM insertion. Of those, three are labelled with a class IC recommendation, four are class IIaB/C, two are IIbC and one is IIIC.

There is consensus of opinion between experts that PM therapy in chronic symptomatic 2AVB or 3AVB, as well as in symptomatic SSS is effective (recommendation class IC). In AV conduction disturbances, expert opinion is in favour of the usefulness of PM therapy in asymptomatic patients with 2AVB (Mobitz I or II) or 3AVB (class IIaC). There is consensus that in asymptomatic SSS PM implantation is not useful (class IIIC). Pacing in asymptomatic patients is accepted in some less frequent conditions such as certain muscular dystrophies and in AV conduction disturbances following catheter ablation or following valve surgery or in the context of an acute MI.

3.3.2 United States guideline on cardiac pacing

This GL considers pacing in bradycardia as well as resynchronisation therapy for heart failure and implantable defibrillator therapy for the prevention of sudden death.[4] The latter two indications are beyond the scope of this report. The documentation of a relationship between symptoms and rhythm is more emphasised in the US as compared to the European GL. It strictly defines symptomatic bradycardia as "a documented brady-arrhythmia that is directly responsible for development of the clinical manifestations of syncope or near syncope, transient dizziness or lightheadedness, or confusional states resulting from cerebral hypoperfusion attributable to slow heart rate. Fatigue, exercise intolerance, and congestive heart failure may also result from bradycardia. (…) Definite correlation of symptoms with a brady-arrhythmia is required."

The US GL formulates 50 recommendations on bradycardia pacing (recommendations on pacing mode excluded). Each recommendation is assigned a level of evidence and a class of recommendation as indicated in Table 6.

Table 6: Classes of recommendation and levels of evidence in the US guideline

Classes of recommendation	
Class I	Treatment SHOULD be administered
Class IIa	IT IS REASONABLE to administer treatment
ClassIIb	Treatment MAY BE CONSIDERED
Class III	Treatment SHOULD NOT be administered since it is not helpful and may be harmful
Levels of Evidence	
Level A	Data derived from multiple randomised clinical trials or meta-analyses
Level B	Data derived from a single randomised clinical trials or nonrandomised studies
Level C	Only consensus opinion of experts, case studies, or standard of care

Source: Epstein et al.[4].

Whereas the European GL requires 3AVB to be symptomatic in order to obtain a class I recommendation, the US GL accepts asymptomatic 3AVB as a class I indication in a number of strictly defined high-risk groups (ACC#12-18-19). The US GL considers AF with prolonged pauses as an indication for pacing, whereas AF is not discussed in ESC GLs. In the most recent US GL, it is contended that "in the setting of AF, a prolonged pause (e.g. >5 seconds) should be considered to be due to advanced 2AVB". Hence recommendation ACC#13 was added: "Permanent PM implantation is indicated for 3AVB and advanced 2AVB at any anatomic level in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer (class IC)."

If one compares the US GLs from 1998 on, no clinically important changes can be discerned as far as the indications for bradycardia pacing are concerned. This is confirmed by other authors who found no major changes in US guidelines between 1991 and 2006.[18] As far as the mode of pacing is concerned, recommendations in the US GL are less affirmative than in the European. The choice for a single or dual chamber device is reported to depend on "the *desire* for AV synchrony", "the *desire* for rate response" or "the *desire* for atrial pacing".

3.3.3 Guidelines related to the management of atrial fibrillation

In order to identify GLs related to pacing in patients with AF, a PubMed search was undertaken by introducing the following search string:

((guideline[pt] OR practice guideline[pt] OR "Guidelines as Topic"[Mesh] OR recommendation*[ti] OR standard*[ti] OR guideline*[ti])) AND ("Atrial Fibrillation"[Mesh]) AND ("Pacemaker, Artificial"[Mesh])

This resulted in 19 hits. These references were obviously also identified in the previously mentioned search for pacing guidelines in general ("pacemaker AND guidelines"). Only 1 out of the 19 references thus retrieved was a genuine pacemaker GL: the 1998 ESC pacing guidelines.[34] The other references were mostly either narrative reviews or articles focussed on the prevention of AF by means of permanent pacing. The Medline search was subsequently extended by searching databases from the National Guideline Clearinghouse and GIN for "atrial fibrillation", from which we retrieved five additional relevant recent GLs.

3.3.3.1 ESC 1998

The 1998 ESC GL includes a chapter dedicated to PM therapy in AF.[34] Class I recommendations (defined as "agreement that a PM should be implanted") are applicable to patients with chronic AF and symptomatic bradycardia, in 3AVB, or in bradycardia due to the concomitant use of AVN depressant drugs that cannot be avoided. A class I indication also applies to patients with symptomatic pauses after spontaneous termination of (paroxysmal) AF and to prevent pause-dependent AF in bradycardia-tachycardia syndrome.

3.3.3.2 New Zealand Guidelines Group 2005

PM therapy in this GL is discussed in relation to AVN catheter ablation, where it is concluded that AVN ablation with PM implantation should be offered only as a last resort, when ventricular rate in AF remains poorly controlled despite optimal medical therapy, or where there is severely symptomatic paroxysmal AF. Furthermore, (atrial or physiologic) pacing is recommended (class B: "recommendation supported by fair evidence") for its use as a potential therapy for non-pharmacological maintenance of sinus rhythm in selected patients with paroxysmal AF and symptomatic bradycardia.

3.3.3.3 NICE 2006 GL.33

This GL was prepared by the National Collaborating Centre for Chronic Conditions (NCC-CC), for the NHS in England and Wales. The NCC-CC is funded by the National Institute for Health and Clinical Excellence (NICE).

As in other GLs discussed so far, PM therapy is only briefly mentioned in this NICE GL as well. It concludes that: "Other than recognised indications for PM implantations such as sinus node disease, symptomatic bradycardia and chronotropic incompetence, no evidence was found to specifically identify other patients with AF who should be referred for PM implantation."

3.3.3.4 Joint ACC/AHA/ESC 2006 GL.29

This GL has been jointly prepared by the ACC/AHA task force on practice guidelines and the ESC Committee for Practice Guidelines, and was developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Hence they can be considered as an update of the European 1998 and the US 2001 GLs.

PM therapy in these GLs is primarily discussed in relation with AVN ablation. It is also mentioned that, "although atrial-based pacing is associated with a lower risk of AF and stroke than ventricular-based pacing in patients requiring pacemakers for brady-arrhythmias, the value of pacing as a primary therapy for prevention of recurrent AF has not been proven."

3.3.3.5 Haute Autorité de Santé 2007/2008 GL32

This document is originating from France. It is mainly based on the 2006 GLs issued by ACC/AHA and the 2006 NICE GL, both discussed above. PM therapy is discussed in the context of AVN ablation therapy and in patients in whom bradycardia is induced by anti-arrhythmic drugs.

3.3.3.6 Institute for Clinical Systems Improvement 2008 GL.30

This GL also refers to the ACC/AHA/ESC 2006 GL, adding no additional information in relation to PM therapy. Its mentions that pacing may allow the use of anti-arrhythmic drugs that are contraindicated due to bradycardia, and that it may be considered in combination with AVN ablation in patients with poorly controlled ventricular response.

Key points

- **The clinical indications for PM therapy mainly rest on many years of clinical experience and expert opinion.**
- **Historical data indicate that PM therapy improves symptoms and prolongs life in patients with (symptomatic) complete heart block.**
- **In general, PM therapy is deemed appropriate in patients with (1) a documented bradycardia (2) that leads to symptoms (3) and in whom there is a definite correlation between the symptoms and the bradycardia.**
- **There are no prominent differences between the European and the US guidelines, but the documentation of a direct relationship between symptoms and heart rhythm is more emphasized in the US as compared to the European guideline.**
- **The ESC 1998 GL on atrial fibrillation recommends PM therapy in case of symptomatic bradycardia, whether occurring spontaneously or due to necessary heart rate lowering drugs.**

4 BELGIAN PACING PRACTICE - THE BEHRA REGISTRY

The Belgian Heart Rhythm Association (BeHRA), formerly the Belgian Working Group on Cardiac Pacing and Electrophysiology (BWGCPE), is a working group of the Belgian Society of Cardiology, established in 1980. From 1981 onwards, it started with the systematic registration of clinical PM activity in Belgium.[8] The BeHRA yearly summarises the clinical pacing activity in Belgium based on the forms provided by its members on a voluntary base. For the present report, BeHRA has provided the KCE with data from their database. It was agreed with BeHRA not to link this database with other databases in order to guarantee privacy (both of patients and hospitals). Because of this, the data originating from the BeHRA registry are presented separately in this chapter to distinguish them clearly from the other databases.

4.1 BEHRA – THE ASSOCIATION

On its website, BeHRA introduces itself as follows: "*The Belgian Heart Rhythm Association (BeHRA) has been created as a working group of the Belgian Society of Cardiology in 1980. Initially, it was composed of a limited number of outstanding cardiologists who were interested in creating a dynamic group of discussion about the evolving domain of Cardiac Pacing. Due to the rapidly growing interest in electrocardiology, electrophysiology and later in implantable defibrillators and ablation, the Group became much more important. It is now composed of all the centers which regularly implant pacemakers and which are actively involved in electrophysiology and/or ablation.*" (source: www.behra.be)

As stipulated earlier, implantation centers (CCP "P") by law must engage in a peer review of their PM related clinical practice. In that context PM centers are requested to send a duplicate of their PM prescription forms. BeHRA collects and aggregates these data and adds "some quality indicators" to it. Every participating centre yearly receives an overview of national data and a personalised feedback including a separate report with the centre-specific data only. As such, centres can benchmark their individual data with national-based activities. The initiators hoped that exchanging these data would enable every centre to conduct a kind of 'self-examination'.(source: http://www.behra.be/peereviewpacing.htm)

4.2 BEHRA'S DATABASE

For the present report, KCE received the BeHRA[a] database for the period 1993-2007. Data allowing direct or indirect identification of the patient were removed. The process was approved by the KCE medical supervisor. The names of the centres were also replaced by a random number to avoid identification and to respect the guaranteed confidentiality of BeHRA towards its members.

4.2.1 Data collection and content

This part provides an overview of variables included in the BeHRA database. They originate from the items the cardiologist or the surgeon indicates on the European PM ID Card at the time of the implantation. A copy of this Card is depicted in the appendix to this chapter. The Card offers codes for symptoms, ECG indications, aetiology, pacing mode, generator and lead changes and file closure. Figure 5 represents a detail of the card, with the code explanations used in it.

a In the remaining of the text, the abbreviation BeHRA will be used systematically to refer both to the former BWGPCE and current BeHRA association.

Figure 5: Detail from the European Pacemaker Patient Identification Card

Code explanation for implantation

Symptoms (before implant)

category -	*code*	*specification*
Unspecified	A1	Unspecified (default)
	A2	Uncoded
Syncope	B1	Syncope
	B2	Dizzy spells
	B3	Bradycardia
Tachycardia	C1	Tachycardia
Other	D1	None / Prophylactic
	D2	Dyspnea / Heart Failure
	D3	Cerebral dysfunction
	D4	Chest pain
	D5	Aborted sudden death

Aetiology

category -	*code*	*specification*
Unspecified	A1	Unspecified
	A2	Uncoded
Unknown	B1	Unknown
	B2	Conduction tissues disease
Ischaemic	C1	Ischaemic
	C2	Post-infarction
Congenital	D1	Congenital
Iatrogenic	E1	Surgical complication
therapeutic	E2	Surgical
	E3	Ablation
	E4	Drug induced
Autonomic nervous	F1	Carotid sinus syncope
system	F2	Vasovagal syndrome
	F3	Orthostatic hypotension
Cardio myopathies	G1	Cardiomyopathy unspecified
	G1A	Cardiomyopathy hypertropic
	G1B	Cardiomyopathy dilated
Valvular	G2	Myocarditis
	G3	Valvular heart disease
	G6	Endocarditis
Hearttransplantation	G7	Heart transplant
	G8	Ionizing radiotion

ECG indications

category -	*code*	*specification*
Unspecified	A1	Rhythm unspecified (default)
	A2	Rhythm uncoded
Sinus rhythm	B1	Normal sinus rhythm
	B2	NSR + abnormal EPS
AV block	C1	1' heart block
	C2	2' heart block - unspecified
	C3	2' heart block - Wenkebach
	C4	2' heart block - Mobitz
	C5	CHB - QRS unspecified
	C6	CHB - narrow QRS
	C7	CHB - wide QRS
	C8	Chronic A fib + AV block
Bundle branch block	D1	BBB - unspecified
	D2	RBBB - incomplete
	D3	RBBB - complete
	D4	LBBB
	D5	LAHB
	D6	LPHB
	D7	RBBB + LAHB + normal PR
	D8	RBBB + LPHB + normal PR
	D9	RBBB + LAHB + long PR
	D10	RBBB + LPHB + long PR
	D11	LBBB + long PR
	D12	LBBB + RBBB (alternans)
Sinus node disease	E1	SSS - unspecified
and atrium	E2	SSS - SA exit block
	E3	SSS - SA arrest
	E4	SSS - bradycardia
	E5	SSS - brady / tachy
	E6	Chronic A fib + brady
	E7	Interatrial block
	E8	Chronotropic incompetance
	F1	Atrial tachy unspecified
	F2	AV-re-entrant tachycardia
	F3	AV nodal tachycardia
	G1	Ventricular extrasystoles
	G2	Non sustained VT / VF
	G3	Sustained VT / FT
	G4	Torsades de pointes

Code explanation for "mode of pacing"

1	2	3
Chamber(s) paced	Chamber(s) sensed	Response to sensing
O = None	O = None	O = None
A = Atrium	A = Atrium	T = Trigger
V = Ventricle	V = Ventricle	I = Inhibit
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)
4		5
Programmability rate modulation		Antitachyarrythmia function(s)
O = None		O = None
P = Simple programmable		P = Pacing (antitachyarrythmia)
M = Multiprogrammable		S = Shock
C = Communicating		D = Dual (P+S)
R = Rate modulation		

Code explanation for explantation

Generator change

category -	*code*	*specification*
Unspecified	A1	Unspecified
	A2	Uncoded
Elective	B1	Elective
	B2	Recall
	B3	System change heamodynamic
	B4	System change - pm syndrome
	B5	System change - palmitations
	B6	System change electrode problem
	B7	EMG inhibition
	B8	Extracardiac stimulation
Surgical	C1	Mechanical protrusion
	C2	Erosion
	C3	Infection
	C4	Wound pain
Failure minor	D1	Failure - unspecified
	D2	Failure - undersensing
	D3	Failure - oversensing
	D4	Failure - magnetic switch
	D5	Failure - programming
Failure major	E1	Failure - unspecified
	E2	Failure - no output
	E3	Failure - low output
	E4	Failure - low rate
	E5	Failure - high rate
	E6	Failure - connector
	E7	Failure - encapsulation
Failure battery	F1	Normal E.O.L.
	F2	Premature E.O.L.

Electrode change

category -	*code*	*specification*
Unspecified	A1	Unspecified (default)
	A2	Uncoded
Elective	B1	Elective
	B2	Displacement
	B3	Exit block
	B4	EMG inhibition
	B5	Extracardiac stimulation
	B6	Perforation
	B7	Undersensing
	B8	Recall
Surgical	C1	Infection / Ulceration
Failure	D1	Connector failure
	D2	Insulation failure
	D3	Conductor break

Indication for file closure

category -	*code*	*specification*
Unspecified	A1	Unspecified (default)
	A2	Uncoded
Death	B1	Death unrelated to pacemaker
	B2	Death related to pacemaker
	B3	Death - sudden
	B4	Death - cause unknown
	B5	Death related to lead
Lost to follow-up	C1	Lost to follow-up
	C2	Hospital transfer
	C3	Pacemaker removed

Based on the European PM ID Card, data on several items are gathered by BeHRA. Table 7 lists an overview of the variables from the BeHRA database that are considered in this report.

Table 7: Overview of variables in the BeHRA database

Variable	Description	Remarks
'Year'	year of implantation	The exact implantation date was removed to assure patients' privacy.
'Center'	Number of the implantation centre	Names of the centres were replaced by a number to prevent identification and respect the guaranteed discretion of BeHRA towards its members.
'Age at implantation'	Age at moment of (re-)implantation	Calculated using the year of implantation and the year of birth.
'Patname'	Patient name	This variable was removed to assure patients' privacy.
'Birthday' 'Datimpl'	Date of birth Date of implantation	These two variables were removed from the database (to assure patients' privacy) after the age at the moment of implantation was calculated.
'Sex'	Gender	
'Symptom'	Symptoms	Symptoms leading to decision for pacemaker implantation.
'ECG'	ECG indications	The Dutch variable name is EKG (elektrokardiogram). We will systematically use the English abbreviation (ECG, Electrocardiogram).
'Aetiol'	Aetiology	Aetiology of the disease leading to symptomatic bradycardia.
'Nature'	First implantation or replacement	
'BIV'	Biventricular pacemaker	Before 2001, this variable was not registered. From 2001 till 2005, this variable was called 'PacCHF'. In 2006 and 2007 it was named 'BIV'. We will systematically use the name 'BIV'.
'GenCHG'	Generator change	Information available for the period 1993-2005.
'VTLCHG'	Ventricular lead change	Information available for the period 1993-2005.
'ATLCHG'	Atrial lead change	Information available for the period 1993-2005.

For the variables 'Gen CHG', 'VTLCHG' and 'ATLCHG', it is possible that the variable name has changed or was encoded differently in 2006-2007. In the following description, data are only presented for the variables that explicitly mentioned the same variable name (i.e. excluding 2006 and 2007 for these three variables)

Some variables are not included in this list since they were a duplicate of another variable (e.g. sex and gender or datimpl and impldate), a recoding (e.g. a number was given for the (group of) outcomes of several variables such as 'symptom', 'ECG', and 'Aetiol'), or a derived variable which we preferred to recalculate using the original values (e.g. age based on birthday and implantation date). The variable 'indication for file closure' was also removed due to missing values (<0.1% recoded since 1995). Other variables indicating the serial number or model of generators or leads (GENmod, CHFmod, VTLmod, ATLmod, VTLser, ATLser) were not taken into account because of the non-standardised way of encoding. Mode of pacing was excluded since it does not necessarily reflect how a certain pacemaker was actually programmed. Moreover, the selection of pacing mode was beyond the scope of this project.

The possibility of patient identification is blocked by removing the patient's name, day of birth, and day of implantation. The last two variables were used to calculate the patients' age in the implantation year before removing them from the database. As indicated earlier, the name of the PM centre had to be removed as well to respect the confidentiality of BeHRA towards its members. A numeric identifier that was already available in the original database (ranging from 1 to 290) was retained instead.[b] It should be noted that this hospital anonymity requirement only holds for the BeHRA database, not for the other national databases discussed further in this report.

- The descriptive statistics of the variables that are presented in the next section are based on the original raw databases received from BeHRA. Due to the variation in registered interventions (e.g. the drop in 1998), the results will mainly be expressed in relative units.

[b] Comparing data of a specific hospital over several years should be done carefully due to the impact of mergers over the years.

4.2.2 Basic Descriptive Statistics

Table 8 provides some basic descriptive statistics of the BeHRA data. There are 117,663 *pacemaker implantation registrations* over the period 1993-2007, with a mean of 7,844 yearly registrations (range: 5,816 in 1998 and 8,748 in 2003). In 1998, there is a relatively large drop in the number of registrations and in the *participating centres* as well. Especially centres with a relatively small number of registrations (i.e. less than 25/year) did not take part in the register during that year (Figure 6).

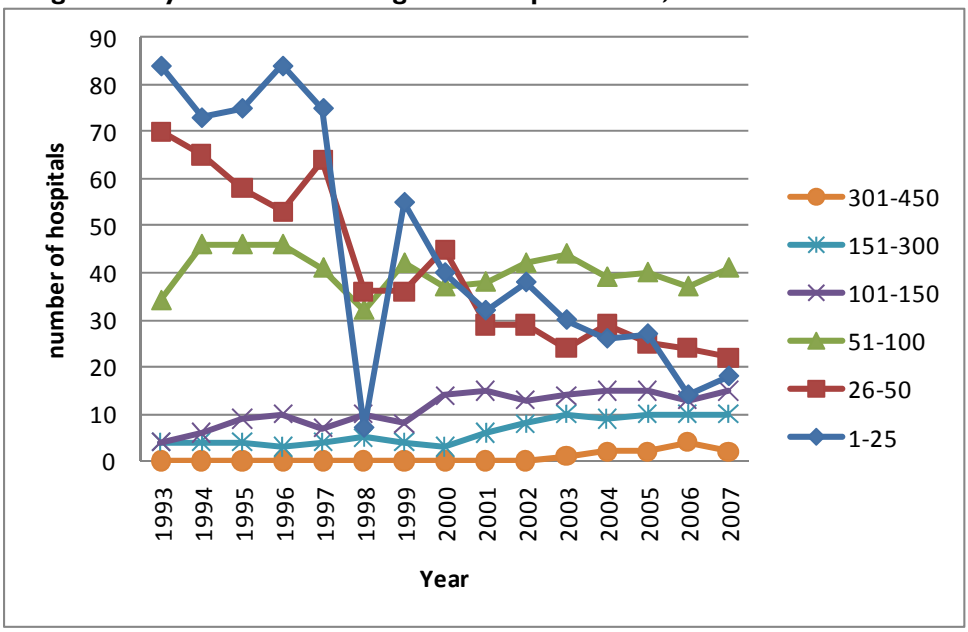
Table 8: General data from the BeHRA database

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	total
Number of registrations (n)	7545	7977	8210	8069	7699	5816	6810	7218	7151	8010	8748	8416	8651	8675	8668	117663
First implantations	6197	6551	6428	6292	5884	4426	5025	5050	4950	5619	6328	6226	6276	6171	6013	87436
Replacements	1348	1426	1782	1777	1815	1390	1785	2168	2201	2391	2420	2190	2375	2504	2655	30227
% first	82.1%	82.1%	78.3%	78.0%	76.4%	76.1%	73.8%	70.0%	69.2%	70.1%	72.3%	74.0%	72.5%	71.1%	69.4%	74.3%
missing (n)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gender (% male)	52.2%	52.6%	52.4%	52.2%	53.6%	54.1%	55.7%	50.4%	56.1%	52.3%	50.7%	51.0%	53.2%	53.1%	53.0%	52.8%
First implantations	51.8%	52.4%	52.0%	52.2%	54.4%	53.8%	55.3%	50.4%	56.3%	52.0%	50.7%	51.0%	53.8%	53.2%	52.9%	
Replacements	54.3%	53.6%	54.0%	52.1%	50.8%	55.0%	56.8%	50.3%	55.6%	53.1%	50.6%	51.0%	51.5%	52.7%	53.2%	
missing (n)*	3	0	3	0	2	46	0	0	0	0	0	0	0	0	0	54
missing (%)	0.04%	0.00%	0.04%	0.00%	0.03%	0.79%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.05%
Mean and median age	74.5	74.3	74.9	74.9	74.6	74.7	75.2	75.4	75.2	75.5	75.4	75.8	76.0	76.1	76.4	75.3
at implantation (years)	76	76	76	76	76	76	77	77	77	77	77	78	78	78	79	77
First implantations	74.7	74.4	75.0	74.8	74.6	74.8	75.3	75.3	75.1	75.2	75.1	75.7	75.8	76.0	76.0	
Replacements	73.3	73.9	74.7	75.3	74.7	74.2	75.1	75.7	75.5	76.1	76.1	76.1	76.6	76.2	77.3	
missing (n)	698	658	804	709	2090	469	496	562	739	591	842	757	566	511	619	11111
missing (%)	9.25%	8.25%	9.79%	8.79%	27.15%	8.06%	7.28%	7.79%	10.33%	7.38%	9.63%	8.99%	6.54%	5.89%	7.14%	9.44%
exclusion (n, age < 0)	71	36	18	12	10	4	0	12	0	0	0	0	0	0	0	163

*: The number or percentage of missing data is in relation to the number of registrations (not in comparison with the actual number of pacemaker (re-)implantations). Remark on age: for a minor amount of yearly registrations (maximum 0.94% in 1993) the data are implausible, as there is a negative difference between the day of implantation and the day of birth. This problem did not occur anymore after the year 2000. There is also a wide variation in missing values to calculate age at (re-)implantation, ranging between 5.89% (2006) and 27.15% (1997).

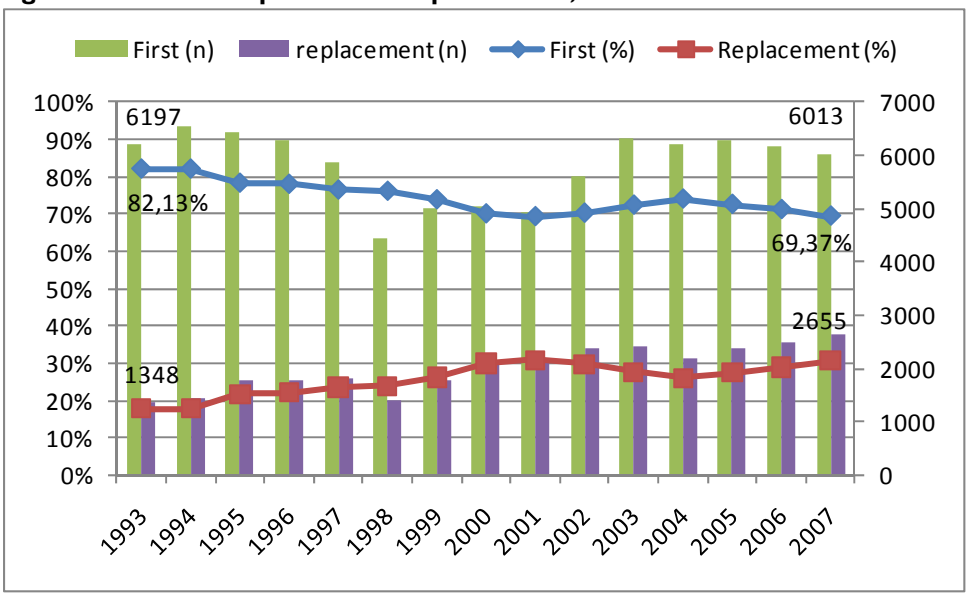
The main determinant of the decreasing number of participating centres over time are mergers of hospitals. This can also be deducted from Figure 6 which shows that there were much more participating centres with few patients (i.e. <25 or 50 registered interventions) in the 1990s versus recent years, and vice versa for relatively large centres (with a maximum of 407 registrations by one centre in 2006).

Figure 6: Number of hospitals participating in the BeHRA registration, categorised by the volume of registrations per centre, 1993-2007



There are no missing data in the database for the *nature of intervention*, i.e. primo implantation or replacement (Table 8). The database contains 87,436 primo implantation registrations and 30,227 replacements. The share of replacements out of the total number of registered implantations increased continuously from roughly 18% in 1993 to 30% in 2000, remaining on that level until 2007 (Table 8 and Figure 7). There is a clear trend in the absolute and relative increase of replacements, which resulted in almost a doubling of the number of registered replacements from 1993 to 2007 (Table 8 and Figure 7).

Figure 7: First and replacement implantations, 1993-2007



4.2.3 Age and gender

On average 53% of registered patients were male (Table 8 and Figure 8). There are almost no missing values for this variable.

Registered patients are predominantly septuagenarians or octogenarians. The age standardized numbers show that the intervention is mainly addressing octogenarians (Figure 9). It appears that: 1) there are relatively more male patients in the registry and 2) the relative number of male nonagenarians increases (although this remains a small group in absolute numbers).

For primo implantations, over the period 1993-2007, on average 53% were male patients (yearly range 50.42% – 56.26%). For replacements this was about the same (average 53%, range 50.32% – 56.84%). Over the same period, the yearly percentage of 65+ was on average 87% (range 85.60% – 88.51%) for first implantations and 86.36% (range 83.44% – 88.53%) for replacements.

Figure 8: Number of registrations by gender and year, 1993-2007

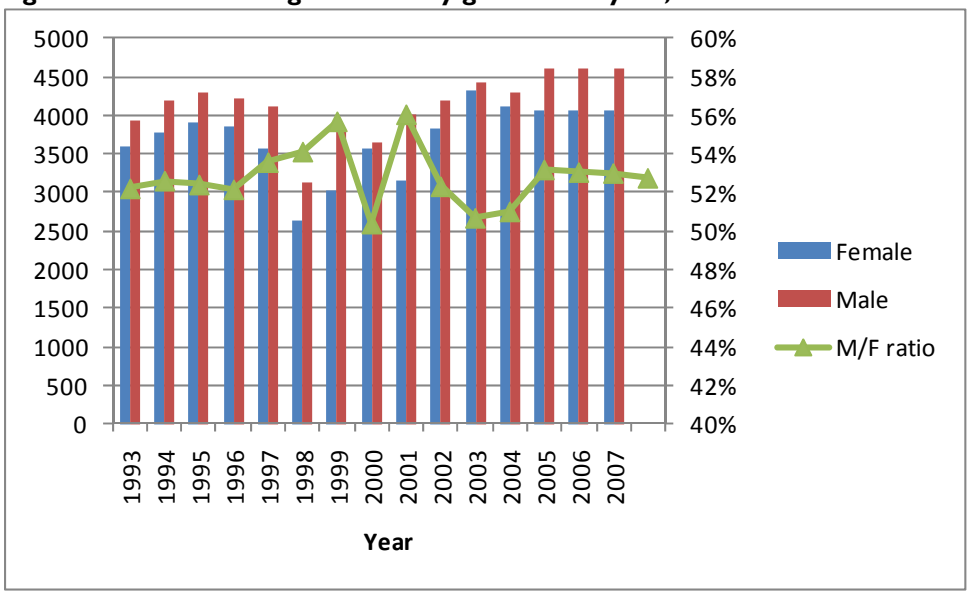
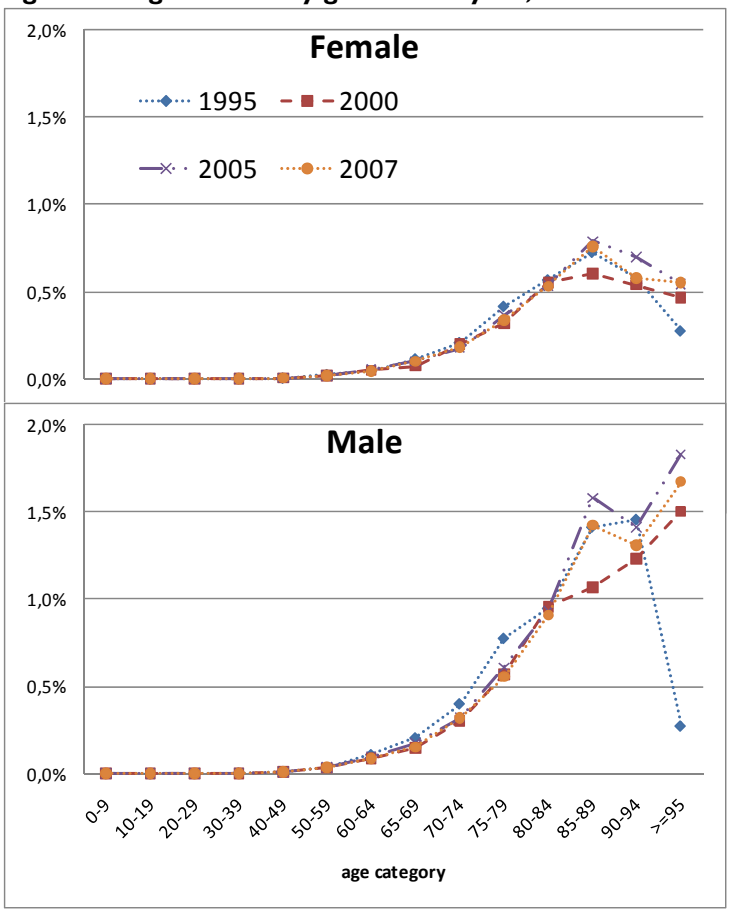


Figure 9: Registrations by gender and year, in % of the total population



4.2.4 Symptoms leading to PM implantation

For the variables 'symptoms', 'ECG', and 'aetiology', we restrain our description to primo implantations (excluding replacements).

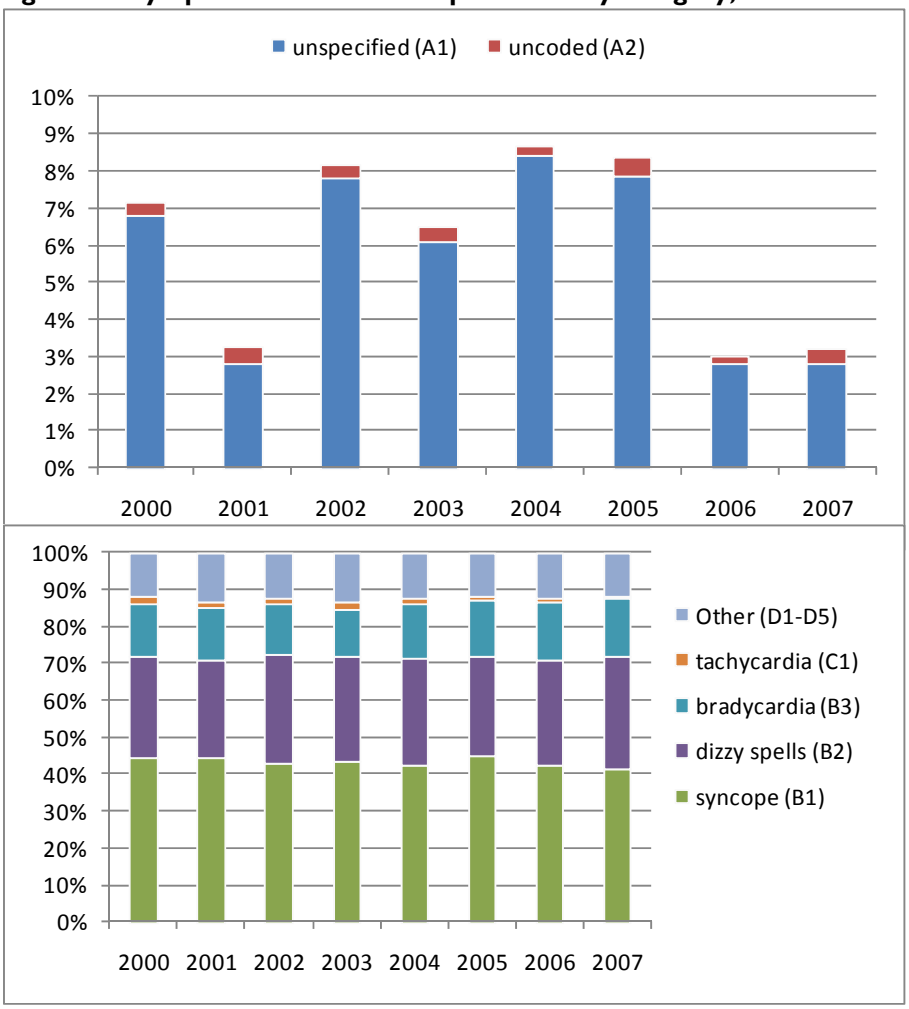
'*Symptoms*' are listed as follows:

Symptoms (before implant)

category -	*code*	*specification*
Unspecified	A1	Unspecified (default)
	A2	Uncoded
Syncope	B1	Syncope
	B2	Dizzy spells
	B3	Bradycardia
Tachycardia	C1	Tachycardia
Other	D1	None / Prophylactic
	D2	Dyspnea / Heart Failure
	D3	Cerebral dysfunction
	D4	Chest pain
	D5	Aborted sudden death

Over the period 1993-2007, on average 17% of all registered symptoms are unspecified or uncoded amounting to 56% in 1997. In 1998 it was drastically reduced to about 11% and declined further to about 3% in 2007. Since registration improved a lot during the late 1990s, only data from the period 2000-2007 are presented. Out of the registered symptoms (Figure 10, at the bottom), during 2000-2007, syncope is most commonly encoded (43%), followed by dizzy spells (28%) and bradycardia (14%). In 2007, excluding the unspecified or uncoded registrations, these three categories represents about 87% of all registered symptoms (Figure 10 - bottom).

Figure 10: Symptoms before first implantation by category, 2000-2007



Remarks: In 2000, there was only 1 missing value apart from the 'unspecified' or 'uncoded' registrations – the unregistered implantations not taken into account. In 2001, the variable A1 was entirely missing in the database but a new item was introduced (D1), most probably corresponding to the absent variable A1. In the figures, D1 is considered as A1.

4.2.5 Electrocardiographic abnormality leading to PM implantation

The variable '*ECG (Electrocardiogram) indications*' is categorised as follows:

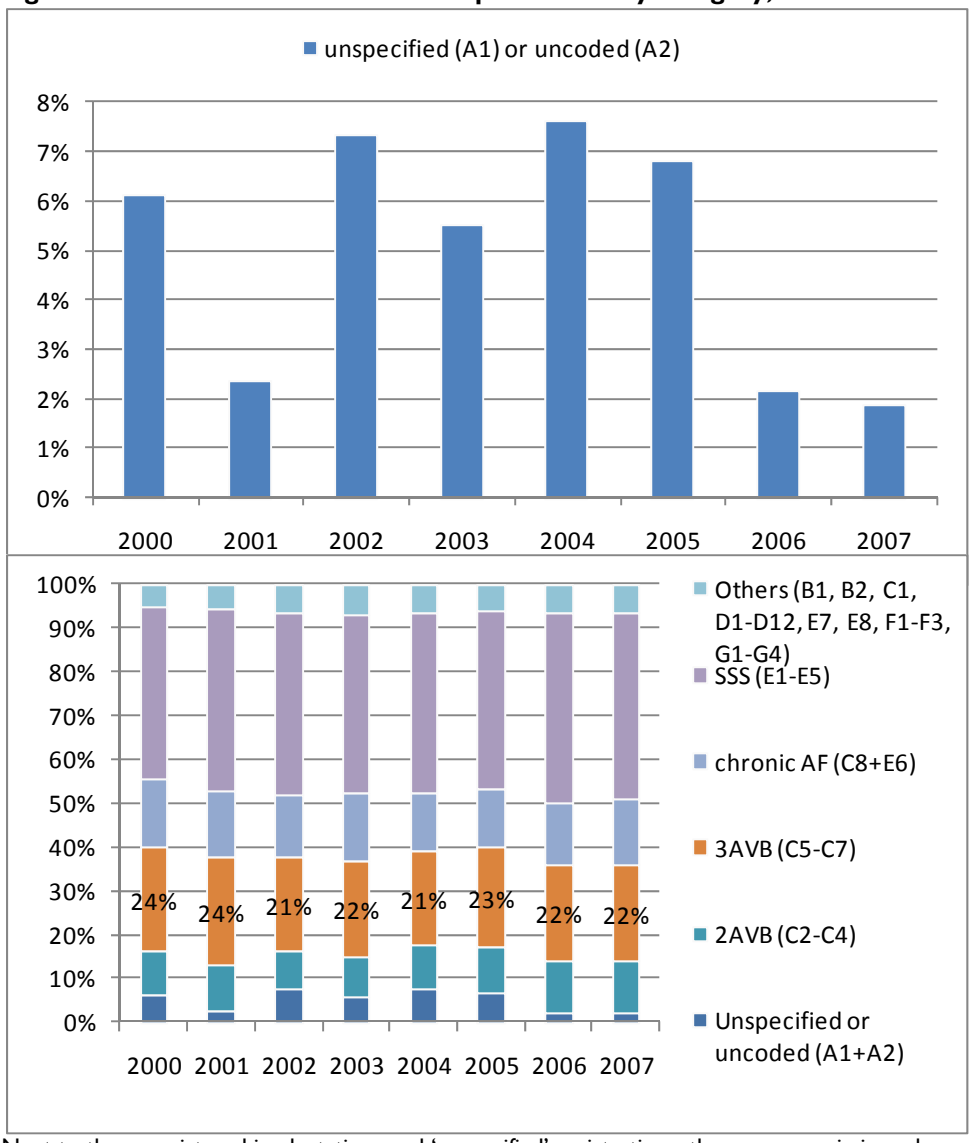
ECG indications

category -	*code*	*specification*
Unspecified	A1	Rhythm unspecified (default)
	A2	Rhythm uncoded
Sinus rhythm	B1	Normal sinus rhythm
	B2	NSR + abnormal EPS
AV block	C1	1' heart block
	C2	2' heart block - unspecified
	C3	2' heart block - Wenkebach
	C4	2' heart block - Mobitz
	C5	CHB - QRS unspecified
	C6	CHB - narrow QRS
	C7	CHB - wide QRS
	C8	Chronic A fib + AV block
Bundle branch block	D1	BBB - unspecified
	D2	RBBB - incomplete
	D3	RBBB - complete
	D4	LBBB
	D5	LAHB
	D6	LPHB
	D7	RBBB + LAHB + normal PR
	D8	RBBB + LPHB + normal PR
	D9	RBBB + LAHB + long PR
	D10	RBBB + LPHB + long PR
	D11	LBBB + long PR
	D12	LBBB + RBBB (alternans)
Sinus node disease and atrium	E1	SSS - unspecified
	E2	SSS - SA exit block
	E3	SSS - SA arrest
	E4	SSS - bradycardia
	E5	SSS - brady / tachy
	E6	Chronic A fib + brady
	E7	Interatrial block
	E8	Chronotropic incompetance
	F1	Atrial tachy unspecified
	F2	AV-re-entrant tachycardia
	F3	AV nodal tachycardia
	G1	Ventricular extrasystoles
	G2	Non sustained VT / VF
	G3	Sustained VT / FT
	G4	Torsades de pointes

NSR: normal sinus rhythm. CHB: complete heart block. BBB: bundle branch block. RBBB: right bundle branch block. LBBB: left bundle branch block. LAHB: left anterior hemiblock. LPHB: left posterior hemiblock. SSS: Sick Sinus Syndrome.) A fib: atrial fibrillation. AV: atrioventricular. VT: ventricular tachycardia. VF: ventricular fibrillation.

As for the previous variable, there were a lot of unspecified and uncoded registrations in the late 1990s (with a maximum of 52% in 1997). Therefore, data are only presented for the period 2000-2007. If one does not consider the unspecified A-categories (Figure 11, bottom), SSS is the most common ECG indication (about 43% in 2007), followed by 3AVB (22% in 2007), AF (15% in 2007), and 2AVB (12% in 2007).

Figure 11: ECG Indications for first implantations by category, 2000-2007



Next to the unregistered implantations and 'unspecified' registrations, there are no missing values for this variable for registered first implantations.
Remark: When the 'unspecified' (A1) and 'uncoded' (A2) registrations are included, 3AVB is registered in 21%-24% of cases.

4.2.6 Aetiology of symptomatic bradycardia

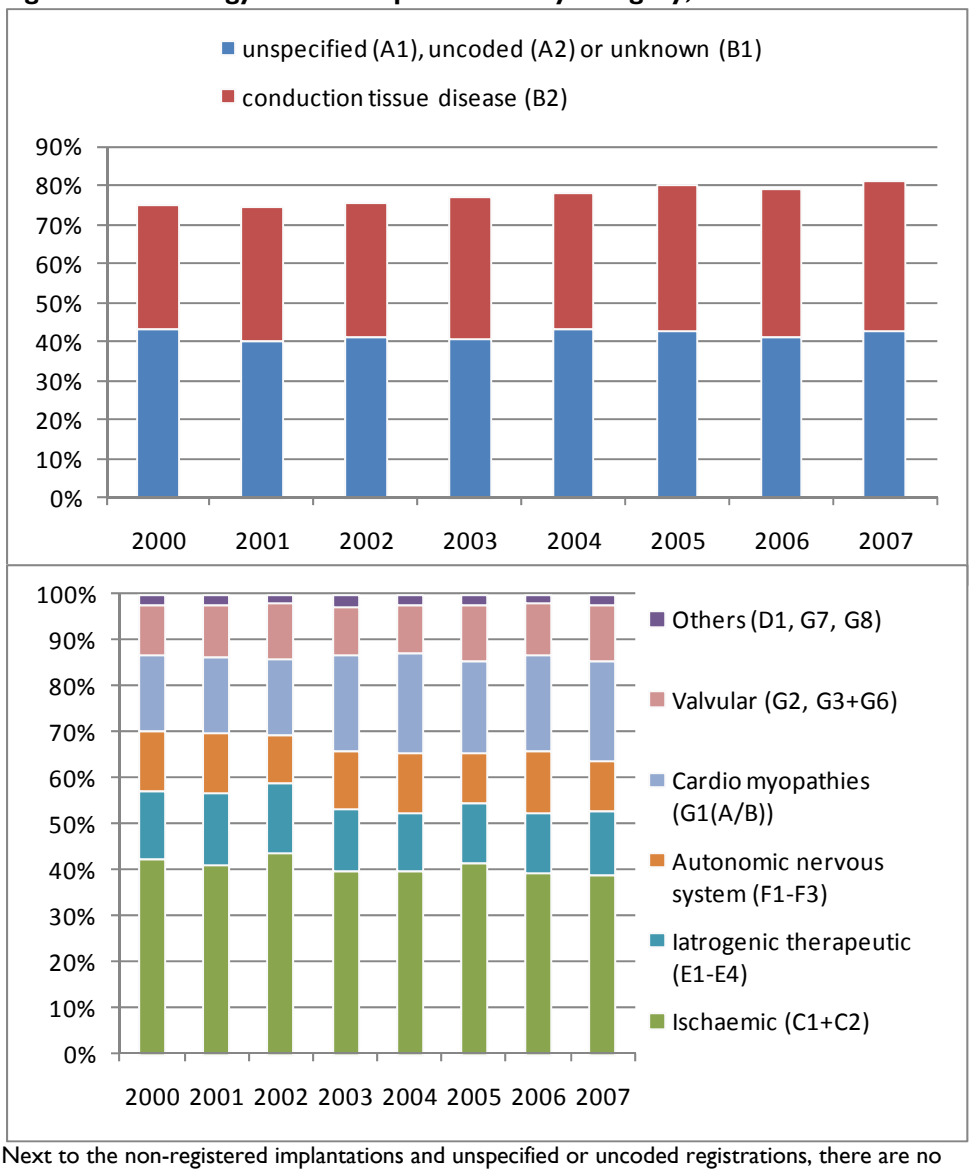
The aetiology of a disease, in this case "symptomatic bradycardia" refers to the cause of the disease. In most cases of AVB and SSS, no clear aetiology of the "symptomatic bradycardia" can be identified, and most cases are believed to result from an age dependent degeneration of conductive tissue of the heart.[I] The variable '*Aetiology*' is classified as follows in the BeHRA registry:

Aetiology

category -	*code*	*specification*
Unspecified	A1	Unspecified
	A2	Uncoded
Unknown	B1	Unknown
	B2	Conduction tissues disease
Ischaemic	C1	Ischaemic
	C2	Post-infarction
Congenital	D1	Congenital
Iatrogenic	E1	Surgical complication
therapeutic	E2	Surgical
	E3	Ablation
	E4	Drug induced
Autonomic nervous	F1	Carotid sinus syncope
system	F2	Vasovagal syndrome
	F3	Orthostatic hypotension
Cardio myopathies	G1	Cardiomyopathy unspecified
	G1A	Cardiomyopathy hypertropic
	G1B	Cardiomyopathy dilated
Valvular	G2	Myocarditis
	G3	Valvular heart disease
	G6	Endocarditis
Hearttransplantation	G7	Heart transplant
	G8	Ionizing radiotion

Although the variable '*Aetiology*' contains a large number of different categories, the aetiology is very often encoded as unspecified (A1), uncoded (A2), unknown (B1) or conduction tissue disease (B2). Figure 12 (top) shows that over the period 2000-2007, in almost 40% of cases the outcome 'unspecified', 'uncoded' or 'unknown' was registered. Together with the outcome 'conduction tissues disease' (B2), this represents about 80% of registered outcomes. Of the remaining 20%, the ischaemic group (C1+C2) represents the largest part (Figure 12, bottom), but in relation to all registered outcomes, this represents less than 10%.

Figure 12: Aetiology for first implantations by category, 2000-2007

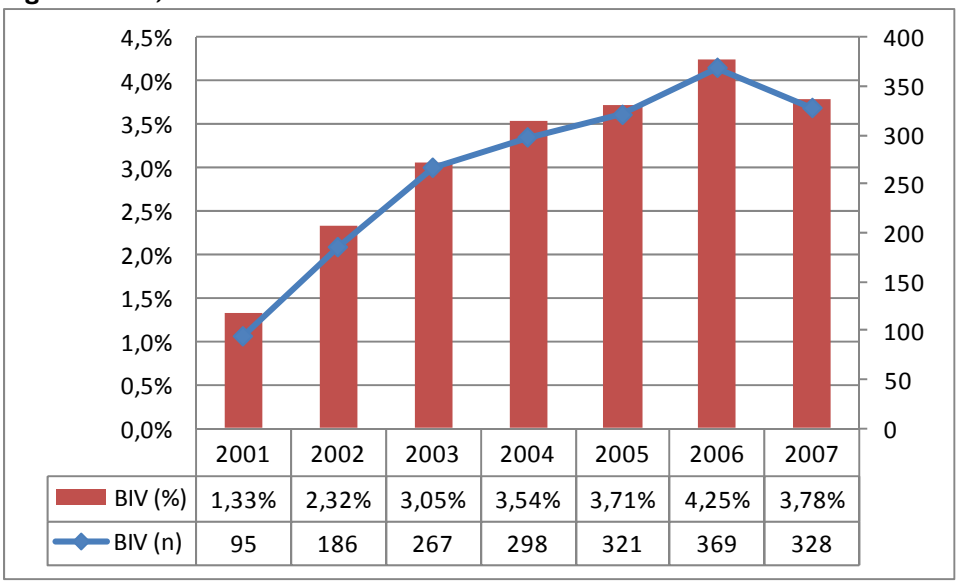


Next to the non-registered implantations and unspecified or uncoded registrations, there are no missing values for this variable for first implantations.

4.2.7 Cardiac resynchronization therapy

Cardiac resynchronization therapy (CRT) is a pacing modality that has been developed for the treatment of heart failure. With this therapy, the aim of pacing is not to prevent bradycardia but to synchronise the contraction of the ventricles of the heart to improve cardiac output. Therefore, this mode of pacing is also referred to as "biventricular pacing". The technology can be used in combination with a conventional pacemaker where it is called a "CRT-P", or in combination with an implantable defibrillator where it is called a "CRT-D". The topic of CRT pacing is beyond the scope of the present report. They are however included in the BeHRA database and since 2001, the variable '*biventricular pacemakers*' has been included in the database. It was encoded from 1.3% in 2001 to 3.8% in 2007 of all registrations (Figure 13).

Figure 13: Biventricular pacemakers, in total numbers and in % of all registrations; 2001-2007



	2001	2002	2003	2004	2005	2006	2007
BIV (%)	1,33%	2,32%	3,05%	3,54%	3,71%	4,25%	3,78%
BIV (n)	95	186	267	298	321	369	328

4.2.8 Replacements of PMs and leads

When the battery of a PM reaches its "end of life (E.O.L.)", the PM has to be replaced. In the database, PM replacement because of E.O.L. of the battery is encoded in the database as "Generator change – Elective – Elective" (code B1), occurring in about 85% of the PM replacement registrations. A PM replacement can also more rarely be indicated because of infection, recall by the manufacturer, upgrading to a more sophisticated device (dual chamber, CRT, ICD), a.s.o. The electrode that connects the device with the inner side of the heart can mostly be left in place and be plugged into the new PM device. In some cases, the physician decides to replace a lead, e.g. because of insulation break or infection. The BeHRA register contains three variables that are related to a replacement procedure: 'generator change', 'atrial lead change', and 'ventricular lead change'.

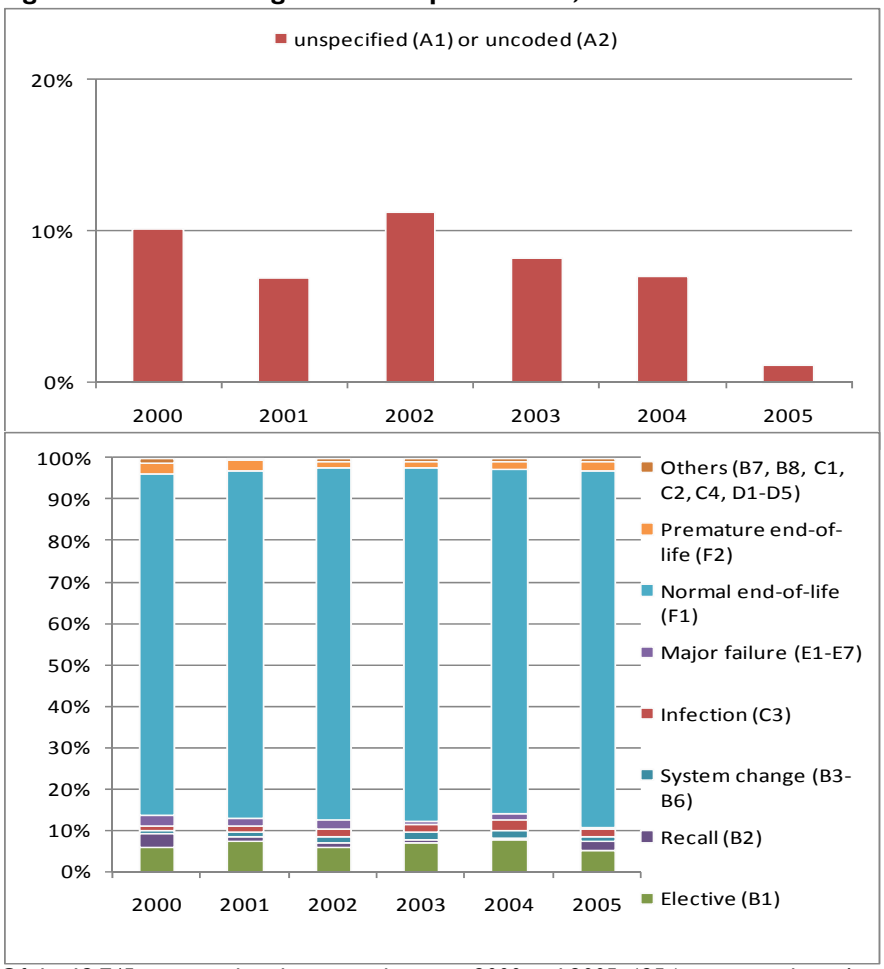
The variable '*generator change*' (= PM replacement) is classified as follows:

Generator change

category -	*code*	*specification*
Unspecified	A1	Unspecified
	A2	Uncoded
Elective	B1	Elective
	B2	Recall
	B3	System change heamodynamic
	B4	System change - pm syndrome
	B5	System change - palmitations
	B6	System change electrode problem
	B7	EMG inhibition
	B8	Extracardiac stimulation
Surgical	C1	Mechanical protrusion
	C2	Erosion
	C3	Infection
	C4	Wound pain
Failure minor	D1	Failure - unspecified
	D2	Failure - undersensing
	D3	Failure - oversensing
	D4	Failure - magnetic switch
	D5	Failure - programming
Failure major	E1	Failure - unspecified
	E2	Failure - no output
	E3	Failure - low output
	E4	Failure - low rate
	E5	Failure - high rate
	E6	Failure - connector
	E7	Failure - encapsulation
Failure battery	F1	Normal E.O.L.
	F2	Premature E.O.L.

Figure 14 shows the proportions of registered indications for PM replacement over the period 2000-2005. Before that period, relatively more replacements were encoded as 'unspecified' or 'uncoded' (A1+A2) (e.g. almost 60% in 1997). Over the period 2000-2005, excluding the 'unspecified' and 'uncoded' categories, on average 85% replacements are because of normal end-of-life, 6.43% are categorized as 'elective', 1.42% as 'recalls', 1.44% as 'system changes', 1.73% as 'infections', 0.24% as 'minor failures', 1.56% as 'major failures', and 1.89% as 'premature end-of-life' (Figure 14 - bottom).

Figure 14: Reason for generator replacements, 2000-2005



Of the 13.745 registered replacements between 2000 and 2005, 625 'generator change' outcomes were missing.

The following entries can be encoded for '*atrial lead change*' and '*ventricular lead change*':

Electrode change

category -	*code*	*specification*
Unspecified	A1	Unspecified (default)
	A2	Uncoded
Elective	B1	Elective
	B2	Displacement
	B3	Exit block
	B4	EMG inhibition
	B5	Extracardiac stimulation
	B6	Perforation
	B7	Undersensing
	B8	Recall
Surgical	C1	Infection / Ulceration
Failure	D1	Connector failure
	D2	Insulation failure
	D3	Conductor break

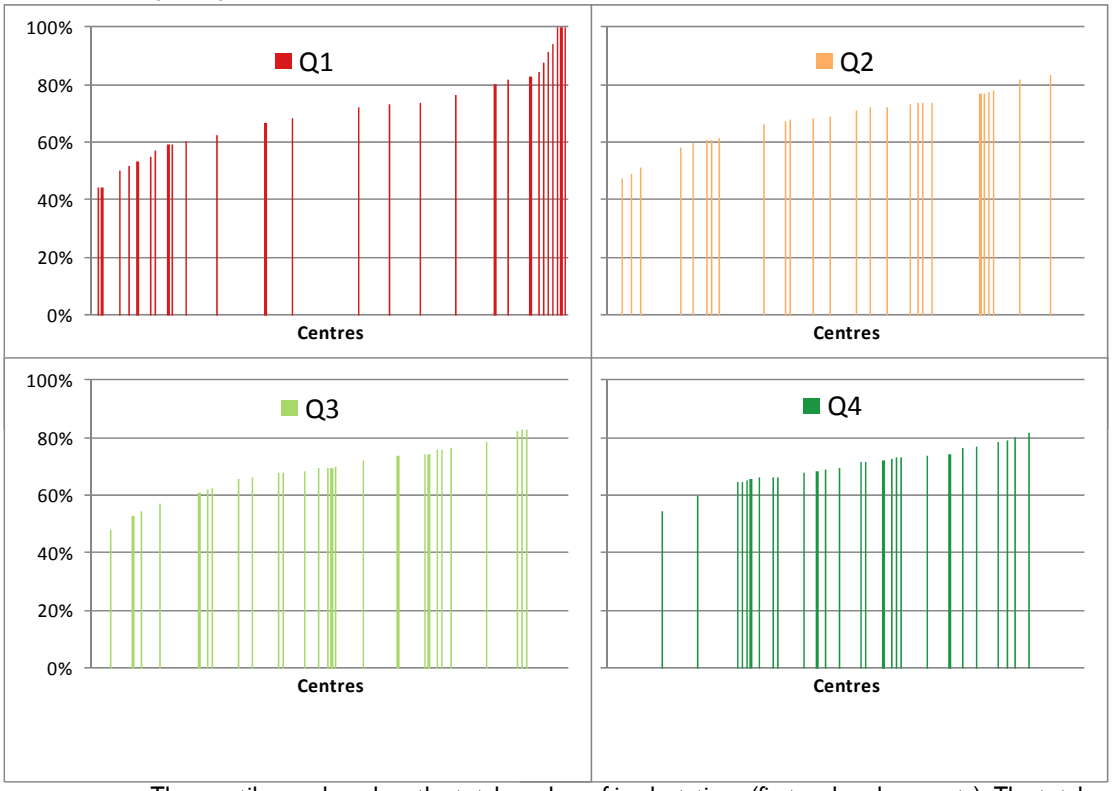
There are on average 268 and 218 yearly registered ventricular and atrial lead replacements between 1993 and 2005, the largest part of outcomes being encoded as 'unspecified' or 'uncoded' (A1+A2). No further details are provided on this variable because of the very small number of registrations.

4.2.9 Hospital variation of PM practice

In the following, we illustrate the hospital variation in some of the parameters from the BeHRA database without naming those centres to respect the guaranteed confidentiality of BeHRA towards its members.

Figure 15 shows the percentage of first replacements in relation to the total number of registered implants per centre. This number varies widely, being 0% for one centre and 100% for three other centres. These extreme values are observed for centres with a small number of total implants (see 1st quartile (Q1) in Figure 15). However, even for centres with a relatively large number of registered implants, the variation is wide, e.g. 47% - 83% in the 3rd quartile (Q3) and 55% - 82% in the 4th (Q4).

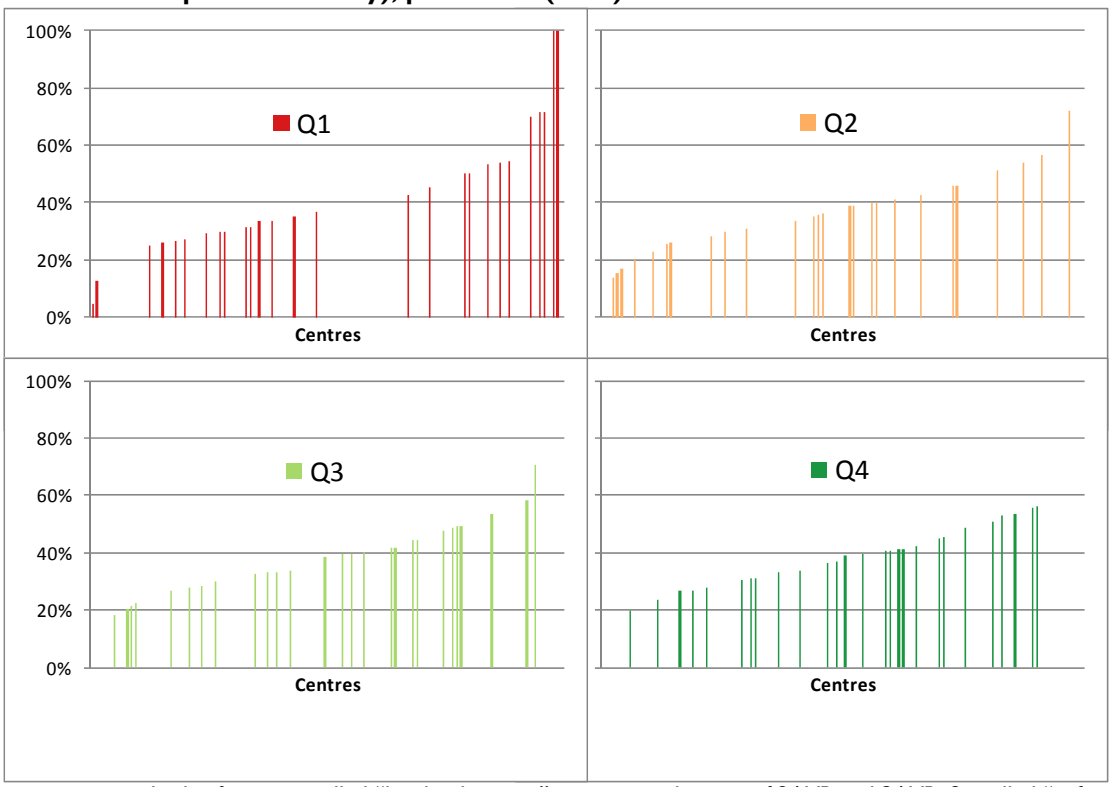
Figure 15: Percentage of first replacements vs total implants, per centre (2007)



The quartiles are based on the total number of implantations (first and replacements). The total number of implants was <=35 in Q1 (minimum: 1), >35 and <= 61 in Q2, >61 and <=100 in Q3, and >100 in Q4 (maximum: 394).

In its yearly review, BeHRA proposes a ratio of so-called 'hard' versus 'soft' indications for PM implantation in a given PM centre, as a quality indicator for its practice: [(2AVB + 3AVB) / (SSS + AF)]. This is the ratio of the number of patients treated in a given centre because of second or third degree AVB and patients treated with a PM because of SSS or slow AF. Figure 16 depicts this ratio per centre for the year 2007. Similar to the previous figure, most extreme values are seen in centres with few registrations (between 5% and 100% in Q1). A wide variation however also exists for centres with a relatively large number of registrations (18% - 71% in Q3 and 20% - 56% in Q4).

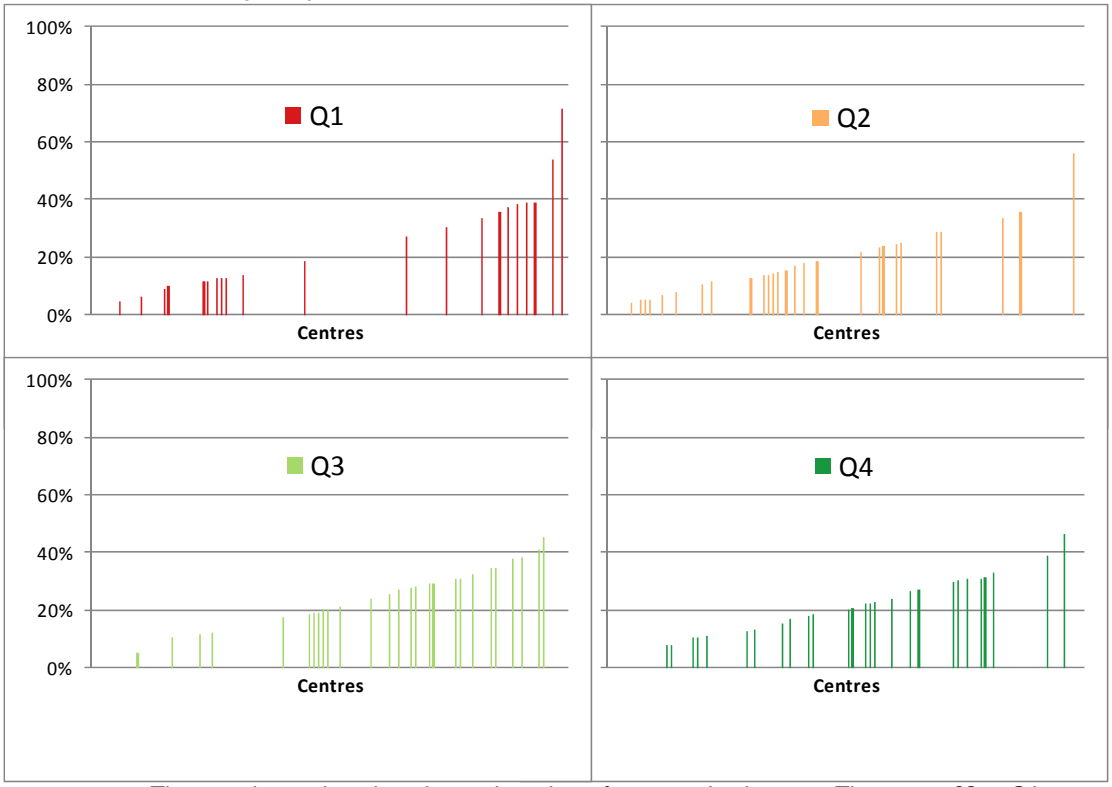
Figure 16: Percentage of 'hard' vs 'hard + soft' indications (first implantations only), per centre (2007)



In this figure, so-called "hard indications" represents the sum of 2AVB and 3AVB. So-called "soft indications" represents the sum of SSS and AF (see also chapter 4.3 where this matter is further discussed). The quartiles are based on the total number of "hard" and "soft" indications. This was <=22 in Q1 (minimum: 1), >22 and <= 39 in Q2, >39 and <=62 in Q3, and >62 in Q4 (maximum: 252).

The percentage of PM patients with 3AVB in a given PM centre could alternatively be considered as a quality indicator. We calculated the percentage of patients in the BeHRA database with 3AVB versus all indications for each Belgian centre. The distribution is shown in Figure 17. Again, wide variations are not only seen in centres with a small number of registrations, but also in the larger centres.

Figure 17: Percentage of 3AVB v all registered ECG indications (first implantations only, inclusive the category 'unspecified or uncoded'), per centre (2007)



The quartiles are based on the total number of registered indications. This was <=23 in Q1 (minimum: 1), >23 and <= 43 in Q2, >43 and <=67 in Q3, and >67 in Q4 (maximum: 287).

4.3 DISCUSSION

The Belgian Health Care Knowledge Centre (KCE) appreciates the willingness of BeHRA to share its database. Our descriptive analysis is based on the raw data that we received, and not on the yearly reports diffused by BeHRA to its members. It was agreed with BeHRA not to disclose the names of centres in this study.

In this voluntary registry, data on almost 117,600 pacemaker implantations over the period 1993-2007 were encoded, including ~87,400 first implantations and ~30,200 replacements. The comparison to insurers' data in section 5.3 shows that in 2007 BeHRA accounts for roughly 80% of all registered implants in Belgium. The relative share of replacements has slightly increased over the years up to 30.6% in 2007. About 53% of all patients are male and the average age is 75.3 years (median: 77 years).

The European PM Patient ID Card that is used as the data source for the BeHRA register offers codes for symptoms, ECG indications, aetiology, pacing mode, generator and lead changes and file closure. These items are recorded at the time of implantation. Unfortunately, encoding of these items as "unspecified" or "uncoded" is specifically allowed for, which is uninformative. Furthermore, the item "symptoms" includes "bradycardia" and "tachycardia" which, strictly speaking, are no symptoms but rather clinical findings. Data on longitudinal data of patients after the implantation is limited to instances where device replacements are involved. Information on complications such as lead dislocation or traumatic injury (bleeding, pneumothorax) is lacking.

Of the registered symptoms, over the period 2000-2007 and after excluding the category 'uncoded' or 'unspecified', the most frequent symptoms for first implantations are syncope (43%), followed by dizzy spells (28%) and bradycardia (14%). For ECG indications, these are SSS (43%), 3AVB (24%), AF (15%), and 2AVB (11%). The aetiology was encoded as 'unspecified', 'uncoded' or 'unknown' in about 40% of all cases or as 'conduction tissues disease' (up to 40%). Most PM replacements are encoded as being due to 'normal end-of-life' (~85%). Data on lead changes is often "unspecified" or "uncoded".

One of the stated goals of the BeHRA registry is to improve the quality of PM practice in Belgium. This goal encompasses several aspects of PM therapy, such as the *appropriateness of PM therapy* in a given patient and the quality of the delivered care including the surgical procedure, the X-ray burden to the patient or the occurrence of complications. As discussed earlier, in the BeHRA registry, the ratio [(2AVB+3AVB)/(slow AF+SSS)] is considered as an appropriateness indicator for a given PM centre. A methodological difficulty with this parameter is however that both the numerator and the denominator of the equation include a variety of indications upon which experts may disagree as being either "hard" or "soft". 3AVB (numerator) and SSS with ventricular pauses provoking recurrent syncope (denominator) would be accepted by most experts to represent hard indications. On the other hand, asymptomatic Wenckebach 2AVB (numerator) or AF with ventricular pauses of 2.5 sec (denominator) are "softer" indications for PM treatment. To our knowledge, objective quality indicators for the assessment of the appropriateness of PM therapy are lacking. This is at least partly related to the fact that PM therapy is mainly based on expert opinion.

In its current structure, the BeHRA register may in principle contribute to a quality assessment and improvement by confronting individual cardiologists with the PM practice of peers ('self-examination'). However, the voluntary nature of the registry and the lack of follow-up data as well as an audit impinge upon this goal.

Assessing *the "technical" quality of the delivered care* by means of a register is a more realistic goal. The occurrence of both early and late complications has been documented in international registers. These data can be used as a benchmark for individual practitioners. Currently, BeHRA does not register these events, but they could be included in the on-line web based application that is being implemented by the NIHDI and is expected to be operational by January 2011. Registration will become mandatory and will be linked to the reimbursement of the device. The advantage is that all PM implants that are performed in Belgium will be registered. As an improvement before starting the register, its goals should be clearly proclaimed, together with the explicit definition of the requested data that are needed to support those goals. Moreover, one could add data to those that are already available from the European PM ID Card. The register should also include follow-up data to allow for an assessment of recalls, the service life of PMs, the dislocation of leads and infections. We recommend to regularly assess the quality of the registry, to audit its content and to discuss and implement corrective measures that may potentially improve PM practice. We are convinced that these measures are needed to increase the benefits of the registry as well as to justify the costs related to its set up. The registry of the Danish Pacing Group may serve a model. As early as 1997, the Danish Pacing Group collected data on top of those available from the European PM Patient ID Card. They include the mode of pacing, venous access route to the heart, skin-to-skin time, fluoroscopy time, the implanters experience, peri-operative complications and late complications at 3 months. Those parameters allow for some quality checks of pacing practice.[35]

Key points:

- **The BeHRA (Belgian Heart Rhythm Association) pacemaker database is a voluntary registry that contains information on Belgian pacemaker implantations. The European PM Patient ID Card is used as its data source.**
- **The usefulness of the registry for the qualitative and quantitative assessment of the Belgian PM practice is limited by a number of factors such as its voluntary nature, the absence of a formal audit and validated quality indicators, and the inherent shortcomings of the European PM Patient ID Card.**
- **The NIHDI plans to introduce an on-line web-based application in 2011 for the prescription and the registration of PM implantation. Registration will become mandatory and will be linked to the reimbursement of the device. The goals and the contents of this new registry should be clearly proclaimed in advance, as well as the measures that will be taken to assess the quality of the registry.**
- **On the one hand, the registry's contribution with regard to the appropriateness of PM implantation in the Belgian practice will remain limited, as long as evidence for a variety of PM indications has not been demonstrated by good studies. On the other hand, if properly conducted, the registry may help to assess and to improve the quality of surgical procedures, and in the long term the quality of care.**

5 BELGIAN PACING PRACTICE – INSURERS' DATA

5.1 DATA SOURCES AND SELECTION

5.1.1 IMA-AIM data

The purpose of the Common Sickness Funds Agency (IMA-AIM) is to organize and manage a common interface to the health care use and patient characteristics data that are collected by all seven Belgian Sickness Funds. The IMA-AIM database contains four types of data: data about all reimbursed health care use per attestation per patient; demographic data (e.g. date of birth, gender, municipality, decease date); data on the insurance status; data on professional status. A detailed description of these data sources and the technicalities of the construction can be found in the authorization[c] of the SCSZG[d] (Sectoral Committee of Social Security and Health care, a subdivision of the Belgian Privacy Commission) [e].

Data for all patients with procedures related to pacemaker interventions throughout the years 2002 to 2007, i.e. covering six years, were retrieved.

5.1.2 Minimal Clinical Data – Minimal Financial Data

The registration of the Minimal Clinical Data (MCD) is mandatory for every hospital in Belgium since 1991.[f] This means that for each hospitalized patient, information such as birth date, sex, postal code of domicile and other information such as length of hospital stay, hospital ward and bed type occupation, has to be recorded, along with ICD-9-CMCM encoding of relevant diagnoses as well as diagnostic and therapeutic procedures performed. Diagnostic and procedure codes are collected per hospital department.

Since 1997, the MCD records are linked to the Minimal Financial Data (MFD). MCD-MFD linkage is performed by a legally instituted 'Technical Cell for the processing of hospital data' (TCT). This procedure is approved by the Belgian Privacy Commission. The linkage process takes about 2 years to completion and full validation. Linkage percentages exceed nowadays 95% overall. This means that the relationship between treated pathology and the costs to the health care system can be studied.

Data for all patients with procedures related to pacemaker interventions throughout the years 2002 to 2006, i.e. covering five years, were retrieved. Year 2007 data could not be provided due to longer delays until availability.

5.1.3 Primary Selection of data

IMA expenditure and patient characteristics data for patients for which one of the NIHDI codes shown in Table 32 in the appendix were reimbursed between January 1, 2002 and December 31, 2007, were requested. MCD-MFD hospital stay data from 2002 to 2006 were coupled to the IMA expenditure database.

5.1.4 Defining and recoding interventions

Related to pacemakers, we distinguish between three types of implantations: primo implantations, regular replacements and early replacements. In principle each of these implantation types is identified by a separate device code as specified by the nomenclature. However, due to changes in the nomenclature classification over time and due to the quality of encoding, it was necessary to recode the implantation type for some interventions in order to identify properly the kind of implantation. For instance, regular replacements of pacemakers are identified by a separate nomenclature code only since July 2005. Before that date all regular replacements were encoded as a primo implantation.

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c Authorization 09/064 of September , 15 2009 (http://www.privacycommission.be).

d Sectoraal Comité voor de Sociale Zekerheid en de Gezondheidszorg.

e A description of the layout of the database and available variables can be found in.[36]

f The text of this subchapter was partly adapted from chapter 4.1.1, KCE Report 113.[37]

Moreover, even after July 2005, there are cases of multiple primo implantations within one and the same patient. By definition, however, every individual can have only one primo implantation, such that subsequent implants must be recoded. A detailed account of the definitions and recodification procedures is described in the appendix to this section.

5.1.5 Other data sources

5.1.5.1 Belgian Demographic Data

Demographic data covering the time period 2002 to 2007 was acquired from Statistics Belgium on the level of municipalities, 5-year age categories and gender (*Statistics Belgium – Population*). These will be used to test, whether regional differences the age-sex distribution of the population drive differences in implantation rates across Belgian regions.

5.1.5.2 Belgian Mortality Tables

Mortality tables on the Belgian population from 2007 were retrieved from the document "sterftetafels_tcm325-63732" from Statistics Belgium.[38] These are used to compare survival rates of pacemaker patients to the Belgian population.

5.1.5.3 Eucomed

Eucomed (www.Eucomed.org) – an international association of manufacturers and suppliers of medical technology – provides data on the total number of pacemaker devices sold in Belgium during 2004 to 2008.[39]

5.1.5.4 INAMI-RIZIV

INAMI-RIZIV provides the number of pacemakers reimbursed by reimbursement date. Data on the number and costs of pacemaker devices from 2002 to 2007 have been retrieved for the device codes as laid out in Table 33 in the appendix to section 5.1.4.

5.1.5.5 Structural contributors to geographic variation in implantation rates

Fiscal revenues per capita

Data on fiscal revenues per capita was retrieved from Statistics Belgium.[40] It is meant to serve as a proxy for income differences between Belgian regions. Data is available on the level of the Belgian municipalities (588 municipalities in 2007).The variable of interest retrieved from the documents is "fisc1993_2007_fr_tcm326-33413", i.e. the fiscal revenues per capita from 2002 to 2007. These will be used to test, whether regional differences in the fiscal revenues per capita of the population drive differences in implantation rates across regions.

Foreign share of the population

Data on the foreign share of the population in 2008 was retrieved from the Portaal Vreemde Afkomst.[41] The variables of interest retrieved from the document "Table-2008-VA-aantal" is "% Vreemdelingen", i.e. the percentage of foreigners within each municipality, as well as "% Vreemde afkomst", i.e. the percentage of the population with foreign origin from "Tabel-4-Vreemde-afkomst". The detailed definition of the population of foreign origin is given on the webpage of the Portaal Vreemde Afkomst. Similarly to fiscal revenues per capita, these will be used to test, whether regional differences in the foreign share of the population also drive differences in implantation rates across regions.

OECD Health Data 2009

Data on the share of the population aged 65 and more, health expenditures as a percentage of GDP and GDP per capita in $purchasing-power-parities for the time period 2003-2006 have been retrieved for several West European countries from OECD Health Data.[42] The data will be used in an international comparison of total implantation rates in a multivariate regression framework.

EUROSTAT

Data on total and foreign population for the time period 2003-2006 have been retrieved for several West European countries from Eurostat.[43, 44] The data will be used in an international comparison of total implantation rates in a multivariate regression framework.

5.2 DESCRIPTIVE RESULTS

5.2.1 The number of pacemakers implanted, sold and reimbursed

Eucomed (www.eucomed.org) – an international association of manufacturers and suppliers of medical technology – provides data on the total number of pacemaker devices sold in Belgium during 2004 to 2009. This number should correspond to the number of pacemakers implanted in a given year, provided that there is no reselling of acquired pacemakers to other countries, pacemakers are not stocked to be used in the following year and there are no recalls of pacemakers by the industry. Following the information given by UNAMEC, Belgian providers of healthcare are not reselling pacemakers to other countries and there is only very incomplete data available as recalls are concerned as discussed in a previous chapter. Stocking should occur rather in hospitals performing many pacemaker implantations. However, because in Belgium there are very few hospitals providing more than 100 pacemaker implantation per year, stocking will not be a big issue.

Eucomed provides only cumulated data for Belgium and Luxemburg. However, based on the assumption that implantation rates in Belgium and Luxemburg are identical, Table 9 gives an estimate of the number of implants sold in Belgium only. In Table 10 we compare the number of pacemakers reimbursed from different data sources with the number of pacemakers sold.[g] The number of pacemakers sold is always highest. A deviation of the number of devices reimbursed according to IMA-AIM and RIZIV-INAMI is reported by IAM-AIM experts to be due to differences in the exact time window considered per calendar year. All following calculations are based on the number obtained from IMA-AIM, as this is our primary data source.

Table 9: Estimated number of pacemakers sold in Belgium; 2004-2007

Category	2004	2005	2006	2007
Belgium + Luxemburg				
Implantation rates (PM and CRT-Ps)	1,107	1,051	1,111	1,162
Population Belgium (in millions)	10.40	10.45	10.51	10.58
Population Luxemburg (in millions)	0.45	0.46	0.47	0.48
Implants sold (estimated)	12,012	11,463	12,199	12,853
Belgium				
Implants sold (estimated)	11,509	10,979	11,678	12,299

Notes: Own calculations based on IMA-AIM, *Statistics Belgium – Population* Statistics, [44] and [39]; see section 5.1 for data sources.

g The reported number of pacemakers implanted includes upgrades to CRT-P as well as data for which individual patient characteristics such as age or sex are missing. It is smaller than the original number of implants registered, because some implants have been recoded according to the procedure as described in the appendix to section 5.1.4. For 2007, this accounts for 1.7% of all implants.

Table 10: Comparison of the number of pacemakers reimbursed and sold in Belgium according to different sources; 2004-2007

Category	2004	2005	2006	2007
Implants				
Devices reimbursed (IMA-AIM)	10,341	10,263	10,916	10,914
Devices sold* (Eucomed)	11,509	10,979	11,678	12,299
Devices reimbursed (RIZIV-INAMI)	11,501	10,512	10,864	11,480
Comparison				
Difference Eucomed/IMA-AIM in %	11.3%	7.0%	7.0%	12.7%
Difference RIZIV-INAMI/IMA-AIM in %	11.2%	2.4%	-0.5%	5.2%
Implied implantation rates per million population based on				
Devices reimbursed (IMA-AIM)*	995	982	1,038	1,031
Devices sold	1,107	1,051	1,111	1,162
Devices reimbursed (RIZIV-INAMI)	1,106	1,006	1,034	1,085

Notes: *estimated, see Table 9; Own calculations based on IMA-AIM, *Statistics Belgium – Population Statistics*, [39] and RIZIV-INAMI; see section 5.1 for data sources.

5.2.2 Reimbursements by insurers related to pacemaker and lead devices

Based on data from RIZIV-INAMI (2010), Table 11 shows the total reimbursement related to pacemaker and lead devices as listed in the appendix in Table 33 and

Nomenclature code	Description
685731	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685753	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685775	Implanteerbare myocardiale elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685790	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685742	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685764	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685786	Implanteerbare myocardiale elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685801	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode

These exclude costs related to the surgical procedure, the hospital stay, peri-operative diagnostic tests, costs related to regular follow-up and complications. The reimbursements related to pacemaker and lead devices totalled 357.4 million € from 2002 to 2007, with 307.1 million € reimbursed for pacemakers and 50.3 million € for leads (Table 11). From 2002 to 2007, annual total reimbursement costs increased by 6.4 and 17.6% for pacemakers and leads, respectively. The mean annual reimbursement for pacemakers and leads was at the level of 59.6 million €.

In 2007, the average reimbursement was 4,419 € for a pacemaker device and 571 € for a lead device (Table 12). From 2002, the average reimbursement has decreased by 11.1% for pacemakers and 3.9% for leads.

Table 11: Total reimbursements related to pacemaker and lead devices; in million €, 2002-2007

Device	2002	2003	2004	2005	2006	2007	Mean of 2002-2007	Sum of 2002-2007
Pacemakers								
Sum	47.7	53.9	56.1	50.5	48.2	50.7	51.2	307.1
Indexed	100.0	113.1	117.7	105.9	101.1	106.4		
Leads								
Sum	7.4	8.4	8.8	8.6	8.4	8.7	8.4	50.3
Indexed	100.0	113.7	118.9	115.4	113.8	117.6		
Total								
Sum	55.1	62.4	64.9	59.0	56.6	59.4	59.6	357.4
Indexed	100.0	113.2	117.9	107.2	102.8	107.9		

Notes: Own calculations based on RIZIV-INAMI; see section 5.1 for data sources.

Table 12: Mean reimbursement for pacemaker and lead device; in €, 2002-2007

Device	2002	2003	2004	2005	2006	2007	Mean of 2002-2007
Pacemakers							
Sum	4,971	4,852	4,879	4,802	4,434	4,419	4,720
Indexed	100.0	97.6	98.1	96.6	89.2	88.9	
Leads							
Sum	595	577	576	573	572	571	577
Indexed	100.0	97.1	96.8	96.4	96.3	96.1	
Total per pacemaker							
Sum	5,744	5,610	5,645	5,616	5,211	5,178	5,494
Indexed	100.0	97.7	98.3	97.8	90.7	90.2	

Notes: Own calculations based on RIZIV-INAMI; see section 5.1 for data sources.

5.2.3 Pacemaker interventions – amount and evolution from 2002 to 2007

There were 10,914 implants in 2007. This number is relatively constant since 2003 (Table 13). The corresponding total implantation rate in 2007 is at the level of 1,031 implants per million inhabitants in 2007. Sliced up by implantation types, in 2007 there were 7,487 primo implantations, 3,179 regular replacements and 248 early replacements. In 2007 the primo implantation rate reached 707 implants per million population.[h]

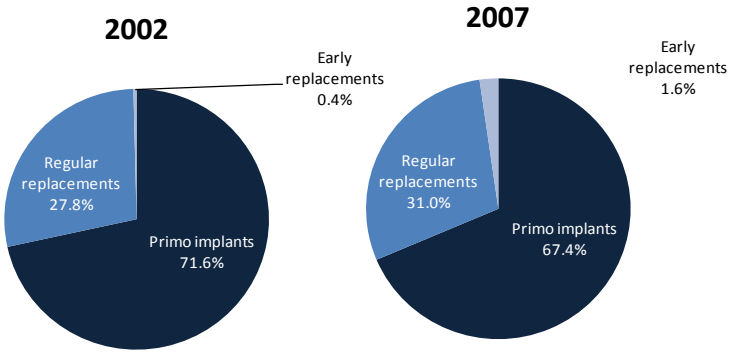
Table 13: General statistics; 2002-2007

Category	2002	2003	2004	2005	2006	2007
Implants						
First implants	6,841	7,614	7,729	7,499	7,635	7,487
Regular replacement	2,677	2,771	2,555	2,665	3,060	3,179
Early replacement	38	69	57	99	221	248
Total	9,556	10,454	10,341	10,263	10,916	10,914
Population (in Mio.)	10.3	10.4	10.4	10.4	10.5	10.6
Implantation rates (per 10,000 inhabitants)						
First implants	6.6	7.4	7.4	7.2	7.3	7.1
Regular replacement	2.6	2.7	2.5	2.6	2.9	3.0
Early replacement	0.0	0.1	0.1	0.1	0.2	0.2
Total	9.3	10.1	9.9	9.8	10.4	10.3

Notes: Own calculations based on IMA-AIM and *Statistics Belgium – Population*; see section 5.1 for data sources.

Tendentiously, the share of primo implantations is decreasing, while the share of replacements is increasing (Figure 18). Primo implantations made up 71.6 and 67.4% of all implants in 2002 and 2007, respectively. The decrease in the percentage of primo implantations is matched by the percentage increase in replacements from 27.8 to 31.0% in 2002 and 2007, respectively. This reflects, most probably, that each year there is a growing population of people with pacemaker implants, which automatically increases the amount of replaceable devices. There is also a growing amount of early replacements, part of which may probably be explainable by upgrading to CRT-devices.

Figure 18: Distribution of implants by interventions type; in % of total, 2002 and 2007



Notes: Own calculations based on IMA-AIM; see section 5.1 for data sources.

h In our data, we do not see a significant "pacemaker tourism" to Belgium. In 2007 there were only 10 implantations in foreigners living outside of, but having been treated in Belgium. However, there is still the possibility that there are more foreigners receiving pacemaker implants in Belgium, but not being registered in our data base.

5.2.4 Gender and age

The mean age of patients with primo implantations has increased over the period 2002 to 2007 and, in 2007, has reached 75.2 years for men and 78.1 years for women (Table 14). Figure 19 shows that the share of patients with primo implantations increases very slowly until the age of 65, in order to jump to nearly 25% for those aged between 80-84 and decreases thereafter.

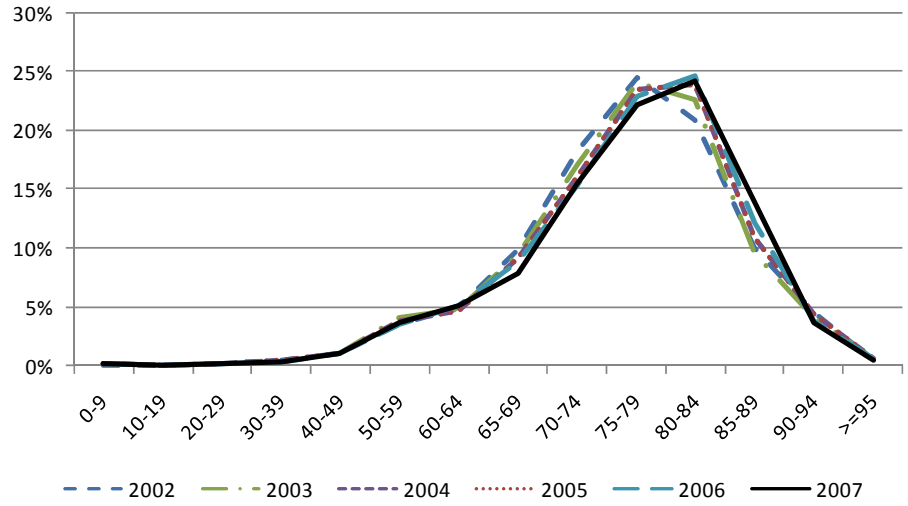
In 2007, 85% of all primo implantations in men (92% for women) occurred in patients older than 65 years, 36% in men aged 80 years and more (50% for women) (Table 15). There is a gradual shift of the distribution towards older ages, which may be explainable by a better accessability of older patients to healthcare services as well as a growing preference and acceptance for treatment by patients in these age groups (Figure 20).

Table 14: Mean age and share of patients with primo implantations; by sex, 2002-2007

Category	2002	2003	2004	2005	2006	2007
Mean age						
Men	74.38	74.37	74.92	75.02	75.27	75.17
Women	77.47	77.42	77.72	77.75	77.75	78.13
Share of patients						
Men	52.2%	52.6%	53.9%	53.5%	53.8%	53.1%
Women	47.8%	47.4%	46.1%	46.5%	46.2%	46.9%

Notes: Own calculations based on IMA-AIM; see section 5.1 for data sources.

Figure 19: Percentage distribution of primo implantations; by age category, 2002 - 2007



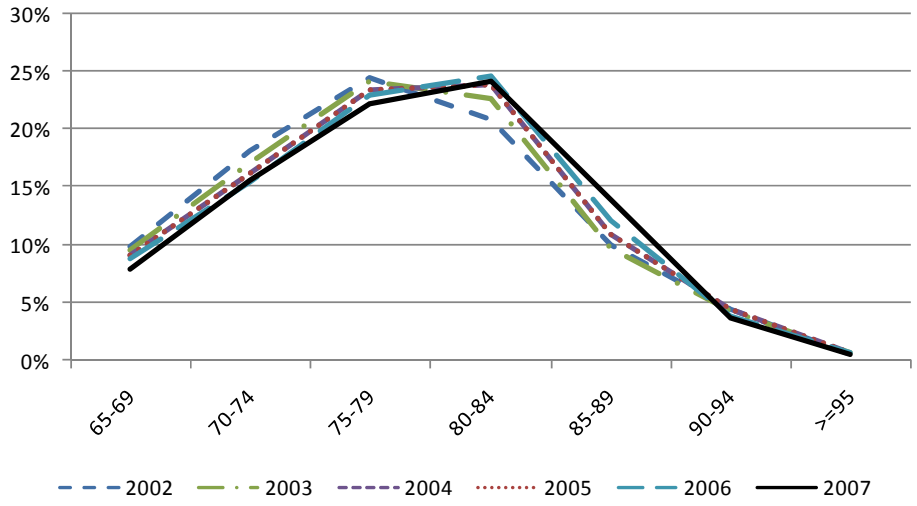
Notes: Own calculations based on IMA-AIM; see section 5.1 for data sources.

Table 15: Share of patients with implants aged 65+ and 80+; in %, by gender, 2002-2007

Category	Men		Women	
	2002	2007	2002	2007
Primo implantations				
65+	86.2%	85.0%	91.1%	91.5%
80+	29.3%	36.0%	43.2%	49.6%
Replacements				
65+	86.4%	86.5%	91.4%	91.9%
80+	37.2%	44.1%	50.6%	57.1%
Total				
65+	86.3%	85.4%	91.2%	91.5%
80+	31.5%	38.4%	45.3%	52.0%

Notes: Own calculations based on IMA-AIM; see section 5.1 for data sources.

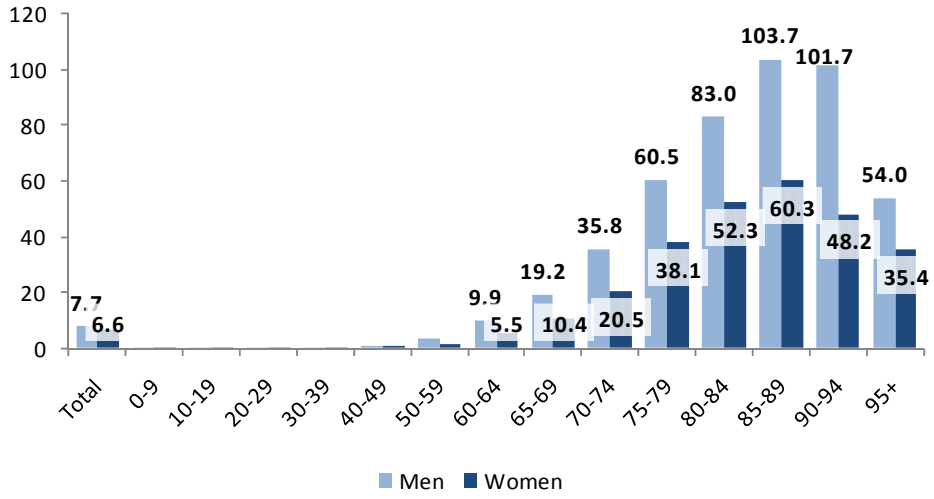
Figure 20: Percentage distribution of primo implantations for those aged 65 and more, 2002 - 2007



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

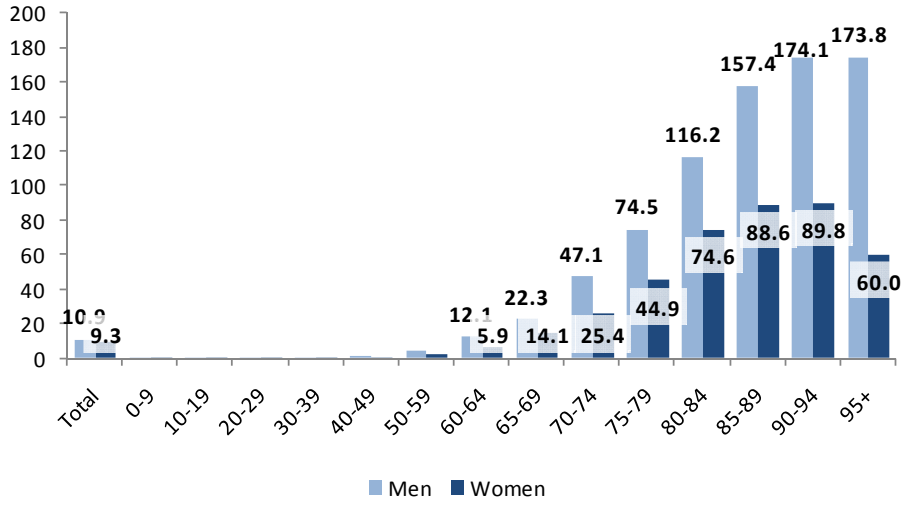
53% of all primo implantations are implanted in men and 47% in women. This distribution stayed relatively constant over 2002 to 2007(Table 14). Because in Belgium there are more women than men at higher age categories, this implies that within the same age group the probability to receive a pacemaker is considerably higher for men than for women. The implantation rate per 10,000 population in patients aged 60-64 years is 9.9 for men and 5.5 for women (Figure 21). At ages above 60, very roughly this implies a ratio between the male and female age specific implantation rate of around 2:1. This is also the case, if total implantation rates per age group are considered (Figure 22).

Figure 21: Primo implantation rates per 10,000 inhabitants; by sex and age category in 2007



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

Figure 22: Total implantation rates per 10,000 inhabitants; by sex and age category in 2007



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

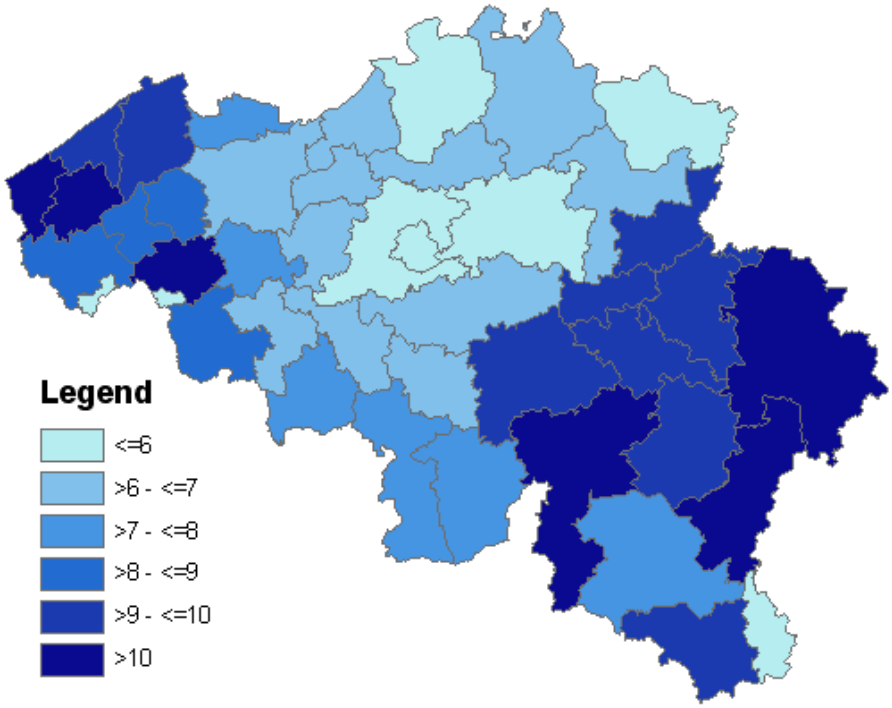
5.2.5 Regional variation in implantation rates

Comparing regional implantation rates can be informative on many accounts. In this chapter, it is supposed to reveal which areas have a relatively low and which areas have a relatively high supply of pacemaker implantations. This information can further serve as a basis of an analysis trying to reveal the causal factors behind these differences.

The calculation of regional implantation rates is based on the patients' place of residence at the time of implantation. The observed differences in primo implantation rates between *arrondissements* are remarkable (Figure 23). They range from 4.2 to 12.3 implants per 10,000 inhabitants in Mouscron and Veurne, respectively.[i] To a certain degree, differences in observed implantation rates are random. This may be accounted for by estimating confidence intervals. These define with a 95% certainty the expected upper and lower limits of implantation rates given the national mean implantation rate and the regional number of inhabitants. Regional implantation rates that surpass the upper (lower) limit can be considered to be significantly above (below) the national average at the 5% statistical significance level (i.e. there is a 5% chance that the true implantation rate is still within limits even if we observe it to be outside the limits).

Figure 24 shows the average observed primo implantation rates throughout 2002 to 2007 on the level of municipalities.[j] We find several regions to be outside of the expected limits (Figure 24 and Figure 25), significantly surpassing or falling below the expected implantation rates.[k]

Figure 23: Observed primo implantation rates per *arrondissement*; per 10,000 inhabitants, per *arrondissement* in 2007



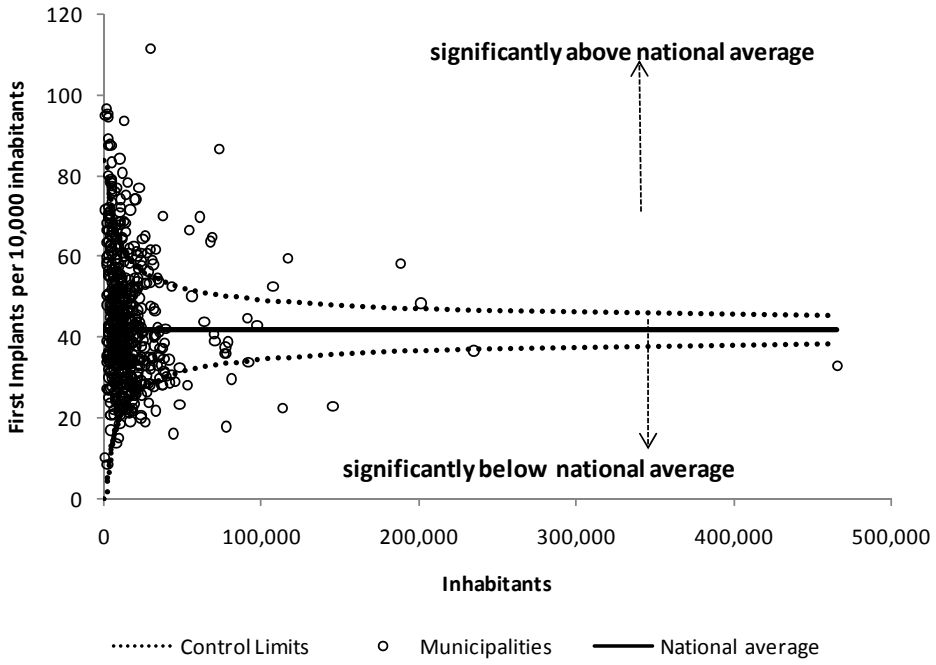
Notes: Own calculation based on IMA-AIM and *Statistics Belgium – Population*; see section 5.1

[i] A map with with the names of the *arrondissements* is in the appendix to this section in. The population of each arrondissement is in Table 43.

[j] We use the cumulative primo implantation rates 2002 to 2007, because on community level it has an impact in which year an implant is done.

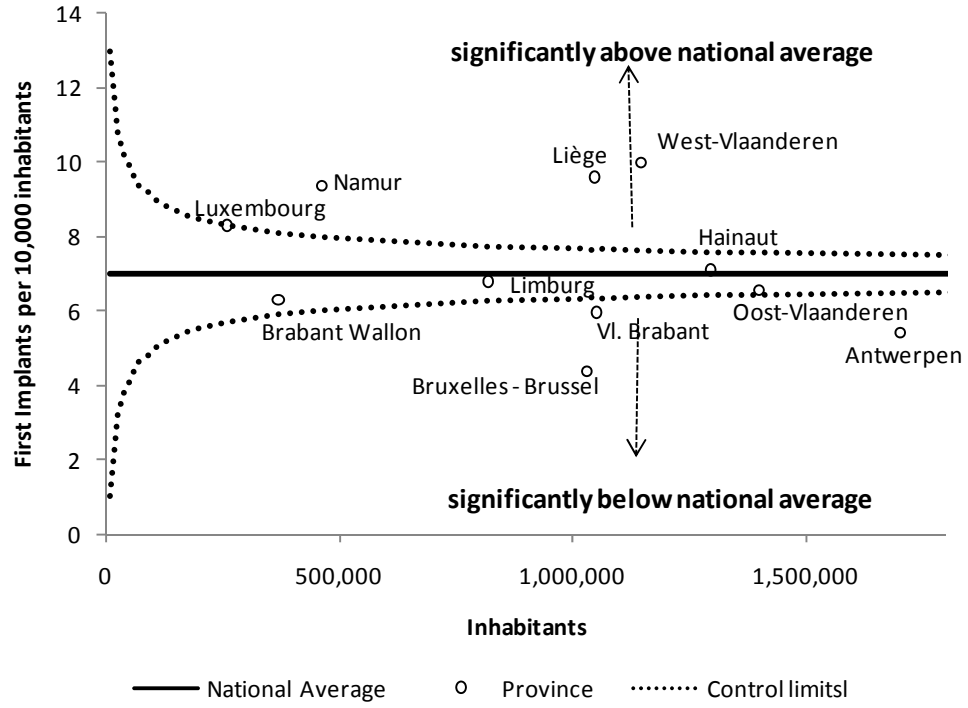
[k] The median primo implantation rate on the level of municipalities is 675, and thus very close to the mean of 699. We thus restrict the comparison of regional implantation rates to the mean implant rate of Belgium.

Figure 24: Cumulative observed primo implantation rates from 2002-2007; per municipality



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

Figure 25: Observed implantation rates compared to national average; per province in 2007



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

As shown above, the probability of a pacemaker implantation varies largely with age and sex. In general, the age and sex distribution varies from region to region. It is, therefore, essential to account for sex-age differences in the regional distribution of the population, in order to be able to make a first regional comparison of implantation rates. Above age and sex, health and health care use may vary by socioeconomic status of the population. For instance, individuals with a poor socioeconomic status as described by low income and low educational attainment have been found to spend more days in hospital and have more contacts with physicians.[45][l] In the following, we therefore adjust for the regional variation of some potential structural factors, which may explain the regional variation in pacemaker implantation rates. The factors are: sex, age, fiscal revenues per capita and the share of the foreign population on the level of municipalities. The general direction of the impact of these factors on implantation rates is:

a. Age: A higher share of the population aged 65 years and more goes along with higher implantation rates.
b. Sex: A higher share of the male in total population goes along with higher implantation rates.
c. Fiscal revenues per capita: Higher fiscal revenues per capita go along with lower implantation rates.
d. Foreigners: A higher share of foreigners goes along with lower implantation rates.[m]

For a more detailed description of the methodology related to these results, see the appendix to this chapter.

The adjustment of the crude primo implantation rates as in Figure 23 by age, sex, fiscal revenues per capita and the foreign share of the population has the effect of considerably narrowing the differences in implantation rates between the *arrondissements* (Figure 26). While still Figure 26 shows that even after adjustment regional differences in implantation rates exist, they are in fact in most cases negligible and minor on conventional statistical significance levels (footnote n). Figure 27 and Figure 28 show that most of the implant rates of municipalities and provinces are within the expected limits, i.e. after taking account of random variation in implant rates. On the level of provinces, only Brussels has still a significantly lower primo implant rate.

Consequently, after the adjustment the deviations of regional first implantation rates from the Belgian average in 2007 are considerably narrowed (Figure 29). Based on estimated coefficients from a multivariate regression framework – as laid out in the appendix to the chapter – we find that a 1% increase in regional fiscal revenue per capita goes along with a 0.85% decrease in the primo implantation rate.[o] Similarly, a 1% increase in the foreign share of the population in associated with a 0.12% decrease in the primo implantation rate.

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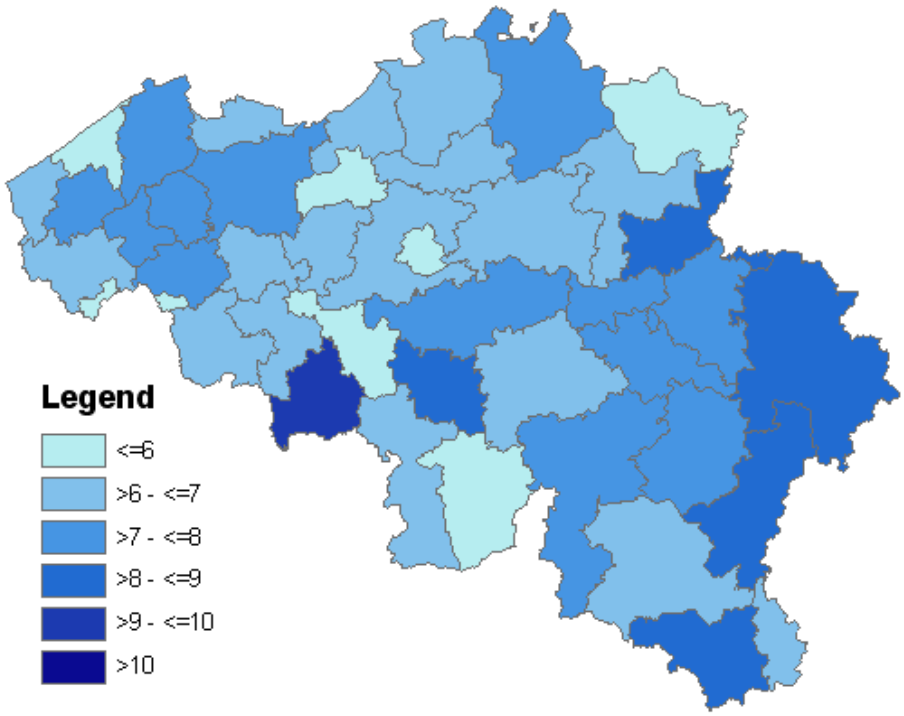
l Using data from the city of Winnipeg in Canada, Roos and Mustard (1997) have found that rates of medical discharges vary strongly with socioeconomic status, while pacemaker implantation rates were not related to the socioeconomic status of patients.

m There is no change in this result, if the percentage of the population with foreign origin is used instead of the percentage of foreigners only. The reason is the high correlation between these two measures on the level of communities (96.2%).

n Figure 63 and Figure 64 in the appendix show the corresponding crude and adjusted implantation rates with the statistical confidence intervals.

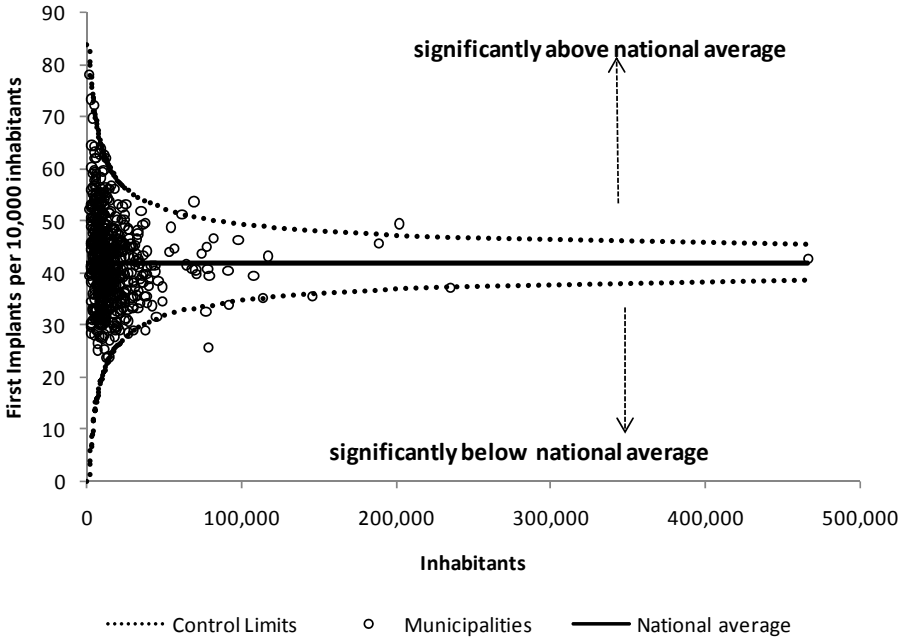
o It has to be kept in mind, that the estimated elasticities are valid only locally. They cannot be used to estimate the impact e.g. the impact of a 10% increase in the explanatory variables, without further investigations.

Figure 26: Adjusted primo implantation rates per *arrondissement*; adjusted by sex, age, fiscal revenues per capita and foreign share of the population, per 10,000 inhabitants, per *arrondissement* in 2007



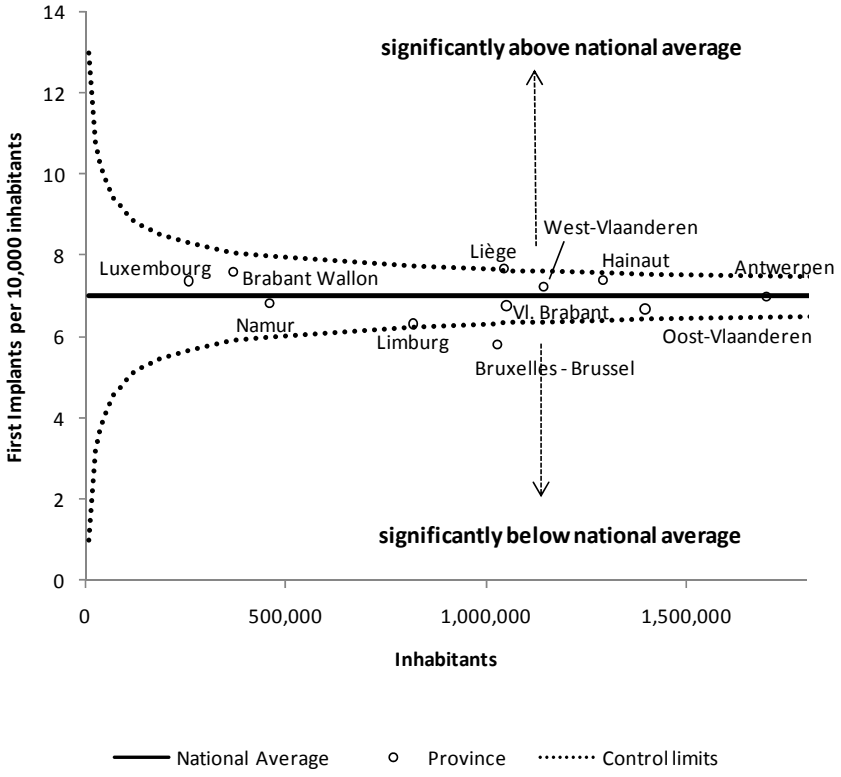
Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources..

Figure 27: Cumulative first implantation rates from 2002-2007 standardized by sex, age, fiscal revenues per capita and share of foreigners; per municipality



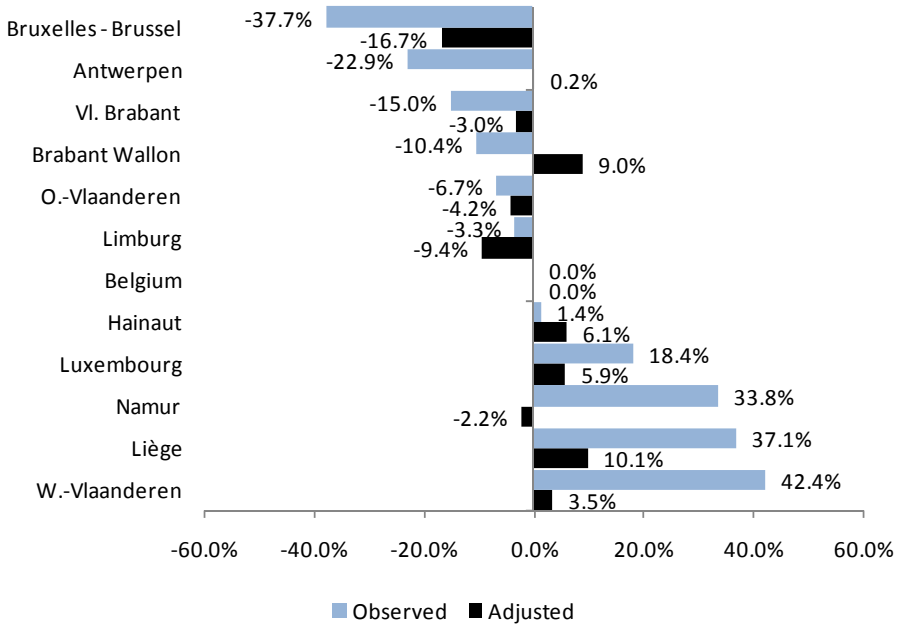
Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

Figure 28: First implantation rates standardized by sex, age, fiscal revenues per capita and share of foreigners; per province in 2007



Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

Figure 29: Observed and adjusted deviations of regional first implantation rates from the national average; adjusted by sex, age, fiscal revenues per capita and share of foreigners, per province in 2007



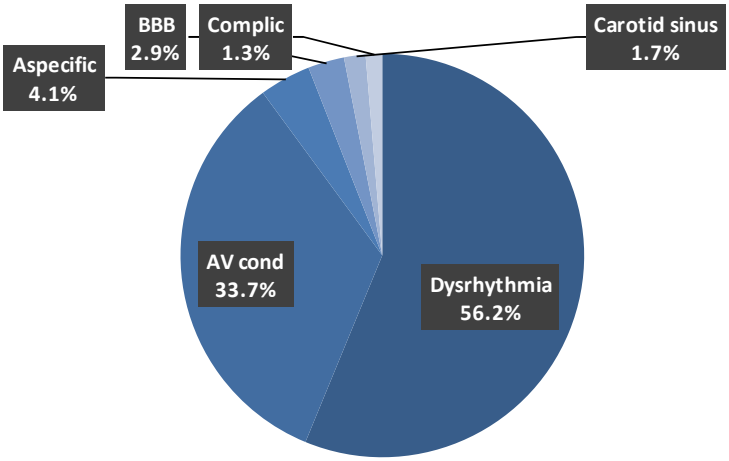
Notes: Own calculation based on IMA-AIM and Statistics Belgium – Population; see section 5.1 for data sources.

5.2.6 Indications for pacemaker interventions

Out of the 37,318 first pacemaker implants throughout 2002 to 2006, 91.7% could be linked to the main indication. The following calculations are done on the basis of the given indications only, excluding the 8.3% of missing data. It is important to keep in mind that because the encoding of the diagnoses is not audited, the quality of the data may suffer.

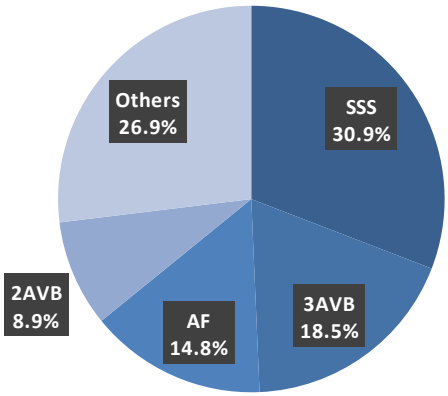
Because the reported frequencies and percentages are quite stable throughout the years 2002 to 2006, only the averages for the whole period of observation are reported. Based on the grouping of ICD-codes, as retrieved from the MCD-MFD data and as presented in the appendix, with 56% dysrhythmias are reported as the most frequent diagnosis group (Figure 30). This is followed with 34% by AV conduction disturbances. On the lower level of indications (Figure 31), the most frequent reporting is SSS (31%), followed by 3AVB (19%), AF (15%) and 2AVB (9%).

Figure 30: Indications for PM interventions per diagnosis group; 2002-2006



Notes: AV cond = AV conduction disorders; BBB = Bundle branch block; Complic = Complication; Excluding missings; Notes: Own calculation based on IMA-AIM and MCD-MFD; see section 5.1 for data sources.

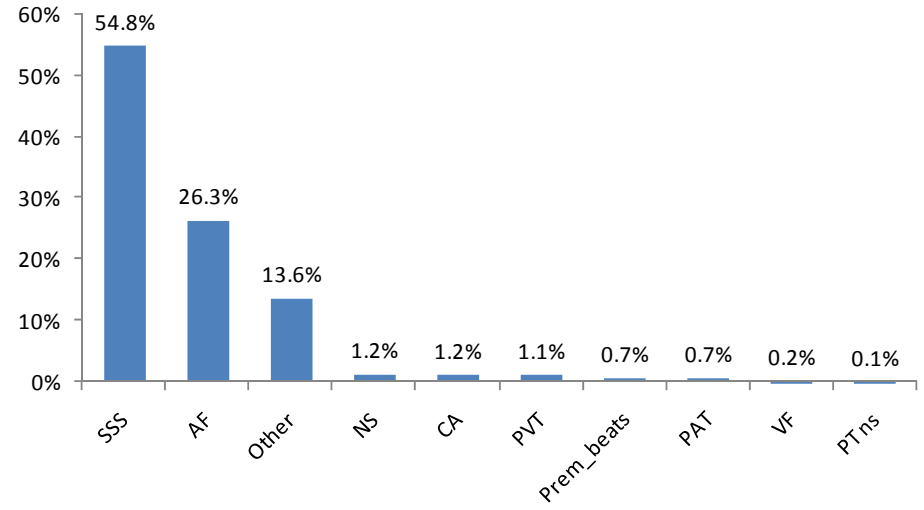
Figure 31: Most frequent indications for primo implantations per main indications; 2002-2006



Notes: SSS = sick sinus syndrome; 3AVB = complete heart block (third degree AVB); AF = atrial fibrillation or flutter; 2AVB = second degree AVB; Others = other indications excluding missings; Own calculation based on IMA-AIM and MCD-MFD; see section 5.1 for data sources.

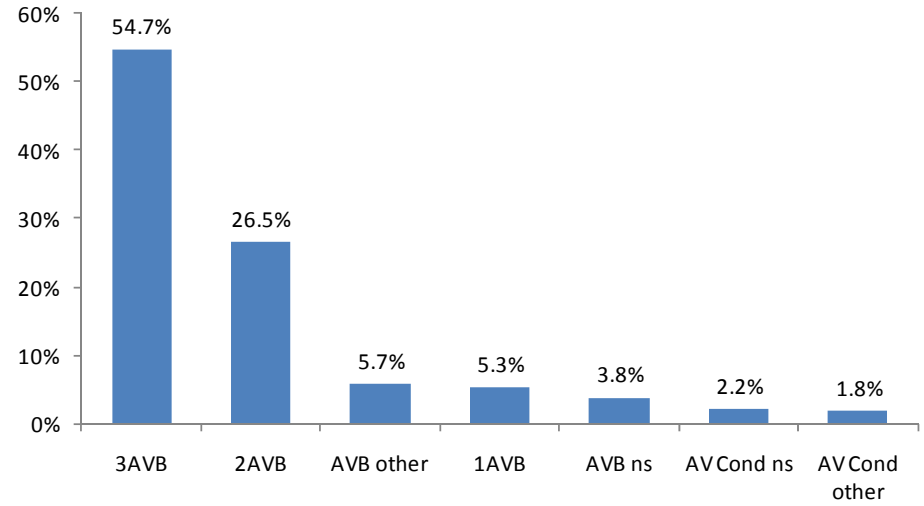
Within the group of dysrhythmias (Figure 32), 55% of indications are reported as SSS, 26% as AF, followed by several indications of minor quantitative importance. Within the diagnosis group of AV conduction disorders (Figure 33), 3AVB is the most frequent indication (55%), followed by 2AVB with 27%.

Figure 32: Indications for primo implantations per diagnosis group - Dysrhythmias; 2002-2006



Notes: PAT = Paroxysmal Supraventricular Tachycardia; PVT = Paroxysmal Ventricular Tachycardia; PT ns = unspecified Paroxysmal Tachycardia; AF = atrial fibrillation or flutter; VF = ventricular fibrillation or flutter; CA = cardiac arrest Prem_beats = premature beats; SSS = sick sinus syndrome; Other = other specified cardiac arrhythmias; NS = unspecified specified cardiac arrhythmias; Own calculation based on IMA-AIM and MCD-MFD; see section 5.1 for data sources.

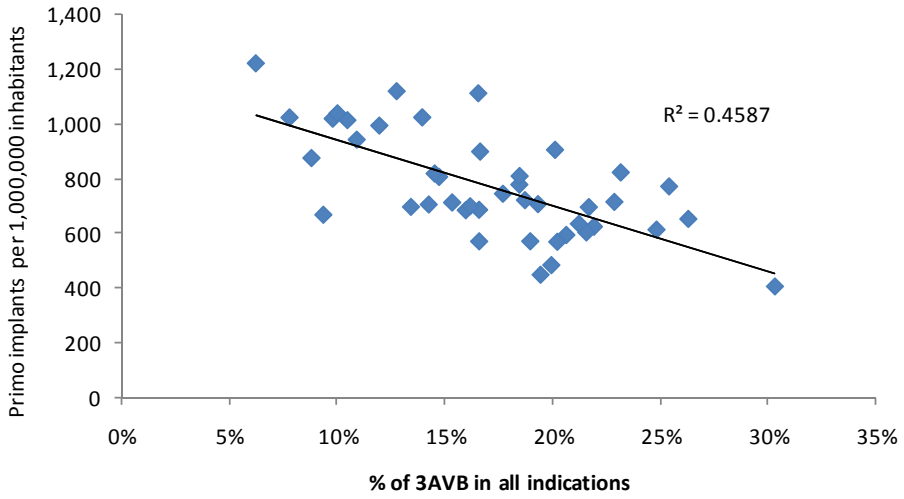
Figure 33: Indications for primo implantations per diagnosis group - AV conduction disorders; 2002-2006



Notes: AVB III = complete heart block (third degree AVB); AVB ns = unspecified AVB; AVB I = first degree AVB; AVB II = second degree AVB; AVB other = other types of heart block; AV Cond other = other specified conduction disturbances; AV Cond ns = unspecified conduction disturbances; Own calculation based on IMA-AIM and MCD-MFD; see section 5.1 for data sources.

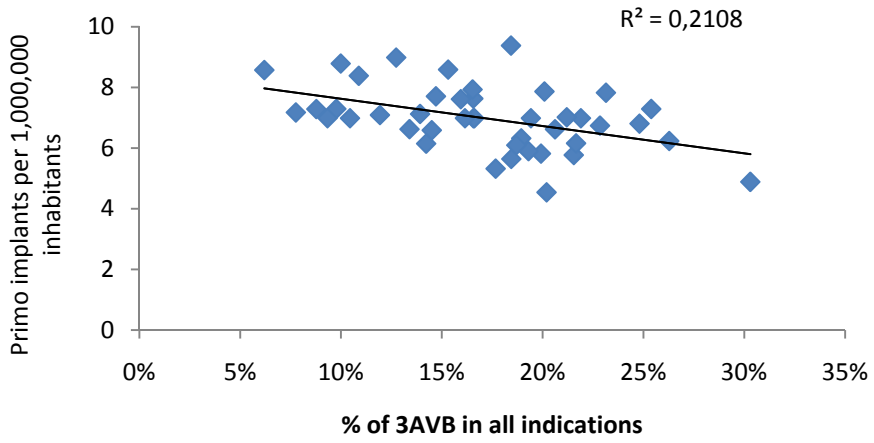
When it comes to the regional variation of primo implantation rates, there is an apparent negative association between the primo implantation rates and the percentage of 3AVB in all indications. This is true for both observed primo implantation rates (Figure 34) as well as after adjustment by sex, age, fiscal revenues per capita and the foreign share of the population (Figure 35).This relationship remains stable also in a multivariate regression framework, which is explained in the appendix to the chapter. Expressed as an elasticity, a 1% increase in percentage of 3AVB goes along with a 0.20% decrease in the primo implantation rate.

Figure 34: Relationship between observed primo implantation rates and the % of 3AVB in all indications; by *arrondissements* in 2006



Notes: Own calculation based on IMA-AIM, MCD-MFD and *Statistics Belgium - Population*; see section 5.1 for data sources.

Figure 35: Relationship between adjusted primo implantation rates and the % of 3AVB in all indications; adjustment based on sex, age, fiscal revenues per capita and foreign share of population; by *arrondissements* in 2006

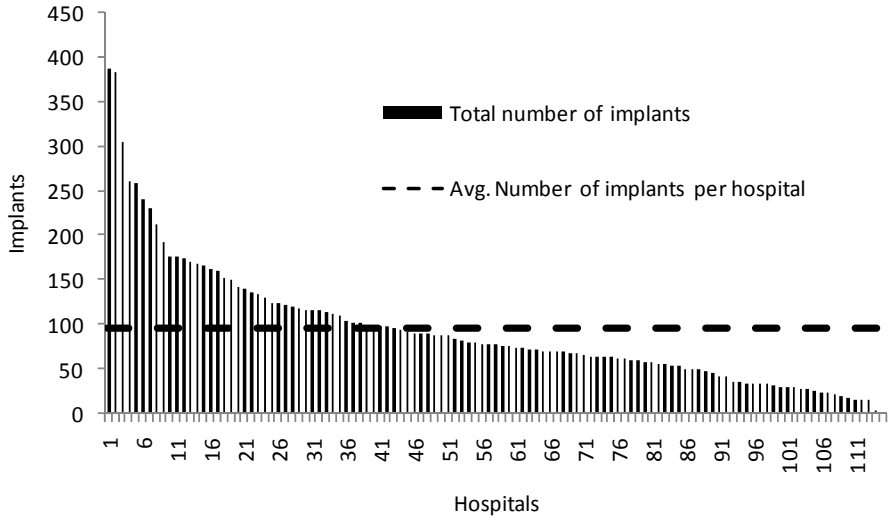


Notes: Own calculation based on IMA-AIM, MCD-MFD, *Statistics Belgium – Population,* [40] *and* [41]; see section 5.1 for data sources.

5.2.7 Hospitals

In general, every acute-care hospital in Belgium has a cardiac care program "A" and a Cardiac Care Program "P" as well, entitling it to perform pacemaker implantations. In 2007 114 hospitals were implanting pacemakers. The total number of implants per hospital ranges between 1 and 387. 10% of hospitals had fewer than 25 implants, 25% had less than 50, 50% had less than 77, 25% had more than 116 and 10% had more than 173 implants. The distribution of implants per hospital is depicted in Figure 36. Because of the relatively low numbers of implants per hospital, each hospital is contributing only a small share of total implants (On average 0.85%; own calculation). Still, there are some considerable differences in terms of implants provided between groups of hospitals. While 30 hospitals with the highest number of implants provide 50% of all implants in Belgium, the lowest 50 hospitals provide around 18% of all implantations.

Figure 36: Number and type of implants per hospital; 2007



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

In 2007 the "biggest" three hospitals provided on average 359 total implants, five further hospitals were within the range of 200 to 300 implants, 30 hospitals within the range of 100 to 200 implants and 76 hospitals were below 100 implants (Table 16). A higher number of implants does not seem to be the result of overly high shares in regular or early replacements. In fact, largely irrespective of the number of implants provided, the share in primo implantations is around 69%, the share in replacements is roughly 31% (Table 17).

Table 16: Distribution of implants; by category of the mean number of implants per hospital, 2007

Hospital category	Hospitals	Implants			
		First implants	Regular replacements	Early replacements	Total
300cases+	3	248.3	98.0	12.3	358.7
200to300cases	5	164.2	72.0	5.2	241.4
100to200cases	30	95.1	40.0	3.0	138.1
less100cases	76	40.3	17.3	1.3	58.8
Total	**114**	**65.6**	**27.8**	**2.2**	**95.6**

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Table 17: Shares of implantation types grouped by the total number of implants, 2007

Hospital category	Shares			
	First implants	Regular replacements	Early replacements	Total
300cases+	69.2%	27.3%	3.4%	100.0%
200to300cases	68.0%	29.8%	2.2%	100.0%
100to200cases	68.9%	29.0%	2.1%	100.0%
less100cases	68.5%	29.4%	2.1%	100.0%
Total	**68.7%**	**29.1%**	**2.3%**	**100.%**

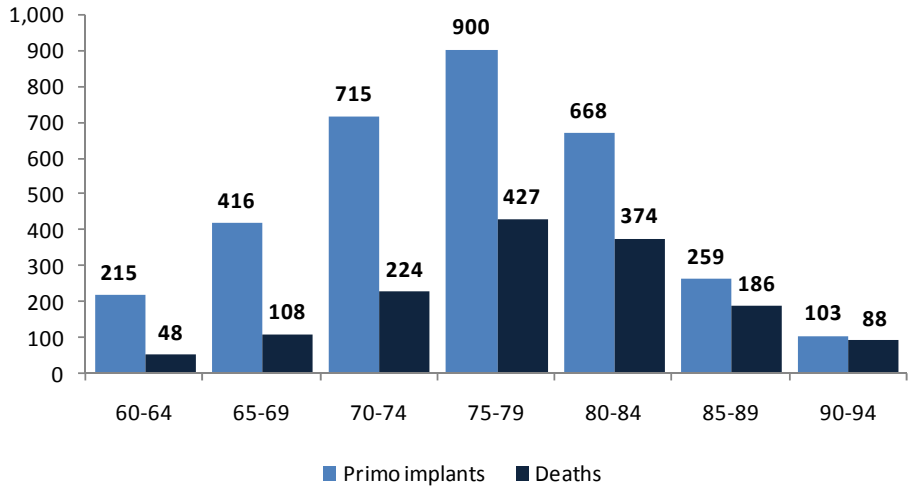
Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

5.2.8 Patient survival

Due to the short time span of the data of only six years, estimations of survival times of patients after a first implantation of pacemakers are not straightforward and bound with relatively large uncertainty. A longer observational period, such as the one in the Danish Pacemaker Statistics 2007 covering a period of 25 years is clearly preferable. Nevertheless, the results presented in this subchapter can be taken as a good approximation for the true survival probabilities of pacemaker patients, until longer observational time periods are available. Because of a very low number of patients aged younger than 60 and few patients aged more than 95 years, these are disregarded in most of the following analyses. The analyses are also restricted to survival of patients after their first implantation in the year 2002, because only for those patients we have an observational period of at least 5 years.

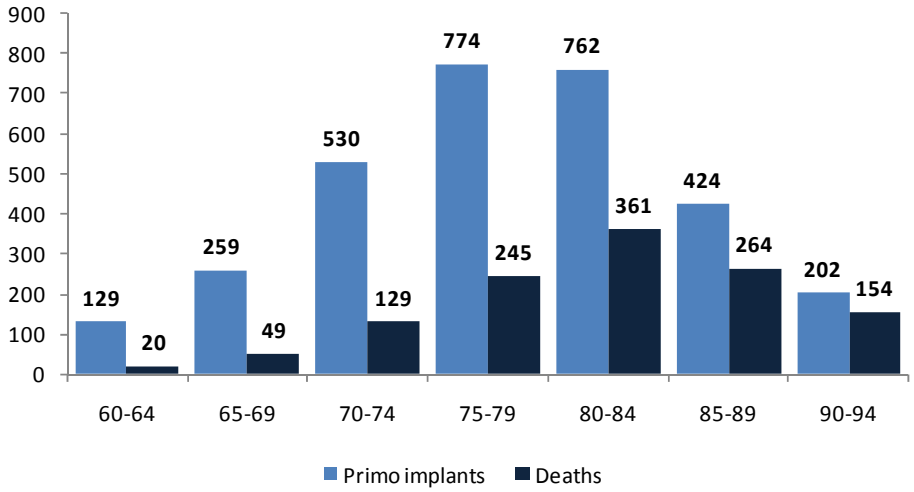
Figure 37 and Figure 38 show the number of primo implantations in 2002 in male and female patients and the according number of deaths within an observational period of 5 years by age groups. 1,222 out of 3080 female patients and 1,455 out of 3,276 male patients between the age of 60 to 94 died within the observational period. This accounts for roughly 44% of male and 40% of female patients in these age groups. The according 5-year survival rates of the patients groups are further compared to 5-year survival rates of the Belgian population. Survival rates of PM patients are always below those of the Belgian population, as would be expected (Figure 39 and Figure 40). It is important to keep in mind, that the Belgian population is not a control group for PM patients in the sense of a scientific experiment. Therefore, this comparison is in the end purely informative and no conclusions on the effectiveness of pacemaking can be drawn solely on the basis of these figures. The appendix to this chapter shows further analyses related to patient survival.

Figure 37: Number of primo implantations in 2002 in male patients and deaths within an observational period of 5 years; by age groups



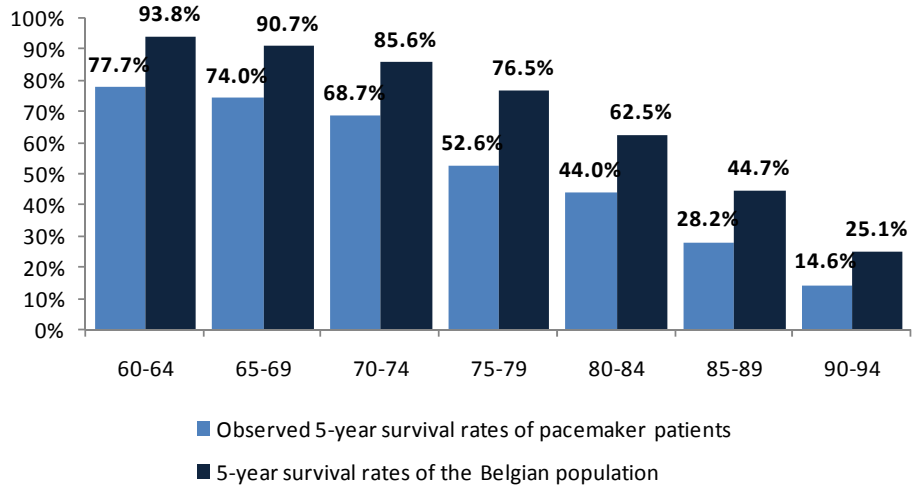
Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Figure 38: Number of primo implantations in 2002 in female patients and deaths within an observational period of 5 years; by age groups



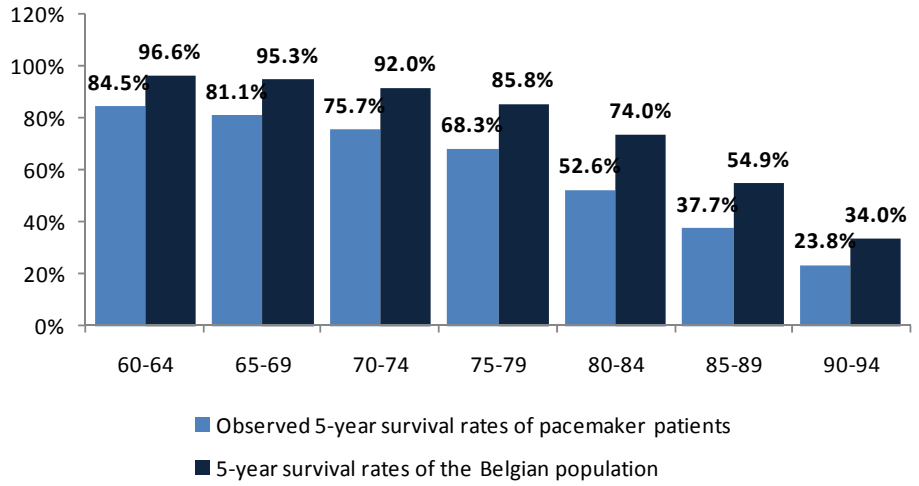
Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Figure 39: 5-year survival of male patients with primo implantations in 2002 compared to the Belgian population



Notes: Own calculation based on IMA-AIM and [38]; see section 5.1 for data sources.

Figure 40: 5-year survival of female patients with primo implantations in 2002 compared to the Belgian population



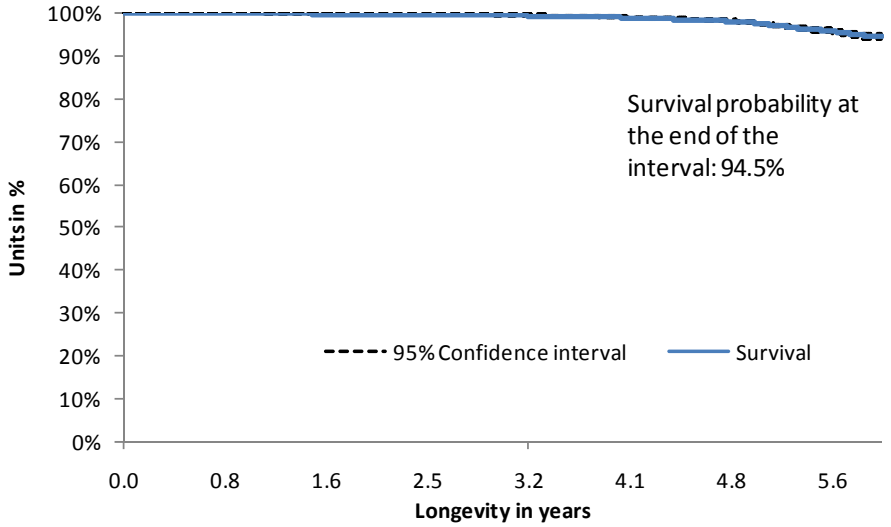
Notes: Own calculation based on IMA-AIM and [38]; see section 5.1 for data sources.

5.2.9 Pacemaker service life

Similarly as in the analysis of patient survival, due to the short time span of only six years, estimations of the service life of pacemakers are quite restricted with the given data. A longer observational period, such as the one in the Danish Pacemaker Statistics 2007 covering a period of 25 years is clearly preferable. During the time span of six years, there are a total of 157 regular and 373 early replacements within the 44,805 patients, for whom the date of first implantation is observed. As such, generator reliability for the first six years after implantation is very high reaching 94.5% for all replacements (Figure 41).

Based on results from the BWGCPE working group, the mean longevity of pacemakers is 7.6 years (+/- 2.6 years).[46]

Figure 41: Pacemaker service life - regular and early replacements; 2002-2007

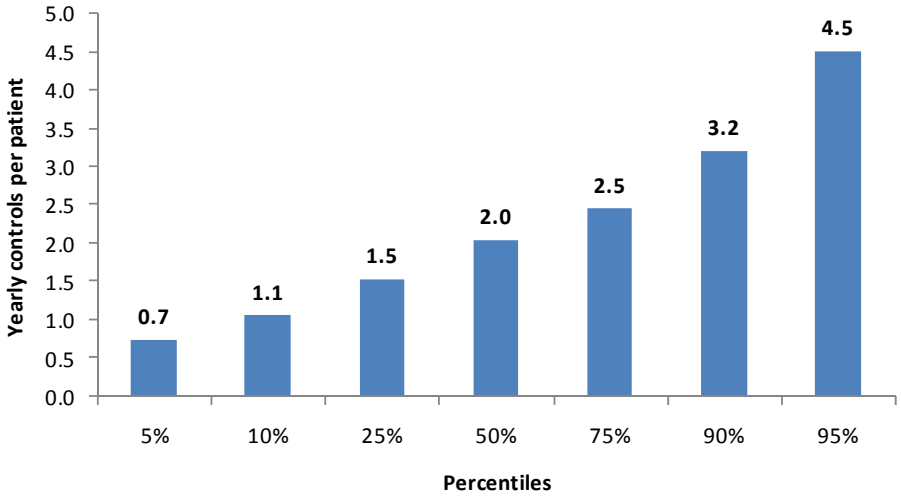


Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

5.2.10 System integrity check

We count the number of system integrity checks[P], as defined by the nomenclature codes in Table 35 in the appendix, in the following. These checks are done on a regular base in order to test the adequate functionality of the implanted pacemaker and lead system. The count is restricted to patients having received a primo implantation in the year 2002, in order to have as long a period of follow-up as possible. For the 6,841 primo implantations in 2002, there are a total of 13,546 PM integrity checks registered. Taking into account the exact duration of observation of patients in the data, we see the following distribution of integrity checks per patient per year. The medium number of annual checks per patient is 2.0. At the 25%-percentile, 1.5 annual checks are performed and at the 75%-percentile 2.5 controls are performed. These numbers are in accordance with European guidelines.[2]

Figure 42: Distribution of the number of system integrity checks per year for patients with a first pacemaker implantation in 2002



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

P "System integrity check" is the English notation used in this report to refer to the Dutch "controle van de deugdelijkheid van de PM" and the French "contrôle de la qualité du stimulateur cardiaque".

5.2.11 Revision of leads

Due to problems with proper encoding of revisions of PM leads, these could not be analysed with given data.

5.3 IMA AND MCD DATA COMPARED TO THE BEHRA REGISTRY

As compared to the insurers data, BeHRA counted 20.6% fewer implants in 2007 (Table 18). The percentages of primo implantations and replacements in all pacemaker implants are at the same level in IMA as in the BeHRA data (Table 19). The average age of patients is slightly higher in IMA than in BeHRA (Table 20). The age distributions by implantation type as well as in total are very similar in both databases (Table 21).

A major difference appears in the comparison of the most frequent PM implantation indications (Table 22). In 2006, SSS is reported in 43% of all cases in the BeHRA registry, while it only accounts for 32% of indications in the IMA data. The percentage of 3AVB is with 22% also higher in BeHRA than in IMA (18%). However, as mentioned already in the analysis of the two databases, the encoding of the diagnoses is not audited, such that the quality of the data may suffer. In fact, it is not possible to say which database provides more accurate data in this respect.

In the appendix to this section, some more comparison tables are presented.

Table 18: Comparison of the total number of implants between IMA and BeHRA; 2002-2007

BeHRA	2002	2003	2004	2005	2006	2007
Primos	5619	6328	6226	6276	6171	6013
Replacements	2391	2420	2190	2375	2504	2655
Total	**8010**	**8748**	**8416**	**8651**	**8675**	**8668**
Missing implants in comparison to IMA	-1,546	-1,706	-1,925	-1,612	-2,241	-2,246
Missings in % of IMA	***-16.2%***	***-16.3%***	***-18.6%***	***-15.7%***	***-20.5%***	***-20.6%***

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 19: Comparison of the distribution of implants by implantation type between IMA and BeHRA; 2002 and 2007

Implantation type	2002		2007	
	BeHRA	IMA	BeHRA	IMA
Primos	70.1%	71.6%	69.4%	68.6%
Replacements	29.9%	28.4%	30.6%	31.4%
Total	100.0%	100.0%	100.0%	100.0%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 20: Comparison of the average age of patients between IMA and BeHRA; 2002 and 2007

Source	2002	2007
BeHRA	75.5	76.4
IMA	76.2	77.0

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 21: Comparison of age distribution of patients between IMA and BeHRA for men and women; 2007

Age distribution	Primo implantations		Replacements		Total	
	IMA	BeHRA	IMA	BeHRA	IMA	BeHRA
0-9	0.23%	0.33%	0.09%	0.26%	0.20%	0.31%
10-19	0.07%	0.12%	0.22%	0.19%	0.11%	0.14%
20-29	0.15%	0.18%	0.22%	0.38%	0.16%	0.24%
30-39	0.32%	0.50%	0.38%	0.56%	0.34%	0.52%
40-49	1.15%	1.41%	1.32%	1.62%	1.21%	1.48%
50-59	3.71%	4.17%	3.55%	4.44%	3.66%	4.26%
60-64	5.18%	4.42%	3.96%	3.31%	4.85%	4.08%
65-69	7.91%	7.10%	7.01%	6.21%	7.61%	6.83%
70-74	15.56%	13.72%	12.49%	10.85%	14.55%	12.84%
75-79	22.21%	20.57%	19.28%	17.82%	21.35%	19.73%
80-84	24.22%	22.14%	23.59%	22.67%	24.08%	22.30%
85-89	13.97%	13.72%	18.12%	17.36%	15.19%	14.84%
90-94	3.66%	3.34%	6.61%	6.10%	4.50%	4.19%
>=95	0.55%	0.67%	2.01%	2.11%	1.01%	1.11%
Missing	1.12%	7.60%	1.13%	6.10%	1.18%	7.14%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 22: Comparison of the distribution of the most frequent indications for patients with primo implantations between MCD and BeHRA; 2002 and 2006

Indications	2002		2006	
	MCD	BeHRA	MCD	BeHRA
SSS	31.25%	41.5%	32.24%	43.2%
3AVB	17.64%	21.1%	18.12%	21.9%
AF	15.58%	14.2%	14.30%	14.1%
2AVB	7.73%	9.0%	9.58%	11.9%
Other	27.80%	14.2%*	25.76%	9.0%*

Notes: *The category 'other' includes all other registered outcomes (inclusive the category 'unspecified' and 'uncoded'); missing observations excluded. Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources (2007 MCD data were not available within this study).

Key points

- **From 2002 to 2007, the accumulated reimbursements related to pacemakers and leads were 357.4 million € with a mean annual reimbursement of 59.6 million €.**
- **In 2007, the average reimbursement was 4,419 € for a pacemaker and 571 € for a lead. From 2002, the average reimbursement has decreased by 11.1% for pacemakers and 3.9% for lead devices.**
- **The total implantation rate in 2007 is at the level of 10.3 and the primo implantation rate is at the level of 7.1 implants per 10,000 inhabitants.**
- **Tendentiously, the share of primo implantations is decreasing, while the share of replacements is increasing. Primo implantations made up 71.6 and 67.4% of all implants in 2002 and 2007, respectively.**
- **The mean age of patients with primo implantations has increased over the period 2002 to 2007 and, in 2007, has reached 75.2 years for men and 78.1 years for women.**
- **In 2007, 85% of all primo implantations in men (92% for women) occurred in patients older than 65 years.**
- **Within the same age group the probability to receive a pacemaker is considerably higher for men than for women.**
- **There are considerable regional differences in observed primo implantation rates.**
- **Once regional primo implantation rates are standardized by the age-sex distribution of the population as well as fiscal revenues per capita and the share of the foreign population, the regional differences in primo implantation rates are no longer statistically significant different from zero for most of the regions.**
- **With 56%, dysrhythmias are reported as the most frequent diagnosis group followed with 34% by AV conduction disturbances.**
- **On the level of indications, throughout the years 2002 to 2006, the most frequent reporting is SSS (31%), followed by 3AVB (19%).**
- **As compared to the insurers' data, BeHRA counted 20.6% fewer PM implants in 2007. With reference to the percentage of primo implantations and replacements and the sex and age distribution, the IMA-AIM and BeHRA data are comparable. A major difference between the two data bases appears in the comparison of the most frequent reported indications for the PM implantation.**

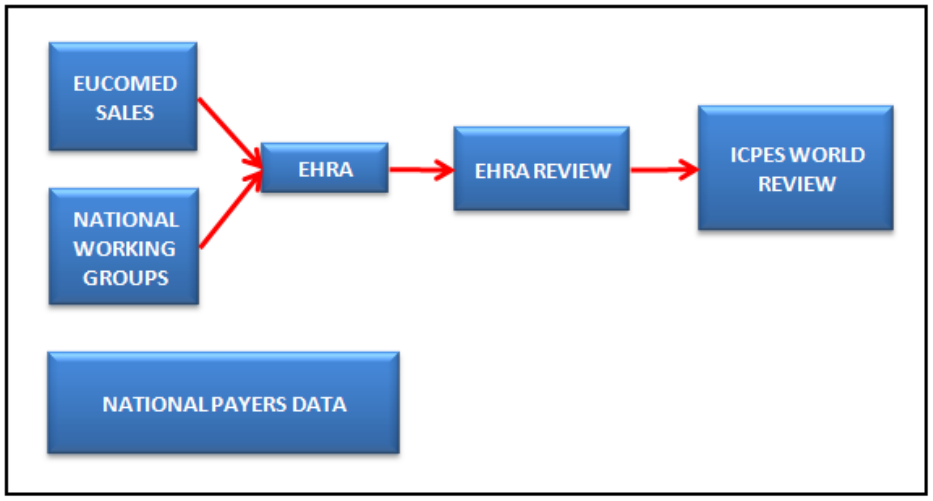
6 INTERNATIONAL PM REGISTERS

A literature search was performed using Medline via PubMed to obtain information on pacing practice abroad, by introducing the following search string: "Registries"[Mesh] AND "Pacemaker, Artificial"[Mesh] and via EMBASE, introducing 'register'/exp AND 'artificial heart pacemaker'/exp. Four main sources of data on implantation rates in various countries thus emerged:

1. Eucomed, the European Medical Device Trade Organisation, gathers information on the sales of medical technology from its member manufacturers. Information on PMs is limited to raw data from yearly sales of devices. Specific information on how many of the devices are actually implanted, the ratio of primo implantations vs. replacements, or patient related data are not available.[47] A few graphs related to implantation rates of cardiac devices from 2004 to 2008, are publicly available from its website (www.eucomed.org).
2. National Working Groups on cardiac pacing and electrophysiology collect mostly on a voluntary basis data on PM practice in their country, based on the "European Pacemaker Patient ID Cards". Besides the numbers of primo implantations and replacements, these data include clinical and electrocardiographic information as well. The Working Groups are invited to forward annual aggregated data to the EHRA Register. In addition, some countries (Germany, Spain, Portugal, France, Italy) publish more detailed data in journals, often in the local language. Some countries, such as Belgium and the Netherlands, limit the availability of detailed data to their members. Still others, such as Denmark and the UK provide yearly updated and publicly available comprehensive data on Working Group websites.
3. The European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC) keeps a registry of PM related procedures, based on data provided to them on a yearly basis by the national Working Groups.[48] This registry was established in the late 1970s. Comparative results between countries are published in scientific articles and presented at international meetings.
4. Every four years, the International Cardiac Pacing and Electrophysiology Society (ICPES) publishes a worldwide survey of cardiac pacing and ICD practice. The most recent survey from 2008 covers the year 2005.[49] The data from European countries is based on the European PM Registry. For countries outside Europe, data are based on questionnaires sent to selected physicians and complemented with data from PM companies.

Obviously, the numerical data provided by these different data sources (Eucomed, national Working Groups, EHRA, ICPES) are interrelated, as diagrammatically shown in Figure 43.

Figure 43: Interrelationship between data sources



Source: KCE.

The number of PMs sold in a given country may differ from the number of actual PM implants because of reselling of acquired PMs from one country to another, stocking of PMs, or recalls of PMs by the industry. However, based on statements from authors in scientific articles,[48, 50, 51] from external experts that took part in the preparation of this report, and from members of Unamec (a Belgian association of distributors and importers of medical devices), the sales data provided by Eucomed can be considered to reliably approximate the PM implantation rate in a given country.

The completeness of the implant numbers originating from the Working Groups, and by extension those from EHRA and ICPES, is uncertain. In most countries, implant numbers are collected on a voluntary basis and are most often not scrutinised for their correctness. Consequently, Working Groups often collect only a fraction of total implants. Authors that present European data on PM practice adjust their data to those obtained from manufacturers.[48] As laid out in a previous chapter, the Belgian BeHRA register roughly reports on 80% of the total number of implants. In Denmark and Germany the completeness of the data is reported to be almost 100%, and a formal quality control is established. In Denmark an audit of the correctness of the reporting of implantation complications was conducted by Swedish cardiologists.[35] Germany introduced in 2002 a mandatory external quality control of PM procedures, and from 2003 on, financial sanctions have been imposed on centres that did not furnish statistical data on their PM activities.In Italy less than data on 60% and in Spain less than 40% of data is collected. It is, however, not clear to what extent these collected data are for the entire clinical pacing practice in the respective countries representative with respect to implantation types, patient characteristics or indications.

As discussed in a previous chapter, the data from the Working Groups are derived from the European PM Patient ID Card that has been introduced in 1978. This form contains identification data of the patient and of the implanted devices (PM, leads), as well as information on symptoms, electrocardiogram, underlying disease, and indications for the replacement of the PM or the lead(s). Some of the items that are listed are however uninformative. For example in all sections, a choice can be made to encode "unspecified" or "uncoded". In the section "Symptom", items such as "bradycardia" or "tachycardia" are meaningless because these terms indicate whether a patient's heart rate is slow or fast but they do not represent symptoms. These formal anomalies in the European PM Card limit the quality of national Working Group data.

Besides the data sources mentioned above, data on the use of PMs should also be available from the insurers and the payers in the different countries. These data can be expected to most reliably reflect the number of PM implants, at least in countries with a general coverage of PMs. To our knowledge, no such data have been published from European countries. Insurers data related to PM practice in Belgium have been presented earlier in the present report. They indicate that for most of the years the number of implants in Belgium closely correspond to the Eucomed sales data, as discussed further.

6.1 PACEMAKER IMPLANTATION RATES IN EUROPE

6.1.1 Eucomed data

The Eucomed website (www.eucomed.org) provides data of PM sales per million inhabitants in 16 European countries for the years 2004 through 2008. Data related to conventional PMs sales in 2005-2008 are depicted in Table 23 and Figure 44. The numbers related to Belgium include those from Luxemburg as well. We have to assume that the implantation rates are identical in Belgium and Luxemburg. The Eucomed data are also incorporated in a recently published overview of pacing practice in Europe.[47] The latter publication also provides the average Western European conventional PM sales per million inhabitants per year. PM sales gradually increased in Western Europe from 831 per million inhabitants in 2004 to 907 per million in 2008 (+9%). This trend is almost universal. According to these data, the highest number of PMs sold per million inhabitants is in Germany, followed by Belgium and Italy. In 2008 this was 1,196 PMs per million in Germany, 1,126 in Belgium and 1,028 in Italy. This order also prevails, if the actual number of pacemakers implanted (1,031 per million) or reimbursed (1,085 per million) in Belgium in 2007 are compared to sales in other countries.[q]

There is some overlap in the clinical indications for a conventional bradycardia PM and a CRT-P device, the latter intended for patients with heart failure. In a patient with bradycardia and intractable heart failure, a physician may consider to implant a CRT-P instead of a conventional PM. Because of these overlapping indications, it might be argued that one has to add the number of CRT-P's to the number of bradycardia PMs in order to fairly compare the number of implants between countries. However, because of the low number of CRT-Ps, they contribute little to the overall sum (Table 23). The result is that in Belgium on average 25% more PMs per million inhabitants are implanted as compared to the Western European average.

Table 23: Sales of conventional PMs and CRT-Ps per million inhabitants in selected European countries, 2005-2008

	PM				CRT-P				PM	PM+CRTP
	2005	2006	2007	2008	2005	2006	2007	2008	2005-2008 average	
AUSTRIA	893	884	908	909	32	26	29	29	899	928
BELGIUM+LUX	1005	1064	1116	1126	46	47	46	46	1078	1124
DENMARK	704	748	643	713	43	37	36	33	702	739
FINLAND	667	672	753	802	15	14	11	14	724	737
FRANCE	933	955	952	986	33	32	31	33	957	989
GERMANY	1134	1176	1200	1196	15	15	15	13	1177	1191
GREECE	527	714	559	776	10	10	8	7	644	653
IRELAND	553	505	419	490	16	7	3	3	492	499
ITALY	956	965	1013	1028	29	26	26	26	991	1017
NETHERLANDS	588	616	652	677	35	32	29	25	633	664
NORWAY	494	482	537	570	25	25	27	23	521	546
PORTUGAL	695	677	720	745	9	9	9	11	709	719
SPAIN	645	657	677	710	9	12	11	12	672	683
SWEDEN	816	880	868	905	37	54	50	54	867	916
SWITZERLAND	630	676	676	706	14	16	15	17	672	688
UK	496	583	603	630	20	23	30	32	578	604
WESTERN EUROPE*	835	868	887	907	23	25	25	25	874	899
RATIO BEL/W.EU.	1,20	1,23	1,26	1,24	2,00	1,88	1,84	1,84	1,23	1,25

Data from Eucomed website. *Average Western European numbers obtained from van Veldhuisen.[47]

[q] See chapter 22 for the number of pacemakers implanted, sold and reimbursed in Belgium.

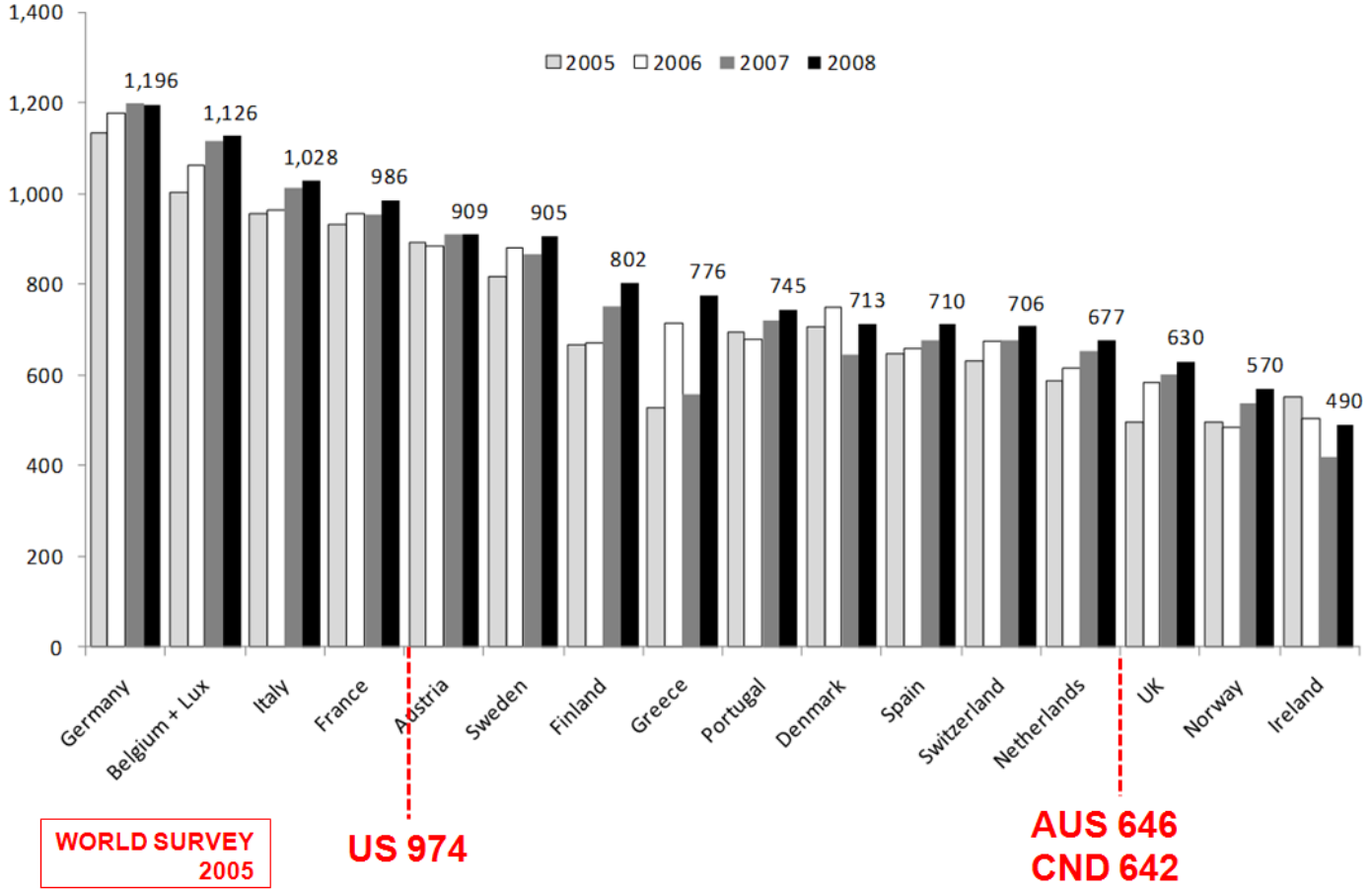
Table 24 shows the rate of ICD implants in Western European countries. The relatively high number of CRT-P implants in Belgium (Table 23) is compensated by a lower rate of CRT-D implantations. This is most probably related to the fact that, in contrast to PM implantations, ICD therapy in Belgium is more strictly regulated.

Table 24: Sales of ICDs per million inhabitants in selected European countries, 2005-2008

	ICD				CRT-D			
	2005	2006	2007	2008	2005	2006	2007	2008
AUSTRIA	97	108	129	136	32	42	57	68
BELGIUM+LUX	88	85	104	112	26	28	40	39
DENMARK	100	104	137	180	32	43	50	59
FINLAND	60	70	84	89	5	13	20	25
FRANCE	55	67	71	77	25	38	47	52
GERMANY	171	193	232	264	55	70	84	103
GREECE	46	51	53	81	8	12	17	28
IRELAND	126	158	120	135	29	8	31	37
ITALY	115	129	149	167	73	93	114	134
NETHERLANDS	106	141	171	194	53	72	87	94
NORWAY	37	74	85	91	18	21	24	22
PORTUGAL	41	45	59	68	18	22	27	31
SPAIN	48	51	57	63	16	19	25	27
SWEDEN	48	54	71	75	21	30	37	38
SWITZERLAND	80	78	95	103	29	38	45	51
UK	50	63	65	74	18	35	39	47
WESTERN EUROPE*	92	110	126	140	38	52	63	74
RATIO BEL/W.EU.	0,96	0,77	0,83	0,80	0,68	0,54	0,63	0,53

Data from Eucomed website. *Average Western European numbers obtained from van Veldhuisen.[47]

Figure 44: Sales of conventional pacemakers in selected Western European countries per million inhabitants, 2005-2008



Based on data from the Eucomed website (accessed May 10, 2010): http://www.eucomed.org/press/~/media/F7C3D59B04AA40F6A8B6142A6FE95C46.ashx. Source population data: Eurostat. Numbers on graph refer to 2008 data (cf. Table 23). Numbers do not include CRT-P devices. Data related to US, Canada (CND) and Australia (AUS) shown at the bottom of the graph, retrieved from Mond et al.[49, 52] and discussed in next paragraph on "World survey of cardiac pacing".

6.1.2 European Heart Rhythm Association data

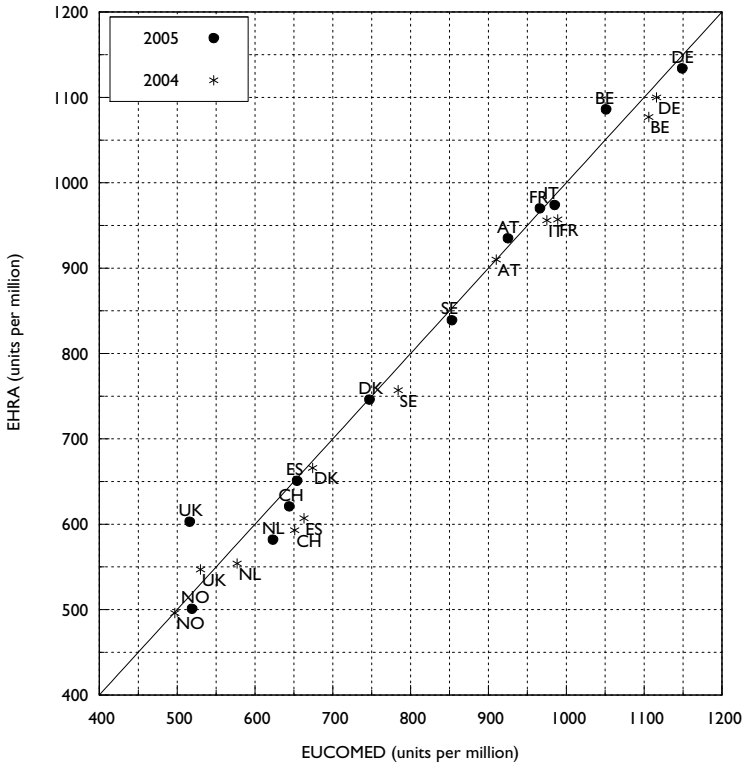
6.1.2.1 Total implantation rates

As discussed earlier, a second source of data on pacing practice in Europe is derived from the European Pacemaker Registry. The most recently published report from the EHRA is related to the use of PMs in the years 2003 through 2005.[48] The authors report that for some countries, data were obtained from device manufacturers (and not from national Working Groups), but it is not clear to which countries this applies and to what extent this is the case. The data that are provided all relate to the sum of conventional PMs and CRT-P devices. Except for the Netherlands and Denmark, CRT-P's reportedly account for less than 5% of the total number of implants. In addition to the number of implants, the EHRA article also mentions the number of replacements, data on different types of PM and leads, the number of PM centres and also data on patient ECG characteristics.

Across Europe, the median number of centres that perform PM implantations per million inhabitants was 4.26/4.88/3.62 in the years 2003/2004/2005. The lowest centre density is in Denmark with 2.72 centres/million and the highest in Belgium (12.1/million) and Germany (11.9/million). However, centres vary in the size, so they are not comparable in a straightforward manner across countries, as their size is unknown. In the years 2003/2004/2005, a total PM implantation rate of 559/621/503 per million inhabitants has been registered in European countries, including some Eastern European countries (Croatia, Czech republic, Latvia, Lithuania, Russia, Slovak republic, Slovenia). The number of PM implants per million varies considerably across countries: the European median total implantation rate is 559/621/503. The highest number of PM implants occurs in Germany where the total number per million inhabitants was 1,068/1,100/1,134 in 2003/2004/2005. The number of implants in Belgium are 1,121/1,077/1,086 per one million inhabitants in 2003/2004/2005.

The available data permit a comparison of Eucomed sales data with the EHRA implant numbers for the years 2004 and 2005 only. As can be inferred from Figure 45, the data largely correspond to one another.

Figure 45: Relationship between the reported number of pacemakers sold (Eucomed) and the number of pacemakers implanted (EHRA), 2004 and 2005



Implantation rates in different countries related to the years 2004 and 2005. Eucomed data from van Veldhuisen et al.[47] and EHRA data from Ector et al.[48]

6.1.2.2 Primo implantation rates

In contrast to Eucomed data, EHRA does not only provide total, but also primo implantation rates. In 2003/2004/2005 the median rate of primo implantations in European countries was 424/435/447 with an average of 426/472/381 respectively. The highest rates are observed in Belgium with 813/807/789 primo implantations in 2003/2004/2005. In Germany, the corresponding rates are 629/756/NA. The share of PM replacements in the total number of PMs implanted is on average 20 to 25%. However, this percentage varies substantially across countries, from a minimum of 9% in Lithuania (2005) to a maximum of 41% in Germany (2003).

As far as patient data are concerned, the European review publishes no detailed data. For comparison of PM indications across countries, it reports a calculated ratio of electrocardiographic characteristics of patients: (sick sinus/slow atrial fibrillation)/(second degree/third degree AV block). According to the authors, this should correct for unspecified indications. The validity of this parameters has been discussed in a previous chapter.

6.2 WORLD SURVEY OF CARDIAC PACING

The most recent survey from the International Cardiac Pacing and Electrophysiology Society (ICPES) was published in 2008 covering the year 2005. It is anticipated that a 2009 survey will be conducted for the World Symposium to be held in 2011 in Greece.[49] The data for European countries is based on the European PM Registry. Therefore they obviously correspond to those in the European 2003-2005 survey that we mentioned earlier.[48] In this review, for countries outside Europe, data were based on questionnaires sent to selected physicians and complemented with data from PM companies. A summary table with data on primo implant rates from a selected number of countries is depicted in Table 25.

Table 25: PM primo implantation rates in a selection of countries, 1997, 2001, 2005

	1997	2001	2005
BELGIUM	585	685	789
US	571	786	752
CANADA	368	591	550
AUSTRALIA	345	486	590
NEW ZEALAND	228	245	275

Data from Mond et al.[49, 52]

In the 2005 World Survey, Belgium had the highest total number of PM implants per million inhabitants (1,076), followed by the US with 974. Data from Germany were not available in this World Survey, but we know from the EHRA data discussed above that the implantation rate in Germany in 2005 was slightly higher than in Belgium (1,134).

The share of replacements in the total of PM implanted ranges from 8.8% in Australia to 32.3% in the Netherlands. The percentage of PM implants in males is larger than in females in most countries. In European countries, the percentage of male PM patients varies between a low 45% in the UK to 62% in the Slovak Republic. The age of male and female recipients is very similar across countries with females being slightly older.

In contrast to the EHRA report[48], the World Report provides details about the electrocardiographic indications for the primo implantation. The major ECG indications are summarized in Table 26.

Table 26: Indications for initial pacemaker implantation, 2005

COUNTRY	High degree AVB (%)	SSS (%)	AF (%)	OTHER or MISSING (%)
BELGIUM	23	40	13	24
CROATIA	36	21	22	21
CZECH REPUBLIC	20	40	22	18
DENMARK	32	32	14	22
FRANCE	25	23	9	43
GREECE	14	20	6	60
ITALY	21	21	13	45
LATVIA	30	38	18	14
NETHERLANDS	25	32	11	32
RUSSIA	36	25	16	23
SLOVAKIA	29	33	11	27
SPAIN	38	23	17	22
SWEDEN	23	33	19	25
SWITZERLAND	26	37	14	23
UK	28	26	17	29
ARGENTINA	68	25	5	2
BRAZIL	52	13	9	26
CANADA	38	34	18	10
ISRAEL	37	35	10	18
NEW ZEALAND	49	28	16	7

Data calculated from [49]. AVB: Atrioventricular block. High degree AVB includes third degree AVB and second degree AVB with a block of 2 or more consecutive P waves.[53] SSS: sick sinus syndrome. AF: atrial fibrillation. Other: bundle branch block, carotid sinus syndrome, AV ablation, hypertrophic cardiomyopathy, congestive cardiomyopathy. Percentages refer for the indication of the initial implantation. 2005 data related to Germany are not provided in this world survey. As discussed later, Markewitz reports the following distribution of indications for primo implants: 3AVB: 23.0%, SSS: 38.3%, AF: 18.2%, other: 9.1%.

Across countries there is a wide range of variation in the percentage of primo implantations for high-degree AV block. Belgium is reported to have 23% of pacemaker patients being treated with a PM because of high-degree AV block.

6.3 THE DANISH PACEMAKER REGISTER

In the next paragraphs, we summarise data that were made publicly available by European national Working Groups. Some of the relevant data are summarised in Table 27 where we also juxtapose implantation rates as reported by the Working Groups alongside the sales numbers reported by Eucomed.

Table 27: Core data related to clinical pacemaker practice (CRT-P inclusive) in Western European countries

Country, year	Eucomed sales per mio	WG total per mio	WG repl % of total	WG data source	3AVB (%)	Age at primo implant
Denmark 2007	679	732	27,1	IT	30,5	Median: 77,6. M: 76,0; F: 79,9
France 2002	NA	869	28,0	Journal	NA	Median: M: 77,25; F: 79,50
Germany 2006	1191	1040	24,1	Journal	23,8	Mean: M: 73,8; F: 77,5
Netherlands 2004	542	532	27,2	IT	24,4	Mean: M: 72,3; F: 75,9
Portugal 2003	NA	601	16,8	Journal	NA	NA
Spain 2008	710	708	26,0	Journal	33,8	Mean: 76,3; M: 75,8; F: 77,0, 81% > 69 yrs.
Italy 2007	1042	529 (60%)	28,3	Journal	23,6	Median: 79

Eucomed sales data derived from van Veldhuisen [47]. WG: national Working Group. IT: WG's website. 3AVB(%): % of primo implantations for third degree atrioventricular block. Population of countries from article, or if not mentioned, obtained from OECD statistics (http://stats.oecd.org/index.aspx?queryid=254). References to WG data sources (journal or website) provided in text.

The Danish PM register was initiated in 1982. In 1989, a register on ICDs was added to it. The register is based at the department of cardiology of the Odense university hospital. From 1997 on, the data originating from the European PM Card were supplemented with information on the quality of PM implantations with respect to the mode of pacing, duration of the procedure and fluoroscopy time, early and late complications. The data collection is based on self-reporting from the individual centres. In order to insure data quality, 20% of pacemaker implantations from 1999 were randomly selected for an external audit performed by Swedish cardiologists. Individual centres were visited and full access to the patient records was obtained. The data sheets sent to the pacemaker register were compared with the information in these records, with special emphasis on the correct reporting of procedural complications.[35] The audit revealed 24 peri-operative complications of which 19 had been reported to the Register and 9 late complications of which 7 had been reported. The seven unreported complications were seen in five different centres.

In 2007, the Danish ICD register was moved to an internet based platform and the data collection was expanded. The latter was done according to the proposal known as the Cardiology Audit & Registration Standards (CARDS) developed by the European Society of Cardiology in 2004. It was the intention of the register managers to also provide by the end of 2008 an internet access to the PM registry in accordance with the CARDS proposal.

The Danish Register provides detailed data on PM practice, quality of practice, demographic data and device related information for each of the 14 Danish centres separately. Here we report on the Danish clinical pacing activity in the year 2007, that are available from the Danish Working Group website (http://www.pacemaker.dk/stat2007.pdf). Some core data are provided in Table 27.

The total number of PM implants in Denmark in 2007 was 3,756, equivalent to 732/million inhabitants.[20] There were 2,740 (534/million) first implants and 1,016 (198/million) replacements, in 14 implanting hospitals (2.7 centres/million). Nineteen implants were performed in Greenland, but otherwise the smallest centre performed 76 and the largest centre 402 first implants with an average of 209 per centre. Overall median age was 77.6 years. There were 1,522 male patients (55.5%) with a median age of 76.0 years and 1,218 female patients with a median age of 79.9 years. 2AVB (code C2-C4) was the indication in 8.6%, 3AVB in 30.5%, SND (code E1-E5) in 33.0% and slow AF (code C8+E6) in 17.2% of the patients. Among the 2,740 patients with a first implantation, 1,251 (45.7%) had syncope and 701 (26.6%) dizzy spells as their presenting symptom.

From 1982 through 2007, a total of 56,672 generators were implanted. Almost half (46.8%) of the generators were still functioning after 10 years and one quarter (25.2%) after 15 years.

6.4 THE UK NATIONAL SURVEY

The registration data in the United Kingdom is contributed on a voluntary basis by PM implanting hospitals. The data is held in the National Pacemaker Database, established in 1977 and part of the Central Cardiac Audit Database (www.ccad.org.uk). Yearly, a UK National Survey is published, describing in detail device implants per hospital referral regions. This document provides graphical data from England, Wales and Scotland but no numerical or aggregated UK data.[54]

There have since long been concerns in the UK that PM therapy had been underused. This concern was based upon a relatively low number of implants per million inhabitants as compared to other European countries, a significant inequality of provision of devices over the country, and the documented delays to PM implantations in patients with an accepted indication for pacing.[55] Related to this issue, the authors of the UK National Survey have introduced the concept of "target national implantation rate" in order to indicate the "deficit" or "excess" implantation rates in different PCTs (Primary Care Trust). A target of 700/million of new PM implants was used, reportedly based on the European average new implantation rate for 2004. This target number is however in contradiction with the published data that we considered earlier in the present report. According to EHRA, the average 2004 primo implantation rate in Europe was 472/million.[48]

6.5 THE GERMAN REGISTER

A PM activity report related to 2006 has been released by the *Fachgruppe Herzschrittmacher und Bundesgeschäftsstelle Qualitätssicherung*. Germany introduced in 2002 a mandatory external quality control of PM procedures, and from 2003 on, financial sanctions have been imposed on centres that did not provide statistical data on their PM activities. These administrative measures had an important impact on the number of reported procedures: in 2001, 26,657 interventions were recorded, in 2003 this number increased by more than 10,000 units to 36,812 and following the introduction of financial sanctions, the number of reported interventions in 2003 as compared to 2001 increased by 150% to 68,430 cases.

The 2006 German register covers 94,210 in-hospital PM procedures, including primo implantations, replacements and revisions.[19] An estimated 5,000 procedures (5%) that were performed on an ambulatory basis were not taken into account. In 2006, 788/million primo implantations and 251/million replacements were registered. Almost 12% of PM procedures were revisions. The mean age of patients at primo implantation was 73.8 years for men and 77.5 for women.

A quarter of ECG indications were complete heart block (3AVB) and a third were SSS. Almost a third of patients (31.5%) received a PM because of syncope, and another third (31.0%) because of dizziness.

The German register provides comprehensive data on implantation related procedural complications. The following complications were considered: pneumothorax, wound haematoma, dislocation of lead (atrial or ventricular), wound infection, and a group of miscellaneous complications (asystole, ventricular fibrillation, pericardial effusion, haemothorax). In 2006, in 4.2% of primo implantations (in 2005: 4.7%), at least one of these complications occurred. The most often occurring complications were dislocations of atrial (1.6% of primo implanted atrial leads, vs. 1.4% in 2005) or ventricular (1.1% of primo implanted ventricular leads) leads. An increase in the number of atrial lead dislocations over the years of PM practice was noticed. The number of centres that recorded less than 1% dislocations decreased both in absolute and relative terms, whereas the number of centres in which more than 5% of atrial leads dislocated increased. The authors of the report suggest that this negative trend might be related to an observed increase in the number of small centres. The number of German PM centres increased from 1,001 in 2005 to 1,029 in 2006. In 2006, 14.1% of centres performed less than 20 interventions as compared to 13.2% in 2005.

6.6 THE DUTCH REGISTER

Since 1976, a national register of the Dutch PM practice has been collected by the Stichting Pacemaker Registratie Nederland (SPRN), based on data from the European PM ID Card provided by different PM centres.[7] In 2008, the SPRN register has been transferred to the DIPR (Dutch ICD and Pacemaker Registry), that introduced an on-line database.[r] Aggregated data from the SPRN database used to be publicly available, whereas access to the DIPR is limited to participating centres. Data provided below are originating from the 2004 SPRN report that we could retrieve from the SPRN website but they apparently are no longer available on the internet. Some core data are depicted in Table 27. A substantial number of CRT-P devices are implanted in the Netherlands, in 2004 constituting 13.8% of all PM implants.

In 2002/2003/2004, 5,585/5,914/6,307 primo implantations and 2,410/2,320/2,350 replacements respectively where registered, totalling 7,995/8,234/8,657 PMs for a total population of about 16.2 million. These numbers indicate an increase in the total number of primo implantations, the number of replacements being fairly constant. The share of replacements in the total number of implants slightly decreased from 30 to 27% over these years. In females, 65% of implants took place in patients over 70 years of age and 85% in patients over 60 years of age. In males, 76% took place in patients above 70 years of age and 90% in patients above 60 years of age. Syncope was encoded as the presenting symptom in about 28% of patients and "dizzy spells" in 24%. An ECG diagnosis of 3AVB accounted for 26.8/24.5/24.4% of primo implantations in 2002/2003/2004 respectively.

6.7 THE SPANISH PACEMAKER REGISTRY

The Spanish PM Registry regularly publishes an "Official report of the Spanish Society of Cardiology Working Group on Cardiac Pacing". The most recent report was published in 2009 and describes PM practice from 1994 through 2008.[56] For the year 2008, data from 11,855 European Identification Cards, voluntary submitted by 116 PM centres were collected. They reportedly cover 36.3% of all PMs implanted during 2008. In 2008 708.3 generators were implanted per million inhabitants. The mean age of the patients who were implanted a PM was 76.3 years, while those who underwent replacement were slightly older, 76.6 years. 80.78% of patients were older than 69 years of age (Table 27). The clinical manifestations responsible for the primary indication of implantation were syncope in 44.5% of the cases, and dizziness in 26.5%. Complete heart block accounted for 33.8% of the ECG indications for the primo implantation, SSS in 20.9% of the cases, and slow atrial fibrillation in 16.5%.

[r] http://www.nvvc.nl/?MID=852

6.8 PORTUGUESE "REGISTO NACIONAL DE PACING"

Only limited data related to the year 2003 are published in a paper originating from the Portuguese Working Group.[57] The EHRA article mentioned above does not provide data from Portugal, whereas the available Eucomed data are limited to the years 2004 through 2008. For 2004, Eucomed reports a total PM implantation rate of 682/million inhabitants. The Portuguese WG reports a total implantation rate in 2003 of 601/million; 16.8% of these are replacements.

6.9 FRENCH «REGISTRE FRANÇAIS DE LA STIMULATION CARDIAQUE»

The most recent article we could retrieve from the French WG are from the year 2002.[58] It describes very limited data originating from 334 centers that implanted 33,850 PMs, representing 65% of PM implantations in France. This indicates that the total number of implants equals 52,077, or 869 implants/million, 28% of which are replacements (Table 27).

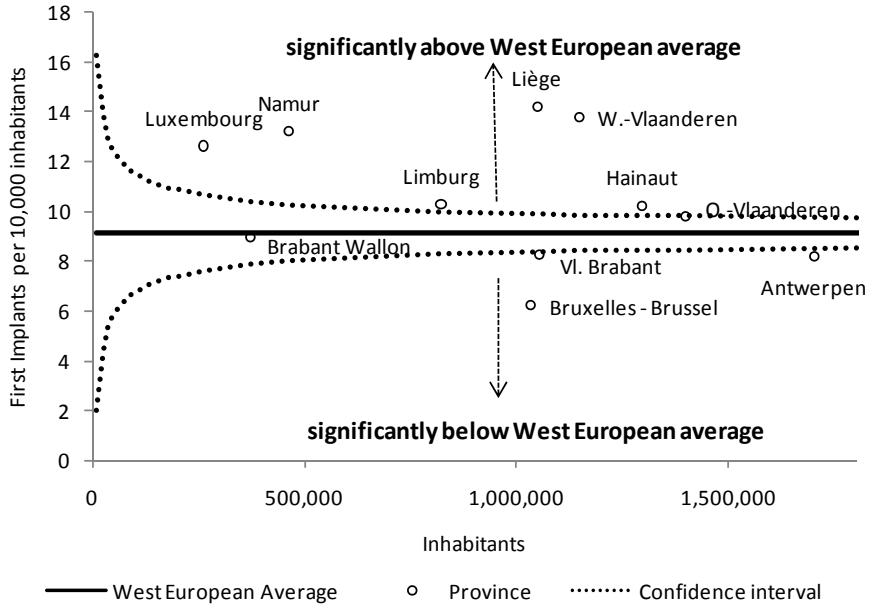
6.10 ITALIAN PACEMAKER REGISTRY

Very recently, a report from the Italian Pacemaker Registry (IPR) was published.[50] It presents Italian PM data from 2003 through 2007. Information was obtained from nearly 60% of the actual implants as indicated by national sales data from a trade organization. For the year 2007, 22,326 primo implantations and 8,820 (28.3%) replacements were registered. These numbers were stable from 2003 through 2007. About 70% of Italian centres participated in the IPR. The median age of patients receiving their first PM was 79 years (inter quartile range: 73-84). The ECG indications were also constant over the years: in 2007 23.6% of PMs were implanted because of 3AVB, 26.8% because of SSS and 18.1% because of slow AF (Table 27).

6.11 COMPARISON OF BELGIAN PRACTICE WITH INTERNATIONAL DATA

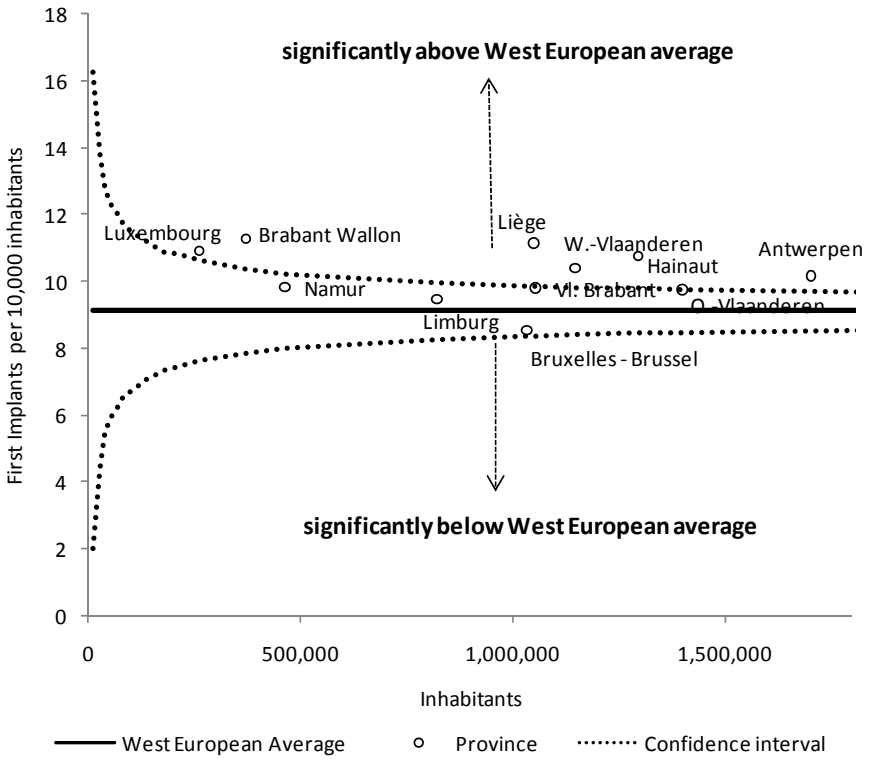
Based on Eucomed data, the total West European implantation rate including conventional pacemakers and CRT-Ps was at the level of 9.1 implants per 10,000 inhabitants in 2007. A comparison of this implantation rate with Belgian implantation rates on the level of provinces reveals to what extent there are statistically significant deviations of the Belgian from the West European total implantation rates. For the actual observed total implantation rates in Belgium, we find Brussels and Antwerpen to fall below the expected limits. In contrast, Luxembourg, Namur, Limburg, Liège, West-Vlaanderen and Hainaut exceed the expected limits, having as such significantly higher total implantation rates than the West European average (Figure 46). Once Belgian implantation rates are adjusted for regional differences in the sex-age distribution, as well as fiscal revenues per capita and the share of foreigners, we find that Luxembourg, Brabant Wallon, Liège, West-Vlaanderen, Hainaut and Antwerpen significantly exceed the West European average (Figure 47).

Figure 46: Observed total Belgian implantation rates per provinces compared to the West European average, per province in 2007



Notes: Own calculations based on IMA-AIM, *Statistics Belgium – Population* and [39]; see section 5.1 for data sources.

Figure 47: Adjusted total Belgian implantation rates per provinces compared to the West European average; including CRT-Ps, adjusted by sex, age, fiscal revenues per capita and the share of foreigners, per province in 2007



Notes: Own calculations based on IMA-AIM, *Statistics Belgium – Population* and [39]; see section 5.1 for data sources.

Countries are heterogeneous in many respects, making comparisons between them difficult and often perceived as unfair. Especially the comparison of observed pacemaker implantation rates without accounting for differences in the demographic and socioeconomic structure of the population might lead to erroneous conclusions. As a first attempt to achieve a fairer comparison, we try in the following to explain international differences in total implantation rates by several structural factors in a multivariate regression framework.[s] Based on OECD, Eurostat and Eucomed data (see chapter 5.1.5), we account for international differences in the share of the population aged 65 and more, the total (public and private) health expenditures as % of GDP, the GDP per capita in $ purchasing-power-parities, the share of the foreign population and annual trends in the growth of implantation rates. The ad hoc choice of the variables is based on the limited availability of data and does not pretend to be comprehensive. In the model framework, the explanatory variables in the year *t* are regressed on the total implantation rate in year *t+1*. The time lag is supposed to strengthen the causal link between the values of explanatory variables, which timely precede the following years' implantation rates. A major constraint of the analysis is the low number of observations: 53 observations for a total of 15 countries. Bigger panels may give better insights into the here mentioned issues, especially because annual changes in the variables are usually small, so a larger time frame is preferable for this kind of analysis. However, misspecification tests carried out after the regression did not point out any technical problems with the regression framework. Therefore, it seems worthwhile not to restrain from presenting the results, which are in fact a first attempt for a fairer comparison of international implantation rates.

After having accounted for differences in these variables between countries, the model reveals whether differences in total implantation rates between countries are still significant at conventional statistical significance levels (Table 28). Only Germany has a significantly higher implantation rate than Belgium. All of the remaining countries included in the estimation – except Italy - have significantly lower total implantation rates. Out of the structural variables, only changes in the share of the foreign population are related to changes in the total implantation rates at statistically significant levels (The same kind of relationship was also revealed at the level of the Belgian communities.).[t] There is also a statistically significant time trend, revealing that compared to the year 2004, implantation rates have risen internationally to higher levels in 2006 and 2007.

[s] The methodology used is a fixed-effect regression framework. For an introduction into this topic see e.g. [59].

[t] When year dummies are excluded, the total healthcare costs as % of GDP, and the GDP per capita are positively and statistically significant related to the change in implantation rates. This signals, that within the available data healthcare costs and GDP per capita must have risen in a majority of countries in question.

Table 28: Determinants of total implantation rates for a sample of 15 West European countries in the time period 2004-2007

Explanatory variables		Coefficient	t-value
Share of pop aged 65+		-0.42	-0.83
Health expenditures as % of GDP		0.43	1.56
GDP per capita		0.09	0.26
Share of foreign population		-0.26**	-2.68
Countries level of implantation rates as compared to Belgium			
Germany		0.16**	2.76
Finland		-0.71***	-4.23
France		-0.24***	-3.28
Greece		-0.56***	-4.72
Ireland		-0.92***	-4.48
Italy		-0.16	-1.36
Netherlands		-0.79***	-6.45
Norway		-0.96***	-8.39
Portugal		-0.68***	-3.01
Sweden		-0.30***	-5.38
Switzerland		-0.32***	-3.05
Spain		-0.41***	-3.53
UK		-0.68***	-6.34
Austria		-0.15***	-4.18
Year trend (Basis 2004)			
	2005	0.05	1.67
	2006	0.08*	2.02
	2007	0.13*	1.99

Notes: 15 countries with a total of 53 observations; R^2= 0.042; F-test for validity of the regression model F(7,31) = 6.43; all variables (except country and year dummies) in logs, as such coefficients show elasticities; Fixed-effect regression model; constant included; Tested for misspecification using STATA's Hausman test, Random-effect model rejected; tested for non-normal distribution and heteroscedesticity of the residuals using Shapiro-Wilk test for normality and the Cook and Weisberg test for heteroscedasticity; All calculations done with STATA 9.2; ***Indicates significance at 1% level; **at 5% level; *at 10% level; Own calculations based on IMA-AIM, *Statistics Belgium – Population*, [39], [43, 44] and [42]; see section 5.1 for data sources.

- **Key points**
- **PM implantation rates in different countries can most reliably be obtained from sales data, delivered by Eucomed, the European Medical Device Trade organisation. Unfortunately, manufacturers' data only deal with the total number of PM sales per country.**
- **By their voluntary nature registries from cardiology associations almost invariably suffer from incompleteness.**
- **Based on Eucomed data, the total West European implantation rate including conventional pacemakers and CRT-Ps was at the level of 9.1 implants per 10,000 inhabitants in 2007. This implantation rate is significantly lower than the implantation rates of six Belgian provinces.**
- **After having accounted for differences in structural factors of regional variation in the use between countries, differences in total implantation rates between countries are still significant at conventional statistical significance levels. Only Germany has a significantly higher implantation rate than Belgium.**

7 DISCUSSION

7.1 THE EVIDENCE THAT SUPPORTS THE USE OF PACEMAKERS

In the present Good Clinical Practice report, the clinical effectiveness of PM therapy has been derived from clinical guidelines as published in the scientific literature. It was beyond the scope of the report to perform a systematic review of the literature on PM effectiveness. PM therapy has been introduced more than 50 years ago for the treatment of complete heart block (CHB) complicated by syncope (so-called "Adams Stokes attacks"). The resulting immediate clinical improvement in these cases is almost miraculous. Over the years, the use of PMs was expanded towards other types of bradycardia, such as sick sinus syndrome (SSS) and slow atrial fibrillation (AF). These arrhythmias represent a heterogeneous mix of conditions, characterised by different grades of severity and a wide variety of symptoms, ranging from recurrent syncope to dizziness. No clinical trials have ever been performed to clearly define the clinical effectiveness of PM therapy in these conditions. Clinical practice of PM therapy mainly rests on expert opinion and consensus. None of the European recommendations on the appropriate use of PM therapy reaches a level of evidence A, indicating that scientific evidence is derived from multiple randomised trials (RCT) or meta-analyses. Only 12 out of 40 recommendations (30%) are supported with a level B evidence (i.e. based on data from a single RCT or large non-randomised studies), whereas the remainder (70%) are essentially based on expert opinion. Out of the 12 level B recommendations, two are related to unexplained syncope and have been attributed a class IIaB recommendation, indicating that "Weight of evidence/opinion is in favour of usefulness/efficacy". Five of the level B recommendations are related to uncommon pacing indications (acute myocardial infarction, muscular dystrophy) and 5 are recommendations against pacing.

The most solid scientific support for PM therapy is for symptomatic patients with complete heart block (3AVB). For this condition, historic evidence demonstrates that permanent pacing abolishes symptoms and increases survival. For some other indications, such as asymptomatic 3AVB, or SSS with prolonged ventricular pauses complicated by recurrent syncope, circumstantial evidence indicates a symptomatic benefit. For others, such as asymptomatic AF with ventricular pauses, or lower grades of AV block, the clinical effectiveness is less certain.

7.2 CONTRIBUTORS TO VARIATION IN THE USE OF PACEMAKERS

Since many years, both in Belgium and in some countries abroad, concerns have been raised about the high number of PMs implanted.[8, 60] In the year 1997, Belgium was reported to have the highest number of primo implantations in the world (585/million), closely followed by the US (571/million) and France (552/million). Among European countries, Belgium reportedly had the highest number of implanting hospitals per million inhabitants: 19.5/million versus a European median of 5.3/million. 2008 Eucomed data confirm the enduring Belgian top ranking with PM sales of 1,126 per million in Belgium, second only to Germany with 1,196 per million (Figure 44).[47] In the UK an opposite story is told, and since many years concerns have risen about a potential underuse of PM therapy, based upon a relatively low number of implants as compared to other European countries and a significant inequality in the provision of devices over the country.[55]

A number of factors that may contribute to the geographic variation in the reported use of PMs are listed in Table 29. These are discussed further in this chapter.

Table 29: Potential contributors to the geographic variation in the reported use of pacemakers

DATA QUALITY and REPORTING BIAS
STRUCTURAL CONTRIBUTORS
DEMOGRAPHIC STRUCTURE
WEALTH
HEALTH CARE SYSTEM
DISEASE and HEALTH CARE RELATED CONTRIBUTORS
DISEASE PREVALENCE and DETECTION
LEVEL OF SCIENTIFIC EVIDENCE
PATIENT'S PREFERENCES
PHYSICIAN'S PREFERENCES

Source: KCE

7.2.1 Data quality

Since many decades, cardiology societies throughout Europe made major efforts to collect data on the use of PMs for treating bradycardia. In Belgium also, a registry based on a voluntary participation has been established since decades. Unfortunately, by their voluntary nature, such registries almost invariably suffer from incompleteness. The data gathered in many of these registries is limited to data available from the European PM Patient ID Card. As explained earlier, this form contains identification data of the patient and of the implanted devices (PM, leads), as well as information on symptoms, electrocardiogram, underlying disease, and indications for the replacement of the PM or the lead(s). However, some of the items are uninformative or unclear. Furthermore, the Card fails to provide information on technical aspects of the surgical procedure, or on early and late complications. As early as 1997, the Danish Pacing Group has collected additional data to those available from the European PM Patient ID Card such as mode of pacing, the reason for deviation from the mode suggested by international guidelines, venous access to the heart, skin-to-skin time, fluoroscopy time, the implanters experience, peri-operative complications and 3 months late complications.[35]

The shortcomings in a number of the international registries make international comparisons difficult, if not impossible. A relatively reliable database – as far as international comparisons of total implantation rates are concerned, is sales data delivered by Eucomed, an international association of manufacturers and suppliers of medical technology. The advantage is that this data comes from one source and provides the number of PMs sold per country. The disadvantage is that, due to international trade, the number of PMs sold may differ from the number of PMs implanted. Also, Eucomed does not provide patient related data.

7.2.2 Structural contributors to regional variation in implantation rates

7.2.2.1 Variation in the use of pacemakers within Belgium

The observed differences in primo implantation rates between Belgian geographic areas are remarkable. In 2007, they ranged from 4.2 to 12.3 implants per 10,000 inhabitants in the *arrondissements* Mouscron and Veurne, respectively. However, several structural factors that impact on the use of PMs between regions may vary and should therefore be accounted for. We find that, if regional implantation rates in Belgium are adjusted by the regional variation in the sex-age distribution of the population, regional fiscal revenues per capita and the share of the foreign population, there are nearly no more significant differences in regional implantation rates.

7.2.2.2 *International variation in the use of pacemakers*

Countries are heterogeneous in many respects, making comparisons between them difficult and often perceived as unfair. However, according the UK's national director for heart disease, "there is increasing evidence from European surveys of heart disease that the epidemiology of conditions for which an implantable device is indicated is similar across that geography".[54] Still, the comparison of observed pacemaker implantation rates without accounting for differences in the demographic and socioeconomic structure of the population might lead to erroneous conclusions. In order to achieve a fairer comparison it is thus important to account for several structural factors, such as depicted in Table 29. In a multivariate regression model we account for differences in some selected factors, such as the share of the population aged 65 and more, the total (public and private) health expenditures as % of GDP, the GDP per capita, the share of the foreign population and annual trends in the growth of implantation rates. Even after this correction, we confirm that in Western Europe only Germany has a significantly higher implantation rate than Belgium.

7.2.3 Disease and health-care related contributors to regional variation

Both AVB and SSS are most often induced by an age dependent degeneration of cardiac structures, and in many patients no specific medical condition that leads to bradycardia can be identified.[1] This is illustrated by the fact that in national registries, for the majority of patients, the reason for a PM primo implantation ("aetiology") in the European PM Patient ID Card is encoded as unspecified (A1), uncoded (A2), unknown (B1) or as conduction tissue fibrosis (B2). In the BeHRA register, between 1993 and 2007, these codes were used between 73.2 and 85.8% of cases. In the Danish 2007 register, in 79.6% of primo implantations, aetiology was encoded as "unknown".

There are no data indicating that in some Western European countries bradycardia provoking diseases are more prevalent than in others. On the other hand, their detection rates may vary. As early as in 1980, it was noticed that unsuspected SSS was progressively more detected because of the increasing use of 24-hours ECG monitoring, potentially leading to an increasing number of PM implants.[10] In a US study, an age standardised increase in the use of PMs from 1990 through 2002 was found to be due to an increase in the number of PM implants because of SSS, the number of PM implants for 3AVB remaining constant.[18]

It has been shown that the less solid the science supporting a given clinical practice, the higher the geographic variation in its application and the higher the number of controversial indications.[61, 62] In this respect, Wennberg has defined "effective care" and "preference sensitive care". *Effective care* consists of evidence-based interventions for which the benefits substantially exceed the harms. This is the case for PM therapy in patients with symptomatic 3AVB and in those with SSS or AF with cardiac arrests in whom it is documented that the bradycardia is directly responsible for the clinical manifestations.[4] *Preference sensitive care* on the other hand encompasses treatment decisions where attitudes or beliefs of patients or doctors may vary. An (unknown) number of cases of PM therapy because of mildly symptomatic SSS or slow AF may be part of this spectrum. This is further illustrated by the fact that both European and US guidelines include not one single class IA recommendation for permanent PM therapy. The propensity to proceed to PM implantation in uncertain cases may differ among physicians, based on the appreciation of a patient's symptoms, the perceived correlation between the symptoms and documented electrocardiographic tracings, the patient's preferences, or the belief of the physician in the technology.

8 CONCLUSIONS

1. The answer to the question whether the Belgian pacing practice is appropriate remains elusive for two main reasons:
   - The clinical guidelines for choosing PM therapy in patients with bradycardia are mainly based on expert opinion and have little rigorous science to back them up.
   - Owing to its voluntary nature, the BeHRA registry inevitably remains incomplete, both with respect to the number of implantations being reported as to the clinical conditions justifying these implantations. The latter limitation holds true for the data originating from the MCD/HBD as well. None of these databases reliably identify the clinical reasons for PM implantations and hence, they cannot be used to assess to what extent international PM guidelines are followed by Belgian cardiologists.
2. The forthcoming mandatory web-based application for PM implantations represents an opportunity to further optimise the registrations. It may also assist in a quality enhancement of the delivered care by registering and surveying the technical aspects of the intervention (lead positioning, X-ray burden, complications) and follow-up issues (device performance).
3. Within Belgium, observed primo implantation rates vary considerably. This variation is strongly related to regional differences in the demographic structure of the population and its socioeconomic characteristics, such as income and the percentage of foreigners. Moreover, within the abovementioned limitations, the data show that Belgian *arrondissements* with lower primo implantation rates have higher percentages of PMs that are implanted because of complete heart block, constituting the most solid indication for PM therapy.
4. Because of the incompleteness of registries and the fact that international insurers' data are not publicly available, one has to rely on sales data provided by manufacturers (Eucomed) to estimate the number of PMs implanted in a given country. Together with Germany and Italy, Belgium has the highest PM sales rate per 10,000 inhabitants in Europe, with figures lying 25% above the Western European average. The reasons for the observed differences across Europe are unclear.

9 APPENDIX

9.1 PACEMAKER AND LEAD RECALLS

9.1.1 European governing context

The enforcement of the harmonised European legislation concerning medical devices is the task of the European member states. The Medical Devices Directives establish specific procedures which the national authorities need to follow when they consider that an unsafe medical device must be withdrawn from the market ("safeguard clause") or when a CE marking is unjustifiably affixed to a device or missing ("wrongly affixed CE marking").

The Federal Agency for Medicines and Health Products (FAMHP, a.k.a. FAGG or AFMPS in respectively the Dutch and French language) is Belgian's national competent agency (NCA) burdened with, amongst other tasks, medical device vigilance.

In this context of European Commission's "comitology", pacemakers and their leads fall into the special category of active implantable medical devices (AIMDs) governed by the European Active Implantable Medical Device Directive (AIMDD).

9.1.2 The medical device vigilance system

The principal purpose of the Medical Device Vigilance System is to improve the protection of the health and safety of patients, users and others by reducing the likelihood of reoccurrence of incidents related to the use of a medical device.

Therefore, the Medical Devices Directives provide that adverse incidents are evaluated and, where appropriate, information is disseminated in the form of a National Competent Authority Report (NCAR) with the objective of preventing repetition of such incidents.[u]

However, it is the task of the manufacturer or his authorised representative to notify the relevant national competent authority about any occurred incidents and field safety corrective actions when the reporting criteria are met. The manufacturer also carries the responsibility for investigating occurred incidents and for taking any corrective actions when necessary.[v]

Nonetheless, and rather remarkably, a 2009 statistics for NCARs report, published by the European Commission's Director General for Health & Consumers, signals for the years 2006 to 2009 a huge discrepancy in the number of NCARs exchanged between NCAs on a European level (see Fig. 1).[w] Forerunner in NCAR exchange is by a large lead Germany, followed by the UK, Ireland, Switzerland and Sweden in that order.

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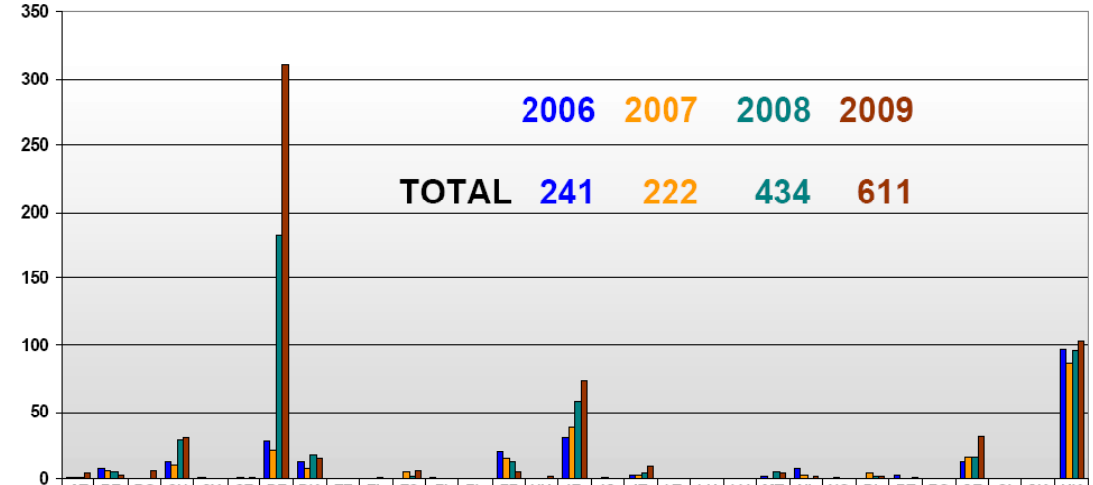
[u] http://ec.europa.eu/enterprise/sectors/medical-devices/market-surveillance-vigilance/index_en.htm

[v] http://ec.europa.eu/enterprise/sectors/medical-devices/files/meddev/2_12_1-rev_6-12-2009_en.pdf

[w] http://ec.europa.eu/enterprise/sectors/medical-devices/files/stats2009_en.pdf

Figure 48: General overview of NCARs exchanged at European level for the years 2006 to 2009



	AT	BE	BG	CH	CY	CZ	DE	DK	EE	EL	ES	FI	FL	FR	HU	IE	IS	IT	LT	LU	LV	MT	NL	NO	PL	PT	RO	SE	SI	SK	UK
2006	1	8		12	1		29	12				1		20		32		3				2	8			3		12			97
2007	1	6		10		1	22	8			5			15		39	1	3					3	1	4			16			87
2008	1	5		30			184	18		1	2			12		58		4				5			2			16			96
2009	4	3	6	32		1	310	15			6			5	2	73		9				4	2		2	1		33			103

9.1.3 The incident reporting system

The manufacturer or his authorised representative must submit an initial incident report to the national competent authority for recording and evaluation. Each initial report must lead to a final report unless the initial and the final report are combined into one report. But not every incident report will lead to a corrective action.

As a general principle, there should be a pre-disposition to report rather than not to report in case of doubt on the reportability of an incident.

Reference to the following considerations may be made in the report, or should be kept on file by the manufacturer in the case of a decision not to report.

Incidents which occurred outside the European economic area (EEA) and Switzerland and do not lead to a field safety corrective action relevant to these geographic areas do not need to be reported. Incidents which occurred outside the EEA and Switzerland and led to a field safety corrective action relevant to the above-mentioned geographical areas must be reported as a field safety corrective action.

9.1.4 Criteria for incidents to be reported by manufacturers to competent authorities

Any event which meets all three basic reporting criteria A – C listed below is considered as an incident and must be reported to the relevant national competent authority. The criteria are that:

A) An event has occurred.

- This also includes situations where testing performed on the device, examination of the information supplied with the device or any scientific information indicates some factor that could lead or has led to an event.
- Typical events include, but are not limited to:

a. A malfunction or deterioration in the characteristics or performance.

A malfunction or deterioration should be understood as a failure of a device to perform in accordance with its intended purpose when used in accordance with the manufacturer's instructions.

b. False positive or false negative test result falling outside the declared performance of the test.

c. Unanticipated adverse reaction or unanticipated side effect

d. Interactions with other substances or products

e. Degradation/destruction of the device (e.g. fire)

f. Inappropriate therapy

g. An inaccuracy in the labelling, instructions for use and/or promotional materials.

Inaccuracies include omissions and deficiencies. Omissions do not include the absence of information that should generally be known by the intended users.

B) The manufacturer's device is suspected to be a contributory cause of the incident

In assessing the link between the device and the incident the manufacturer should take account of:

- the opinion, based on available evidence, of healthcare professionals;
- the results of the manufacturer's own preliminary assessment of the incident;
- evidence of previous, similar incidents;
- other evidence held by the manufacturer.

This judgement may be difficult when there are multiple devices and drugs involved. In complex situations, it should be assumed that the device may have caused or contributed to the incident and the manufacturers should err on the side of caution.

C) The event led, or might have led, to one of the following outcomes:

- death of a patient, user or other person
- serious deterioration in state of health of a patient, user or other person

A serious deterioration in state of health can include:

a. life-threatening illness

b. permanent impairment of a body function or permanent damage to a body structure

c. a condition necessitating medical or surgical intervention to prevent a) or b)

Examples:

- clinically relevant increase in the duration of a surgical procedure
- a condition that requires hospitalisation or significant prolongation of existing hospitalisation

d. any indirect harm as a consequence of an incorrect diagnostic or IVD test results when used within manufacturer´s instructions for use

e. foetal distress, foetal death or any congenital abnormality or birth defects

Note: Not all incidents lead to death or serious deterioration in health. The non-occurrence of such a result might have been due to other fortunate circumstances or to the intervention of healthcare personnel. It is sufficient that:

- an incident associated with a device happened, and
- the incident was such that, if it occurred again, it might lead to death or serious deterioration in health.

9.1.5 Field safety corrective actions

A field safety corrective action (FSCA) is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. Such actions should be notified via a field safety notice (FSN).[x]

More generally speaking, corrective action is any set of actions taken to eliminate the cause of a potential nonconformity or other undesirable situation.[y] Note that there can be more than one cause for non-conformity. Furthermore, corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.

The definition of FSCA has been introduced as an effective synonym for the more commonly used term "recall". The reason is that *there is no harmonised definition of the term "recall" among EEA national competent agencies.*[f]

The FSCA may include:

- the return of a medical device to the supplier;
- device modification;
- device exchange;
- device destruction;
- retrofit by purchaser of manufacturer's modification or design change;
- advice given by manufacturer regarding the use of the device (e.g. where the device is no longer on the market or has been withdrawn but could still possibly be in use)

A device modification can include:

- permanent or temporary changes to the labelling or instructions for use;
- software upgrades including those carried out by remote access;
- modification to the clinical management of patients to address a risk of death or serious deterioration in state of health related specifically to the characteristics of the device. For example:

For implantable devices it is often clinically unjustifiable to explant the device because the clinical risks of explanting the device may outweigh the risks of leaving the device implanted. Corrective action taking the form of special patient follow-up, irrespective of whether any affected unimplanted devices remain available for return, constitutes an FSCA.

- - advice relating to a change in the way the device is used.

9.1.6 Belgian field safety corrective actions as reported by the FAMHP

Belgian field safety corrective actions need to be reported by the manufacturer to the FAMHP, Belgian's national competent agency. Contrary to many other NCAs, the FAMHP has not made its FSCA database publicly available on its website: http://www.fagg-afmps.be (Unfortunately, this also happens to be the case for Eudamed, the European databank for medical devices that could potentially contain FAMPH NCARs.) Upon contacting the FAMPH by e-mail, the FAMHP was able to produce the data needed for this report within the timeframe of approximately one week. Nonetheless, we feel that the barriers to obtaining this kind of information should be kept as low as possible for physicians, patients and the KCE alike.

x, http://ec.europa.eu/enterprise/sectors/medical-devices/files/meddev/2_12_1-rev_6-12-2009_en.pdf
y EN ISO 9000:2000, 3.6.5

Table 1: An overview of the Belgian field safety corrective actions as reported by the FAMHP for the years 2001 to 2007

date	manufacturer	action	trademark	model number	defect	preliminaries	affected implanted devices in Belgium	confirmed prophylactic explantations in Belgium
2001	St Jude Medical	recall	Tempo en Meta IPG	TEMPO: 1102, 1902, 2102, 2902 - META: 1256	Dendritic growth at the hybrid-battery connection site (bridge □short circuit □loss of output or telemetry, abnormal telemetry or premature EOL)	Extension of warning of 2000.06, with specific mentioning of risk of loss of output or abnormal sensing or output.	3014	240
2002.11	St Jude Medical	recall of certain serial numbers	Tempo en Meta IPG	TEMPO 2102 and META 1256D	Dendritic growth at the hybrid-battery connection site (bridge □short circuit □ loss of output or telemetry, abnormal telemetry or premature EOL)		239	no data
2002.11	St Jude Medical	recall	Tempo en Meta IPG	TEMPO: 1102, 1902, 2102, 2902 - META: 1256 certain serial numbers		Extension of warning of 2000.06, with specific mentioning of risk of loss of output or abnormal sensing or output.	346	71
2003.12	St Jude Medical	recall	REGENCY	2400L 2402L 2406L 2407M/S			1	no data
			MICRONY	2525T				
			VERITY	5156				
			IDENTITY	5172				
			ENTITY	5226 5326				
			AFFINITY	5230				
			INTEGRITY	5346				
2002.03	Medtronic	recall	Kappa IPG	700/600 dual chamber series	Risk of fractured wires supplying power to the pacemaker circuitry with sub-muscular implantation		no data	no data
2004.06	Medtronic	recall of non-implanted devices, firmware update via programmer of implanted devices	Kappa IPG	KVDD 701/901: 30 serial numbers	Affected units inaccurately display an error message on the programmer when undergoing interrogation		1	no data
2005.07	Guidant	recall of certain serial numbers	PULSAR MAX	1170, 1171, 1270	A hermetic sealing component experiences a gradual degradation resulting in higher than normal moisture content within the pacemaker case late in device's service life. Risk of loss of pacing or sustained MSR pacing, the latter potentially producing heart failure.		1415	no data*
			PULSAR	0470, 0870, 0970, 0972, 1172, 1272				
			DISCOVERY	1174, 1175, 1273, 1274, 1275				
			MERIDIAN	0476, 0976, 1176, 1276				
			PULSAR MAX II	1180, 1181, 1280				
			DISCOVERY II	0481,0981, 1184, 1186, 1187, 1283, 1284, 1285, 1286				
			VIRTUS PLUS II	1380, 1480				
			INTELIS II	1483, 1484, 1485, 1384, 1385, 1349, 1499				

Table 1: An overview of the Belgian field safety corrective actions as reported by the FAMHP for the years 2001 to 2007 (continued)

date	manufacturer	action	trademark	model number	defect	preliminaries	affected implanted devices in Belgium	confirmed prophylactic explantations in Belgium
2005.09	Guidant	recall	INSIGNIA Entra SSI	0484, 0485	Foreign material within a crystal timing component ☐ Failure modes: Intermittent or permanent loss of pacing without warning, reversion to VVI mode or appearance of a reset warning upon interrogation; no output at implantation		2418	no data*
			INSIGNIA Entra DDD	0985, 0986				
			INSIGNIA Entra DR	1294, 1295, 1296				
			INSIGNIA Entra SR	1195, 1198				
			INSIGNIA Ultra DR	1290, 1291				
			INSIGNIA Ultra SR	1190				
			INSIGNIA Plus SR	1297, 1298				
			INSIGNIA Plus DR	1194				
			INSIGNIA AVT SSI	482				
			INSIGNIA AVT VDD	882				
			INSIGNIA AVT DDD	982				
			INSIGNIA AVT DR	1192				
			INSIGNIA AVT SR	1292				
			NEXUS Entra SSI	1325, 1326				
			NEXUS Entra DDD	1425, 1426				
			NEXUS Entra SR	1395, 1398				
			NEXUS Entra DR	1466, 1494, 1495				
			NEXUS Ultra DR	1490, 1491				
			NEXUS Entra SR	1390				
			NEXUS Plus SR	1394				
			NEXUS Entra DR	1467, 1468				
			NEXUS AVT VDD	1428				
			NEXUS AVT SSI	1328				
			NEXUS AVT DDD	1432				
			NEXUS AVT SR	1392				
			NEXUS AVT DR	1492				
2006.01	Guidant	recall				Extension of 2005.07 recall	3	no data*
2006.06	Guidant	recall	INSIGNIA	482, 484, 485, 882, 982, 985, 986, 1190, 1192, 1194, 1195, 1198, 1290, 1291,1292, 1294, 1295, 1296, 1298	Defect in low voltage capacitor ☐ Intermittent or permanent loss of therapy or premature battery depletion		no data	no data*
			NEXUS	1325, 1326, 1328, 1390, 1392, 1394, 1395, 1398, 1426, 1428, 1432, 1466, 1467, 1468, 1490, 1491, 1492, 1494, 1495				
2006.08	Guidant	information				Update of product advisory letter of 2006.06		
11							7437	311

Note * : A representative of Guidant (now Boston Scientific) confirmed the prophylactic explantation with most patient-dependent patients.

Table 1 lists the pacemaker (not including CRT-P nor pacemaker programmer or other peripherals) and pacemaker lead and adapter related FSCAs as recorded by the FAMPH for the years 2001 to 2007. The year 2001 was included in order to measure possible prophylactic explantation effects for the year 2002.

As can be deduced from this table, there were 11 recorded FSCAs in Belgium, of which one was an informative action and the other 10 constitute a "recall" action that could potentially have led to prophylactic explantations. Over the above-mentioned time period, the latter type of FSCA affected at least 7437 devices in Belgium and resulted in at least 311 confirmed prophylactic explantations, not including the effectively affected devices that were among the reported provoking incidents.

However, the real number of prophylactic explantations is most probably much higher as a representative of Guidant (now Boston Scientific) confirmed the prophylactic explantation with most patient-dependent patients with respect to the 2005-2006 FSCAs of that manufacturer.

In view of Figure 1 indicating a significant higher incidence of NCARs originating from Germany, the FAMPH-reported FSCAs were compared to the FSCAs reported by BFArM, the German national competent agency for the years 2005 to 2007. This data was retrieved from the publicly accessible database on the BFArM website.[z]

Data prior to 2005 was not available.

As can be inferred from Table 2, BFArM registered 8 FSCAs of which 4 (indicated in grey) were not registered by the FAMPH. Cross-checking with the BeHRA database showed that most probably at least one of these 4 FSCAs pertain to pacemaker models that may have been implanted in Belgium. The other 3 FSCAs may anyhow be relevant to Belgian healthcare professionals albeit due to Germany's vicinity.

The above indicates a potential Belgian compliance problem with the reporting of and/or registering of FSCAs. The number of FSCA-affected pacemakers as well as the number of prophylactic explantations can therefore be higher in Belgium than the numbers as inferred from the FAMPH data.

Table 30: An overview of the German field safety corrective actions as reported by the BFArM for the years 2001 to 2007

starting date	corrective action as reported by BFArM	action	reported by FAMPH
2005.11.24	Ausfall der Stimulation bei Ela Medical Herzschrittmachern Symphony und Rhapsody		no
2005.11.24	Rückruf der Guidant -Herzschrittmacher Insignia und Nexus	recall	yes
2005.12.22	Mögliches Therapieversagen bei Sigma-Herzschrittmachern von Medtronic		no
2006.02.16	Rückruf der Untergruppen der Schrittmacher Pulsar, Pulsar Max, Pulsar Max II, Discovery, Discovery II, Meridian, Virtus Plus II und Intelis II von Guidant	recall	yes
2006.07.06	Information zu Untergruppen der INSIGNIA und NEXUS Herzschrittmacher von Guidant		yes
2006.09.06	Information von Guidant zu Untergruppen der INSIGNIA und NEXUS Herzschrittmacher		yes
2007.03.01	Rückruf der implantierbaren Zweikammer-Herzschrittmacher der C- und T-Serie von Vitatron	recall	no
2007.07.17	Rückruf der NEWAY DR Schrittmacher von Sorin	recall	no
8			4

z http://www.bfarm.de/cln_012/nn_424458/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html__nnn=true

9.2 CRITICAL APPARAISAL OF GUIDELINES

The methodological quality of these PM GLs were critically appraised independently by two reviewers (Hans Van Brabandt, Joan Vlayen - KCE) using the AGREE instrument, depicted below. The latter "*assesses both the quality of the reporting, and the quality of some aspects of recommendations. It provides an assessment of the predicted validity of a guideline, that is the likelihood that it will achieve its intended outcome. It does not assess the impact of a guideline on patients' outcomes*". [aa] For the present report, only the recommendations related to conventional PM therapy from these GLs were considered.

Table 31 summarises the result of the appraisal of the European [2] and the US [4] guidelines. Each item is rated on a 4-point scale ranging from 4 (Strongly Agree) to 1 (Strongly Disagree), with two mid points: 3 (Agree) and 2 (Disagree). The table shows per item the individual score and the average of both assessors. Domain scores are calculated by summing up all the scores of the individual items in a domain and by standardising the total as a percentage of the maximum possible score for that domain. If both assessors would award a 4 on each item within a domain, the resulting domain score would be 100%. If they both scored each item a 1, the resulting domain score would be 0%. For the overall assessment, one of four options had to be selected by each appraiser in order to make a judgment as to the quality of the guideline: 'Strongly recommend', 'Recommend (with provisos or alterations)', 'Would not recommend' and 'Unsure'.

Table 31: Appraisal of guidelines by using the AGREE instrument

	European GL			US' GL		
Appraiser #	1	2	Mean	1	2	Mean
Domain 1. Scope and Purpose						
1. overall objective	3	3	3,0	3	3	3,0
2. clinical questions	3	4	3,5	3	4	3,5
3. patient population	2	2	2,0	2	2	2,0
Domain score	*55,6*	*66,7*	***61,1***	*55,6*	*66,7*	***61,1***
Domain 2. Stakeholder Involvement						
4. all relevant professional groups	2	2	2,0	3	4	3,5
5. patients views and preferences	3	1	2,0	3	1	2,0
6. target users	2	3	2,5	2	3	2,5
7. pilot test	1	1	1,0	1	1	1,0
Domain score	*33,3*	*25,0*	***29,2***	*41,7*	*41,7*	***41,7***
Domain 3. Rigour of Development						
8. systematic search	1	1	1,0	2	2	2,0
9. selection criteria	1	1	1,0	3	1	2,0
10. formulation of recommendations	2	1	1,5	3	3	3,0
11. benefits, side effects and risks	4	2	3,0	4	1	2,5
12. explicit link	4	1	2,5	4	4	4,0
13. external review	3	4	3,5	3	4	3,5
14. update procedure	1	1	1,0	3	4	3,5
Domain score	*42,9*	*19,0*	***31,0***	*71,4*	*57,1*	***64,3***
Domain 4. Clarity and Presentation						
15. specific and unambiguous	4	4	4,0	4	3	3,5
16. different options for management	4	2	3,0	4	1	2,5
17. key recommendations	4	4	4,0	4	4	4,0
18. tools for application	3	1	2,0	1	1	1,0
Domain score	*91,7*	*58,3*	***75,0***	*75,0*	*41,7*	***58,3***
Domain 5. Applicability						
19. organisational barriers	4	1	2,5	2	1	1,5
20. possible cost implications	3	1	2,0	4	3	3,5
21. key review criteria	1	1	1,0	1	1	1,0
Domain score	*55,6*	*0,0*	***27,8***	*44,4*	*22,2*	***33,3***
Domain 6. Editorial Independence						
22. editorially independent	2	4	3,0	1	3	2,0
23. conflicts of interest	3	4	3,5	4	4	4,0
Domain score	*50,0*	*100,0*	***75,0***	*50,0*	*83,3*	***66,7***
Number of items (out of 23) scoring ≥3	**13**	**8**	**9**	**15**	**13**	**11**
Number of domains (out of 6) scoring >60%	**1**	**2**	**3**	**2**	**2**	**3**
Recommend?	Would not recommend	Unsure		Recommend (with provisos or alterations)	Recommend (with provisos or alterations)	

Highlighted in yellow (light grey): items with a mean score of max 2. Highlighted in orange (dark grey): items with in both GLs mean score of max 2.

[aa] http://www.agreecollaboration.org/pdf/agreeinstrumentfinal.pdf

Within the domain "Scope and purpose" in the AGREE instrument, a number of important questions remain unanswered regarding the item "Patient population". It is obvious that the overall objective of the GLs is to provide recommendations on the treatment of patients with certain symptoms that occur in combination with distinct electrocardiographic abnormalities, but many of these elements are poorly described. The GLs do not define symptoms such as near-syncope, dizziness, fatigue, reduced exercise capacity or cognitive impairment and light headedness, although these are all considered as potential symptoms of bradycardia that might be amenable to PM therapy. The European GL does not address chronic AF in its GL, although this arrhythmia accounts for up to 22% of primo implantations in EU countries.[49] The US GL defines a prolonged pause in the setting of AF as "greater than 5 seconds", which it considers as advanced second-degree AVB, but otherwise it does not address the issue of PM therapy in chronic AF. The 1998 European GL on AF[34] applies a class I recommendation ("agreement that a PM should be implanted") for PM therapy in patients with chronic AF and symptomatic bradycardia that is related to the concomitant use of necessary AVN depressant drugs. The notion of "necessary drugs" however remains undefined. Unfortunately, in the 2006 GL on AF, jointly prepared by the ACC/AHA the ESC, PM therapy in patients with chronic AF is discussed in relation with AVN ablation only.[29] Both GLs perform inadequately with respect to the methodology that was reportedly followed in the systematic review of the scientific literature (item #8). Details of the strategy used to search for evidence (search terms used, sources consulted and dates of the literature covered) were not provided. As a corollary, criteria for including or excluding evidence identified by the search (item #9) are not provided. Item #10 of the AGREE instrument refers to a description of the methods used to formulate the recommendations and how final decisions were arrived at. Methods could include a voting system, or formal consensus techniques (e.g. Delphi panels). This item is not addressed in any of the GLs, although it might be particularly relevant for a GL in which recommendations are mostly derived from expert consensus (i.e. level of evidence C).

With only 9 out of 23 items on the AGREE instrument scoring 3 (agree) or 4 (strongly agree), the overall assessment of the European GL is at best to be labelled as "unsure", indicating that the appraisers of the GL are in doubt about their "*confidence that the potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice*". The US GL overall appraisal is superior to the European, essentially because of a better score in the "Rigour of development" domain.

9.2.1 The Agree Instrument

Appendix 3. Short appraisal form (please circle your answer)

SCOPE AND PURPOSE

1.	The overall objective(s) of the guideline is (are) specifically described.	Strongly Agree	1 2 3 4 Strongly Disagree
2.	The clinical question(s) covered by the guideline is (are) specifically described.	Strongly Agree	1 2 3 4 Strongly Disagree
3.	The patients to whom the guideline is meant to apply are specifically described.	Strongly Agree	1 2 3 4 Strongly Disagree

STAKEHOLDER INVOLVEMENT

4.	The guideline development group includes individuals from all the relevant disciplines or stakeholders.	Strongly Agree	1 2 3 4 Strongly Disagree
5.	The patients' views and preferences have been sought.	Strongly Agree	1 2 3 4 Strongly Disagree
6.	The target users of the guideline are clearly defined.	Strongly Agree	1 2 3 4 Strongly Disagree
7.	The guideline has been piloted among target users.	Strongly Agree	1 2 3 4 Strongly Disagree

METHODOLOGY

8.	Systematic methods were used to search for evidence.	Strongly Agree	1 2 3 4 Strongly Disagree
9.	The criteria for selecting the evidence are clearly described.	Strongly Agree	1 2 3 4 Strongly Disagree
10.	The methods used for formulating the recommendations are clearly described.	Strongly Agree	1 2 3 4 Strongly Disagree
11.	The health benefits, side effects and risks have been considered in formulating the recommendations.	Strongly Agree	1 2 3 4 Strongly Disagree
12.	There is an explicit link between the recommendations and the supporting evidence.	Strongly Agree	1 2 3 4 Strongly Disagree
13.	The guideline has been externally reviewed by experts prior to publication.	Strongly Agree	1 2 3 4 Strongly Disagree

14.	A procedure for updating the guideline is provided.	Strongly Agree	1	2	3	4	Strongly Disagree

CLARITY AND PRESENTATION

15.	The recommendations are specific and unambiguous.	Strongly Agree	1	2	3	4	Strongly Disagree
16.	The different options for management of the condition are clearly presented.	Strongly Agree	1	2	3	4	Strongly Disagree
17.	Key recommendations are easily identifiable.	Strongly Agree	1	2	3	4	Strongly Disagree
18.	The guideline is supported with tools for application.	Strongly Agree	1	2	3	4	Strongly Disagree

APPLICABILITY

19.	The potential organisational barriers in applying the guideline have been discussed.	Strongly Agree	1	2	3	4	Strongly Disagree
20.	The potential costs implications of applying the recommendations have been considered.	Strongly Agree	1	2	3	4	Strongly Disagree
21.	The guideline presents key review criteria for monitoring and/or audit purposes.	Strongly Agree	1	2	3	4	Strongly Disagree

METHODOLOGY

22.	The guideline is editorially independent from the funding body.	Strongly Agree	1	2	3	4	Strongly Disagree
23.	Conflicts of interest of guideline development members have been recorded.	Strongly Agree	1	2	3	4	Strongly Disagree

OVERALL ASSESSMENT

Would you recommend this guideline for use in practice?

- ☐ Strongly recommend
- ☐ Recommend (with provisos or alterations)
- ☐ Would not recommend
- ☐ Unsure

Adapted from: The AGREE Collaboration. Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument. www.agreecollaboration.org.

9.3 EUROPEAN SOCIETY OF CARDIOLOGY 2007 GUIDELINES

#	RECOMMENDATION	CLASS
	Sinus node disease	
1	Sinus node disease manifests as symptomatic bradycardia with or without bradycardia-dependent tachycardia. Symptom–rhythm correlation must have been (1) spontaneously occurring, or (2) drug induced where alternative drug therapy is lacking	IC
2	Syncope with sinus node disease, either spontaneously occurring or induced at electrophysiological study	IC
3	Sinus node disease manifests as symptomatic chronotropic incompetence: spontaneously occurring drug induced where alternative drug therapy is lacking	IC
4	Symptomatic sinus node disease, which is either spontaneous or induced by a drug for which there is no alternative, but no symptom rhythm correlation has been documented. Heart rate at rest should be <40 b.p.m.	IIaC
5	Syncope for which no other explanation can be made but there are abnormal electrophysiological findings (CSNRT > 800 ms)	IIaC
6	Minimally symptomatic patients with sinus node disease, resting heart rate <40 b.p.m. while awake, and no evidence of chronotropic incompetence	IIbC
7	Sinus node disease without symptoms including use of bradycardia-provoking drugs	IIIC
8	ECG findings of sinus node dysfunction with symptoms not due directly or indirectly to bradycardia	IIIC
9	Symptomatic sinus node dysfunction where symptoms can reliably be attributed to non-essential medication	IIIC
	Acquired atrioventricular block	
10	Chronic symptomatic third- or second-degree (Mobitz I or II) atrioventricular block	IC
11	Neuromuscular diseases (e.g. Myotonic muscular dystrophy, Kearns–Sayre syndrome, etc.) with third- or second-degree atrioventricular block	IB
12	Third- or second-degree (Mobitz I or II) atrioventricular block: (i) after catheter ablation of the atrioventricular junction (ii) after valve surgery when the block is not expected to resolve	IC
13	Asymptomatic third- or second-degree (Mobitz I or II) atrioventricular block	IIaC
14	Symptomatic prolonged first-degree atrioventricular block	IIaC

15	Neuromuscular diseases (e.g. Myotonic muscular dystrophy, Kearns–Sayre syndrome, etc.) with first-degree atrioventricular block	IIbB
16	Asymptomatic first-degree atrioventricular block	IIIC
17	Asymptomatic second-degree Mobitz I with supra-Hisian conduction block	IIIC
18	Atrioventricular block expected to resolve	IIIC
Intraventricular conduction disturbances		
19	Intermittent third-degree atrioventricular block	IC
20	Second-degree Mobitz II atrioventricular block	IC
21	Alternating bundle branch block	IC
22	Findings on electrophysiological study of markedly prolonged HV interval (>100 ms) or pacing-induced infra-His block in patients with symptoms	IC
23	Syncope not demonstrated to be due to atrioventricular block when other likely causes have been excluded, specifically ventricular tachycardia	IIaB
24	Neuromuscular diseases (e.g. Myotonic muscular dystrophy, Kearns–Sayre syndrome, etc.) with any degree of fascicular block	IIaC
25	Incidental findings on electrophysiological study of markedly prolonged HV interval (>100 ms) or pacing-induced infra-His block in patients without symptoms	IIaC
26	Bundle branch block without atrioventricular block or symptoms	IIIB
27	Bundle branch block with first-degree atrioventricular block without symptoms	IIIB
Recent myocardial infarction		
28	Persistent third-degree heart block preceded or not by intraventricular conduction disturbances	IB
29	Persistent Mobitz type II second-degree heart block associated with bundle branch block, with or without PR prolongation	IB
30	Transient Mobitz type II second- or third-degree heart block associated with new onset bundle branch block	IB
31	Transient second- or third-degree heart block without bundle branch block	IIIB
32	Left anterior hemiblock newly developed or present on admission	IIIB
33	Persistent first-degree atrioventricular block	IIIB
Reflex syncope		

34	Recurrent syncope caused by inadvertent carotid sinus pressure and reproduced by carotid sinus massage, associated with ventricular asystole of more than 3 s duration (patient may be syncopal or pre-syncopal), in the absence of medication known to depress sinus node activity	IC
35	Recurrent unexplained syncope, without clear inadvertent carotid sinus pressure, but syncope is reproduced by carotid sinus massage, associated with a ventricular asystole of more than 3 s duration (patient may be syncopal or pre-syncopal), in the absence of medication known to depress sinus node activity	IIaB
36	First syncope, with or without clear inadvertent carotid sinus pressure, but syncope (or pre-syncope) is reproduced by carotid sinus massage, associated with a ventricular asystole of more than 3 s duration, in the absence of medication known to depress sinus node activity	IIbC
37	Hypersensitive carotid sinus reflex without symptoms	IIIC
38	Patients over 40 years of age with recurrent severe vasovagal syncope who show prolonged asystole during ECG recording and/or tilt testing, after failure of ther therapeutic options and being informed of the conflicting results of trials	IIaC
39	Patients under 40 years of age with recurrent severe vasovagal syncope who show prolonged asystole during ECG recording and/or tilt testing, after failure of other therapeutic options and being informed of the conflicting results of trials	IIbC
40	Patients without demonstrable bradycardia during reflex syncope	IIIC

9.4 ACC/AHA/HRS 2008 GUIDELINES

#	RECOMMENDATION	CLASS
	Sinus node dysfunction	
1	Permanent pacemaker implantation is indicated for SND with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms.	IC
2	Permanent pacemaker implantation is indicated for symptomatic chronotropic incompetence.	IC
3	Permanent pacemaker implantation is indicated for symptomatic sinus bradycardia that results from required drug therapy for medical conditions.	IC
4	Permanent pacemaker implantation is reasonable for SND with heart rate less than 40 bpm when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented	IIaC
5	Permanent pacemaker implantation is reasonable for syncope of unexplained origin when clinically significant abnormalities of sinus node function are discovered or provoked in electrophysiological studies.	IIaC
6	Permanent pacemaker implantation may be considered in minimally symptomatic patients with chronic heart rate less than 40 bpm while awake.	IIbC
7	Permanent pacemaker implantation is not indicated for SND in asymptomatic patients.	IIIC
8	Permanent pacemaker implantation is not indicated for SND in patients for whom the symptoms suggestive of bradycardia have been clearly documented to occur in the absence of bradycardia.	IIIC
9	Permanent pacemaker implantation is not indicated for SND with symptomatic bradycardia due to nonessential drug therapy.	IIIC
	Acquired atrioventricular block	
10	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level associated with bradycardia with symptoms (including heart failure) or ventricular arrhythmias presumed to be due to AV block.	IC
11	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level associated with arrhythmias and other medical conditions that require drug therapy that results in symptomatic bradycardia.	IC
12	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients in sinus rhythm, with documented periods of asystole greater than or equal to 3.0 seconds or any escape rate less than 40 bpm, or with an escape rhythm that is below the AV node.	IC

13	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer.	IC
14	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level after catheter ablation of the AV junction.	IC
15	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level associated with postoperative AV block that is not expected to resolve after cardiac surgery.	IC
16	Permanent pacemaker implantation is indicated for third degree and advanced second-degree AV block at any anatomic level associated with neuromuscular diseases with AV block, such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy, with or without symptoms.	IB
17	Permanent pacemaker implantation is indicated for second-degree AV block with associated symptomatic bradycardia regardless of type or site of block.	IB
18	Permanent pacemaker implantation is indicated for asymptomatic persistent third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster if cardiomegaly or LV dysfunction is present or if the site of block is below the AV node.	IB
19	Permanent pacemaker implantation is indicated for second or third-degree AV block during exercise in the absence of myocardial ischemia.	IC
20	Permanent pacemaker implantation is reasonable for persistent third-degree AV block with an escape rate greater than 40 bpm in asymptomatic adult patients without cardiomegaly.	IIaC
21	Permanent pacemaker implantation is reasonable for asymptomatic second-degree AV block at intra- or infra- His levels found at electrophysiological study.	IIaB
22	Permanent pacemaker implantation is reasonable for first or second-degree AV block with symptoms similar to those of pacemaker syndrome or hemodynamic compromise.	IIaB
23	Permanent pacemaker implantation is reasonable for asymptomatic type II second-degree AV block with a narrow QRS. When type II second-degree AV block occurs with a wide QRS, including isolated right bundlebranch block, pacing becomes a Class I recommendation. (See Section 2.1.3, "Chronic Bifascicular Block.")	IIaB
24	Permanent pacemaker implantation may be considered for neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy with any degree of AV block (including first-degree AV block), with or without symptoms, because there may be unpredictable progression of AV conduction disease.	IIbB
25	Permanent pacemaker implantation may be considered for AV block in the setting of drug use and/or drug toxicity when the block is expected to recur even after the drug is withdrawn.	IIbB

26	Permanent pacemaker implantation is not indicated for asymptomatic first-degree AV block.	IIIB
27	Permanent pacemaker implantation is not indicated for asymptomatic type I second-degree AV block at the supra-His (AV node) level or that which is not known to be intra- or infra-Hisian.	IIIC
28	Permanent pacemaker implantation is not indicated for AV block that is expected to resolve and is unlikely to recur100 (e.g., drug toxicity, Lyme disease, or transient increases in vagal tone or during hypoxia in sleep apnea syndrome in the absence of symptoms).	IIIB
	Intraventricular conduction disturbances	
29	Permanent pacemaker implantation is indicated for advanced second-degree AV block or intermittent third degree AV block.	IB
30	Permanent pacemaker implantation is indicated for type II second-degree AV block.	IB
31	Permanent pacemaker implantation is indicated for alternating bundle-branch block.	IC
32	Permanent pacemaker implantation is reasonable for syncope not demonstrated to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia (VT).	IIaB
33	Permanent pacemaker implantation is reasonable for an incidental finding at electrophysiological study of a markedly prolonged HV interval (greater than or equal to 100 milliseconds) in asymptomatic patients.	IIaB
34	Permanent pacemaker implantation is reasonable for an incidental finding at electrophysiological study of pacinginduced infra-His block that is not physiological.	IIaB
35	Permanent pacemaker implantation may be considered in the setting of neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy with bifascicular block or any fascicular block, with or without symptoms.	IIbC
36	Permanent pacemaker implantation is not indicated for fascicular block without AV block or symptoms.	IIIB
37	Permanent pacemaker implantation is not indicated for fascicular block with first-degree AV block without symptoms.	IIIB
	Recent myocardial infarction	
38	Permanent ventricular pacing is indicated for persistent second-degree AV block in the His-Purkinje system with alternating bundle-branch block or third-degree AV block within or below the His-Purkinje system after ST-segment elevation MI.	IB
39	Permanent ventricular pacing is indicated for transient advanced second- or third-degree infranodal AV block and associated bundle-branch block. If the site of block is uncertain, an electrophysiological study may be necessary.	IB
40	Permanent ventricular pacing is indicated for persistent and symptomatic second- or third-degree AV block.	IC
41	Permanent ventricular pacing may be considered for persistent second- or third-degree AV block at the AV node level, even in the absence of symptoms.	IIbB

42	Permanent ventricular pacing is not indicated for transient AV block in the absence of intraventricular conduction defects.	IIIB
43	Permanent ventricular pacing is not indicated for transient AV block in the presence of isolated left anterior fascicular block.	IIIB
44	Permanent ventricular pacing is not indicated for new bundle-branch block or fascicular block in the absence of AV block.	IIIB
45	Permanent ventricular pacing is not indicated for persistent asymptomatic first-degree AV block in the presence of bundle-branch or fascicular block.	IIIB
Reflex syncope		
46	Permanent pacing is indicated for recurrent syncope caused by spontaneously occurring carotid sinus stimulation and carotid sinus pressure that induces ventricular asystole of more than 3 seconds.	IC
47	Permanent pacing is reasonable for syncope without clear, provocative events and with a hypersensitive cardioinhibitory response of 3 seconds or longer.	IIaC
48	Permanent pacing may be considered for significantly symptomatic neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tilt-table testing.	IIbB
49	Permanent pacing is not indicated for a hypersensitive cardioinhibitory response to carotid sinus stimulation without symptoms or with vague symptoms.	IIIC
50	Permanent pacing is not indicated for situational vasovagal syncope in which avoidance behavior is effective and preferred.	IIIC

Highlighted rows: class I (green) or IIa (yellow).

9.5 REIMBURSEMENT NOMENCLATURE CODES OF INTEREST

Amb	Hosp	Label
476210	476221	Monitoring Holter : continu elektrocardiografisch registreren gedurende ten minste 24 uur,door middel van een draagbaar toestel met magneetband of met ingebouwd geheugen, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel, met protocol en mogelijkheid tot reproduceren van de volledige tracés
476232	476243	Herhaling binnen een jaar van verstrekking nr 476210 - 476221
476254	476265	Monitoring Holter : continue electrocardiografische analyse gedurende ten minste 24 uur, door middel van draagbaar toestel, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel met protocol en mogelijkheid tot reproduceren van een deel van de tracés
476276	476280	Uitgebreid electrofysiologisch onderzoek voor het opwekken en beëindigen van tachycardieën met behulp van drie of meer catheters,inclusief afname van bloedstalen, radioscopische en electrocardiografische controles, toediening van farmaca en contraststoffen, met protocol en tracés
476291	476302	Beperkt elektrofysiologisch onderzoek tot studie van de sinusknoopfunctie en van de atrioventriculaire geleiding met behulp van een of meerdere catheters met inbegrip van de electrocardiografische opnamen
476313	476324	Diagnose en/of behandeling van tachycardieën door middel van electrische prikkels via één of meerdere endocavitair geplaatste catheters met inbegrip van de electrocardiografische opnamen
476335	476346	Tilt-test op 60° met minimumduur van 45' of tot optreden van syncope, onder continue electrocardiografische controle en niet-invasieve bloeddrukmonitoring, al dan niet met toediening van farmaca, met protocol
475834	475845	Registratie met kwalitatieve en kwantitatieve analyse van een elektrocardiografie met hoge amplitudo via orthogonale afleidingen ter opsporing van abnormale potentialen, bij gedokumenteerd kamerarythmia-risico, met protocol
687514	687525	Elektrodekatheter(s), intracavitair of in de slokdarm, voor tijdelijk elektrosystolisch stimuleren van het hart
229110	229121	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar
229132	229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar
229154	229165	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar
229176	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
475952	475963	Implantatie langs transveneuze weg van een linker kamer elektrode, verbonden aan een pacemaker of een hartdefibrillator
684530	684541	Eerste implanteerbare hartstimulator, inclusief adaptor
684655	684666	Voortijdige hernieuwing van de hartstimulator (artikel 35, § 11, 4° van de nomenclatuur)
684375	684386	Vervangingshartstimulator, inclusief adaptor
685731	685742	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode

685753	685764	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685775	685786	Implanteerbare myocardiale elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685790	685801	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
691795	691806	Endocardiale uni- of bipolaire of myocardiale pacemaker-elektrode
691810	691821	Single-pass pacemaker-elektrode (VVD)
691832	691843	Percutaan geplaatste linkerventrikel resynchronisatie-elektrode
691854	691865	Epicardiaal geplaatste linkerventrikel resynchronisatie-elektrode
475635	475646	Controle van de deugdelijkheid van een ingeplante hartstimulator door foto-analyse van de prikkel
475893	475904	Controle van de deugdelijkheid en/of herprogrammatie van een hartdefibrillator, met meting van de stimulatie- en gevoeligheidsdrempel en met evaluatie van de performantie van de defibrillator, met protocol en tracés
475856	475860	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
475871	475882	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
589433	589444	Percutane extractie van een elektrode bij een patiënt met een ingeplante hartstimulator of een ingeplante hartdefibrillator of percutaan verwijderen van een intracardiaal vrijzittend vreemd lichaam, met uitsluiting van de farmaceutische produkten, de contrastmiddelen en het wegwerpmateriaal
475930	475941	Herpositioneren van één of meerdere hartelektroden, op een andere dag dan de implantatie
229655	229666	Heelkundige extractie van een met de vaatwand vergroeide intracavitaire elektrode wegens infectie of elektrische malfunctie bij een patiënt met een ingeplante hartstimulator of defibrillator met behulp van de excimer laser, al dan niet gepaard gaande met de vervanging of herpositionering van het hoofdimplantaat (since 1.10.07)

European Pacemaker Patient Identification Card

European Pacemaker Patient Identification Card

National Registration Centres

Austria:
Austrian Working Group on Cardiac Pacing, Wahringerstrab 15/16, A-1090 WIEN.

Belgium:
Belgian Cardiac Pacing Group, Dept. Cardiology, Universit Clinic St. Raphaël, Gasthuisberg, B-3000 LEUVEN.

Bulgaria:
Institute of Cardiovascular Diseases, Pacemaker Centre, BG 1309 SOFIA.

Croatia:
University Clinic of Cardiovascular Diseases, Kispaticeva 12, CF 10000 Zagreb.

Czech Republic:
Czech Working Group on Cardiac Arrythmias and Pacing, Interni Klinika Fakultni Nemocnice, I.P. Pavlova 6, 775 2 OLOMOUC.

Denmark:
Department of Clinical Physiology, Odense University Hospita DK-5000 ODENSE C.

France:
Collège Français de Stimulation Cardiaque, CHU RANGUEI F-31054 TOULOUSE Cedex.

Federal Republic of Germany:
Institut für Medizinische Technik der Justus-Liebig Universiti Giessen, D-6300 GIESSEN, Postfach 66 26.

Working Group on Cardiac Pacing, Medical Clinic, Universi Hospital (Charité), Humboldt University, Schumannstrasse 20-21, D-1040 BERLIN.

Hungary:
National Pacemaker Register, DOTE I - Belklinica, H-401 DEBRECEN Pf 19.

Italy:
Centro Registrazione Pacemaker c/o Istituto di Cardiologi Ospedale Regionale, I-33100 UDINE.

The Netherlands:
Pacemaker Patienten Registratie Afd. Cardiologie Academisc Ziekenhuis, NL-GRONINGEN 9713 EZ.

Norway:
Norwegian Pacing Group, Pacemaker Center, Post 112 Med A. VD, Ullevals Sykehus, N-0407 OSLO 4.

Poland:
Instytut Kardiologii ul. Alpejska 42, PL-04-628 WARSZAWA.

Portugal:
Associação Portuguesa de Pacing Cardiaco, Campo Grand 28-4C - P-1700 LISBON.

Spain:
Spanish Pacing Group, Servicio de Cirurgia Cardiaca, Hospit La Paz, E-28046 MADRID.

Sweden:
Pacemaker Register, Dept. of Cardiology, Karolinska Sjukhuse S-17176 STOCKHOLM.

Switzerland:
Swiss National Pacing and Electrophysiology Group, Division Cardiology, Rosiere 16-CHUV, CH-1011 LAUSANNE.

U.K.:
The British Pacing Group - 47 Wimpole Street, GB-LONDO W1M 7DG.

Yugoslavia:
2nd Surgical University Hospital Pacemaker Centre Vsegradska 26 - YU-BELGRADE 11000.

CODE EXPLANATION FOR IMPLANTATION

① SYMPTOMS (BEFORE IMPLANT)

CATEGORY-CODE		SPECIFICATION
UNSPECIFIED	A1	Unspecified (default)
	A2	Uncoded
SYNCOPE	B1	Syncope
	B2	Dizzy spells
	B3	Brady Cardia
TACHYCARDIA	C1	Tachycardia
OTHER	D1	None / Prophylactic
	D2	Dyspnea / Heart Failure
	D3	Cerebral Disfunction
	D4	Chestpain
	D5	Aborted sudden dead

② ECG INDICATIONS

CATEGORIE-CODE		SPECIFICATION
UNSPECIFIED	A1	Rhythm unspecified (default)
	A2	Rhythm uncoded
SINUS RHYTM	B1	Normal sinus rhythm
	B2	MER + abnormal EPS
AV BLOCK	C1	1° heartblock
	C2	2° heartblock unspecified
	C3	2° heartblock - Wenckebach
	C4	2° heartblock - Mobitz
	C5	CHB-QRS unspecified
	C6	CHB - narrow QRS
	C7	CHB - wide QRS
	C8	Chronic A/fib → AV block
BUNDLE BRANCHE BLOCK	D1	BBB - unspecified
	D2	RBBB - incomplete
	D3	RBBB - complete
	D4	LBBB
	D5	LAHB
	D6	LPHB
	D7	RBBB + LAHB = normal PR
	D8	RBBB + LPHB = normal PR
	D9	RBBB + LAHB = long PR
	D10	RBBB + LPHB = long PR
	D11	LBBB + long PR
	D12	LBBB / RBBB (alternans)
SINUS NODE DISEASE AND ATRIUM	E1	SSS - unspecified
	E2	SSS - SA exit block
	E3	SSS - SA arrest
	E4	SSS - bradycardia
	E5	SSS - brady / tachy
	E6	Chronic A/fib + brady
	E7	Interatrial block
	E8	Chronotropic incompetence
ATRIAL-TACHY	F1	Atrial tachy unspecified
	F2	AV-re-entrant tachycardia
	F3	AV nodal tachycardia
VENTRICULAR TACHY	G1	Ventricular extrasystoles
	G2	Non sustained VT / VF
	G3	Sustained VT / FT
	G4	Torsades de pointe

③ AETIOLOGY

CATEGORY-CODE		SPECIFICATION
UNSPECIFIED	A1	Unspecified
	A2	Uncoded
UNKNOWN	B1	Unknown
	B2	Conduction tissues disease
ISCHEMIC	C1	Ischaemic
	C2	Post-Infarction
CONGENITAL	D1	Congenital
IATROGENIC THERAPEUTIC	E1	Surgical complication
	E2	Surgical
	E3	Ablation
	E4	Drug induced
AUTONOMIC NERVOUS SYSTEM	F1	Carotid sinus syncope
	F2	Vasovagal syndrome
	F3	Orthostatic hypotension
CARDIO MYOPATHIES	G1	Cardiomyopathy unspecified
	G1A	Cardiomyopathy hypertrophic
	G1B	Cardiomyopathy dilated
VALVULAR	G2	Myocarditis
	G3	Valvular heart disease
	G5	Endocarditis
HEARTTR./PL.	G7	Heart Transplant
	G8	Ionizing Radiation

CODE EXPLANATION FOR "MODE OF PACING"

Boxes 1 2 3 4 5

(4) BOX	1	2	3
	Chamber(s) Paced O = None A = Atrium V = Ventricle D = Dual (A+V)	Chamber(s) sensed O = None A = Atrium V = Ventricle D = Dual (A+V)	Response to sensing O = None T = Trigger I = Inhibit D = Dual (T+I)

4	5
Programmability rate modulation O = None P = Simple Programmable M = Multiprogrammable C = Communicating R = Rate Modulation	Antitachyarrythmia function(s) O = None P = Pacing (antitachyarrythmia) S = Shock D = Dual (P+S)

THE NASPE/BPEG Generic (NBG) Pacemaker Code

CODE EXPLANATION FOR EXPLANTATION

⑤ GENERATOR CHANGE

CATEGORY-CODE		SPECIFICATION
UNSPECIFIED	A1	Unspecified
	A2	Uncoded
ELECTIVE	B1	Elective
	B2	Recall
	B3	System change heamodynamic
	B4	System change-pm syndrome
	B5	System change-palpitations
	B6	System change Electrode problem
	B7	EMG Inhibition
	B8	Extracardiac Stimulation
SURGICAL	C1	Mechanical protrusion
	C2	Erosion
	C3	Infection
	C4	Woundpain
FAILURE MINOR	D1	Failure - unspecified
	D2	Failure - undersensing
	D3	Failure - oversensing
	D4	Failure - magnetic switch
	D5	Failure - programming
FAILURE MAJOR	E1	Failure - unspecified
	E2	Failure - no output
	E3	Failure - low output
	E4	Failure - low rate
	E5	Failure - high rate
	E6	Failure - connector
	E7	Failure - encapsulation
FAILURE BATTERY	F1	Normal E.O.L.
	F2	Premature E.O.L.

⑥ ELECTRODE CHANGE

CATEGORY-CODE		SPECIFICATION
UNSPECIFIED	A1	Unspecified (default)
	A2	Uncoded
ELECTIVE	B1	Elective
	B2	Displacement
	B3	Exit Block
	B4	EMG Inhibition
	B5	Extracardiac Stimulation
	B6	Perforation
	B7	Undersensing
	B8	Recall
SURGICAL - FAILURE	C1	Infection / Ulceration
	D1	Connector failure
	D2	Insulation failure
	D3	Conductor break

⑦ INDICATION FOR FILE CLOSURE

CATEGORY-CODE		SPECIFICATION
UNSPECIFIED	A1	Unspecified (default)
	A2	Uncoded
DEATH	B1	Death unrelated to pacemaker
	B2	Death related to pacemaker
	B3	Death - sudden
	B4	Death - cause unknown
	B5	Death related to lead
LOST TO FOLLOW-UP	C1	Lost to follow-up
	C2	Hospital transfer
	C3	Pacemaker removed

9.6 PACEMAKER PRESCRIPTION FORM (RECTO)

PACEMAKER IMPLANTATIE VOORSCHRIFT
HARTSTIMULATOR REGISTRATIEFORMULIER

IMPLANTATIECENTRUM : .....
R.I.Z.I.V.-Nummer van het centrum : .....
Dienst/Geneesheer : .....
Telefoon : ..... **Fax :** .....

NAAM PATIENT : ..... **Dossiernr. :** .....
Geboortedatum : ..../..../..... **Geslacht :** .....

Adres : .....
Postcode : ..... **Gemeente :** .....
Verzekeringsorganisme : ..... **Stamnummer :** .....

IMPLANTATIEGEGEVENS :
Datum : ..../..../..... **Pacing Mode :** .....

		Identificatiecode (R.I.Z.I.V.-lijst)	Fabrikant	Type	Serienummer
Pacemaker	:	.....	.....	.....	.....
Ventric. Elektrode	:	.....	.....	.....	.....
Atriale Elektrode	:	.....	.....	.....	.....
Bijhorigheden	:	.....	.....	.....	.....

INDICATIES (zie keerzijde)	***SYMPTOOM***	***E.C.G.***	***ETIOLOGIE***
	☐☐	☐☐	☐☐

EXPLANTATIEGEGEVENS :
Datum Explantatie : ..../..../..... **Datum Implantatie :** ..../..../..... van het geëxplanteerd toestel

		Identificatiecode (R.I.Z.I.V.-lijst)	Fabrikant	Type	Serienummer	***REDEN VERVANGING***
Pacemaker	:	.....	.....	.....	.....	☐
Ventric. Elektrode	:	.....	.....	.....	.....	☐
Atriale Elektrode	:	.....	.....	.....	.....	☐

INDICATIE/OPMERKINGEN : .....
.....
.....

	Naam	R.I.Z.I.V.-Nummer	Handtekening en datum
- Geneesheer-specialist in de cardiologie [1], verantwoordelijk voor de indicatie en implantatie	.....	.....	.....
- Geneesheer-specialist in de cardiologie [1], medeverantwoordelijk voor de indicatie	.....	.....	.....

[1] één van de twee voornoemde geneesheren kan een specialist in de inwendige geneeskunde zijn die hierbij verklaart dat hij zijn hoofdactiviteit uitoefent in de cardiologie

9.7 PACEMAKER PRESCRIPTION FORM (VERSO)

PACING INDICATION

CODE FOR IMPLANTATION

	Symptom			ECG Indications			Generator Change			Electrode Change	
Unspecified	A1 Unspecified	Unspecified	A1	Rhythm unspecified	Unspecified		A1 Unspecified				
	A2 Unceded		A2	Rhythm unceded			A2 Unceded			A2 Unceded	
Syncope	B1 Syncope	Sinus Rhythm	B1	Normal sinus rhythm	Elective		B1 Elective	Elective		B1 Elective	
	B2 Dizzy Spells	AV Block	C1	1° heart block			B2 Recall			B2 Displacement	
	B3 Bradycardia		C2	2° heart block-unspecified			B3 Sys. change-hemodynamic			B3 Exit block	
Tachycardia	C1 Tachycardia		C3	2° heart block-Wenckebach			B4 Sys. change-pacer syndrome			B4 EMG Inhibition	
Other	D1 Prophylactic		C4	2° heart block-Mobitz			B5 Sys. change-palpitations			B5 Extra cardiac stimulation	
	D2 Heart Failure		C5	CHB-QRS unspecified			B6 Sys. change-electr. problem			B6 Perforation	
	D3 Cerebral dysfunction		C6	CHB-narrow QRS			B7 EMG Inhibition			B7 Undersensing	
	F1 HSSC		C7	CHB-wide QRS			B8 Extra cardiac stimulation	Surgical		C1 Infection-ulceration	
		Bundle	D1	BBB-unspecified	Surgical		C1 Mechanical protrusion	Failure		D1 Connector failure	
		Broncho	D2	RBBB-incomplete			C2 Erosion			D2 Insulation break	
	Aetiologyn	Block	D3	RBBB-complete			C3 Infection			D3 Conductor break	
Unspecified	A1 Unspecified		D4	LBBB-complete unknown			C4 Wound pain				
	A2 Unceded		D5	LAHB	Failure minor		D1 Unspecified				
	B1 Unknown		D6	LPHB-ischaemic			D2 Undersensing				
	B2 Conduction tissue fibrosis		D7	RBBB+LAHB+normal PR			D3 Oversensing				
	C1 Ischaemic		D8	RBBB+LPHB+normal PR			D4 Magnetic Switch				
	C2 Post Infarction		D9	RBBB+LAHB+long PR			D5 Programming				
Congenital	D1 Congenital		D10	RBBB+LPHB+long PR	Failure Major		E1 Unspecified				
Iatrogenic	E1 Surgical complication		D11	LBBB+long PR			E2 No output				
	E2 Surgical	Sick Sinus	E1	SSS-unspecified			E3 Low output				
	E3 Ablation	Syndrome	E2	SSS-SA exit block			E4 Slow rate				
C.S.S.	F1 Carotid Sinus Syndrome		E3	SSS-SA arrest			E5 Fast rate				
Other	G1 Cardiomyopathie		E4	SSS-bradycardia			E6 Connector				
	G2 Myocarditis		E5	SSS-brady-tachy			E7 Encapsulation				
	G3 Valvular Heart Disease		E6	A.Flutter/FLB+bradycardia	Failure Battery		F1 Normal E.O.L				
		Atrial Tachy	F1	Atrial tachycardia			F2 Premature E.O.L				
			F2	Pre-excitation							
		Ventricular	G1	Ventricular extrasystoles							
		Tachy	G2	Ventricular tachycardia							
			G3	Paroxysmal VF							

CODE EXPLANATION FOR MODE OF PACING

BOX 1 Chamber(s) paced	BOX 2 Chamber(s) sensed	BOX 3 Response to sensing	BOX 4 Programmability rate modulation	BOX 5 Antitachyarrhythmia function(s)
O = none	O = none	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	P = Simple Progammable	P = Pacing
V = Ventricle	V = Ventricle	I = Inhibited	M = Multiprogrammable	S = Shock
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)	C = Communicating	D = Dual (P+S)
			R = Rate modulation	

CODE FOR EXPLANTATION

9.8 APPENDIX TO CHAPTER 5.1.3

Table 32: NIDHI reimbursement codes for the primary selection of data

NIHDI Reimburse-ment code	Dutch label	French label
229110 229121	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar	Implantation d'électrodes intramyocardiques par thoracotomie et placement sous-cutané du pace-maker
229132 229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar	Implantation d'électrodes intracavitaires par voie intra-veineuse et placement sous-cutané du pacemaker
229154 229165	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar	Implantation d'électrodes intracavitaires par voie intraveineuse et d'électrode auriculaire par médiastinoscopie et placement sous-cutané du pace-maker
229176 229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode	Remplacement d'un pace-maker sous-cutané ou d'une électrode intracavitaire permanente
475856 475860	Controle van de deugdelijkheid en/of herprogrammatie van een eenkamerpacemaker (SSI), met ondervraging van het geheugen en meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés	Contrôle de la qualité et/ou reprogrammation d'un stimulateur cardiaque, chambre simple (SSI), avec interrogation de la mémoire et mesure du seuil de stimulation et de sensibilité, avec protocole et tracés
475871 475882	Controle van de deugdelijkheid en/of herprogrammatie van een tweekamerpacemaker (DDD), met ondervraging van het geheugen en meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés	Contrôle de la qualité et/ou reprogrammation d'un stimulateur cardiaque, chambre double (D.D.D.), avec interrogation de la mémoire et mesure du seuil de stimulation et de sensibilité, avec protocole et tracés
475952 475963	Implantatie langs transveneuze weg van een linker kamer elektrode, verbonden aan een pacemaker of een hartdefibrillator	Implantation par voie transveineuse d'une électrode ventriculaire gauche, connectée à un pacemaker ou un défibrillateur cardiaque
691795 691806	Endocardiale uni- of bipolaire of myocardiale pacemaker-elektrode	Electrode de stimulateur, endocardiale unipolaire ou bipolaire ou myocardiale
691810 691821	Single-pass pacemaker-elektrode (VVD)	Electrode de stimulateur cardiaque single-pass (VVD)
691832	Percutaan geplaatste	Electrodes de resynchronisation du ventricule

691843	linkerventrikel resynchronisatie-elektrode	gauche placée par voie percutanée
691854 691865	Epicardiaal geplaatste linkerventrikel resynchronisatie-elektrode	Electrodes de resynchronisation du ventricule gauche placée par voie épicardique

Source: KCE.

9.9 APPENDIX TO CHAPTER 5.1.4

We identify primo implantations, regular replacements and early replacements by the device codes as depicted in Table 33.

Table 33 : Nomenclature codes for pacemaker devices

Implantation type	Nomenclature code		Encoded since	Description
	Inpatient	Outpatient		
Primo implantation	684541	684530	01/08/1997	Eerste implanteerbare hartstimulator, inclusief adaptor
Regular replacement	684386	684375	01/06/2005	Vervangingshartstimulator, inclusief adaptor
Early replacement	684666	684655	01/08/1997	Voortijdige hernieuwing van de hartstimulator (artikel 35, § 11, 4° van de nomenclatuur)

Source: KCE.

A simple count of the number of devices shows a total of 11,097 implants in 2007 (Table 34).

Table 34: Number of implants given by the original codification in the IMA data; 2002-2007

Implantation type	2002	2003	2004	2005	2006	2007
Regular Replacement	0	0	0	1221	2664	3021
Early Replacement	6	10	19	31	57	52
Primo implantation	9,919	10,845	10,707	9,363	8,438	8,024
Total	9,925	10,855	10,726	10,615	11,159	11,097

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

In a first recodification step, we identify potential regular replacements that have been originally coded as primo implantations. For this purpose, we check whether a patient with a device that has been originally encoded as a primo implantation, has undergone a system integrity check of the pacemaker before. By definition, a system integrity check can, however, only be done after a primo implantation. Therefore, all these device codes must be recoded as replacements. System integrity check are identified by the nomenclature codes, as depicted in Table 35.

Table 35: Nomenclature codes for pacemaker system integrity checks

Outpatient	Inpatient	Description
475635	475646	Controle van de deugdelijkheid van een ingeplante hartstimulator door foto-analyse van de prikkel
475893	475904	Controle van de deugdelijkheid en/of herprogrammatie van een hartdefibrillator, met meting van de stimulatie- en gevoeligheidsdrempel en met evaluatie van de performantie van de defibrillator, met protocol en tracés
475856	475860	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
475871	475882	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés

Source: KCE.

Recodification results in Table 36. The percentage terms relate to the original number of implants as given by the IMA data in Table 34. For instance, 25% of all primo implantations in 2002 have been recoded as replacements.

Table 36: Number of implants after recodification of primo implantations as replacements, if a related quality check is encoded before the day of the implantation; 2002-2007

Implantation type	2002	2003	2004	2005	2006	2007
Regular Replacement	2452	2924	2737	2946	3345	3465
% of initial number	-	-	-	*241%*	*126%*	*115%*
Early Replacement	6	10	19	31	57	52
% of initial number	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Primo implantation	7,467	7,921	7,970	7,638	7,757	7,580
% of initial number	*75%*	*73%*	*74%*	*82%*	*92%*	*94%*
Total	9,925	10,855	10,726	10,615	11,159	11,097
% of initial number	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

In the second recodification step, a detailed matrix of all relevant nomenclature codes for the proper identification of the appropriate implantation type is defined for each patient. The matrix summarizes the combination of all relevant events for each patient, allowing thus for each patient case to check – and if appropriate – to recode the implantation type. The relevant nomenclature codes are shown in Table 37. The matrix counts, how many times a specific combination of nomenclature codes appears. For instance, the combination of the codes 229143 and 684541 can be observed 33,231 times throughout 2002-2007 (Table 38). All combinations with less than 10 counts have not been taken into account for recodification purposes. Rather, the original codification has been retained.

Recodification taking into account changes induced by the classification matrix results in Table 38. The main result is here that the total number of implants has been reduced, mainly due to recodification of several implants as revisions.

Table 37: Nomenclature codes for classification of implant types

Nomenclature code		Description
Inpatient	Outpatient	
229121	229110	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar
229143	229132	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar
229165	229154	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar
229180	229176	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
684541	684530	Eerste implanteerbare hartstimulator, inclusief adaptor
684386	684375	Vervangingshartstimulator, inclusief adaptor
684666	684665	Voortijdige hernieuwing van de hartstimulator
691806	691795	Endocardiale uni- of bipolaire of myocardiale pacemaker-elektrode
691821	691810	Single-pass pacemaker-elektrode (VVD)
691843	691832	Percutaan geplaatste linkerventrikel resynchronisatie-elektrode
691865	691854	Epicardiaal geplaatste linkerventrikel resynchronisatie-elektrode
685742	685731	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 – 684541 of de verstrekking 684375-684386, per elektrode
685764	685753	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 – 684541 of de verstrekking 684375-684386, per elektrode
685786	685775	Implanteerbare myocardiale elektrode voor de verstrekking 684530 – 684541 of de verstrekking 684375-684386, per elektrode
685801	685790	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 – 684541 of de v erstrekking 684375-684386, per elektrode

Source: KCE.

Table 38: Classification matrix for identification of implant types; 2002-2007

Classification	Inplanten van elektroden in het myocardium door thoracotomie n onderhuids plaatsen van de hartprikk 229121	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartpr 229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode doo 229165	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode 229180	Primo implants 684541	Regular replacement 684386	Early replacement 684666	Endocardiale uni- of bipolaire of myocardiale pacemaker-elektrode 691806	Single-pass pacemaker-elektrode (VVD) 691821	Percutaan geplaatste linkerventrikel resynchronisatie-elektrode 691843	Epicardiaal geplaatste linkerventrikel resynchronisatie-elektrode 691865	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 – 684541 of de verstrek 685742	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 – 684541 of de verstrekk 685764	Implanteerbare myocardiale elektrode voor de verstrekking 684530 – 684541 of de verstrekking 684375- 685786	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 – 684541 of de verstre 685801	Count
Primo implant		1			1								1			33,231
Replacement				1	1											7,263
Replacement				1		1										4,353
Primo implant			1		1								1			3,035
Primo implant		1			1							1	1			2,863
Primo implant		1			1							1				2,384
Replacement		1		1	1								1			1,542
Primo implant			1		1							1	1			844
Replacement		1			1											588
Primo implant					1								1			504
Primo implant		1			1										1	423
Replacement				1	1								1			396

Classification	229121	229143	229165	229180	684541	684386	684666	691806	691821	691843	691865	685742	685764	685786	685801	Count

Replacement		1				1							1		379
Primo implant and replacement		1		1	1	1							1		215
Replacement		1				1									161
Replacement					1										154
Replacement				1		1							1		130
Primo implant (and revision)		1		1	1							1	1		120
Primo implant	1				1									1	112
Primo implant	1				1								1		111
Primo implant	1	1			1								1		109
Primo implant			1		1							1			103
Primo implant (and revision)			1	1	1								1		87
Replacement						1									86
Primo implant and replacement		1			1	1							1		82
Primo implant and replacement				1	1	1									79
Primo implant		1			1								1	1	76
Primo implant					1							1	1		75
Primo implant (and revision)		1		1	1										72
Primo implant					1							1			70
Replacement		1		1		1							1		62
Replacement			1			1							1		51
Primo implant		1	1		1								1		50
Primo implant and replacement		1		1	1		1						1		43
Primo implant (and revision)		1		1	1							1			36

Classification	229121	229143	229165	229180	684541	684386	684666	691806	691821	691843	691865	685742	685764	685786	685801	Count
Primo implant		1			1									1		32
Replacement		1		1		1										29
Primo implant			1		1											29
Replacement		1				1						1				28
Replacement				1	1							1				25
Primo implant			1		1								1	1		23
Primo implant					1									1		21
Primo implant		1			1		1						1			18
Replacement		1				1						1	1			18
Primo implant	1				1											17
Primo implant and replacement				1	1	1							1			17
Replacement			1			1										16
Primo implant	1	1			1								1	1		16
Primo implant (and revision)	1	1		1	1								1			16
Primo implant (and revision)			1	1	1							1	1			16
Replacement	1			1	1								1			15
Primo implant			1		1										1	13
Replacement				1			1									13
Replacement				1	1							1	1			13
Primo implant			1		1							1		1		13
Primo implant and replacement			1	1	1	1							1			11
Replacement				1	1		1									11
Primo implant			1		1									1		11
Replacement				1		1						1				10
Primo implant (and revision)		1		1	1	1										10
Primo implant					1										1	10
Replacement						1							1			10

Source: KCE.

Table 39: Number of implants after using the classification matrix for recodification of implant types; 2002-2007

Implant type		2002	2003	2004	2005	2006	2007
Regular Replacement		2712	2833	2598	2743	3228	3373
	% of initial number	-	-	-	*225%*	*121%*	*112%*
Early Replacement		3	7	14	21	53	54
	% of initial number	*50%*	*70%*	*74%*	*68%*	*93%*	*104%*
First implant		6,841	7,614	7,729	7,499	7,635	7,487
	% of initial number	*69%*	*70%*	*72%*	*80%*	*90%*	*93%*
Total		9,556	10,454	10,341	10,263	10,916	10,914
	% of initial number	*96%*	*96%*	*96%*	*97%*	*98%*	*98%*

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

In the last recodification step, regular replacements are recodified as early replacements, if they occur within five years after the last implant. This results in an augmentation in the number of early replacements and a decrease in the number of regular replacements. Table 40 shows the final counts of implant types per year.

Table 40: Recode replacements as early replacements if within 5 years of last implant

Implant type	2002	2003	2004	2005	2006	2007
Regular Replacement	2677	2771	2555	2665	3060	3179
% of initial number	-	-	-	*218%*	*115%*	*105%*
Early Replacement	38	69	57	99	221	248
% of initial number	*633%*	*690%*	*300%*	*319%*	*388%*	*477%*
Primo implantation	6,841	7,614	7,729	7,499	7,635	7,487
% of initial number	*69%*	*70%*	*72%*	*80%*	*90%*	*93%*
Total	9,556	10,454	10,341	10,263	10,916	10,914
% of initial number	*96%*	*96%*	*96%*	*97%*	*98%*	*98%*

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

9.10 APPENDIX TO CHAPTER 5.2.2

Table 41: Nomenclature codes for pacemaker leads

Nomenclature code	Description
685731	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685753	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685775	Implanteerbare myocardiale elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685790	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685742	Implanteerbare endocardiale unipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685764	Implanteerbare endocardiale bipolaire elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685786	Implanteerbare myocardiale elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode
685801	Implanteerbare endocardiale single-pass elektrode voor de verstrekking 684530 - 684541 of de verstrekking 684375 - 684386, per elektrode

Source: KCE.

9.11 APPENDIX TO CHAPTER 0

This subchapter shows step by step, how the standardization of the observed regional first implantation rates by age and sex, fiscal revenues per capita and the foreign share of the population is done as well as the result of the standardization.

General methodology

Belgium is taken as the standard population. Given its population and socioeconomic characteristics, we calculate the national implantation rates within each of the categories of interest, such as age, sex, fiscal revenues per capita and the share of foreign population. Then, we multiply those implantation rates by the population numbers in each of Belgian *arrondissements* to arrive at the expected (standardized) number of implants. Diving the observed by the expected number of implant by region results in the standardized implant ratio. A further multiplication of the ratio by the Belgian implantation rates results then in the standardized implantation rates by region.

Adjustment by sex and age

Standardization is done by sex and in the age categories from 0-9, 10-19, ..., 50-59, 60-64, 65-69,..., 90-94 and 95 plus. The shares of the population above the ages of 64 and 79 vary considerably (Figure 49), which will clearly affect implantation rates. The effect of sex-age standardization of primo implantation rates per province is depicted in Figure 50.Overall, standardization of regional implantation rates by sex and age leads to a lower variation of implantation rates relative to the mean of Belgium. While the standard deviation of actual regional implantation rates on the level of *arrondissements* from the Belgian mean primo implantation rate was 200 in 2007, it was 191 after standardization. Thus, while reducing overall variation, it is far from eliminating it (Figure 51).

Figure 49: Shares of the population above the ages of 64 and 79; by provinces in 2007

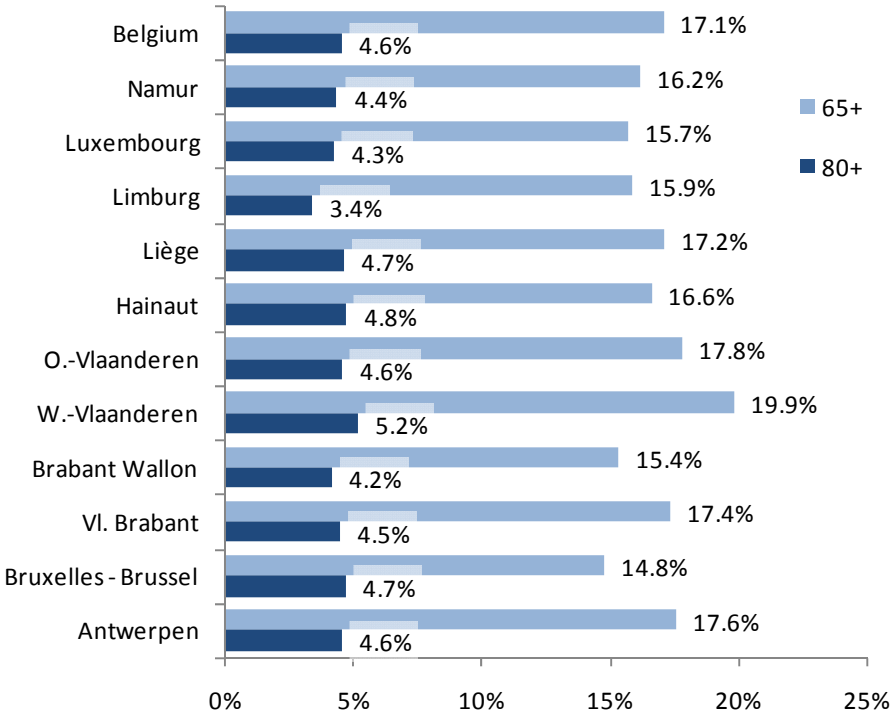
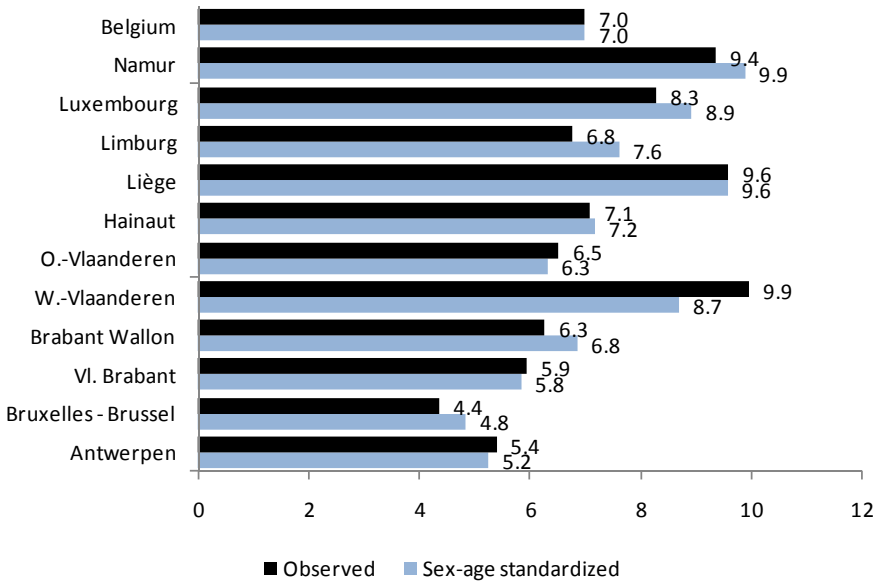
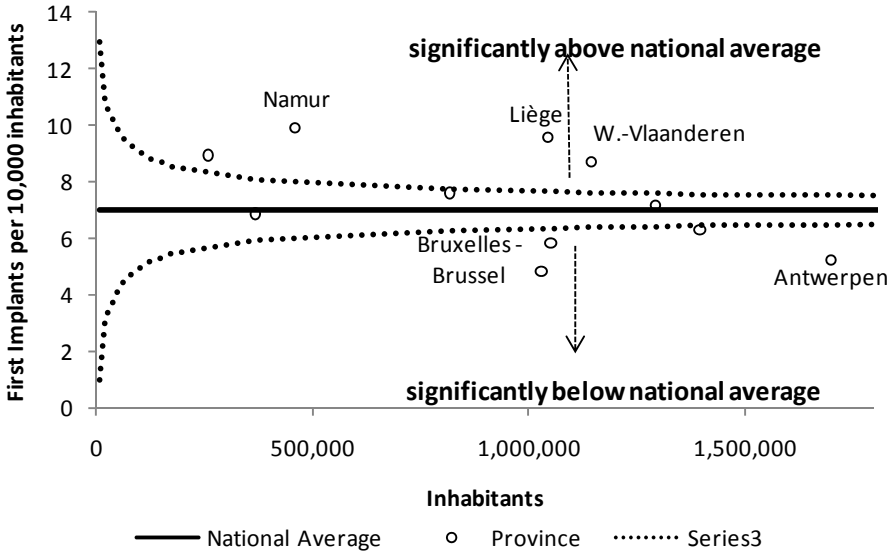


Figure 50: Actual versus sex-age standardized primo implantation rates per province; per 10,000 inhabitants, 2007



Notes: Own calculation based on IMA-AIM and *Statistics Belgium - Population*; see section 5.1 for data sources.

Figure 51: Sex-age standardized primo implantation rates per province and expected limits; per 10,000 inhabitants, 2007



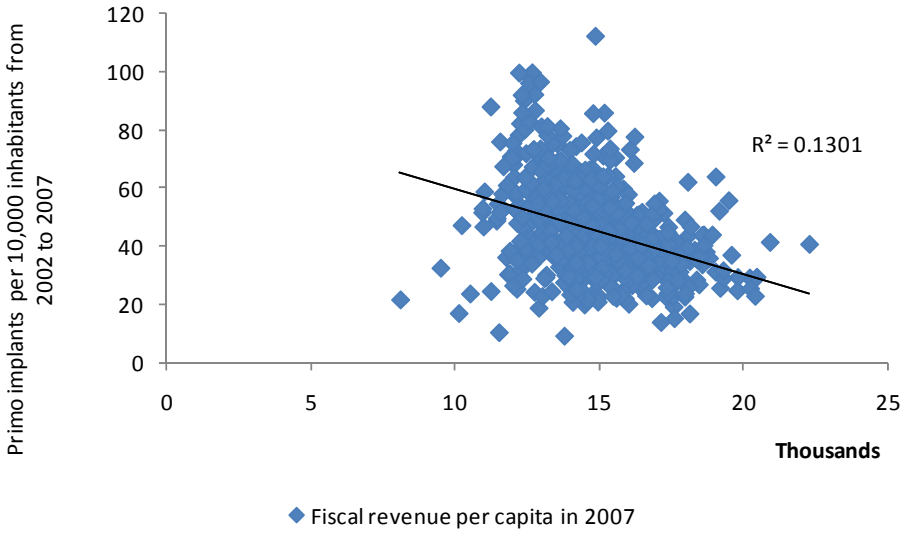
Notes: Own calculation based on IMA-AIM and *Statistics Belgium - Population*; see section 5.1 for data sources.

Adjustment by fiscal revenues per capita

Regional fiscal revenues per capita differences are approximated by differences in the fiscal revenue per capita in 2007. Fiscal revenue per capita varies between roughly 8,000 to 23,000 Euros per municipality (Figure 52). Overall, there is a negative relationship between the fiscal revenue per capita and regional primo implantation rates. The standardization of implantation rates by the additional factor of fiscal revenues per capita is done by quintiles of fiscal revenues per capita on the level of *arrondissements*.

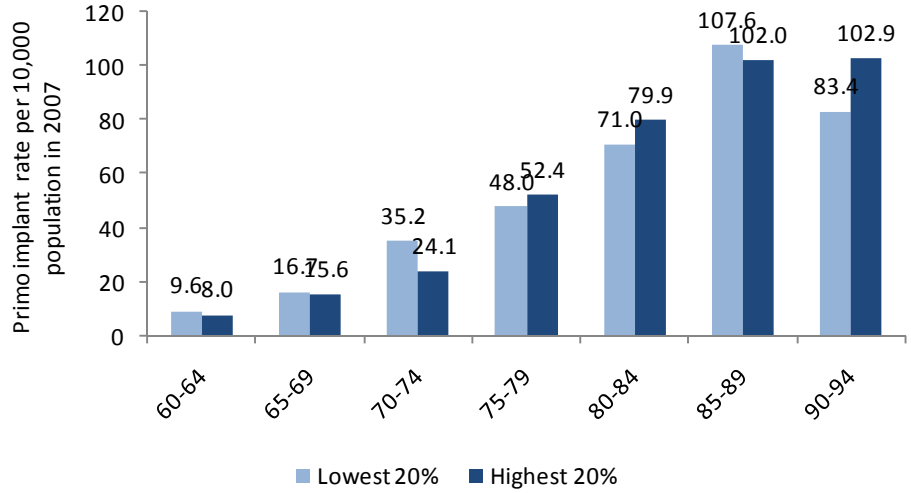
When subdivided by age groups and sex, the relationship between fiscal revenues per capita quintiles and implantation rates gets more variegated. In some age groups a higher fiscal revenues per capita goes along with higher implantation rates, in some in this the other way round (Figure 53andFigure 54). Further standardization of implantation rates by regional fiscal revenues per capita differences has the effect of narrowing the differences in primo implantation rates between regions (Figure 55 and Figure 56).

Figure 52: Mean fiscal revenue per capita in 2007 and cumulative primo implantation rate per 10,000 inhabitants per municipality



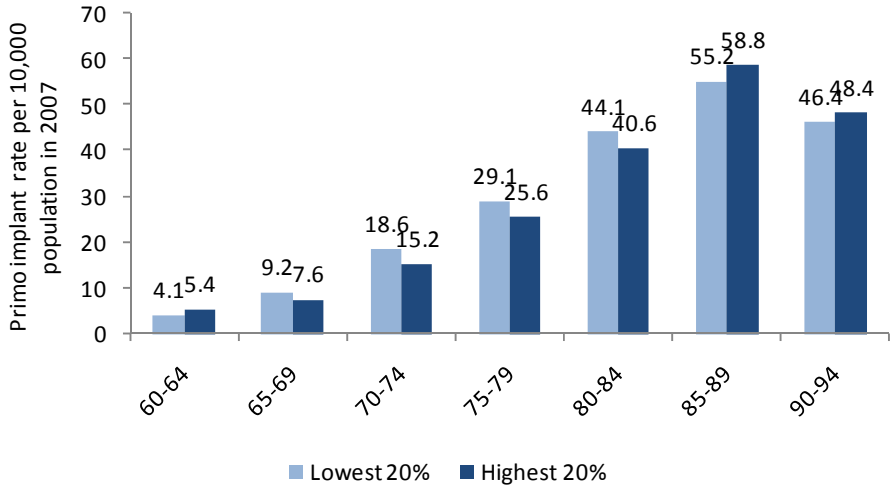
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [40]; see section 5.1 for data sources.

Figure 53: Male primo implantation rates; comparison of *arrondissements* with lowest 20% to highest 20% fiscal revenue per capita; 2007



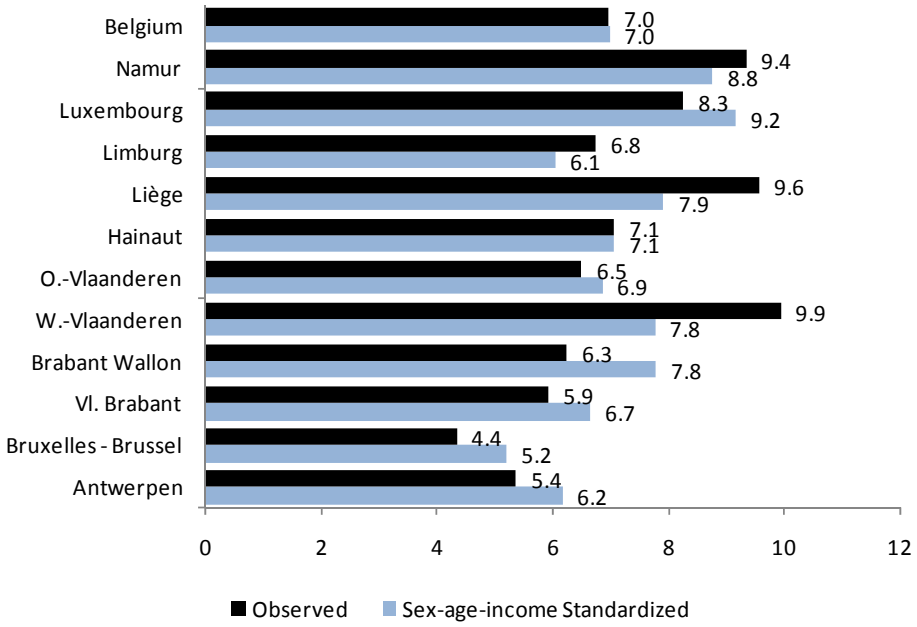
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [40]; see section 5.1 for data sources.

Figure 54: Female primo implantation rates; comparison of *arrondissements* with lowest 20% to highest 20% fiscal revenue per capita; 2007



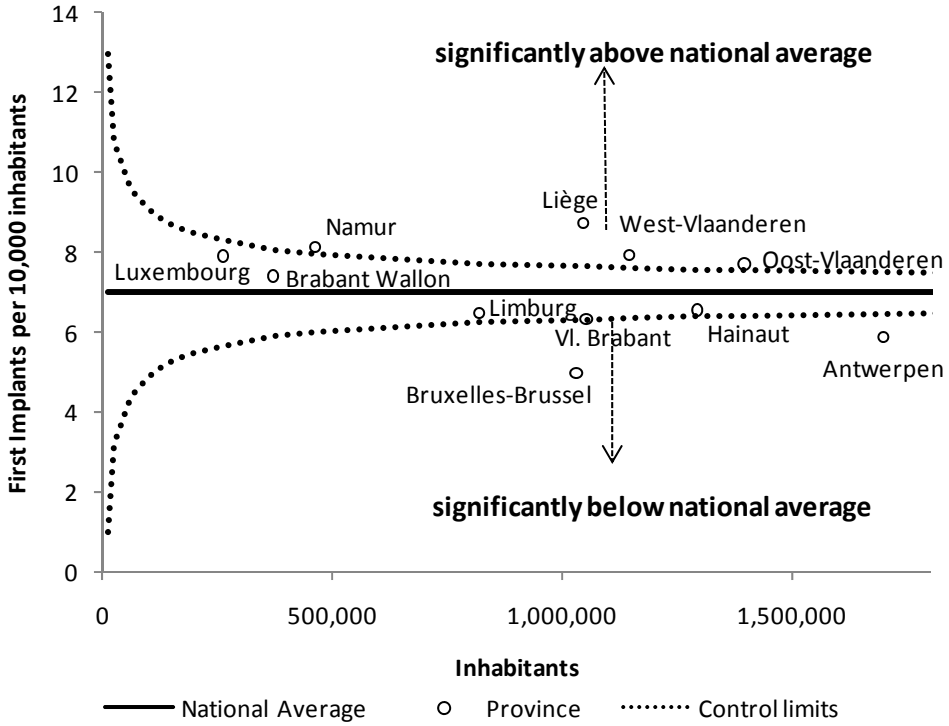
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [40]; see section 5.1 for data sources.

Figure 55: Actual versus sex-age-fiscal revenues per capita standardized primo implantation rates per province; per 10,000 inhabitants, 2007



Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [40]; see section 5.1 for data sources.

Figure 56: Sex-age-fiscal revenues per capita standardized primo implantation rates per province and expected limits; per 10,000 inhabitants, 2007

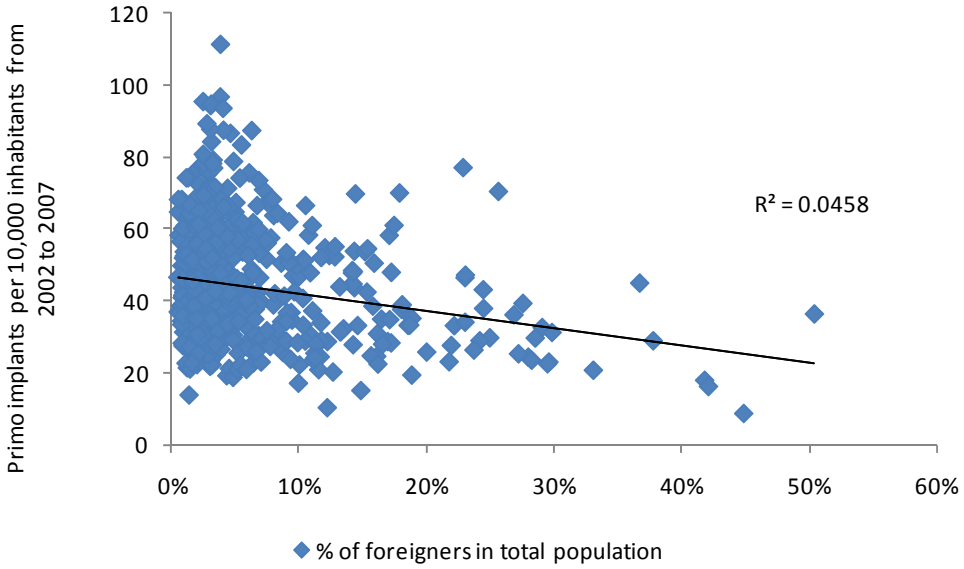


Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [40]; see section 5.1 for data sources.

Adjustment by the share of foreigners in the population

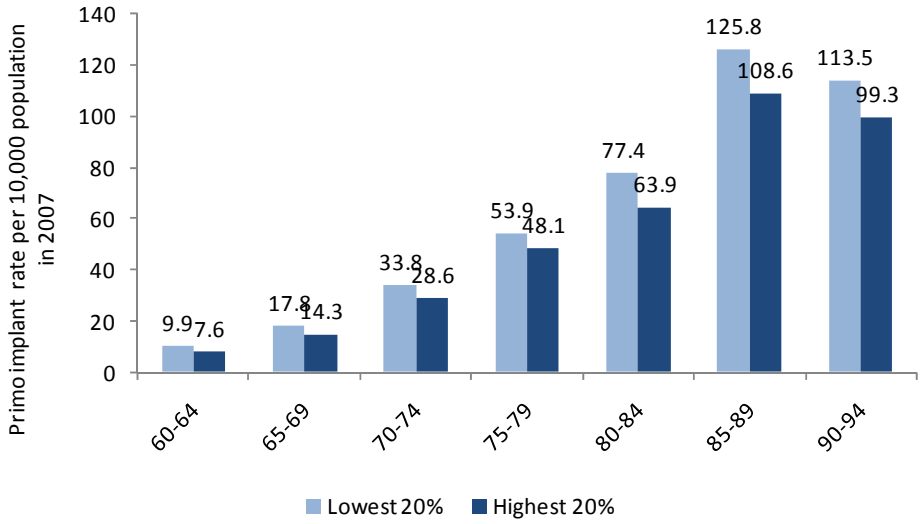
Overall, there is a negative relationship between the share of foreigners and regional primo implantation rates (Figure 57). The standardization of implantation rates by the additional factor of the share of foreigners in the population is done by quintiles of share of foreigners on the level of *arrondissements*. When subdivided by age groups and sex, we see that in all higher age groups implantation rates are higher when the share of foreigners is lower (Figure 58 and Figure 59). Standardization of sex-age adjusted implantation rates by regional differences in the share of foreigners has the effect of narrowing the differences in primo implantation rates between regions (Figure 60 and Figure 61).

Figure 57: Mean share of foreigners in the population and cumulative primo implantation rates per 10,000 inhabitants per municipality



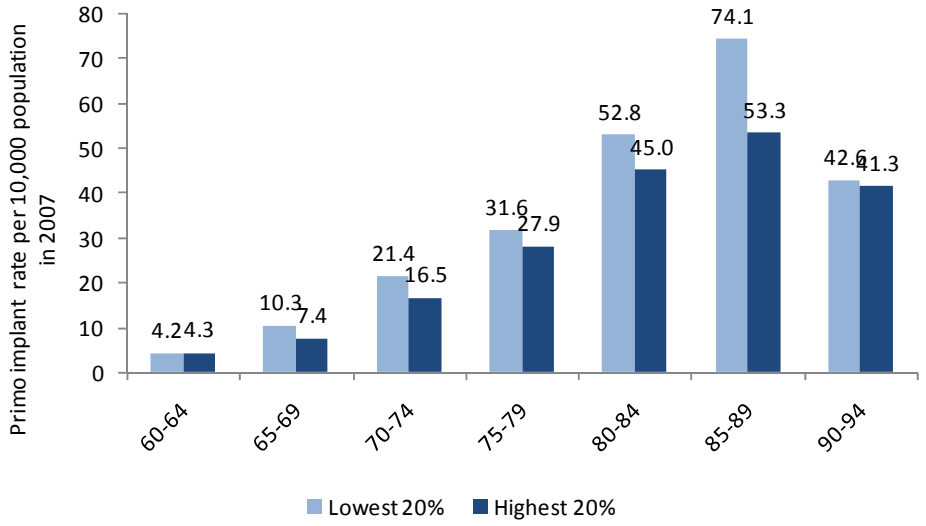
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

Figure 58: Male primo implantation rates; comparison of *arrondissements* with lowest 20% to highest 20% share of foreigners in the population; 2007



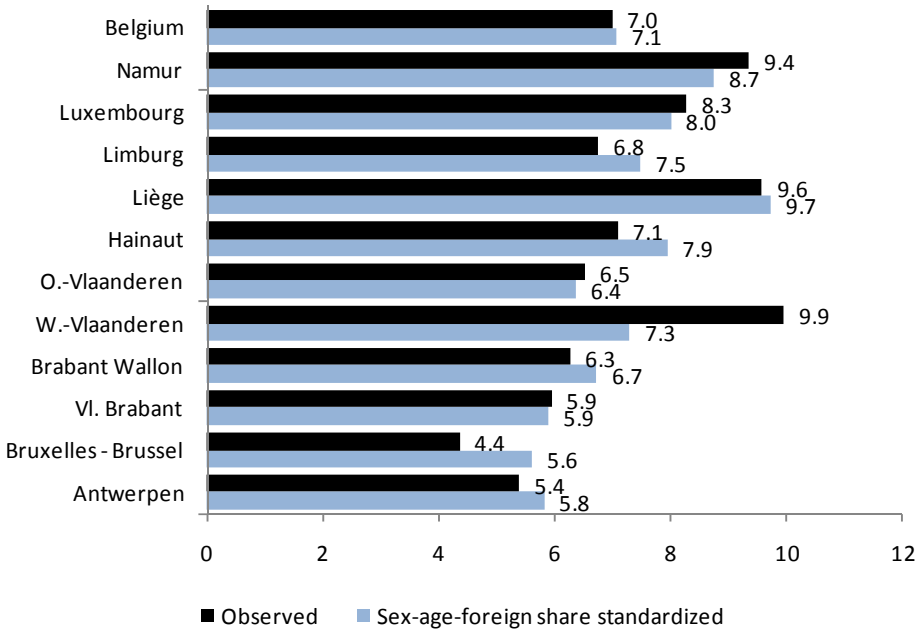
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

Figure 59: Female primo implantation rates; comparison of *arrondissements* with lowest 20% to highest 20% share of foreigners in the population; 2007



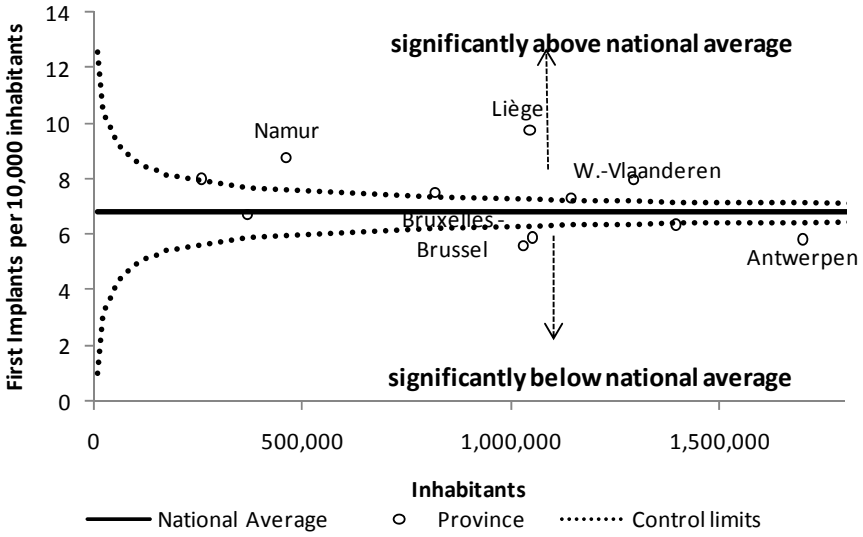
Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

Figure 60: Actual versus sex-age -foreign share standardized primo implantation rates per province; per 10,000 inhabitants, 2007



Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

Figure 61: Sex-age-foreign share standardized primo implantation rates per province and expected limits; per 10,000 inhabitants, 2007



Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

Table 42 summarizes the results of adjustment of cumulative primo implantation rates at the level of communities by use of a multivariate regression model. The estimated coefficients of the explanatory variables are presented as elasticities and reveal the percent change in primo implantation rates due to a one percent change in the explanatory variables. We find that the regional fiscal revenue per capita, the foreign share of population, the share of men in population older then 60, and the share of people aged 75-79 and 80-84 are related to the regional levels of primo implantation on conventional statistical significance levels. For instance, a 1% increase in regional fiscal revenue per capita goes along with a 0.85% decrease in the primo implantation rate.[bb] Similarly, a 1% increase in the foreign share of the population in associated with a 0.12% decrease in the primo implantation rate. Similar interpretations hold for the other statistically significant variables.

[bb] It has to be kept in mind, that the estimated elasticities are valid only locally. They cannot be used to estimate the impact of a, i.e. 10% increase in the explanatory variables, without further investigations.

Table 42: Association between the cumulative primo implantation rate from 2002 to 2007 and socioeconomic variables; by municipality

Variables (Year 2007)	Coefficient	t-value
Fiscal revenue per capita	-0.86***	-7.83
Foreign share of the population	-0.12***	-7.27
Share of men in population older than 60	-1.47***	-3.65
Share of population in age groups		
60-64	-0.11	-0.71
65-69	0.35	1.87
70-74	-0.25	-1.15
75-79	0.39**	2.41
80-84	0.42**	2.11
85-89	-0.15	-1.32
90+	-0.06	-1.03

Notes: Total number of municipalities without missing data is 588; R^2= 0.33; F-test for validity of the regression model F(10,577) = 29.33; all variables in logs, as such coefficients show elasticities; Huber-White robust standard errors; constant included; Tested for misspecification of the model using STATA's linktest and ovtest; tested for non-normal distribution and heteroscedesticity of the residuals using Shapiro-Wilk test for normality and the Cook and Weisberg test for heteroscedasticity; Calculated the variance inflation factor for the independent variables using the vif test; All calculations done with STATA 9.2; ***Indicates significance at 1% level; **at 5% level; *at 10% level; Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources

Figure 62: Belgian *arrondissements*

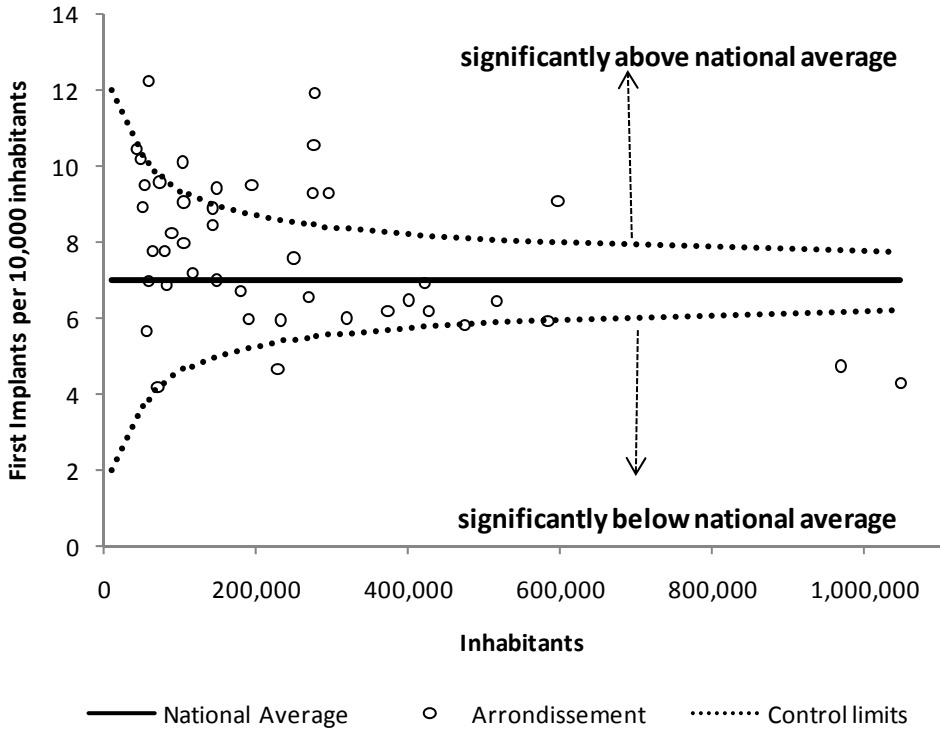
Source: KCE.

Table 43: Population per *arrondissement* in 2007; in thousands

Code	*Arrondissement*	Population
11000	Arr. Antwerpen	961.13
12000	Arr. Mechelen	316.22
13000	Arr. Turnhout	423.22
21000	Bruxelles - Brussel	1031.22
23000	Arr. Halle-Vilvoorde	580.41
24000	Arr. Leuven	472.06
25000	Arr. de Nivelles	370.46
31000	Arr. Brugge	274.77
32000	Arr. Diksmuide	48.57
33000	Arr. Ieper	104.8
34000	Arr. Kortrijk	278.16
35000	Arr. Oostende	148.33
36000	Arr. Roeselare	142.78
37000	Arr. Tielt	89.18
38000	Arr. Veurne	59.3
41000	Arr. Aalst	267.27
42000	Arr. Dendermonde	189.64
43000	Arr. Eeklo	80.55
44000	Arr. Gent	512.41
45000	Arr. Oudenaarde	117.13
46000	Arr. Sint-Niklaas	231.26
51000	Arr. d'Ath	81.83
52000	Arr. de Charleroi	422.6
53000	Arr. de Mons	249.88
54000	Arr. de Mouscron	70.72
55000	Arr. de Soignies	180.15
56000	Arr. de Thuin	147.48
57000	Arr. de Tournai	142.2
61000	Arr. de Huy	104.76
62000	Arr. de Liège	594.58
63000	Arr. de Verviers	274.97
64000	Arr. de Waremme	73.11
71000	Arr. de Hasselt	398.06
72000	Arr. Maaseik	228.03
73000	Arr. Tongeren	194.18
81000	Arr. Arlon	55.59
82000	Arr. de Bastogne	43.44
83000	Arr. de Marche-en-Famenne	53.12
84000	Arr. de Neufchâteau	58.15
85000	Arr. de Virton	50.87
91000	Arr. de Dinant	104.02
92000	Arr. de Namur	294.32
93000	Arr. de Philippeville	63.65

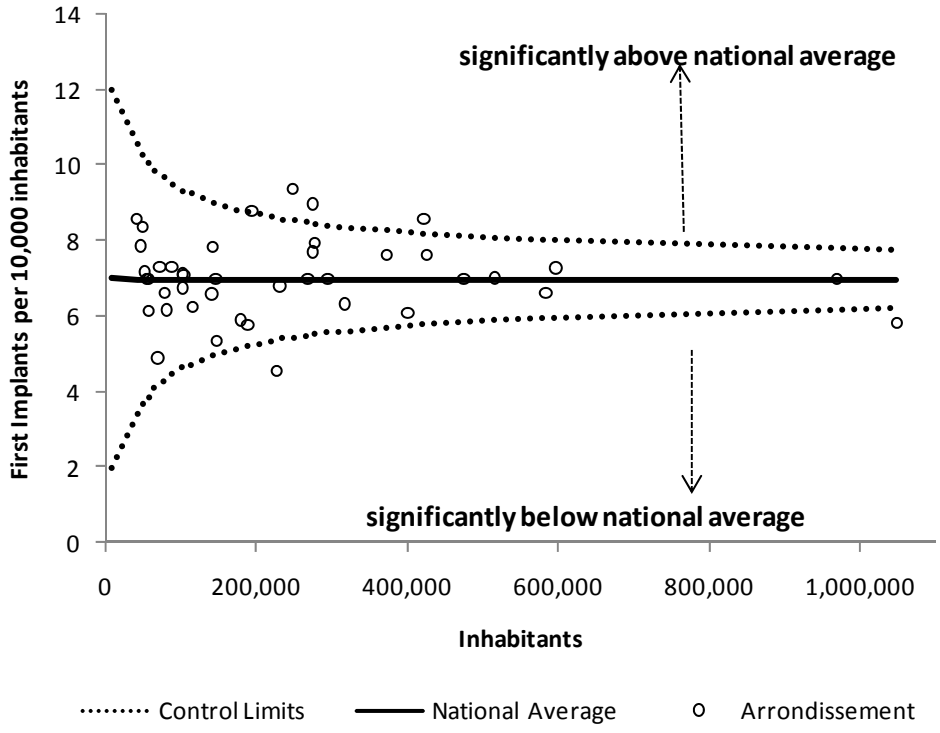
Notes: Statistics Belgium – Population; see section 5.1 for data sources.

Figure 63: Observed implantation rates compared to national average; per *arrondissement* in 2007



Notes: Own calculation based on IMA-AIM and *Statistics Belgium – Population*; see section 5.1 for data sources.

Figure 64: First implantation rates standardized by sex, age, fiscal revenues per capita and share of foreigners; per *arrondissement* in 2007



Notes: Own calculation based on IMA-AIM and *Statistics Belgium – Population*; see section 5.1 for data sources.

9.12 APPENDIX TO CHAPTER 5.2.6

Table 44: Grouping of diagnoses in MCD-MFD data

ICD-code	Group	Subgroup	Label
7802	Aspecific	Aspecific	syncope and collapse
7850	Aspecific	Aspecific	tachycardia, unspecified
7851	Aspecific	Aspecific	palpitations
V421	Aspecific	Aspecific	cardiac transplant
V4501	Aspecific	Aspecific	postoperative status, PM in situ
V4502	Aspecific	Aspecific	postoperative status, defibrillator in situ
V5331	Aspecific	Aspecific	implantation and adjusting of PM
V5332	Aspecific	Aspecific	implantation and adjusting of defibrillator
4260	AV Cond	AVB III	conduction disturbances, complete heart block (third degree AVB)
42610	AV Cond	AVB ns	conduction disturbances, unspecified AVB
42611	AV Cond	AVB I	conduction disturbances, first degree AVB
42612	AV Cond	AVB II	conduction disturbances, second degree AVB, Mobits type II type
42613	AV Cond	AVB II	conduction disturbances, second degree AVB, Wenckebach type (or Mobits type I)
4266	AV Cond	AVB other	conduction disturbances, other types of heart block
4267	AV Cond	AV Cond other	conduction disturbances, preexcitation syndrome
42681	AV Cond	AV Cond other	idem as Dutch
42689	AV Cond	AV Cond other	other specified conduction disturbances
4269	AV Cond	AV Cond ns	unspecified conduction disturbances
74686	AV Cond	AVB other	Congenital heart block
4262	BBB	BBB_L	conduction disturbances, left bundle branch hemi block (anterior or posterior)
4263	BBB	BBB_L	conduction disturbances, other type of left bundle branch block
4264	BBB	BBB_R	conduction disturbances, right bundle branch block
42650	BBB	BBB other	conduction disturbances, unspecified bundle branch block
42651	BBB	BBB_bil	conduction disturbances, right bundle branch AND left posterior bundle branch block
42652	BBB	BBB_bil	conduction disturbances, right bundle branch AND left anterior bundle branch block
42653	BBB	BBB_bil	conduction disturbances, other bilateral bundle branch block
42654	BBB	BBB_tri	conduction disturbances, trifascicular block
3370	Carotid sinus	Carotid sinus	Carotid sinus syndrome
99601	Complic	Complic	mechanical complication resulting from PM implant
99604	Complic	Complic	mechanical complication resulting from defibrillator implant
99661	Complic	Complic	infection of an implanted cardiac device
99672	Complic	Complic	infection of an implanted cardiac device - other
4270	Dysrhythmia	PAT	Paroxysmale Supraventriculaire Tachycardia
4271	Dysrhythmia	PVT	Paroxysmale Ventriculaire Tachycardia
4272	Dysrhythmia	PT ns	unspecified Paroxysmale Tachycardia
42731	Dysrhythmia	AF	atrial fibrillation
42732	Dysrhythmia	AF	atrial flutter
42741	Dysrhythmia	VF	ventricular fibrillation
42742	Dysrhythmia	VF	ventricular flutter
4275	Dysrhythmia	CA	cardiac arrest
42760	Dysrhyth	Prem_beats	unspecified premature beats

	mia		
42761	Dysrhythmia	Prem_beats	supraventricular (or atrial) premature beats
42769	Dysrhythmia	Prem_beats	other premature beats
42781	Dysrhythmia	SSS	sino atrial dysfunction or sick sinus syndrome or SSS
42789	Dysrhythmia	Other	other specified cardiac arrhythmias
4279	Dysrhythmia	NS	unspecified specified cardiac arrhythmias

Source: KCE.

See explanations to Table 42 in the appendix to chapter 0.

Table 45: Association between the cumulative primo implantation rate from 2002 to 2007 and 3AVB by municipality

Variables (Year 2007)	Coefficient	t-value
Fiscal revenue per capita	-0.83***	-8.35
Foreign share of the population	-0.12***	-8.11
Share of 3AVB in all indications	0.20***	-8.34
Share of men in population older than 60	-1.23***	
Share of age groups in total population		-3.19
60-64	-0.16	-1.23
65-69	0.44	2.67
70-74	-0.08	-0.47
75-79	0.34*	1.97
80-84	0.31**	2.15
85-89	0.004	0.04
90+	-0.09	-1.65

Notes: Total number of municipalities without missing data is 572; R^2= 0.44; F-test for validity of the regression model F(11,560) = 40.88; all variables in logs, as such coefficients show elasticities; Huber-White robust standard errors; constant included; Tested for misspecification of the model using STATA's linktest and ovtest; tested for non-normal distribution and heteroscedesticity of the residuals using Shapiro-Wilk test for normality and the Cook and Weisberg test for heteroscedasticity; Calculated the variance inflation factor for the independent variables using the vif test; All calculations done with STATA 9.2; ***Indicates significance at 1% level; **at 5% level; *at 10% level; Notes: Own calculation based on IMA-AIM, *Statistics Belgium – Population* and [41]; see section 5.1 for data sources.

9.13 APPENDIX TO CHAPTER 5.2.7

In Belgium, one distinguishes between three types of hospitals by their academic status: university hospitals, university-related hospitals and non-academic hospitals. University hospitals combine research, teaching and medical activities and are often considered to provide state-of-the-art innovative medical services. University hospitals are recognized by royal decree.[cc] University-related hospitals must have at least 75% "university" beds and conform to the criteria of royal decree.[dd] In 2007 there were 7 university, 15 university-related and 89 non-academic hospitals that performed pacemaker interventions. Due to mergers, the number of independently operating hospitals in our sample decreased from 121 in 2002 to 114 in 2007.

Table 46: Hospitals by academic type; 2002-2007

Hospital type	2002	2003	2004	2005	2006	2007
University	7	7	7	7	7	7
University-related	14	14	14	14	14	15
Non-academic	88	88	88	88	88	89
Not assigned	12	5	5	5	5	3
Total	**121**	**114**	**114**	**114**	**114**	**114**

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Due to differences in the number of hospitals and implants provided by the academic type of hospitals (Table 47), university hospitals provided around 9% of all implants, while they make up 6% of all hospitals. Also university-related hospitals have with 16% a relatively high share in total implants (Figure 65).

Table 47: Number of implants by the academic type of hospitals; 2002-2007

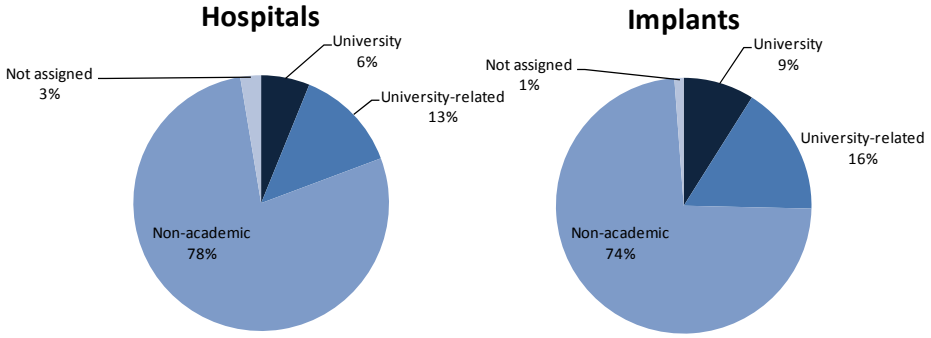
Hospital type	2002	2003	2004	2005	2006	2007
Implants						
University	872	1044	1071	927	1153	976
University-related	1619	1718	1700	1724	1860	1793
Non-academic	6604	7296	7218	7325	7592	8017
Not assigned	461	396	352	287	311	128
Total	**9556**	**10454**	**10341**	**10263**	**10916**	**10914**

Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

cc http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=2005081088&table_name=loi

dd http://www.ejustice.just.fgov.be/cgi_loi/loi_a1.pl?language=fr&la=F&cn=2002042549&table_name=loi&&caller=list&F&fromtab=loi&tri=dd+AS+RANK&rech=1&numero=1&sql=%28text+contains+%28%27%27%29%29#Art.38
Non-academic hospitals:
http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=1989013033&table_name=loi

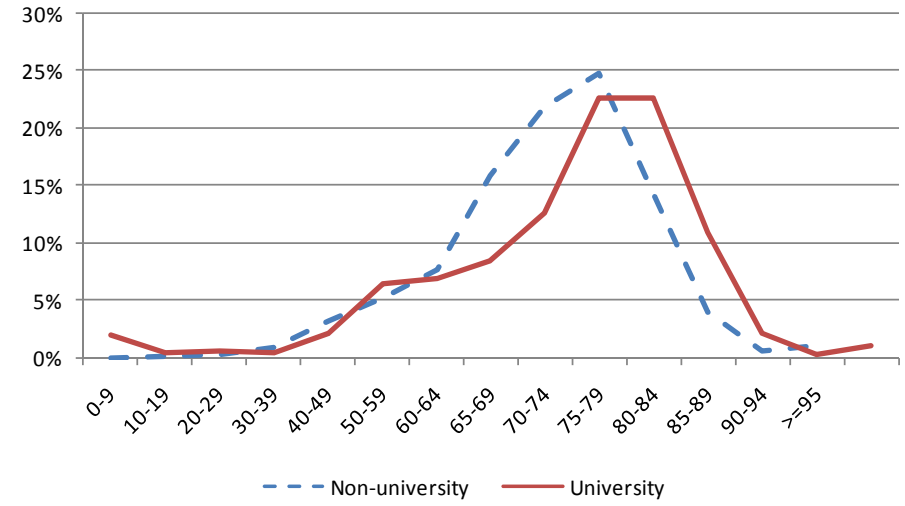
Figure 65: Distribution of the number of total implants by the academic type of hospitals; 2002-2007



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

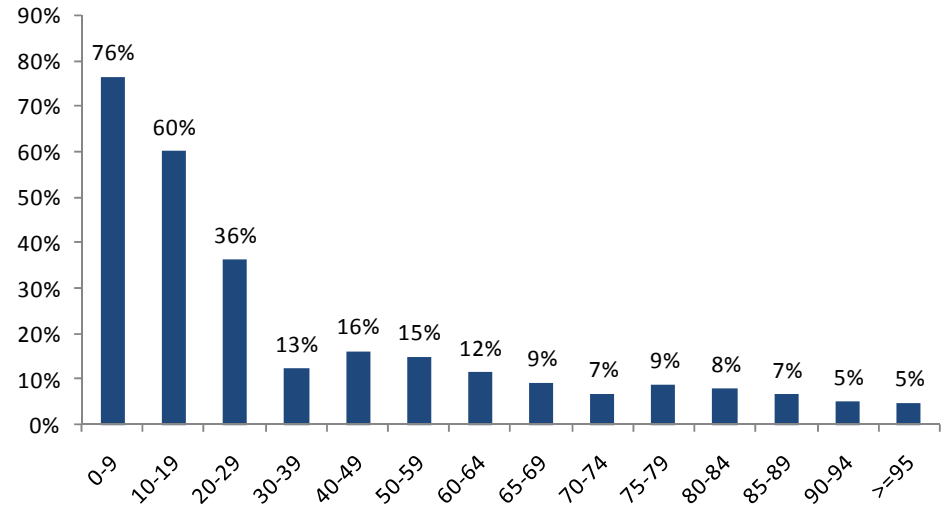
The share of patients below the age of 30 and above the age of 80 provided with primo implantations are relatively high at university as compared to non-academic hospitals (Figure 66). In fact, in 2007 university hospitals treated 76% of all patients with primo implantations below the age of 10, and an overproportional share of patients as compared to the number of university hospitals until the age of 65 (Figure 67).

Figure 66: Age distribution of patients with primo implantations in universities versus non-universities; in %, 2007



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Figure 67: Share of university primo implantations in total implants; by age category in 2007

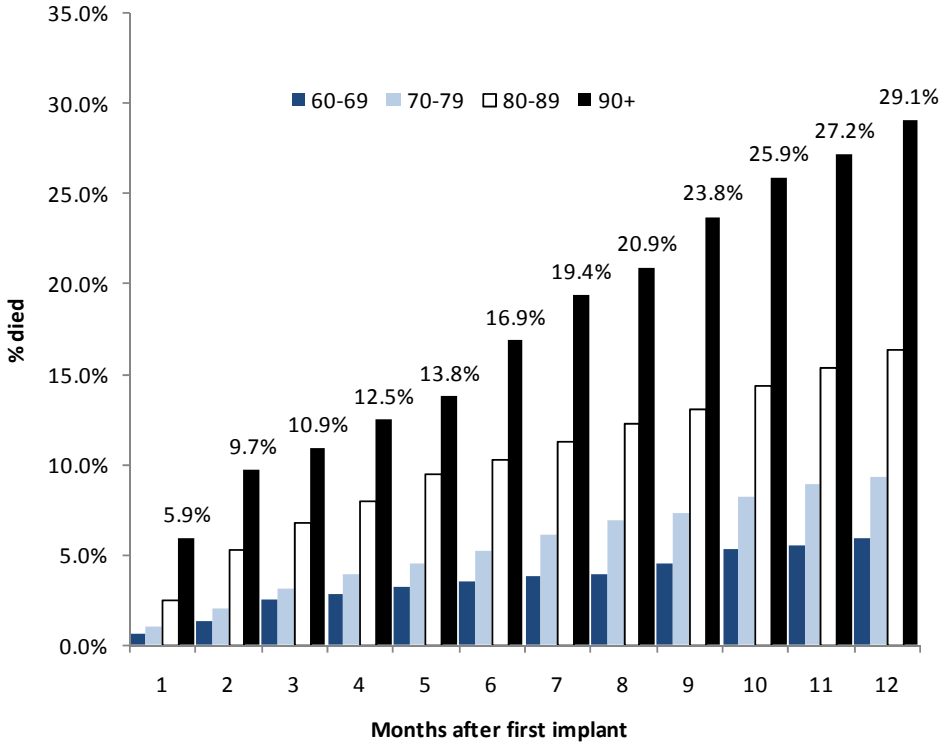


Notes: Own calculation based on IMA-AIM; There are only 4 Belgian hospitals accredited to deliver therapy in congenital heart disease (cardiac care program C), being thus allowed to implant pacemakers in children; see section 5.1 for data sources.

9.14 APPENDIX TO CHAPTER 5.2.8

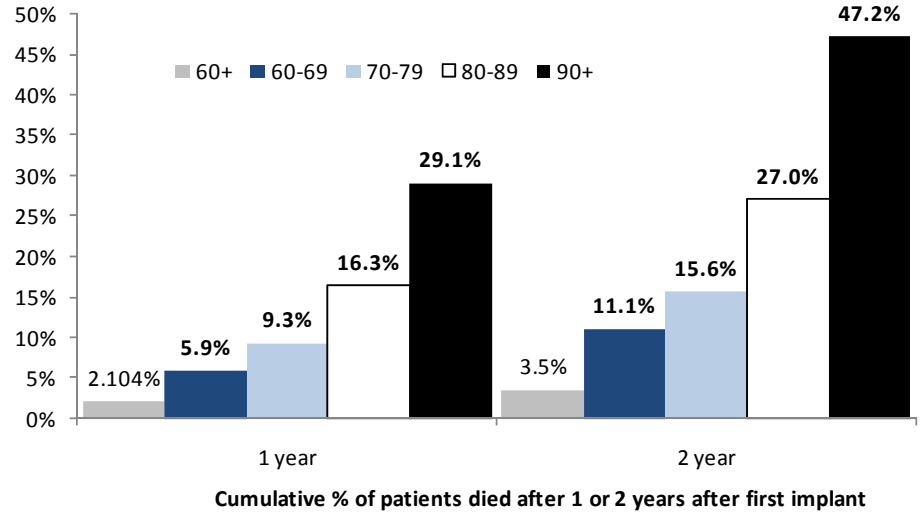
For the groups of patients aged 60-69, 70-79, 80-89 and 90+, Figure 68 shows the monthly cumulative percentages of patients that died within the first year of the primo implantation. For instance, 17.0% of patients aged 90+ died within 6 months and 29% died within the first year after the primo implantation. The cumulative percentages within the first as well as within the first two years are depicted in Figure 69. Around 16% of patients aged 80-89 die within the first year and 27% within two years. 47% of patients aged 90 and more die within two years after the first implant.

Figure 68: Cumulative percentage of patients with primo implantations in 2002 that died within the first year after a primo implantation; by age groups and per month



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

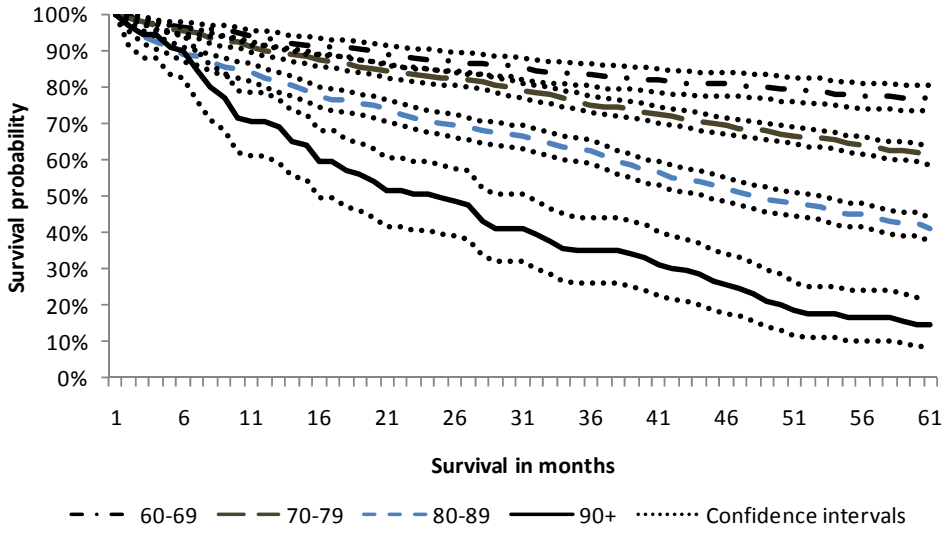
Figure 69: Cumulative % of patients dying within the first two years after a primo implantation; by age groups; 2002-2007



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

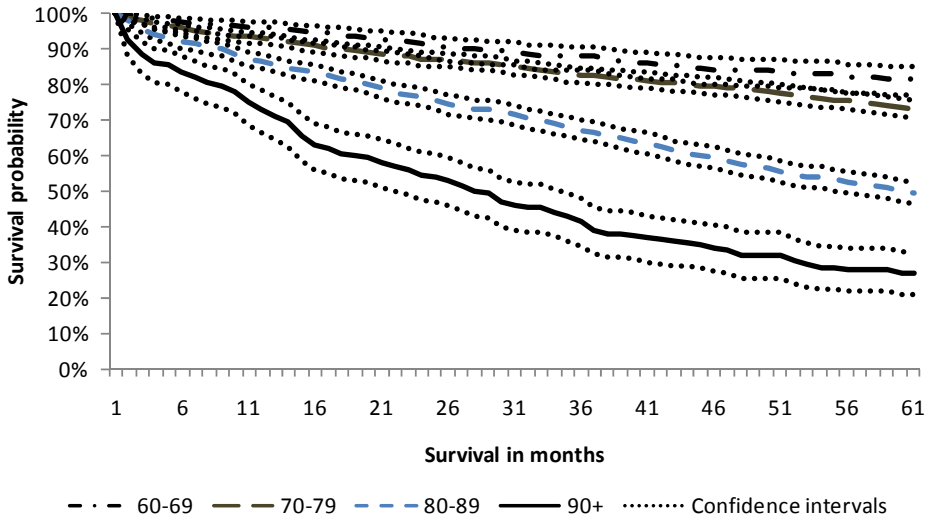
Clearly, survival time after first implantation depends on age and sex. Whereas the survival probability after 36 months of male patients aged 60 to 69 years old is still about 90%, the expected survival probability for those aged 90 and more decreases to around 50% (Figure 70). Within the same age groups female patients have in general a higher survival probability then male patients at any given point of time. For instance, the survival probability after 36 months for females aged 90 and more is 60%, which is 10% more than in the case of male patients (Figure 71).

Figure 70: Survival probability for male patients with primo implantations in 2002



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

Figure 71: Survival probability for female patients with primo implantations in 2002



Notes: Own calculation based on IMA-AIM; see section 5.1 for data sources.

9.15 APPENDIX TO CHAPTER 5.3

Table 48: Comparison of age distribution of male patients between IMA and BeHRA; 2007

Age distribution	Primo implantations		Replacements		Total	
	IMA	BeHRA	IMA	BeHRA	IMA	BeHRA
0-9	0.23%	0.38%	0.00%	0.21%	0.17%	0.33%
10-19	0.08%	0.19%	0.24%	0.28%	0.12%	0.22%
20-29	0.18%	0.28%	0.24%	0.42%	0.19%	0.33%
30-39	0.35%	0.47%	0.36%	0.50%	0.36%	0.48%
40-49	1.53%	1.92%	1.69%	1.77%	1.57%	1.87%
50-59	4.90%	5.22%	4.23%	5.24%	4.67%	5.22%
60-64	6.26%	5.44%	5.50%	4.25%	6.07%	5.07%
65-69	8.90%	7.67%	7.43%	6.87%	8.48%	7.42%
70-74	17.14%	15.21%	15.71%	12.54%	16.68%	14.39%
75-79	22.97%	21.24%	19.27%	17.28%	21.86%	20.02%
80-84	21.56%	20.45%	21.69%	21.81%	21.67%	20.87%
85-89	11.51%	11.31%	16.19%	16.01%	12.84%	12.75%
90-94	2.61%	2.48%	4.77%	4.89%	3.18%	3.22%
>=95	0.35%	0.38%	1.45%	1.70%	0.69%	0.78%
Missing	1.43%	7.38%	1.21%	6.23%	1.44%	7.03%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 49: Comparison of age distribution of female patients between IMA and BeHRA; 2007

Age distribution	Primo implantations		Replacements		Total	
	IMA	BeHRA	IMA	BeHRA	IMA	BeHRA
0-9	0.23%	0.28%	0.20%	0.32%	0.23%	0.29%
10-19	0.06%	0.04%	0.20%	0.08%	0.10%	0.05%
20-29	0.11%	0.07%	0.20%	0.32%	0.14%	0.15%
30-39	0.29%	0.53%	0.39%	0.64%	0.31%	0.56%
40-49	0.71%	0.85%	0.92%	1.45%	0.80%	1.03%
50-59	2.37%	3.00%	2.82%	3.54%	2.51%	3.17%
60-64	3.96%	3.29%	2.30%	2.25%	3.47%	2.97%
65-69	6.78%	6.47%	6.56%	5.47%	6.64%	6.16%
70-74	13.77%	12.05%	8.99%	8.93%	12.16%	11.10%
75-79	21.35%	19.82%	19.29%	18.42%	20.77%	19.40%
80-84	27.22%	24.03%	25.66%	23.65%	26.79%	23.91%
85-89	16.76%	16.43%	20.21%	18.91%	17.85%	17.19%
90-94	4.85%	4.31%	8.60%	7.48%	5.98%	5.28%
>=95	0.77%	0.99%	2.62%	2.57%	1.36%	1.47%
Missing	0.77%	7.84%	1.05%	5.95%	0.90%	7.27%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 50: Comparison of sex distribution of patients with primo implantations between IMA and BeHRA; 2002-2007

Category	2002	2003	2004	2005	2006	2007	Average 2002-2007
Men							
IMA	52.2%	52.6%	53.9%	53.5%	53.8%	53.1%	53.2%
BeHRA	52.0%	50.7%	51.0%	53.8%	53.2%	52.9%	52.3%
Women							
IMA	47.8%	47.4%	46.1%	46.5%	46.2%	46.9%	46.8%
BeHRA	48.0%	49.3%	49.0%	46.2%	46.8%	47.1%	47.7%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

Table 51: Comparison of the sex distribution of patients with replacements between IMA and BeHRA; 2002-2007

Category	2002	2003	2004	2005	2006	2007	Average 2002-2007
Men							
IMA	52.4%	52.5%	51.9%	51.5%	52.0%	52.6%	52.2%
BeHRA	53.1%	50.6%	51.0%	51.5%	52.7%	53.2%	52.0%
Women							
IMA	47.6%	47.5%	48.1%	48.5%	48.0%	47.4%	47.8%
BeHRA	46.9%	49.4%	49.0%	48.5%	47.3%	46.8%	48.0%

Notes: Own calculations based on IMA-AIM and BeHRA; see section 5.1 for data sources.

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131. Continuïteit van de medicamenteuze behandeling tussen ziekenhuis en thuis. D/2010/10.273/37.
132. Is Neonatale Screening op Mucoviscidose aangewezen in België? D/2010/10.273/41.
133. Optimalisatie van de werkingsprocessen van het Bijzonder Solidariteitsfonds. D/2010/10.273/44
134. De vergoeding van slachtoffers besmet met het hepatitis C-virus of het HIV-virus door bloedtransfusie. D/2010/10.273/47.
135. Spoedeisende psychiatrische hulp voor kinderen en adolescenten. D/2010/10.273/49.
136. Bewaking op afstand van patiënten met geïmplanteerde defibrillatoren. Evaluatie van de technologie en breder regelgevend kader. D/2010/10.273/53.
137. Pacemakertherapie voor bradycardie in België. D/2010/10.273/56.