Drempelwaarden voor kosteneffectiviteit in de gezondheidszorg

KCE reports 100A

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
2008

Het Federaal Kenniscentrum voor de Gezondheidszorg

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VOORWOORD

Het Federaal Kenniscentrum voor de Gezondheidszorg (KCE) maakt nu al vijf jaar kritische evaluaties van gezondheidsinterventies, zogenaamde Health Technology Assessments (HTA). Deze HTA rapporten bevatten meestal ook een economische evaluatie. Wanneer een interventie betere resultaten voor de gezondheid oplevert maar meer kost, kan de kosteneffectiviteit berekend worden, uitgedrukt als een Incremental Cost-Effectiveness Ratio (ICER). Deze ICER geeft aan hoeveel het kost om een bijkomende eenheid gezondheidseffect aan te kopen.

Het is onduidelijk hoe Belgische beleidsmakers met dit soort informatie omgaan. Dit rapport is een inleiding tot de methodologische basis en betekenis van ICERs en drempelwaarden voor ICERs. Er worden vragen gesteld over het gebruik van ICERs in beleidsbeslissingen; kennen en gebruiken Belgische beleidsmakers ICERs?

Voor dit onderzoek hebben we gretig gebruik gemaakt van de ervaring van de beleidsmakers en we zijn de deelnemers van de Commissie voor Tegemoetkoming van Geneesmiddelen en de Commissie Tegemoetkoming Implantaten erg dankbaar voor hun medewerking.

Dit rapport is een methodologisch rapport, vergelijkbaar met het rapport 'Richtlijnen voor Farmaco-economische Evaluaties in België' (KCE rapport 78A). Sinds deze richtlijnen in april 2008 werden gepubliceerd, moedigt het RIZIV de farmaceutische bedrijven aan om deze richtlijnen te volgen wanneer ze een farmaco-economische evaluatie indienen bij een aanvraag tot terugbetaling van een geneesmiddel. Met dit rapport hopen we de beleidsmakers en andere belanghebbenden te informeren over het gebruik, de relevantie en de valkuilen van economische evaluaties voor beslissingen binnen de gezondheidszorg. Indien we met dit rapport een iets beter begrip van moeilijke economische concepten en onderzoeksresultaten voor beleidsmakers kunnen verwezelijken zijn we in ons opzet geslaagd.

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Samenvatting

ACHTERGROND

Health Technology Assessments (HTA) bevatten vaak een kosteneffectiviteitsanalyse (KEA). Het doel van een KEA is beleidsmakers te informeren over de kost van de maatschappelijke meerwaarde die een interventie biedt (de zogenaamde *value for money* van een interventie). De noodzaak tot het evalueren van de verhouding tussen maatschappelijke meerwaarde en kost ontstaat vanwege het feit dat keuzes onvermijdelijk zijn wanneer de middelen beperkt zijn. Beleidsmakers in de gezondheidszorg hebben er vaak moeite mee om de resultaten van kosteneffectiviteitsanalyses correct te interpreteren en bij de beleidsvorming te gebruiken. Vandaar de vraag van de Raad van Bestuur van het Federaal Kenniscentrum voor de Gezondheidszorg (KCE) om de basisbegrippen van gezondheidseconomische evaluatie en de interpretatie van kosteneffectiviteitsratio's toe te lichten in een toegankelijk rapport bestemd voor niet-gezondheidseconomisten.

DOELSTELLINGEN

De doelstellingen van het rapport zijn:

- het introduceren van de basisbegrippen van gezondheidseconomische evaluatie: kosteneffectiviteitsanalyse (KEA), incrementele kosteneffectiviteitsratio (Incremental Cost-Effectiveness Ratios - ICERs) en ICER- drempelwaarden.
- het uitleggen van de theoretische basis en relevantie van de ICER-drempelwaarden waarnaar vaak wordt verwezen in gezondheidseconomie.
- beschrijven hoe ICER-drempelwaarden worden gebruikt en kunnen worden gebruikt in het besluitvormingsproces in de gezondheidszorg.
- een overzicht geven van hoe andere landen met ICER- drempelwaarden omgaan.
- onderzoeken hoe twee Belgische adviesorganenorganen op dit moment omgaan met kosteneffectiviteitsvragen in het besluitvormingsproces.

Dit rapport veronderstelt geen voorkennis van gezondheidseconomische evaluaties.

METHODEN

We maakten een narratief overzicht van de wetenschappelijke literatuur, gebaseerd op een incrementele literatuurzoektocht. De verschillende perspectieven t.o.v. ICERs en ICER-drempelwaarden werden weergegeven. De internationale vergelijking was gebaseerd op de lijst van farmaco-economische richtlijnen in verschillende landen die werd gepubliceerd door de *International Society for Pharmacoeconomics and Outcomes Research*. Voor het veldonderzoek deden we twee groepinterviews: één met leden van het Bureau van de Commissie voor Tegemoetkoming van Geneesmiddelen (CTG) en één met leden van de Technische Raad voor Implantaten (TRI).

ECONOMISCHE EVALUATIE IN DE GEZONDHEIDSZORG

Economische evaluatie van interventies in de gezondheidszorg is een vergelijkende analyse van alternatieve handelwijzen, zowel op het vlak van hun kosten als op het vlak van hun uitkomsten. De meest frequent gebruikte technieken voor economische evaluatie in de gezondheidszorg zijn kosteneffectiviteits- en kosten-nutsanalyses. De technieken verschillen in de manier waarop de uitkomsten worden uitgedrukt, maar hebben uiteindelijk hetzelfde doel, nagaan hoe de beperkte middelen moeten worden verdeeld om de totale gezondheid van een populatie te maximaliseren. Een veel gebruikte maat voor 'gezondheid' in kosteneffectiviteitsanalyses is het aantal gewonnen levensjaren door een interventie (*life years gained* - LYG). In kosten-nutsanalyses worden gezondheidseffecten vaak uitgedrukt in termen van het aantal gewonnen gezonde levensjaren (*quality adjusted life years* - QALY's), waarbij de gewonnen levensjaren worden 'gewogen' voor een gekwantificeerde maat voor gezondheidsgerelateerde levenskwaliteit tijdens deze gewonnen levensjaren. In dit rapport wordt KEA gebruikt als de generische term voor beide economische evaluatietechnieken.

DE INCREMENTELE KOSTENEFFECTIVITEITSRATIO

De incrementele kosteneffectiviteitsratio (ICER) is de verhouding van het geschatte kostenverschil tussen twee interventies en het uitkomstenverschil tussen deze twee interventies. De ICER vertegenwoordigt de geschatte bijkomende kost van een interventie per extra eenheid gezondheidseffect ten opzichte van de meest kosteneffectieve alternatieve interventie voor hetzelfde gezondheidsprobleem, de 'comparator'. Het wordt voornamelijk gebruikt om geïnformeerde besluitvorming mogelijk te maken over interventies die zowel duurder als effectiever zijn dan hun comparator.

Er moet rekening worden gehouden met een aantal methodologische problemen met betrekking tot de ICERs.

- Een zinvolle vergelijking tussen ICERs van verschillende interventies is niet altijd mogelijk, vooral niet wanneer de maatstaven voor de gezondheidsuitkomsten niet identiek zijn (bijv. LYG versus gewonnen QALY's) en wanneer de methoden die worden gebruikt om de ICERs te berekenen, verschillend zijn.
- De incrementele kosten en incrementele effectschattingen zijn, per definitie, onzeker en daarom is de ICER ook onzeker. Voor beleidsmakers is de mate van onzekerheid rond de schatting van de ICER relevante informatie waarmee zij mogelijks rekening wensen te houden in het besluitvormingsproces.
- Door het bestaan van tijdsvoorkeur moeten toekomstige kosten en baten verdisconteerd worden. Dit betekent dat de waarde van toekomstige kosten en effecten wordt verminderd om rekening te houden met het feit dat mensen meer waarde hechten aan onmiddellijke gezondheidseffecten en -kosten dan aan toekomstige gezondheidseffecten en -kosten. De relatieve waarde van de discontovoet voor kosten ten opzichte van de discontovoet voor gezondheidsuitkomsten kan een belangrijke impact hebben op de geschatte waarde van de ICER. Of de gezondheidsuitkomsten aan hetzelfde percentage moeten worden verdisconteerd als de kosten is tot op heden een onderwerp van discussie.
- ICERs omvatten typisch kosten en gezondheidsuitkomsten op korte en op lange termijn. Dit betekent dat het nemen van beslissingen op basis van ICERs een invloed heeft op zowel de huidige als de toekomstige verdeling van middelen en gezondheid. Onzekerheid over de toekomst stelt de juistheid van de huidige beslissing altijd in zekere mate in vraag. Met deze onzekerheid moet op gepaste wijze rekening worden gehouden in het besluitvormingsproces.

DE ICER-DREMPELWAARDE

De ICER als zodanig laat beleidsmakers niet toe om conclusies te trekken over de kosteneffectiviteit van een interventie. Voor dergelijke conclusies moet een vergelijking worden gemaakt met een referentiewaarde voor de ICER. Boven deze referentiewaarde wordt een interventie niet langer als kosteneffectief gezien (omdat de bijkomende kosten voor een bijkomende eenheid gezondheidseffect als te hoog worden beschouwd); onder deze referentiewaarde wordt de interventie als kosteneffectief beschouwd. Volgens de neo-klassieke welvaartseconomische theorie, een theorie die ervan uitgaat dat de maatschappelijke welvaart uitsluitend wordt bepaald door het indivuele nut van de leden van die maatschappij, kan men bij een vast budget een ICER-drempelwaarde definiëren boven dewelke een interventie de efficiëntie van de gezondheidssector niet verbetert en onder dewelke een interventie de efficiëntie van de gezondheidssector wel verbetert. Efficiëntie is in deze context gedefinieerd als het maximaliseren van de totale gezondheid met de middelen (het budget) die men beschikbaar heeft voor gezondheidszorg. De ICER-drempelwaarde is de ICER van de laatste interventie in een ranglijst van interventies die nog steeds (volledig of zelfs gedeeltelijk) kan worden gefinancierd met dit vast budget, indien eerst de interventie met de laagste ICER wordt gefinancierd en vervolgens interventies met hogere ICERs tot het budget is uitgeput. Deze ICER-drempelwaarde is gebaseerd op verschillende aannames.

- Het budget voor gezondheidzorg is vast, d.w.z. het kan niet worden overschreden.
- Het enige doel van beleidsbeslissingen in de gezondheidszorg is om gezondheid, uitgedrukt in termen vanvan QALYs of LYG's, te maximaliseren binnen de populatie..
- Men beschikt over volledige informatie over de ICERs van alle mogelijke interventies.
- Programma's zijn perfect deelbaar, d.w.z. ze kunnen worden gereduceerd tot elk gewenst niveau.
- Programma's hebben constante schaalopbrengsten, dit wil zeggen dat een uitbreiding van een programma eenzelfde proportionele toename zowel in kosten als in effecten teweegbrengt: het reduceren of uitbreiden van een programma (in dezelfde doelpopulatie) heeft geen invloed op zijn ICER.
- Gezondheidsprogramma's zijn onafhankelijk van elkaar, dit betekent dat wijzigingen in één programma geen invloed hebben op andere programma's.

Deze ICER-drempelwaarde is het resultaat van een gezondheidsmaximalisatiemodel dat van toepassing is op een specifieke context (welbepaald budget, model van gezondheidszorgorganisatie en ziekteverzekering), op een specifiek tijdsmoment en onder specifieke omstandigheden. Daarom is de ICER-drempelwaarde geen statische waarde, maar wijzigt ze in de loop van de tijd omdat ze onderhevig is aan budgetwijzigingen, financieringing van (nieuwe) interventies en veranderende productiviteit in de gezondheidszorg. De context van een vast budget vereist een variabele ICER-drempelwaarde. Voor een vaste ICER-drempelwaarde daarentegen, is een flexibel gezondheidszorgbudget nodig.

THEORIE VERSUS PRAKTIJK

De theoretische aannames voor een ICER-drempelwaardebenadering zijn onrealistisch. Ten eerste kan de theoretische ICER-drempelwaarde niet worden *geïdentificeerd* in de praktijk omwille van een gebrek aan informatie. Ten tweede, zelfs indien de ICER-drempelwaarde zou kunnen worden geïdentificeerd, zou deze niet kunnen worden *toegepast* omdat bepaalde theoretische voorwaarden niet zijn vervuld: budgetten zijn niet noodzakelijk strikt vast, gezondheidsmaximalisering is niet het enige doel voor beleidsmakers in de gezondheidszorg, billijkheid is altijd een overweging wanneer middelen moeten worden verdeeld, gezondheidsprogramma's vertonen niet altijd constante schaalopbrengsten en programma's zijn niet noodzakelijk perfect deelbaar.

Sommige van deze voorwaarden kunnen als belangrijker worden beschouwd dan andere.

In een gemengd publiekprivaat systeem, waar patiënten remgelden moeten betalen, is het toepassen van de ICER-drempelwaarde niet waardevrij: de ICER- drempelwaarde suggereert wel welke interventies het waard zijn geïmplementeerd te worden, maar helpt niet om het optimale niveau van terugbetaling te bepalen (hoeveel van de totale kosten worden betaald uit het overheidsbudget gezondheidszorg). Ondoordacht gebruik van een unieke ICER-drempelwaarde kan dan vanuit maatschappelijk standpunt leiden tot een ongewenst niveau van eigen bijdragen voor specifieke patiëntenpopulaties en bijgevolg tot een verminderde financiële toegankelijkheid van de gezondheidszorg.

Het gebruik van een expliciete ICER-drempelwaarde kan er ook toe leiden dat de economische evaluaties die worden voorgelegd om terugbetaling van een product te bekomen worden gemanipuleerd naar die drempelwaarde toe. Vooral indien geen standaard methodologie wordt vereist voor economische evaluatie kan dit gebeuren. Maar zelfs met een standaard methodologie is manipulatie tot op zekere hoogte toch nog altijd mogelijk (bijv. selectief gebruik van inputgegevens in een economisch model of het 'optimaliseren' van de prijs van de interventie). Bovendien bestaat het risico dat de ICER-drempelwaarde als een rechtvaardiging op zich wordt gebruikt, terwijl beleidsmakers soms misschien meer nadruk willen leggen op andere criteria dan gezondheidsmaximalisering.

ALTERNATIEVEN VOOR ICERS EN ICER-DREMPELWAARDEN

In de literatuur werden alternatieven voorgesteld voor de ICER-drempelwaarde volgens de neoklassieke welvaartseconomische theorie. Deze alternatieven verschillen in de mate waarin zij het idee van een ICER-drempelwaarde ondersteunen als richtinggevend voor het verdelen van middelen.

- De ICER-drempelwaarde wordt niet langer gedefinieerd als de ICER van de minst kosteneffectieve interventie die nog wordt gefinancierd, maar als de maatschappelijke bereidheid-tot-betalen (BTB) voor een gewonnen QALY (of LYG). Een ICER-drempelwaarde die zo wordt gedefinieerd, vereist een flexibel budget aangezien dit inhoudt dat in principe elke interventie met een ICER onder de maatschappelijke BTB voor een QALY moet worden gefinancierd. De maatschappelijke BTB-benadering is aantrekkelijk omdat ze expliciet gebaseerd is op de maatschappelijke waarde van gezondheidszorg, maar het lijkt moeilijk, zoniet onmogelijk, om de maximum maatschappelijke BTB voor een generische QALY (of LYG) te bepalen; het is moeilijk om zich een beeld te vormen van de waarde van een QALY (of LYG) los van enige concrete context. Een alternatief is het herdefiniëren van de maatschappelijke BTB voor een QALY per individueel geval. Hierdoor vermijdt men het probleem van de meting van de maatschappelijke BTB voor een generische QALY die niet aan een context gebonden is maar loopt men het risico dat dit leidt tot onhoudbare budgetvereisten. Een andere manier die werd gesuggereerd om de maatschappelijke BTB voor een QALY te bepalen, is zich te baseren op beslissingen uit het verleden. Maar de empirische ICER-drempelwaarden of een hele reeks ICER-drempelwaarden uit vroegere beslissingen, moeten altijd worden geïnterpreteerd binnen hun budgettaire, maatschappelijke en politieke context. Aangezien beslissingen zelden of nooit alleen op economische overwegingen gebaseerd zullen zijn, kunnen beslissingen uit het verleden nooit een zuivere schatting zijn van de maatschappelijke BTB voor een QALY (of LYG). Ze kunnen slechts een indicatie geven van welke waarden maatschappelijk aanvaardbaar kunnen.
- De ICER kan impliciet of expliciet worden afgewogen tegen andere elementen in het besluitvormingsproces. Deze benadering vereist het meten en/of objectiveren van elk van de relevante elementen die moeten worden afgewogen. In deze context kan de vergelijking van de ICER met een ICER-drempelwaarde een manier zijn om efficiëntieoverwegingen binnen het besluitvormingsproces te brengen.

- Het eigenlijke gewicht van elk beslissingselement kan expliciet naar voren worden gebracht, of impliciet blijven in het beslissingsproces. Impliciet blijven over het relatieve gewicht van de beslissingscriteria komt de transparantie van het besluitvormingsproces echter niet ten goede. Het expliciet definiëren van het relatieve belang (i.e. gewicht) van de criteria vermindert de noodzaak van herhaalde discussies over het relatieve gewicht dat elk beslissingscriterium moet krijgen maar het eigenlijke gewicht van een criterium bepalen is niet eenvoudig. Discussies zullen altijd nodig blijven omdat elke beslissing mede wordt bepaald door specifieke omstandigheden.
- Eerder dan een drempelwaarde voor de ICER te definiëren, kan een drempelwaarde worden gedefinieerd voor de gemiddelde kosteneffectiviteitsratio. Het gemiddelde Bruto Nationaal Product (BNP) per capita zou zo'n drempelwaarde kunnen zijn, waarbij het gemiddelde BNP per capita wordt aanzien als een reflectie van het 'billijke aandeel' van iedere burger in de totale rijkdom van het land. Deze benadering zou echter kunnen leiden tot een situatie waarbij het volledige BNP (of zelfs meer) zou moeten worden besteed aan gezondheidszorg.
- Bij de opportuniteitskostenbenadering wordt afgestapt van de idee van een ICER als leidraad voor beslissingen. Hier wordt gesteld dat de interventies die worden afgebouwd of volledig verlaten om de nieuwe interventie te kunnen financieren moeten worden gespecificeerd. De 'verloren' gezondheidsbaten van deze interventies moeten vervolgens worden vergeleken met de potentiële 'gewonnen' gezondheidsbaten van de nieuwe interventie. Op nationaal vlak kan implementatie van deze benadering ingewikkeld zijn, vooral indien het gezondheidszorgbudget niet strikt vast is; op lokaal niveau, zoals een individueel ziekenhuis, kan dit mogelijks wel toepasbaar zijn.
- De benadering vanuit kosten-gevolgen pleit ervoor alle economisch relevante elementen in detail uit te splitsen: zowel de inputs in het economisch model als de outputs die in de ICER-schatting 'verborgen' zitten. Zo kan de beleidsmaker expliciet de economische elementen afwegen tegen de andere elementen.

Elk van deze benaderingen zoekt naar een manier om economische overwegingen expliciet te maken in het besluitvormingproces in de gezondheidszorg. Ze mogen niet worden gezien als elkaar wederzijds uitsluitende methoden, maar eerder als elkaar aanvullende methoden die kunnen helpen om de besluitvorming transparanter te maken.

DE ROL VAN ECONOMISCHE EVALUATIES BIJ DE BESLUITVORMING IN DE GEZONDHEIDSZORG

Besluitvorming is een veel ingewikkelder proces dan een geïnformeerde en rationele evaluatie van problemen, het afwegen van alternatieven en het formuleren van optimale oplossingen. Rationaliteit is inherent begrensd, beslissingen incrementeel en besluitvormingsprocessen politiek van aard. Beslissingen worden niet genomen op basis van wetenschappelijke of technische informatie alleen, maar op basis van een verscheidenheid aan informatiebronnen. Dit betekent dat in de realiteit economische evaluaties alleen niet zullen volstaan om beleidsmakers te informeren bij de besluitvorming. Effectiviteit en kosteneffectiviteit zijn slechts twee van de vele overwegingen bij het maken van beleidskeuzes. Noch de theorie, noch de empirie wijzen op een evolutie van de ICER-drempelwaarde naar een uniek beslissingcriterium. Bevindingen uit KEA kunnen als input worden gebruikt in een deliberatief, op evidence gebaseerd besluitvormingsproces waarin de standpunten en belangen van meerdere belanghebbenden in overweging worden genomen.

Er worden niettemin inspanningen gedaan om de beslissingen in de gezondheidszorg te "rationaliseren" door informatie en kennis aan te bieden die op een degelijke methodologische basis werd verzameld.

Kennis en wetenschappelijke bewijsvoering kunnen op drie verschillende manieren worden gebruikt door de beleidsmakers: direct, selectief en ter verduidelijking. Er werden echter verschillende hinderpalen en faciliterende elementen geïdentificeerd voor een geïnformeerde besluitvorming. Hinderpalen bij het gebruik van economische evaluaties in besluitvorming zijn meestal gerelateerd aan de *toegankelijkheid* van wetenschappelijke bewijsvoering en de *aanvaardbaarheid* ervan. Het vermogen om economische analyses te begrijpen, de houding ten overstaan van economische evaluaties (waaronder bezorgdheid over de basis van de analyses en hun gebruik), de draagwijdte van de economische onderzoeksvragen in vergelijking met de draagwijdte van de beleidsvragen, belemmeren het gebruik van KEA bij de besluitvorming.

Een onderzoekstak concentreert zich op kennis makelarij (*knowledge brokering*). Voor het proces van 'knowledge brokering' werden vier modellen geïdentificeerd: een informatie push model, een informatie pull model, een uitwisselingsmodel en een geïntegreerd model.

Omwille van de praktische moeilijkheden die samenhangen met de besluitvorming, zou men, vanuit het standpunt van sociale rechtvaardigheid en democratie, tenminste mogen verwachten dat het besluitvormingsproces transparant is en dat de beleidsmakers verantwoordelijk zijn voor hun beslissingen.

HET GEBRUIK VAN ICER-DREMPELWAARDEN IN ANDERE LANDEN

Geen van de 10 landen die in dit rapport worden bestudeerd, gebruikt een unieke ICER-drempelwaarde. Momenteel gebruikt het Verenigd Koninkrijk (VK) een ICER-drempelwaarde *bereik* van £20 000 tot £30 000 per gewonnen QALY, maar de discussie over het gebruik van ICER-drempelwaarden, en het niveau ervan, is echter wel nog steeds aan de gang in het VK.

Sommige landen hebben getracht een impliciete ICER-drempelwaarde af te leiden uit vroegere beslissingen over de verdeling van middelen: in Australië vond men AU$69 900/QALY, in Nieuw-Zeeland NZ$20 000/QALY en in Canada vond men een aanvaardingsbereik van kosten van dominante interventies (met name minder dure én meer effectieve interventies) tot CAN$80 000/QALY met een bereik voor negatief advies met betrekking tot terugbetaling van CAN$31 000 tot CAN$137 000/QALY.

We vonden ICER-drempelwaarden of bereiken, voorgesteld door personen of instellingen in de Verenigde Staten ($50 000/QALY), Nederland (€80 000/QALY) en Canada (CAN$20 000 - CAN$100 000/QALY).

Zelfs in het enige land dat een expliciet bereik van drempelwaarden hanteert (VK), wordt de besluitvorming niet alleen gebaseerd op overwegingen van kosteneffectiviteit. Een typisch aanvullend beslissingscriterium is billijkheid. Onlangs werden in het Verenigd Koninkrijk de relatieve maatschappelijke waarden gemeten voor gezondheidsbaten volgens de populaties waarbij deze baten werden gerealiseerd, met als doel in KEA "billijkheidsgewichten" toe te kennen aan gewonnen QALYs.

In geval van hoge ICERs kunnen andere beoordelingselementen aan belang winnen. In de meeste landen blijkt dat de waarschijnlijkheid dat een interventie wordt aanvaard voor terugbetaling groter is als de ICER lager is. Deze relatie voor België onderzoeken lag buiten het opzet van deze studie.

HET GEBRUIK VAN ICER-DREMPELWAARDEN IN BELGIE

Hoewel er inspanningen worden geleverd om het besluitvormingsproces te 'rationaliseren' en vragen tot terugbetaling wetenschappelijk te onderbouwen, blijft de besluitvorming in België voornamelijk een interactief deliberatieproces. Klinische effectiviteit is het belangrijkste wetenschappelijke criterium dat in het besluitvormingsproces van zowel de Commissie voor Tegemoetkoming van Geneesmiddelen (CTG) als van de Technische Raad voor Implantaten (TRI) wordt gebruikt. Kosteneffectiviteit wordt soms in overweging genomen in de CTG maar slechts zelden in de TRI. Door beide Commissies wordt de budgettaire impact als een belangrijker factor gezien dan de ICER.

CONCLUSIE

De ICER kent een aantal zwakke punten als maat voor het evalueren van het vermogen van een interventie om de efficiëntie in de gezondheidszorg te verhogen. De ICER-drempelwaarde waarmee de ICERs van interventies moeten worden vergeleken, is onbekend en varieert in de tijd. Dit is echter geen argument *tegen* het gebruik van economische overwegingen bij de besluitvorming in de gezondheidszorg. Economische overwegingen negeren is onethisch, aangezien het besteden van middelen aan één gezondheidszorgprogramma de beschikbare middelen voor andere gezondheidszorgprogramma's vermindert.

AANBEVELINGEN

- Efficiëntie moet één van de criteria zijn in de besluitvorming rond gezondheidszorg, aangezien het onethisch is om economische efficiëntie te negeren in beleidsbeslissingen. Dossiers die worden ingediend ter ondersteuning van het beleid moeten bijgevolg steeds een economische evaluatie bevatten.
- Economische modellen moeten op een transparante manier worden beschreven. Alle informatie die in het model wordt gebruikt moet zodanig worden weergegeven dat beleidsmakers in staat zijn om de gemaakte aannames te verifiëren, de invloed van onzekerheden te beoordelen en het belang van deze aannames en de onzekerheden voor de beslissing af te wegen.
- De resultaten van economische evaluaties moeten uitgesplitst worden weergegeven. Dit houdt in dat men de ICER 'uitpakt', maar ook dat men economisch relevante parameters voorlegt die kunnen worden afgeleid uit de economische evaluatie maar die niet noodzakelijk zichtbaar zijn in de ICER-schatting.
- Naast de uitgesplitste presentatie van economisch belangrijke elementen, moet men ook de ICER, berekend volgens standaard methodologische richtlijnen, blijven voorleggen.
- In het besluitvormingsproces over de verdelingverdeling van middelen in de gezondheidszorg moet wetenschappelijk onderzoek een plaats blijven krijgen. Dit laat beleidsmakers toe om hun argumenten wetenschappelijk te onderbouwen.
- Beleidsmakers moeten de criteria die aan de basis liggen van hun beleidsbeslissingen, en het relatieve belang van de verschillende criteria in elke beslissing, transparanter maken.

Scientific summary

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GLOSSARY

Beveridge-type health care system	Taxation-funded public health service system (named after William Beveridge, 20th century British economist and politician).
Bismarck-type health care system	Health care system where public and private providers are reimbursed by compulsory health insurance funds (named after Otto von Bismarck, 19th century German chancellor).
Confidence interval (CI)	Statistical concept. Interval likely to include the estimated parameter with a given confidence level, for example 95% CI. Results are presented as a point estimate surrounded by its confidence interval.
Cost-benefit analysis	Type of economic evaluation in which all costs incurred and resulting benefits of an intervention are expressed in monetary units (e.g. €) and a net monetary gain/loss or cost-benefit ratio is computed.
Cost-consequence analysis	A variant of cost-effectiveness analysis in which the components of incremental costs and consequences (health outcomes) of alternative programmes are computed and listed, without aggregation into a cost-effectiveness ratio or cost-utility ratio.
Cost-effectiveness acceptability curve	Curve representing the probability of an intervention being cost-effective (Y-axis), given different values for the ICER threshold value (X-axis). The curve reflects the uncertainty around the ICER estimate.
Cost-effectiveness analysis	Method of comparing alternative treatments in which the costs and consequences of the treatments vary. The outcomes of alternative treatments are measured in the same non-monetary (natural) unit (e.g. life years gained, events avoided, …).
Cost-minimisation analysis	Method of comparing the costs of alternative health interventions that are assumed to have an equivalent effect on health outcomes.
Cost-utility analysis	Special form of cost-effectiveness analysis in which the costs per unit of 'utility' are calculated. The term is also frequently used for economic evaluations that take the impact of an intervention on health-related quality of life into account, irrespective of whether the outcome measure can be regarded as a true utility measure in its theoretical economic sense. The most commonly used outcome measure in cost-utility analyses is the quality-adjusted life year (QALY).
Credibility interval	Confidence interval around a cost-effectiveness ratio resulting from an economic model. In contrast to statistical confidence intervals, the values within a credibility interval are not actually observed but result from a mathematical model, making assumptions about the relationships and distributions of input variables.
Discounting	Economic concept to handle time-preference, using a method of calculation by which costs and benefits occurring at different moments in time can be compared. Discounting converts the value of future costs and benefits into their present value to account for positive time preferences for benefits (preference for current benefits as compared to future benefits) and negative time preferences for costs (preference for future costs as compared to current costs).
Economic evaluation	Comparative analysis of alternative courses of action in terms of both their costs and consequences.
Effectiveness (effectiviteit/doeltreffendheid; efficacité réelle/efficacité pratique	The extent to which health interventions achieve health improvements in real-life settings.
Efficacy (efficaciteit/werkzaamheid; efficacité théorique/efficacité expérimentale/efficacité	The extent to which health interventions achieve health improvements under ideal controlled conditions (as for example in randomised controlled trials)

potentielle)	
Efficiency (efficiëntie/doelmatigheid; efficience)	In economic theory defined as the condition in which no productive resources are wasted in the manufacture of a certain product; i.e. where output is produced at minimum cost or the level of output is maximised at a given cost (i.e. cannot be increased). In health care, efficiency implies that choices should be made so as to derive the maximum total health benefit from the available resources. 'Allocative efficiency' occurs when the outcomes achieved with the available resources match the priorities of society.
Health-related quality of life	A multidimensional construct measuring the physical, social and emotional aspects that are relevant and important to a patient's well-being.
Health maximisation	Maximisation of relevant health outcomes. In health economics often maximisation of the number of LYG or the number of QALYs gained.
Health outcome	Result of health intervention for the health of a patient or a population.
ICER threshold value	Benchmark for ICERs (incremental cost-effectiveness ratios) to assess an intervention's cost-effectiveness. Interventions with an ICER below the ICER threshold value are considered cost-effective, interventions with an ICER above the ICER threshold value are not cost-effective.
Incremental analysis	Analysis of additional costs and additional health outcomes associated with different treatments.
Incremental cost-effectiveness ratio (ICER)	Ratio of additional costs and additional health outcomes associated with different treatments: $(C_2 - C_1)/(E_2 - E_1)$, where C_2 and C_1 represent the costs of intervention 2 and 1 respectively and E_2 and E_1 represent the health outcomes (effects) of intervention 2 and 1 respectively.
League table	Table ranking health interventions according to their incremental cost-effectiveness ratio with the purpose to guide resource-allocation decisions.
Opportunity costs	The costs of resources consumed expressed as the value of the next best alternative for using these resources.
Private insurance based health care system	System where health care is funded from premiums paid to private insurance companies.
Quality-adjusted life year	Measure for health outcomes that includes both quality and quantity of life a patient is expected to have. Quality-adjusted life years are calculated by estimating the total life years gained from a treatment and weighting each time period within these life years gained with a quality-of-life score between 0 (dead) to 1 (perfect health) that reflects the health-related quality of life in that period.
Sensitivity analysis	Technique used in economic evaluation to allow for uncertainty by testing whether plausible changes in the values of the main variables affect the results of the analysis.
Societal Willingness to Pay (WTP)	Societal willingness to pay refers to the maximum amount society is willing to pay for a unit of health gain (e.g. QALY or life-year gained). It reflects what society is willing to sacrifice in terms of other goods or services for a unit of health gain.
Uncertainty	A state in which the true value of a parameter or the structure of a process is unknown.
Utility	A measure of the preference for, or desirability of, a specific level of health status or specific health outcomes.

ABBREVIATIONS

CADTH	Canadian Agency for Drugs and Technologies in Health
CBA	Cost-Benefit Analysis
CEA	Cost-Effectiveness Analysis
CEDAC	Canadian Expert Drug Advisory Committee
CTG/CRM	Drug Reimbursement Committee (Commissie Tegemoetkoming Geneesmiddelen/Commission de Remboursement des Médicaments) (=DRC) (Belgium)
CUA	Cost-Utility Analysis
CVZ	Dutch Health care Insurance Board (College voor zorgverzekeringen)
DACEHTA	Danish Centre for Health Technology Assessment
DRC	Drug Reimbursement Committee (=CTG/CRM) (Belgium)
FOD/SPF	Federal Public Service (Federale Overheidsdienst / Service Public Fédéral) (=FPS) (Belgium)
FPS	Federal Public Service (=FOD/SPF) (Belgium)
GDP	Gross Domestic Product
HPV	Human Papillomavirus
HRQoL	Health-Related Quality of Life
ICER	Incremental Cost-Effectiveness Ratio
KCE	Belgian Health Care Knowledge Centre (Federaal Kenniscentrum voor de Gezondheidszorg / Centre fédéral d'expertise des soins de santé (Belgium)
MCDA	Multi-Criteria Decision Analysis
MRI	Magnetic Resonance Imaging
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence (UK)
NIHDI	National Institute for Health and Disability Insurance (=RIZIV/INAMI) (Belgium)
PBAC	Pharmaceutical Benefits Advisory Committee (Australia)
PET	Positron Emission Tomography
PHARMAC	Pharmaceutical Management Agency (New Zealand)
QALY	Quality-Adjusted Life Year
RIZIV/INAMI	National Institute for Health and Disability Insurance (Rijksinstituut voor Ziekte- en Invaliditeitsverzekering/National d'Assurance Maladie-Invalidité) (=NIHDI) (Belgium)
TCI	Technical Council for Implants (=TRI/CTI) (Belgium)
TRI/CTI	Technical Council for Implants (Technische Raad voor Implantaten/Conseil Technique des Implants) (=TCI) (Belgium)
WTP	Willingness-To-Pay

1 GENERAL INTRODUCTION

1.1 BACKGROUND

One of the research domains of the Belgian Health Care Knowledge Centre (KCE) is Health Technology Assessment (HTA). HTA aims to inform health care decision makers about the (most likely) clinical, economic, organisational and ethical implications of implementing and financing health interventions. In comparison with existing health interventions, new interventions may reduce mortality or morbidity, improve health-related quality of life (HRQoL), deliver similar care for less money or enhance the organisation of health care. Unfortunately, although many of these technologies have their own intrinsic value, society cannot afford all of them simultaneously. Therefore, the assessment of the *'value for money'* of health interventions is an important part of any HTA. It usually takes the form of a cost-effectiveness or cost-utility analysis.

This report is written at the request of the Board of the Belgian Health Care Knowledge Centre (KCE). Some of the KCE HTA-reports present cost-effectiveness analyses and incremental cost-effectiveness ratios (ICERs). For people who are not trained in health economics it may not be clear, however, what ICERs represent and what their contribution can be for health care policy making. Therefore a demand was formulated to explain to lay people the concept of ICERs and their potential use in daily practice.

1.2 PROBLEM STATEMENT

Economic evaluation assesses the relative *'value for money'* of health interventions.[1]

Health interventions are to be interpreted in a broad sense. They include preventive health programmes, curative health care, rehabilitation services and palliative care and within these health interventions, use of drugs, medical devices, behavioural therapy etc.[2-4]

The basic goal of economic evaluations is to inform health care policy makers about the best way to allocate limited resources in health care in order to maximize health gains. They help decision makers to evaluate whether funding a particular (high cost) technology is worthwhile.

A commonly used measure for the assessment of an intervention's relative value for money is the incremental cost-effectiveness ratio (ICER). The ICER represents the additional cost per extra unit of *'effect'* generated by an intervention compared with an appropriate comparator. This comparator is an alternative intervention for the same condition or no intervention when none is currently available. While costs are normally expressed as monetary values (for a given year), effects can be expressed in various units, such as life years gained (LYG), quality-adjusted life years (QALY) gained, or natural units (e.g. number of infections avoided).[2-4]

If an intervention offers better outcomes at a lower cost than its comparator, i.e. it is more effective and less costly, it is straightforward to conclude that it offers better value for money (see 2.3). More often, however, an intervention offers better outcomes at a higher cost. For the evaluation of these cases, economic evaluation can be helpful to policymakers, especially when deciding about the reimbursement of health interventions because reimbursement has implications for the efficiency of the allocation of the scarce health care resources.

However, it is not so straightforward to give a meaning to ICERs or to use them in a decision making context. For example, is €60 000 per QALY gained reasonable to decide for reimbursement or is it too high? Where do we draw the line of acceptability? Without ways to deal with these questions, economic evaluations and their resulting ICERs will be of limited value to health care decision makers.

1.3 SCOPE OF THIS REPORT

This report is written to support non-economically trained people involved in health care decision making. Therefore, the aim of this report is primarily didactic and it does not pretend to be a fully elaborated scientific (theoretical and methodological) study.

The central questions in this report are: "*When can interventions be considered cost-effective*" and *"Is there a threshold for the ICER above which interventions can no longer be considered cost-effective?*".

This report offers information to health care policy makers about economic evaluations in health care, their results and their relevance for health care policy. It gives an introduction on how the results of economic evaluations should be interpreted, whether a threshold value for the ICER can be defined above which an intervention cannot be considered cost-effective and how the ICER can be used in health care policy decision making. Recommendations are formulated for health care policy makers on how to deal with results of economic evaluations within decision making contexts and also for researchers on how to make the results of economic evaluations more useful for policy makers.

1.4 OBJECTIVES

This report describes the basic concepts of cost-effectiveness analysis (CEA), incremental cost-effectiveness ratios (ICERs) and ICER threshold values. It aims to explain how they are obtained and tries to explore how they are or could be used in health care decision making contexts.

More specifically, the report addresses six questions:

- What is an ICER and an ICER threshold value and where does it come from, i.e. what is its theoretical background? (sections 2.1 to 2.6)
- What is the external validity of the theoretical assumptions for an ICER threshold value? (section 2.7)
- What are possible alternatives for the ICER threshold value approach? (section 2.8)
- What is the (potential) role of an ICER threshold value in health care decision making contexts? (sections 3.1 to 3.4)
- Are ICER threshold values used in other countries and how are they used? (section 3.5)
- How do specific Belgian advisory councils deal with the issue of *'value for money'* in health care? (section 3.6)

For interested readers, references for further reading are provided.[2-5]

1.5 METHODOLOGY

Given the objectives of this report, we did not perform a systematic review of the literature. We made a narrative review of the literature on ICERs and ICER threshold values using an incremental search strategy: starting from relevant references identified through an explorative search in Medline, (key-words used were 'cost-effectiveness', 'ICER' and 'threshold') and applying the snowball principle to identify additional relevant references. We considered different viewpoints on CEA and ICERs, trying not to exclude or preferentially include any specific perspective.

The methods used for the international comparison of the use of ICER threshold values and for the explorative field study in the Belgian decision making context are detailed in the relevant sections.

1.6 STRUCTURE OF THIS REPORT

First, we briefly describe the basic concepts of economic evaluation and the theoretical foundations for ICER threshold values (question 1). Next, we describe to what extent the theoretical assumptions of the ICER threshold value approach are valid (question 2) and which alternatives are suggested in literature for ICERs and ICER threshold values along with their strengths and weaknesses (question 3).

In a subsequent chapter, we describe decision making processes and the potential place of economic considerations within these (question 4). The application of ICER thresholds in other countries is described (question 5) and we conclude the chapter with a description of the results of an explorative field study within the Belgian decision making context and the place of ICERs and ICER threshold values in two committees that advice the Ministry of Social Affairs about the reimbursement of health interventions (question 6). The field study explores to what extent CEA and ICERs are currently known and used in Belgian health care reimbursement decision making.

The report concludes with a general discussion on the possible role of economic evaluation in health care decision making and the conclusions from this scientific overview. Finally, we formulate some recommendations for Belgian health care policy makers with respect to the potential use of ICERs and ICER threshold values in policy decisions.

2 ICERS AND ICER THRESHOLD VALUES

2.1 GENERAL PRINCIPLES OF ECONOMIC EVALUATION IN HEALTH CARE

Economic evaluation is defined as the comparative analysis of alternative courses of action in terms of both their costs and consequences.[2] In economic evaluation of health care interventions, 'consequences' are most often interpreted as 'health effects' or 'health outcomes'. Both terms will be used interchangeably in this report.

Only evaluations that compare two or more alternatives and consider both costs and consequences are considered full economic evaluations (see Figure 1).[2]

Figure 1: Overview of partial and full economic evaluations

		Are both costs (inputs) and consequences (outputs) of alternatives examined?		
		No		Yes
		Outputs only	Inputs only	
Comparison of 2 alternatives?	No	Outcome description	Cost description	Cost-outcome description
	Yes	Efficacy or effectiveness evaluation	Cost comparison	Cost-utility analysis (CUA), Cost-benefit analysis (CBA), Cost-effectiveness analysis (CEA), Cost-minimisation analysis (CMA)

Partial evaluation

Full economic evaluation

Adapted from Drummond et al. (2005)[2]

Full economic evaluations are classified according to the way in which the health effects are expressed. Health effects can be expressed in physical units (cost-effectiveness analysis, CEA), in terms of utility values (cost-utility analysis, CUA) or in monetary terms (cost-benefit analysis, CBA). A commonly used outcome measure in CEA is the *'number of life years gained'* (LYG) by the intervention under study. In CUA, the number of quality-adjusted life years gained (QALYs) is often used as an outcome parameter, where LYG are 'weighted' for a quantified measure of health-related quality of life (HRQoL) in those LYG. QALYs are often regarded as just another measure of effectiveness rather than as a utility measure in its strict utilitarian sense.[6, 7] Therefore and for the ease of reading, we use the term cost-effectiveness analysis (CEA) for both cost-per-LYG and cost-per-QALY gained analyses throughout this report. CBA, where both costs and effects are expressed in monetary terms, is becoming increasingly unpopular as a technique for health economic evaluations because of the difficulties experienced in valuing health outcomes in monetary terms.[a 3] Therefore, we will concentrate on CEA in this report. Cost-minimisation analysis is a specific case of CEA where the health outcomes of the intervention and its comparator are assumed to be equivalent and where the aim then becomes to obtain those outcomes at the lowest cost.[2-4]

CEA is used to assess efficiency in the production of desirable health outcomes. More specifically, it aims to help identify how the highest number of LYG or QALYs can be achieved by allocating limited resources between all possible health interventions.[2-4]

a In contrast to CEA or CUA, where one specific measure of health effect is chosen for the evaluation (e.g. LYG or QALYs), cost-benefit analysis in principle allows the consideration of non-health effects of an intervention as well. It is therefore a broader form of economic evaluation than CEA or CUA. I.e. if all effects of an intervention could be expressed in monetary units, there is no reason to restrict the analysis to health effects only. Consequently, broader comparisons would become possible with CBA, even with interventions outside the health care sector. An acceptable monetary valuation of all effects remains, however, difficult.

The assumption of CEA in its neo-classical welfarist form is that health care decision makers' primary goal is to maximise health within given budget constraints, making abstraction of other potential concerns decision makers may have in real life, such as equity, political and macro-economic considerations.

Its aim is to show how resources can be allocated to meet the goal of health outcomes maximisation, where health outcomes are strictly defined in terms of LYG or QALYs gained. There is still debate about whether this kind of CEA is useful for decision makers, i.e. as an *imperfect* aid to decision making,[2] or whether CEA should try to incorporate, in some way or another, the other goals health care policy makers might have,[8] for instance by weighting the health outcomes of specific populations more heavily to reflect social preferences for health outcomes allocation, as in the so-called extra-welfarist approach. Although theoretically appealing, there is yet no consensus on *how* other goals besides health maximisation should be incorporated in CEA or *what* other goals should be included.[4, 9-11] CEA, as commonly performed in practice now, still approaches the resource allocation decision problem from the economic efficiency point of view, not explicitly considering other health policy goals such as equity in its framework. Therefore, we focus on this basic approach in this chapter. Chapter 3 elaborates on other possible approaches.

Key points

- **Economic evaluation is the comparative analysis of alternative courses of action in terms of both their costs and consequences.**
- **Cost-effectiveness (CEA) and cost-utility analysis (CUA) are the most frequently used techniques for economic evaluation in health care. In this report CEA is used as the generic term to cover both techniques.**
- **CEA aims to inform health policy makers about the best way to allocate limited health care resources in order to obtain maximal health outcomes in terms of LYG or QALYs gained.**

2.2 THE INCREMENTAL COST-EFFECTIVENESS RATIO (ICER)

The ICER is the ratio of the difference in costs (C) and the difference in outcomes (E, effects) between an intervention and its comparator. Expressed in a formula:

$$ICER = \frac{C_2 - C_1}{E_2 - E_1}$$

where C_2 (E_2) is the cost (effect) of the intervention and C_1 (E_1) is the cost (effect) of the comparator. The costs of the intervention and the comparator include not only the costs of a specific drug, device or act but the cost of the entire treatment path followed by the patients undergoing the treatment, including the costs of follow-up and treatment of potential complications and/or side-effects (lifetime perspective). Also on the effect-side, effects are not limited to the immediate effect of a product, device or act but both the positive and negative health effects associated with the entire treatment path and the potential complications and side-effects. The comparator should be a cost-effective alternative intervention for the same condition.[b 2, 3]

The ICER can be expressed as a cost per LYG or as a cost per QALY gained. It is used for making decisions about interventions that are both more costly and more effective than their comparator (or less effective but cheaper).

b Comparing with an intervention that is not cost-effective will eventually lead to an estimate of the ICER that is unable to inform policy makers about the best way to allocate scarce resources to obtain the highest health benefits (see 2.6.2). It is hence assumed that it is possible to establish the cost-effectiveness of the comparators before the comparison is made. In practice, it is often assumed that 'current practice' is the most appropriate cost-effective comparator.

The ICER of an intervention could be compared to a certain ICER threshold value or to ICERs of other interventions for other conditions. The lower the ICER, the more additional health can be obtained with the same additional value of resource inputs, and thus the more cost-effective an intervention is considered.[2-4]

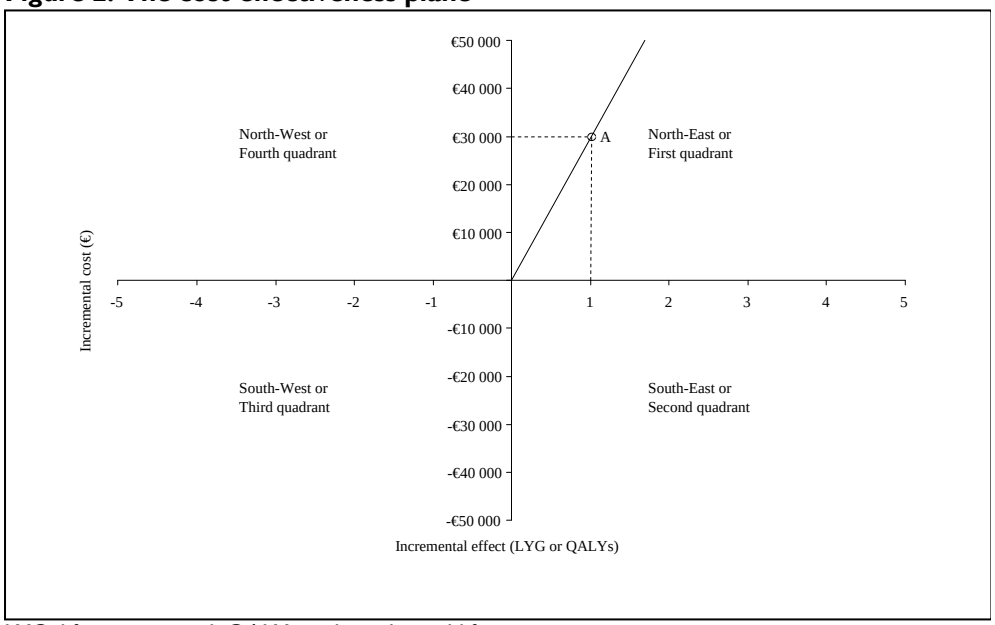
Key points

- **The incremental cost-effectiveness ratio (ICER) is the ratio of the estimated difference between the costs of two interventions and the estimated difference between the outcomes of these two interventions.**
- **The ICER represents the estimated additional cost per extra unit of health benefit generated by an intervention compared with an appropriate comparator. The appropriate comparator is the most cost-effective alternative for the same health condition.**
- **The ICER intends to support informed decision making about interventions that are both more costly *and* more effective than their comparator (or inversely less effective but cheaper).**

2.3 THE COST-EFFECTIVENESS PLANE

The results of a full economic evaluation can be represented graphically on a cost-effectiveness plane (Figure 2).[2]

Figure 2: The cost-effectiveness plane



LYG: life years gained, QALY: quality-adjusted life years

The origin of the plane represents the costs and effects of the comparator, against which the costs and effects of the intervention are compared. The values on the axes are *incremental* values. The horizontal axis represents the difference in health effects between the intervention and the comparator, expressed as either LYG or QALYs gained. The vertical axis represents the cost difference between the intervention and the comparator. The comparator is either no intervention (or current situation) or a relevant cost-effective alternative intervention for the same condition.

The cost-effectiveness plane is subdivided in four parts, called quadrants.

In the second and fourth quadrant it is straightforward which intervention offers the highest value for money, i.e. the intervention with the lowest costs and the largest health effects.

- In the second quadrant, the new treatment is better and cheaper than the alternative; in economic literature this new treatment is then called 'dominant'.
- In the fourth quadrant the new treatment is worse and more expensive, it is 'being dominated'.

The conclusion becomes more difficult if the intervention is situated in the first or the third quadrant.

- In the first quadrant, the intervention is better but also more expensive. In this case an ICER can be calculated.
- In the third quadrant, interventions are cheaper but less effective than their comparator. These can in theory be treated in the same way as interventions in the first quadrant[12], although in practice they are very different. Interventions in the third quadrant would save money, at the expense of worse health. It is often argued, however, that in real life proof of better clinical effectiveness is a necessary (but not sufficient) condition for reimbursement.[13] In other words, before even considering an intervention for reimbursement, policy makers will first look at whether the intervention offers better health outcomes. If this is not the case, costs or savings are often not even considered.
- The third quadrant may also represent situations of disinvestment: reversing a reimbursement decision might potentially result in large savings at the expense of a limited loss in health. Again, in real life these considerations are rarely made.

The value of the ICER is equal to the slope of the line through the origin and the intervention's cost-effectiveness pair (e.g. point A). In the example in Figure 2, the ICER is €30 000 per QALY gained (or LYG depending on the units on the horizontal axis) compared to its comparator.

Key points

- **A cost-effectiveness plane visualises the cost difference (Y-axis) and effect difference (X-axis) between an intervention and its comparator.**
- **If an intervention is more costly and more effective than its comparator (or less costly and less effective), the slope of the line through the origin and the point corresponding to the incremental cost and effect on the plane is equal to the value of the ICER.**

2.4 METHODOLOGICAL ISSUES OF THE ICER

2.4.1 Comparability of ICERs for different interventions

Different considerations have to be made when using and comparing ICERs.

First, ICERs of different interventions can only be compared if their numerator and denominator are expressed in the same units. Incremental costs are generally expressed in monetary units (for a given country and year) but incremental effects can be expressed in different units, for instance as LYG or as QALYs.

Second, the methodology used for calculating incremental costs and incremental effects is important for the comparability of ICERs across interventions. Methodological issues may decrease the comparability of ICERs across interventions and their suitability for health care decision making. Consistency and transparency of economic evaluations is crucial for their credibility and usefulness for health care decision making.

Therefore, several HTA agencies have elaborated methodological guidelines to help those who conduct economic evaluations to calculate ICERs consistently.[14-18]

One of the important elements in all these guidelines is the perspective of the economic analysis: different perspectives lead to different values for the ICER, due to differences in the costs included in the analysis.

For example, productivity losses are costs from the societal perspective but not from the health care payers' perspective. Including or excluding these costs may have an important impact on the ICER estimate.

Another important methodological issue relates to the measure for health gains. Both LYG and QALYs have their weaknesses as measures for health gains.

- Using LYG as the sole outcome measure of interventions could create a decision bias against interventions that only impact upon quality of life.[2]
- QALYs, on the other hand, are often still fraught with measurement problems and are often not comparable between studies due to the variety in measurement techniques for HRQoL. Different measurement techniques give different results (e.g. Griebsch et al.[19], Scuffham et al.[20], Read et al.[21], Hornberger et al.[22], and Marra et al.[23]). As there is no 'gold standard' for measuring HRQoL, it is difficult to determine which measurement technique gives the most appropriate results for the purposes of the evaluation. As long as different measurement techniques for HRQoL are being used in CEAs, ICERs expressed in terms of cost-per-QALY gained will be difficult to compare across interventions.

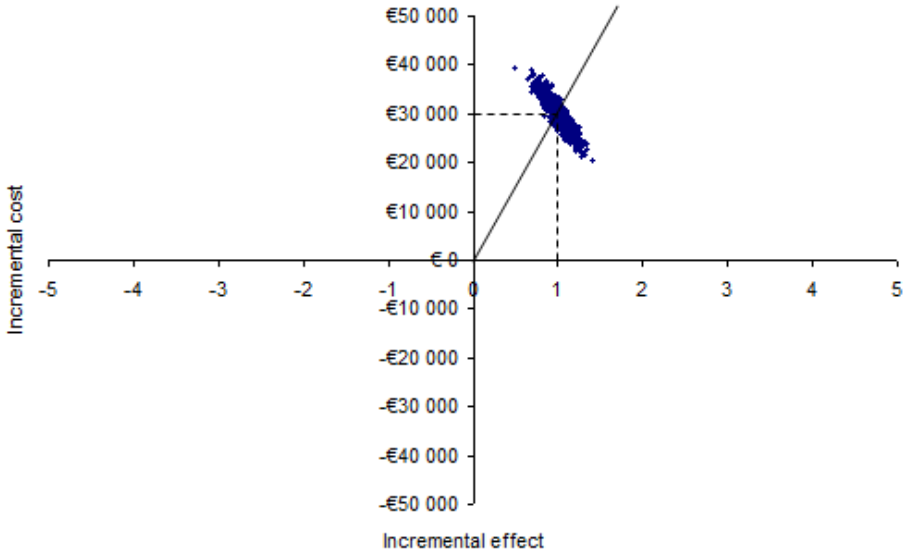
2.4.2 Uncertainty around the ICER

The calculated incremental costs and effects that are used to determine the ICER are both estimates, and estimates are by definition uncertain. The uncertainty of the numerator and denominator of the ICER translates into uncertainty around the ICER estimate.

While the degree of uncertainty may differ between estimates, the uncertainty should not be ignored.[24, 25] Uncertainty may, for example, relate to the expected effectiveness of the treatment in a specific patient population, the proportion of patients complying with the treatment, the costs associated with the organisation of the treatment in routine care, etc... Very often, assumptions have to be made about these parameters, assumptions that are translated into data distributions around a central estimate.

The uncertainty around the ICER estimate can be expressed as a credibility interval, comparable to a confidence interval for empirical data, or graphically on the cost-effectiveness plane as a scatter plot, representing the individual values resulting from probabilistic sensitivity analysis (Figure 3).[26]

Figure 3: Cost-effectiveness plane and presentation of uncertainty around the estimate of the cost-effectiveness ratio



In this example, the Mean ICER is €30 803 (95% credibility interval: 19 433 – 46 747)

2.4.3 When do we incur costs and when do we reap the benefits?

The future is uncertain and this uncertainty has to be dealt with. Costs and outcomes of health interventions usually do not occur at the same time. This raises the issue of valuing future outcomes and costs and choosing the appropriate time horizon for economic evaluations.

The timing issue is dealt with by means of discounting future costs and outcomes.[2, 4, 27, 28] Through discounting the value of future costs and outcomes is reduced to account for the fact that people value future health outcomes and costs less than immediate health outcomes and costs. The choice of the relative discount rate for costs compared to outcomes is important, as a discount rate that is lower for outcomes than for costs leads to relatively lower ICERs for programmes with outcomes in a far-away future as compared to a situation where both costs and outcomes would be discounted at the same rate.[29-31] The debate on whether an equal or differential discount rate should be used for costs and health outcomes is ongoing.[32-36]

A crucial question is "what is a reasonable time horizon for health economic evaluations", knowing that these evaluations will be used for current decision making. By taking decisions *now* on the basis of economic evaluations with a long time horizon, decisions are actually taken about costs and effects occurring now *and* in the future. Uncertainty exists, amongst others, about the emergence of new interventions, the future population eligible for a specific treatment and the long-term effectiveness of an intervention.[37] As a consequence, the expected benefits of an intervention for which decisions are taken *now* might never occur. Some of these uncertainties can be solved by further research while others cannot.[25, 38]

However, this does not imply that it would be better to take decisions only within a short term perspective, as this would preclude the application of preventive interventions and could potentially jeopardize future generations.

Vaccinations are a typical example of interventions with an important upfront cost and with outcomes much further in the future, outcomes that can often only be demonstrated after actual implementation of a large vaccination programme. In other words, the expected ICER might never be realised and maybe resources would have been better spent elsewhere.

Decision makers are forced to make a trade-off between waiting until more evidence becomes available and the risks inherent to taking a decision in a situation of uncertainty.[37, 39-41] Remaining uncertainty can be addressed in extensive sensitivity analyses that lead to an uncertainty range around the ICER point estimate.[24, 25, 38, 42]

Key points

- **Variability across economic evaluations in terms of outcome measures (LYG or QALYs) and methods used to calculate the ICER reduce the comparability of ICERs across interventions.**
- **The ICER of an intervention is by definition an estimate and therefore uncertain.**
- **Future costs and benefits should be discounted. The debate on whether equal discount rates should be used for costs and health outcomes or lower discount rates for outcomes than for costs is still ongoing, but the rates used can have an important effect on the ICER estimate and should be fully appreciated when comparing ICERs.**
- **Future costs and benefits are often uncertain. This uncertainty should be adequately considered in the decision making process.**

2.5 THE ICER THRESHOLD VALUE IN A FIXED BUDGET SETTING

As a stand-alone value the ICER does not offer information about whether an intervention is worth its costs. Health care policy makers still have to decide whether the value of the ICER is acceptable or not.

According to neoclassical welfare economic theory[c], an ICER threshold value can be defined below which an intervention is cost-effective (increases efficiency) and above which it is not.[2] This is subject to specific conditions (see 2.5.1). In this paragraph, the basis and the meaning of this ICER threshold value and the conditions to which it is subject are explained.

2.5.1 Basic assumptions

To be able to define the ICER threshold value, the following basic assumptions have to be fulfilled:[45-47]

- the health care budget is fixed[d]
- the health care policy makers' sole objective is to maximise health given this fixed budget[e]
- full information exists on the costs and effects of *all* available health interventions,
- health programmes are perfectly divisible, meaning that it is possible to realise only part of a programme
- health programmes are independent from one another
- health programmes have constant returns to scale, meaning that reducing a programme does not change its ICER.

A fixed health care budget is in this context *not* a budget that remains constant over time or grows at a constant rate. 'Fixed budget' means that the budget cannot be increased or overspent within a given year.[f]

Perfect divisibility of a health programme would imply that the programme can be implemented or downgraded to whatever extent. Basically, this refers to programmes without fixed costs (see 2.7.3).

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c The difference between welfarims and extra-welfarism is conceptually and methodologically complex. Welfarism asserts that social welfare is a function of individual welfare (approached as utility) obtained only from the consumption of goods and services.43 Extra-welfarism argues that the superiority of one social state (allocation of resources) over another may also depend on the non-utility aspects of each state.43 For example, while in the welfarist approach the aim is to maximise the total number of QALYs, extra-welfarism also includes considerations that are not included in the QALY, such as the allocation of QALYs across patient groups or severity of illnesses. These additional considerations may justify an allocation of resources that is sub-optimal according to the welfarist approach. Relative societal values of health gains (QALYs) have recently been studied empirically in the UK.44 This fits with the extra-welfarist approach.

d A fixed budget is not specifically required for the welfarist approach. Also in a variable budget context the welfarist approach can be applied, but then the meaning of the ICER threshold value is different from the one presented in this section (see 2.8.1 for the meaning of the welfaristic ICER threshold value in a variable budget context).

e This refers to the welfarist approach.

f In some systems, the health care budget will be strictly fixed, i.e. it cannot be increased and resources from other sectors cannot be applied to fill potential gaps. Such a system prevails in countries such as the UK and New Zealand although it should be noted that budgets are never completely fixed. In other systems, the budget is fixed in principle but can be used in a flexible way. For example, in Belgium the health care budget is fixed but due to the prospective financing of some health services (e.g. GP consultations) the budget can exceed the pre-defined budget.

2.5.2 Identifying the ICER threshold value

If these assumptions are fulfilled, it is possible to construct an ICER league table, where interventions are ranked from lowest to highest ICER. The health-maximising allocation of a fixed budget is obtained by financing the interventions with the lowest ICERs first and then moving down in the league table until the budget is exhausted.[45] The ICER of the last intervention still financed from the budget then represents the cost of the marginal (i.e. the last) QALY gained (or LYG) from the budget. This ICER then represents the threshold value for new ICERs: if a new intervention can produce an additional QALY (LYG) at a lower incremental cost (i.e. has a lower ICER) than the last intervention already financed from the budget (the ICER threshold value), it is economically more efficient to produce that additional QALY (LYG) instead of the current marginal QALY (LYG). If the cost of an additional QALY (LYG) from the new intervention is higher than the cost of the marginal QALY (LYG) currently funded, it is not worth replacing the existing marginal intervention with the new one, as it would reduce total health.[45]

Therefore, according to the ICER threshold approach,[2-4]

- intervention A is not cost-effective if $ICER_A$ > ICER threshold value;
- intervention A is cost-effective if $ICER_A$ < ICER threshold value.

An example: consider three health interventions in an exemplary health system. The incremental costs and effects of these interventions, each time relative to their relevant comparator are presented in Table 1. Each intervention treats a different disease. Intervention A offers a treatment to 10 patients, intervention B to 15 patients and C to 8 patients. Based on the incremental costs and effects an ICER can be calculated for each intervention. The ICERs are then ranked from low to high (league table). The higher the ICER, the less cost-effective an intervention is considered. Finally, the budget impact of the interventions in the current year is indicated. With a given budget of €1 100 000, for instance, health interventions A, B and part of C can be financed. In the threshold approach, financing part of a programme is an option, as explained in section 2.5.1. In real life, however, this might not always be the case. We elaborate on this in section 2.7.3.

Consider now a new intervention D with an incremental cost of €800 000 and a budget impact of €700 000. For a decision about the reimbursement of the intervention within the limits of a fixed budget, D's ICER has to be compared with C's ICER. If D's ICER is lower than 20 000€/QALY, say 18 000€/QALY it is worthwhile to implement part of D (up to the point where €100 000 is spent on D) and spend less resources on (disinvest in) intervention C.[g]

Table 1: Resource allocation based on ICERs in the ideal world

	ΔC	ΔE	ΔC/ΔE	Total incremental effectiveness	Total incremental cost	Budget impact in current year
A	100.000	10	10.000	100	1.000.000	200.000
B	200.000	12	16.667	180	3.000.000	800.000
C	100.000	5	20.000	40	800.000	150.000

For every new intervention that is considered to be financed by the same fixed budget, the ICER of that intervention should be compared with the ICER of the last intervention in the league table still financed.[48] If the ICER of the new intervention is higher than the ICER of the last financed intervention (the threshold value), the new programme should not be accepted. If its ICER is lower than the threshold value, financing of this new intervention would increase the total number of QALYs gained and hence a health maximising decision rule would demand the inclusion of the new health programme.

g Note that under these conditions it is not cost-effective to finance the entire programme, as the ICER of D is still higher than the ICER of B. Financing the entire programme would require disinvestment in B, but given the lower ICER of B this would not be efficient.

The decision implies a reduction in the budget spent on the intervention with the highest ICER. If not, under a fixed budget, the new intervention cannot be paid for.

2.5.3 Characteristics of the ICER threshold value in a fixed budget setting

The ICER threshold value has the following characteristics:

1. The threshold changes as the composition of the health programmes funded changes. Because the threshold value is equal to the ICER of the last programme selected before the budget is exhausted, the threshold changes each time a new programme is included in the package of funded programmes.[47, 48] In the previous example, the new ICER threshold value becomes 18 000€/QALY, being the ICER of D, the marginally financed programme.
2. The ICER threshold value depends on the available budget. The higher the budget, ceteris paribus, the higher the threshold will be.[49, 50]
3. The ICER threshold value depends on the productivity in the health care sector. If the productivity increases, meaning that more LYG or more QALYs can be generated with the same amount of resources, and the budget does not change, the threshold value will decrease.

These characteristics suggest that the ICER threshold value is not a static value but changes over time due to changes in budgets, innovations, productivity, etc.[48] In addition, they imply that the ICER threshold value from one country is not necessarily applicable to other countries, as other countries have other budgets, other practices, other productivity, other health programmes already financed etc.[46]

Other reasons explain why ICER threshold values are not easily transferable between countries: the standard methodology used for calculating ICERs may differ, financing systems may differ, budgets may be more or less fixed etc.

2.5.4 Interpretation of the ICER threshold value in a fixed budget setting

The theoretical ICER threshold value as presented above does not take into account societal willingness to pay for a QALY or for a LYG and it is neither an absolute criterion for evaluating the cost-effectiveness of health interventions in real life.[34, 48] Rather, it is the *result* of an economic theoretical model for maximising health gains from a given fixed budget that applies to a specific context, at a specific moment in time and under specific conditions.

The ICER threshold value represents the highest amount of money for a QALY (or LYG) society still *can* pay at a specific moment in time, given its fixed health care budget and its health maximising goal. With every new intervention that enters the package of reimbursed interventions, the ICER threshold value has to be revisited. Therefore, the ICER threshold value cannot be interpreted as a value that stands for a long time. It will only apply for as long as the comparisons with new potential candidates for financing do not lead to the inclusion of new interventions in the funded package.

Key points

The ICER threshold value is a theoretical construct for maximising health within the constraints of a fixed budget.

This theoretical ICER threshold value assumes:

- **A fixed health care budget, defined as a budget that cannot be exceeded.**
- **The one and only aim of health care decisions is to maximise health benefits in terms of QALYs or in terms of LYG.**
- **Complete information on the ICERs of all interventions is available.**
- **Perfect divisibility of health programmes.**
- **Constant returns to scale; i.e. reducing or extending a programme (in the same target population) does not influence its ICER.**
- **Health programmes are independent from each other.**

The ICER threshold value is the ICER of the last intervention in a league table that is still (fully or even partially) financed from the fixed budget.

The ICER threshold value is not a static value but changes over time, subject to changes in the budget, the interventions funded and the productivity of health care.

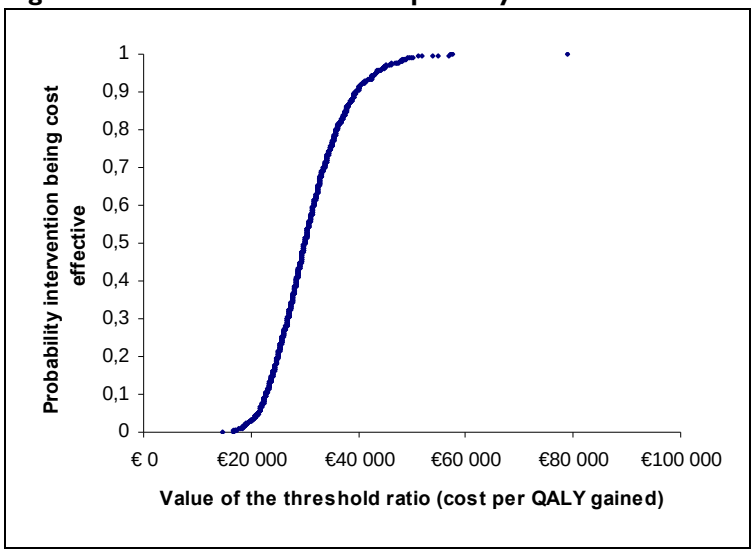
2.6 METHODOLOGICAL ISSUES OF THE ICER THRESHOLD VALUE

2.6.1 Uncertainty around the ICER and the ICER threshold value

As discussed in paragraph 2.4.2 an ICER is an estimate and the exact value is uncertain. This implies that in comparisons with an ICER threshold value, the only possible conclusion is that there is a probability that the ICER falls below the threshold value. This probability can be quantified based on the results of probabilistic sensitivity analyses.

The probabilistic sensitivity analysis calculates a distribution around the ICER. The cost-effectiveness acceptability curve then reflects the proportion of the distribution of the ICER below the threshold value for all possible ICER threshold values.[51] Graphically, it would be the proportion of dots from Figure 3 falling below the ICER threshold value; i.e. to the right of the line through the origin with a slope equal to the ICER threshold value. By varying the ICER threshold value, the proportion of dots falling below the ICER threshold line also varies. As the proportion of dots falling below the ICER threshold line corresponds to the probability that the intervention is considered cost-effective for the pre-defined ICER threshold value, the probability that an intervention is considered cost-effective changes if the ICER threshold changes. The graphical presentation of this probability is called a 'cost-effectiveness acceptability curve' and is shown in Figure 4.[2, 3]

Figure 4: Cost-effectiveness acceptability curve



However, not only the ICER of interventions is uncertain, also the ICER threshold value -being the ICER of the last intervention financed from the budget- is subject to uncertainty. Therefore, the ICER threshold value will not be a single value but rather again a variable with a distribution.[47] For practical use, the ICER threshold value could be defined as a range with limits defined by the upper- and lower limits of the 95% confidence or credibility interval around the ICER of the marginally funded health programme.[h] The cost-effectiveness acceptability curve, however, does not account for the uncertainty around the ICER threshold value.[47]

Given the uncertainty about the precise value of the ICER threshold and its definition in terms of an interval, the kind of conclusions drawn from these curves can no longer be that "there is a probability of Y% that the ICER is below the threshold value" but rather that "the probability that the ICER falls below the ICER threshold value is between X% and Z%." The range for the probabilities is defined by the applied range for the ICER threshold value.

In conclusion, the uncertainty around the ICER threshold value adds to the uncertainty around the ICER estimate, thereby increasing the uncertainty about an intervention's cost-effectiveness.

2.6.2 Comparison with an appropriate comparator

The theoretical ICER threshold value can only be defined if for each intervention in the league table the ICER is calculated relative to a *cost-effective* comparator or relative to *doing nothing*.[3] If the comparator is an alternative intervention (and hence not 'doing nothing') it should be an intervention that is currently financed because it is considered worthwhile given the fixed budget constraint and the health maximisation objective.[i] In other words, the league table approach assumes that all health interventions currently financed from the healthcare budget fit within the health maximisation rationale and are financed only because they are cost-effective. Hence, if a new intervention emerges as an alternative to an existing and already funded intervention, the existing intervention is an appropriate comparator.

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h In case of economic modelling, the term "credibility interval" is used rather than "confidence interval" to make the distinction between variability in directly observed values versus variability in values resulting from an economic model.

i Comparison with an appropriate alternative treatment is recommended in most guidelines for economic evaluation. The WHO's "Guidelines on generalized cost-effectiveness analysis", however, recommend the evaluation of an intervention's cost-effectiveness relative to "doing nothing" (i.e. relative to the natural history of disease) as a standard approach.52 The WHO has a very specific mandate and has therefore specific reasons for electing this approach. For a full discussion on the generalized cost-effectiveness analysis, see WHO (2003).53

If there is no alternative that is already funded for the new intervention, it should be compared with 'doing nothing', because this means that no cost-effective comparator is yet available for this new intervention.

If interventions that are not cost-effective are currently funded, CEA using these interventions as comparator might lead to ICERs that look attractive compared to the ICER threshold value. However, as the comparator should not have been funded in the first place according to the economic efficiency argument, application of the ICER threshold value rule for the new intervention would not lead to maximal health outcomes. The approach hence imposes the strong requirement of being able to establish the cost-effectiveness of the comparator before proceeding to the cost-effectiveness analysis.

2.6.3 Measurement units in nominator and denominator

Because of the clear difference between measures of 'health gain' (e.g. LYG or QALYs), any threshold value should be considered taking explicitly into account the currency used in the numerator and outcome parameter used in the denominator. Although, this remark may seem obvious, it has been observed that often 'round' numbers are preferred, which are easily copied without paying much attention to the units accompanying the number and applied threshold values do not seem to change over time despite changing economic environment and inflation.[42, 54-56]

Key points

- **The ICER threshold value is the result of a health maximisation model that applies to a specific context (fixed budget, country), at a specific moment in time and under specific conditions.**
- **The ICER threshold value is subject to uncertainty and variability. Therefore, the ICER threshold value is not a single value but a range of values. This is important for the kind of conclusions that can be drawn from cost-effectiveness analyses.**
- **The league table approach used to define the ICER threshold value assumes that each intervention's ICER is calculated compared to a cost-effective alternative or to doing nothing if no cost-effective alternative exists.**
- **The units in which the costs and health effects are expressed are important for the interpretation of the ICER threshold value: an ICER threshold value of €30 000/QALY is different from an ICER threshold value of £30 000/LYG.**

2.7 HOW WELL ARE THE THEORETICAL ASSUMPTIONS FOR THE ICER THRESHOLD VALUE FULFILLED IN REAL LIFE?

As explained previously in 2.5.1, the ICER threshold value can be defined as the ICER of the last intervention still financed from a fixed budget, but only if a series of basic assumptions are fulfilled.[45, 57]

The conditions for the appropriate identification of the ICER threshold value are highly theoretical and seldom met in practice.[50] The extent to which the conditions are met depends partly on the characteristics of the health care reimbursement system.

Globally, three main reimbursement models can be identified: the Beveridge model (national health provider paid directly from taxes), the Bismarck model (comprehensive social security based system but mainly paid from contributions of employees) and the private health insurance model.[58-60]

A Beveridge system is characterised by a centrally organised National Health Service (NHS), where health care is provided mainly by public providers.[59] Examples of such systems are found in the UK, Italy and Spain. In Beveridge systems the state is the central actor.

The Ministry of Health prepares the annual health care budget which is considered to be fixed for that year. Health care is primarily financed from public resources obtained through general taxation. As such, the health care budget competes with other spending priorities as a consequence of which the health care budget cannot easily be exceeded.[j] Beveridge systems are, overall, characterised by many public providers and relatively few private providers.[60]

A Bismarck system, as prevailing in Belgium, France and Germany, is a social security based system where social insurance is comprehensive and mandatory.[59] Resources available for social security spending come from social security contributions, mainly from salaried employees. There is generally a strong influence of stakeholders. For instance, reimbursement of health care procedures is often negotiated between health care providers, insurers and government. There is a mixture of private and public providers and the health care budget is considered somewhat more flexible.[60]

In a private insurance system, health care is paid out of premiums paid to private insurance companies. The obvious example of this system is the US, where this system is combined with a few limited social care fallback systems such as Medicare and Medicaid.

2.7.1 Fixed budget

The ICER threshold value approach as described in 2.5.2 is applicable in situations where the health care budget is strictly fixed (while other conditions also apply, see 2.5.1).

A fixed health care budget requires a variable ICER threshold value. Under a fixed budget constraint, an ICER threshold value (with an appropriate range around it representing uncertainty) against which other ICERs should be compared to maximise health outcomes can be defined *at a specific moment in time*. But the ICER threshold value cannot be fixed over time in a fixed budget situation, It has to be revised every time a positive reimbursement decision about a new intervention is taken.[48, 61]

A flexible health care budget does allow the use of a fixed ICER threshold value to a certain extent. The budget will then have to expand every time a new intervention with a lower ICER than the threshold ICER value becomes available.[62-64][k] However, the meaning and hence the interpretation of the ICER threshold value would in that case be completely different (see 2.8.1). It is then no longer the health-maximising threshold criterion for a fixed budget.

As explained previously the health care budget is more fixed in an NHS (Beveridge) system than in a social security (Bismarck) system. In the UK, for instance, the budget of the NHS is mainly exogenously determined by Parliament.[61]

It is a fixed budget that should cover most or all health care expenditures of the citizens.[l] As a consequence, the cost of an intervention is equal to the resources needed from the health care budget.

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j In practice, the health care budget of a given year can be exceeded in a Beveridge system, for example if in a specific year more prescription drugs are used than initially expected. This will, however, be more difficult than in a Bismarck system where budgets are more often negotiated.

k Expansion of the budget every time the ICER of an intervention is lower than the ICER threshold value is not tenable in any system, be it a fixed or flexible budget system. Hence, regular adaptation of the ICER threshold value will always be necessary. In systems with more flexible budgets, the revision of the ICER threshold value might be less frequent than in systems with less flexible budgets (e.g. once a year or every two years, in the context of an evaluation of the health care package funded from public resources and their budgetary consequences). But, the constant revision of the ICER threshold value still requires the satisfaction of the basic (and problematic) assumptions of the 'conventional' ICER threshold value approach: perfect divisibility of health programmes, constant returns to scale and making abstraction of equity considerations across patient populations in case of unweighted QALYs (or LYG). It could be argued that perfect divisibility of programmes and constant returns to scale are less important conditions for the ICER threshold value approach, but this only applies to systems with flexible budgets.

l In practice, the health care budget of a given year can be exceeded in a Beveridge system, for example if in a specific year more prescription drugs are used than initially expected, but this will be more difficult than in a Bismarck system where budgets are much more negotiated.

In a social security system, where patients often pay individual co-payments for the services they consume, the total cost of an intervention is not equal to its total budget impact for the public health care payer. In the case of Belgium, the NIHDI as well as the 'Federal Public Service (FPS) Health, Food Chain Safety and Environment' pay for (part of) the health care services. Together they are the Belgian public (governmental) payers for health care. According to the Belgian pharmacoeconomic guidelines costs are calculated from the perspective of the *health care payer*, i.e. the patient *plus* the public payer.[18] It includes the impact on the governmental health care budget as well as on the patient's health care expenditures. This is a reasonable perspective if the objective of the economic evaluation is to allocate the *health care* budget efficiently, but it implies that the health care 'budget' is less fixed as it includes a patient's co-payment component. Calculating costs from either the government or the patient's perspective alone would not make sense.

Why not? If costs would be calculated from the government's perspective only, interventions with limited reimbursement (i.e. with a limited impact on the health care budget) will generally be more cost-effective than fully reimbursed interventions. The lower the reimbursement is, the lower the ICER will be. As a consequence, if costs are calculated from the government's perspective only, interventions with a low reimbursement rate will lead in the ICER league table. However, basing reimbursement decisions on such a league table has ethical consequences, as interventions that would require a higher reimbursement, e.g. because they would otherwise have a huge impact on patient's income, would not be reimbursed according to the ICER threshold value approach. Hence, taking the government's perspective only for the calculation of costs in the ICER is not useful for resource allocation decisions in a system with patient co-payments.

However, taking the broader perspective of both patient and government as health care payers is also problematic for the application of the ICER threshold value approach for maximising health benefits from a given fixed budget. When the health care payers' perspective is taken, the threshold value shows how the health care payers' collective budget should be allocated to obtain maximal health. *Who* pays, the patient or the government, is considered irrelevant for the approach. In other words, the approach does not determine the optimal level of reimbursement. This means that the ICER threshold value approach gives no indication about how to allocate the government's health care budget in order to obtain maximal health benefits. From a distributive justice point of view, however, the level of reimbursement might not be irrelevant. Suppose two interventions cost the same from the health care payers' perspective but the new intervention, that society wants to see reimbursed at 100% for whatever reason, replaces another intervention that is currently reimbursed at 10%. Then either the reimbursement of the new intervention requires disinvestment in *more* other interventions or the budget has to be adapted, or the decision to reimburse the new intervention at 100% should be revised. But again, we either move away from the 'fixed budget' condition or we take decisions with specific ethical consequences.

In conclusion, in a system with patient co-payments, the health care budget is not as fixed as in a NHS system. This reasoning can be expanded to all economic evaluations performed from a societal perspective. From a societal point of view, it is hard to see what the fixed health care budget would be.[47] The rationale for taking a societal perspective in economic evaluation is that one should strive for an efficient allocation of resources across all sectors, not only within the health sector. Allocation of the budget between sectors is one element of efficient resource use within a society. The ICER threshold value does not, however, help to define the appropriate budget for the health sector.

Thus, the first condition for the ICER threshold value approach is not met in a social security based system or in a system where ICERs are calculated from a societal perspective.

2.7.2 Complete information on costs and effects of all health interventions

The determination of the ICER threshold value requires, among others, full information on the costs and consequences of all health programmes. However, no single health care system, whether NHS, social security or private insurance based, has full information. As a consequence, the real ICER of the marginal intervention covered by the budget is unknown.[4, 61, 64, 65] The health care policy maker may hence be continuously *searching* for an ICER threshold value rather than *setting* one.[61]

There are two ways for dealing with this problem of incomplete information. The first is to make a rough estimate of the value of the threshold.[47] However, because very little empirical evidence exists on the value of the ICER threshold, this approach is not evidence-based and will potentially -if the estimate is wrong- not lead to maximal health from a given budget. If the estimated ICER threshold is higher than the 'real' threshold value in its theoretical sense, i.e. higher than the ICER of the least cost-effective programme still funded, too many technologies will get a positive recommendation.[48] To fund these technologies, funds could have been diverted from other healthcare services which provided better value for money.[66] As a result, maximal health gains are not reached for the given budget. When the threshold value is underestimated, some interventions (i.e. those with an ICER between the threshold value that is too low and the real threshold value) that offer value for money are denied to society. The health budget is under-utilised and less health is gained from the available budget than could have been gained.

A second way for dealing with incomplete information is to define the threshold as the ICER of the intervention that is most likely to be displaced by the new one.[48] In practice this would mean that the decision maker should first consider where the resources for funding the new intervention should come from; i.e. the disinvestments that will have to be made to finance the new intervention. Ideally, this should be the intervention with the highest ICER. The intervention with the highest ICER is, economically, the least efficient and therefore the first candidate for disinvestment. If this intervention cannot be identified, the ICER of the intervention in which the disinvestment can be done should be used as the ICER threshold value against which the ICER of the new intervention is compared. Only if the ICER of the new intervention is lower than the ICER of the intervention that is being replaced, funding the intervention increases efficiency in health care. If, in practice, the ICER of the intervention that will be replaced is at that time unknown, it should be calculated. Otherwise the decision might be wrong from an efficiency point of view.

To illustrate this with an example, suppose a new intervention emerges for the treatment of Alzheimer disease and suppose that for the implementation of this intervention resources will be taken away from a treatment for chronic low back pain. The ICER threshold value against which the ICER of the Alzheimer intervention should be compared is then the ICER of the chronic low back pain treatment. This approach is useful only if the decision maker takes the a priori position that financing of the Alzheimer disease treatment should come from disinvestments in the chronic low back pain intervention. If afterwards another decision with respect to disinvestment is taken, the threshold was wrong and the investment decision should be re-considered in the light of the ICER of the intervention that will actually be displaced. In a real-life decision making context, however, this exercise would rarely be made. Decisions about the reimbursement of health interventions are mainly made on a case by case basis.[67]

2.7.3 Perfect divisibility and constant returns to scale

The condition of perfect divisibility and constant returns to scale is highly theoretical and never fulfilled in real life.[46, 47, 68]

Perfect divisibility means that health care programmes can be 'bought' or downgraded to whatever extent. This might not be the case, however, especially when a health programme requires high investment costs (e.g. an additional MRI or PET scanner, the building of additional premises).[69] For example, to provide a diagnostic work-up involving PET to one patient, the full investment of a PET scanner has to be made. The cost per patient decreases as more patients are included in the diagnostic work-up programme and there will be an optimal occupation rate for the PET scanner that will minimise the cost per patient and hence the ICER. The programme involving PET is therefore not perfectly divisible without changing the ICER of the programme. While the ICER threshold approach assumes that all activities that are worth doing *can* be done in each and every volume, it is unlikely that this is the case in real life for *all* interventions.[m 47] The example given might be an extreme case, but nevertheless illustrates the issue. Many health interventions do not require huge investments, for example drug treatments. The critique with respect to the absence of perfect divisibility of scale is not relevant for these interventions. However, even in these cases it is unlikely that the implementation of only part of a health programme will not affect the ICER of that programme. This relates to the second assumption of constant returns to scale.

Constant returns to scale means that the costs and health benefits of a health programme are reduced (increased) proportionally to the reduction (increment) of the extent of the programme.[47] Consequently, the ICER is assumed to remain constant when a health programme is reduced or increased. This assumption does not hold in cases where the fixed costs of a programme are high or where the incremental effectiveness does not change proportionally with the number of patients treated. The higher the fixed costs, the less proportional the decrease in total cost with a decrease in the number of patients treated and hence the higher the ICER becomes (if effectiveness is not affected, see earlier example of the PET scan). A reduction in the number of patients treated might not proportionally decrease the effectiveness of the programme. For example, a school vaccination programme for HPV will be more effective in reducing the incidence of HPV than opportunistic vaccination because the effect of the vaccination exceeds the direct effect on the individual.[71] As a consequence, the ICER of vaccination will decrease if more children are vaccinated because the effectiveness increases more than proportionally with the costs if the number of vaccinated children increases.

Moreover, the ICERs may differ between sub-groups of patients.[46] While the overall ICER of a health programme may be unfavourable according to the threshold approach, it might well be the case that the ICER of the same programme is below the threshold value for a specific sub-group of patients, e.g. because the programme is more effective for specified sub-populations. In that case, it would be efficient to allocate resources to this specific sub-group but it would not be efficient to implement the entire health programme. Inability to make this distinction may lead to inefficient resource allocation.[n]

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m Mathematical solutions have been developed to address the problem of assumed constant returns to scale and divisibility.70 The practical applicability of the techniques is yet limited because of the high data requirements. The data needed are often not available.

n Commercial companies may try to close an 'all or nothing' deal to cover the entire population although the intervention is only cost-effective for a specific sub-group.72 The requested price is a weighted average of the prices that would render the intervention cost-effective in the different sub-groups. In the sub-group where the intervention is most effective, the price can be relatively high if the intervention is to remain under the threshold value. In sub-groups where the intervention is less effective, the price will have to be lower to remain under the threshold value. At the 'average' price, the intervention will be cost-effective (below the threshold value) for some sub-groups but not for others. 'All or nothing' deals hence lead to sub-optimal resource allocation, as in principle the intervention should only be reimbursed for the sub-group in which the intervention is cost-effective at that price. Claxton et al. (2007) therefore argue that such deals should be rejected. They argue that the price should not be higher than the price that renders the intervention cost-effective in the sub-group with the highest ICER that is still considered

2.7.4 Health programmes are independent from one another

The assumption that health programmes are independent from one another does not hold in real life. In economic evaluation, a health intervention is never looked at in isolation. For example, the costs associated with the implantation of a device (e.g. a coronary stent) exceeds the pure cost of the device, as patients will have to go to hospital, undergo diagnostic procedures before the decision to implant the device is taken, may have to follow an additional medication treatment after the intervention etc. Hence, the ICER of the device cannot be reduced to the pure costs and effects of the device but also depends on the costs and effects of the diagnostic procedures, the drug treatment etc.

For the application of the ICER threshold value approach this might be problematic. Suppose in the previous example that the drug treatment (not preceded by the device implant) is not reimbursed because its ICER is higher than the ICER threshold value. If the ICER of the intervention with the device, but including the drug treatment, is lower than the ICER threshold value, what should the decision be? According to the ICER threshold value approach, the device should be reimbursed. The intervention with the device is only cost-effective, however, because it is followed by the drug treatment. Therefore, the reimbursement of the device cannot be decided without reconsideration of the reimbursement of the drug treatment.

This conclusion has implications for health care systems characterised by separate budgets for different sub-sectors in the health care sector, e.g. for pharmaceuticals, for devices and implants, for physician fees, etc. This is the case in many countries, including Belgium. When pursuing efficient resource allocation in the health care sector it is impossible to stay within the rationale of separate budgets. As demonstrated before, due to dependencies between interventions that are paid for out of different health care sub-budgets, it does not make sense to look at the interventions separately and consider only the impact on one particular sub-budget. Economic evaluation from the perspective of one of the sub-budgets only would not give an accurate idea of the real impact of the interventions on the health care costs and effects and would hence not be useful for the evaluation of allocative efficiency in health care.

2.7.5 Health maximisation as the sole goal of health policy makers

The 'economic efficiency in production'-argument for the use of ICER threshold values, or health maximisation (in terms of QALYs or LYG) as the primary aim of health care decision making, might not adequately reflect the reasons for decisions about resource allocation in health care in real life. This applies to both NHS and social security-based health care systems. There is a large body of literature on distributional concerns in resource allocation based on CEA. They essentially provide an argument for an extra-welfarist approach, where resource allocation decisions take the relative societal value of health gains for different population groups into account.[9-11, 20, 44, 57, 65, 74-92] Much of the discussion is related to the health outcome measures used in economic evaluation. QALYs, for instance, as other outcome measures, typically ignore societal preferences for distributional aspects, such as preferences related to the number of people receiving treatment (more patients receiving QALYs versus fewer patients) and preferences related to the personal characteristics of the individuals receiving treatment (level of severity of the condition).[44, 76]

In a NHS system where the budget is mainly fixed, health maximisation will of course not be pursued at whatever cost in terms of equity. Society has preferences with respect to the allocation of health gains, that have to be taken into account in the health care decision making process.[44]

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acceptable.72 Other authors have argued that appropriation of the social surplus of an innovation to producers is central to the dynamic efficiency in health care (i.e. to ensure continuing efficient R&D investments) and is therefore justified.73

The same applies to a social security system, be it that the ICER threshold value approach would in this system not only impact on health inequality but also on income inequality. It is generally acknowledged that decision makers take other aspects into account besides the ICER of an intervention, to decide whether or not the intervention is worth its cost. Because these factors differ across interventions, a single threshold value for the ICER below which an intervention is considered value for money, is not consistent with how society chooses to make decisions (see also chapter 3).

If it would be possible, however, to include these additional considerations in the ICER, e.g. by weighting the QALYs of populations the society wants to protect more heavily, the ICER threshold value approach might still be applicable.[75] The ICER threshold value would in this case be defined in terms of a cost-per-weighted QALY. The objective is no longer 'health outcome maximisation' but 'weighted health outcome maximisation'. This weighted QALY approach has three potential drawbacks. First, a prerequisite for this approach is transparency of the composition of the weights for QALYs: which criteria are determinant, what value is assigned to each determinant and how are these values combined to obtain a unique weight? Obviously, this is not an easy requirement.

A second potential problem of including additional decision criteria in the cost-effectiveness ratio is the selection of the appropriate cost-effective comparator. If decisions are not purely inspired by a pursuit of maximal health, it might happen that interventions that are not cost-effective according to the theoretical ICER threshold value approach (without QALY weighting) are nevertheless reimbursed. For example, suppose that, despite a high ICER, a specific intervention is reimbursed because there is no alternative treatment for treating a specific serious disease and patients would otherwise be left untreated. Suppose that the conventional ICER of this programme is higher than the ICER threshold value that would imply maximal health outcomes but that the outcomes have been given a higher weight in order to stay below the ICER threshold value. If after the decision is taken a new intervention for this patient population is developed, it might have a low ICER when the existing treatment is used as the comparator in the CEA. Its ICER might be below the ICER threshold value and hence it might be concluded that it is cost-effective. However, the existing reimbursed treatment might not be the relevant comparator, as the reason for initial reimbursement (i.e. non-existence of an alternative treatment for the patients) no longer holds. Previous decision might have to be revised in the light of new developments. This leads to the conclusion that including additional considerations in the ICER and including such 'weighted' ICER subsequently in a league table might complicate their interpretation and their practical usability. Moreover, the risk for misuse or errors in the choice of the appropriate comparator increases.

A third weakness of the weighted QALY approach, if used in combination with a threshold value, is the remaining requirements of perfect divisibility of health programmes and constant returns to scale, two requirements that may not hold in real life (see 2.7.3).

A few attempts have been made to derive an ICER threshold value from past health policy decisions.[65, 93-95] The exercises showed that indeed there is no single threshold value above which the decision is always negative and below which it is always positive. Rather, a range of acceptable ICERs has been identified. This can mean different things: (1) the decision maker does not know the *true* ICER threshold value that would maximise health benefits from a given budget;[61, 64, 96] (2) other considerations than health maximisation determine the acceptability of an intervention with an ICER that is, strictly speaking, above the ICER threshold value[65, 67], (3) different methods are used to obtain the ICER estimates as a consequence of which they are not always comparable, (4) the level of uncertainty around the ICER estimates determines their acceptability and (5) decision makers do not 'trust' all ICER estimates to the same extent. The different reasons probably all apply to some extent.[85] An empirically identified range of ICER threshold values should therefore be interpreted as the range of societal willingness to pay for an additional QALY or LYG at that time, in that specific budgetary and societal context and for those specific interventions rather than as an ICER threshold value in the purely theoretical meaning of an absolute criterion for health maximisation.[65, 96]

2.7.6 Additional caveats

There is a serious risk of bias towards the ICER threshold value, if one is defined.[97] Once a threshold value is set, there is the danger that ICERs of new technologies will converge towards this threshold value by inducing commercial companies to adapt their prices in order to 'satisfy' the cost-effectiveness criterion (ICER<threshold value) or to manipulate economic models (e.g. by changing modelling assumptions) to obtain an 'acceptable' result. In this case, however, no net health benefit will be created if another intervention with an ICER equal to the threshold value is being replaced to fund this alternative. The health benefits resulting from the new technology would offset the health displaced elsewhere.[72]

A second risk of applying an ICER threshold value for health care decision making is that an ICER below a certain threshold value becomes a legitimization in itself, while the decision maker may wish, for legitimate reasons, to deviate from the decision rule based on health maximisation arguments only.[98]

Key points

- **The theoretical requirements for identifying and using a single fixed ICER threshold value are unrealistic:**
  - **The ICER threshold value cannot be *identified* due to a lack of information of the ICERs of all interventions. Fixed budget situations are incompatible with a fixed ICER threshold value over time. In social security systems, with a mix of public and private financing, a fixed ICER threshold value could no longer be the ICER of the last intervention still financed from a fixed budget, as the budget is flexible.**
  - **The ICER threshold value, as defined by the neoclassical welfarist theory cannot be *used* in practice because equity concerns always arise in resource allocation decisions, health programmes may not show constant returns to scale and health programmes may not be perfectly divisible.**
- **A fixed budget context requires a flexible ICER threshold value. A fixed ICER threshold value is only applicable in a context with flexible budgets.**
- **In a mixed public-private system, where patients pay co-payments, applying the ICER threshold value approach would potentially lead to an undesirable income inequality. The ICER threshold value can suggest which interventions are worth implementing but does not suggest the optimal level of reimbursement (how much of the total cost is paid out of the governmental health care budget).**
- **Using an ICER threshold value carries a risk. Once an explicit ICER threshold is defined, there is a risk of manipulation towards this ICER threshold value in economic evaluations. Moreover, the ICER threshold value risks becoming a legitimization in itself, while decision makers may sometimes wish to weigh other criteria than health maximisation more heavily in their decision.**
- **Empirical ICER threshold values or a range of ICER threshold values observed from past decisions should always be interpreted in their budgetary, societal and political context.**

2.8 ALTERNATIVES TO ICERS AND ICER THRESHOLD VALUES

As discussed in the previous chapter, the ICER threshold value approach is based on a number of assumptions that are highly theoretical. Because few practical solutions exist to overcome these issues, the identification and application of an ICER threshold value in its neo-classical welfarist meaning appears to be impossible.

Alternatives to the theoretical ICER threshold value have been suggested in literature. They differ in the extent to which they follow the logic of the CEA, ICERs and ICER threshold values.

Three lines of thought can be identified:

1. those who suggest an alternative definition for the ICER threshold value but stick to the principle that an ICER threshold value should guide health care policy decisions
2. those who abandon the idea of an ICER threshold value but still use ICERs to support health care policy decisions
3. those who abandon the idea of ICERs and CEA and suggest an alternative approach to bring economic considerations into the health-care decision making process.

This chapter gives a brief overview of the alternatives to the ICER threshold value under a fixed budget constraint described in section 2.5. While the alternatives are presented here as stand-alone approaches, it should be appreciated that combinations of these approaches are possible and are being examined. But, because of the particular scope and educational purpose of this report we made a clear distinction between the approaches. The proposed alternatives are classified in Table 2 according to their level of acceptance of the ICER and a single ICER threshold value as a decision criterion.

Table 2: Classification of alternatives to the use of an ICER threshold value in its theoretical meaning according to their level of acceptance of ICERs and a single ICER threshold value as a decision criterion in health care policy decisions.

Alternative	Acceptance of ICER	Acceptance of a single ICER threshold value	Paragraph	References
ICER threshold value as societal willingness to pay	YES	Single or multiple ICER threshold values possible	2.8.1	12, 56, 83
Comparison with past decisions	YES	YES	2.8.2	65, 93, 94
ICER as one element weighed against other elements in the decision making process	YES	Possible but not nece©ssary	2.8.3	8, 65, 67
Average GDP per capita as a threshold value for average cost-effectiveness	CER, not *I*CER	YES	2.8.4	99
Opportunity cost approach	NO	NO	2.8.5	63, 98
Cost-consequences analysis	NO	NO	2.8.6	77

2.8.1 The ICER threshold value as a reflection of societal willingness to pay

The concept of an ICER threshold value as described in 2.5 is used to guide decision makers towards a health-maximising health care resource allocation given a fixed health care budget.

If not defined as the least cost-effective intervention still financed from a fixed health care budget, the ICER threshold value could be defined as the maximum societal willingness to pay (WTP) for an additional QALY (or LYG).[12, 56, 83] The societal WTP for an additional QALY (or LYG) is determined by the relative value of an extra QALY (or LYG) compared to the value of the benefits generated in other sectors.[o][100]

The more benefits from other sectors that the society is willing to give up for additional health, the higher the implied societal WTP for a QALY (or LYG) is.

The societal WTP approach avoids the need for full information on the costs and health outcomes of all interventions, and would allow the evaluation one by one of every new intervention considered for funding. However, defining the ICER threshold value like this has a number of implications and weaknesses, depending on how it would be used. Two possibilities are considered:

- either a generic ICER threshold value (WTP for a QALY) is applied to all new health programmes considered for funding, [12] or
- the societal WTP for a QALY is reconsidered for each new intervention considered for funding or for groups of interventions/conditions that are comparable in terms of their characteristics that determine societal WTP.[101]

Using the societal WTP for a QALY as the ICER threshold value is incompatible with a fixed budget system. As argued in 2.7.1, fixed ICER threshold value requires a flexible budget.[p] The measurement of the societal WTP for *a* (generic) QALY (or LYG) poses a number of methodological problems and it is doubtful that a generic societal WTP value applicable to all kinds of health programmes exists. Indeed, empirical studies suggest that the ICER threshold values often proposed in literature are lower than the actual WTP for a QALY,[56] while others find the opposite result.[83][q] The societal WTP for a QALY (or LYG) is always context-dependent. It is hard to imagine the value of *a* life year, making abstraction of the person and his characteristics (current health status, age, etc). In addition, appropriate measurement of WTP requires that respondents have to make trade-offs and are aware that the value they place on a QALY (or LYG) has implications for the consumption of other goods and services (i.e. opportunity costs). If not, unrealistic and impractical values may be measured.

An increasing amount of literature in health economics focuses on the incorporation of equity considerations in the ICER to overcome the problem of the previously described approach that it does not take societal preferences with respect to the distribution of health gains into acocount.[75, 81, 89, 90] This has been addressed previously in section 2.7.5.[r]

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o The maximum societal willingness to pay for an additional QALY (or LYG) is the amount of "wealth", in terms of benefits from other sectors, society is willing to give up to obtain an additional QALY (or LYG). The health care budget is optimal from a societal point of view if the ICER of the least cost-effective intervention still financed from the health care budget is equal to the societal WTP for a QALY gained (or LYG). As long as society is willing to give up benefits from other sectors to obtain additional benefits in the health care sector (i.e. the value of the benefits foregone in other sectors is lower than the value of the benefits obtained in the health care sector), the budget should expand.

p De facto this means that the maximum WTP for health gains will determine the health care budget. The health care budget thus obtained is the optimal budget from a societal point of view because society would not be willing to trade health for other benefits in other sectors. Note that for an optimal budget from a societal point of view, the societal WTP approach gives the same results as the ICER threshold value approach if all other conditions are fulfilled.

q Note that the results of WTP studies depend heavily on the methods used to measure WTP. Different methods yield different results. As there is no gold-standard, it is difficult to assess the validity of the results.

r This is an extra-welfarist approach.

A way to achieve the incorporation of equity considerations in the ICER metric is by weighting QALYs (or LYG). The weights assigned to the QALYs (or LYG) of specific population groups should reflect societal preferences for the allocation of QALYs to these groups. Hence, QALYs gained by patients the society wishes to favour are valued higher than QALYs gained by patients society does not want to favour. If adequate weights could be defined, reflecting all societal equity concerns (both in terms of health and income distribution in case of a mixed public-private system, see 2.7.5), the ICER threshold value could be defined as the societal WTP for a weighted QALY and the threshold value approach could again be applied, be it with the necessary caveats as presented in 2.7.5. Its advantage would be increased transparency of the decision making process if the determination of the weights could be transparent. The major problem is identifying all relevant parameters from a societal point of view and measuring the weights. Different empirical studies have demonstrated that people indeed do find equity concerns important for resource allocation decisions.[76, 87, 92]

Actual weighting of QALYs (or LYG) has, however, not yet been implemented in routine CEA. It can moreover be argued that, even if it would be feasible to adequately capture and quantify equity (and other) concerns, certain dynamics in the decision making process will remain implicit and variable across health interventions, such as for instance the influence of stakeholders.

Rather than trying to define one generic ICER threshold value representing the WTP of *a* (weighted) QALY (or LYG) in general, the maximum WTP for a QALY (or LYG) could be made dependent on specific characteristics of the intervention or the population (e.g. severity of disease, availability of an alternative treatment). For instance, WTP might be higher for interventions that reduce mortality risk than for interventions that improve quality of life, as already shown in empirical studies.[101] In its most extreme form, societal WTP could be re-assessed on a case-by-case basis for every individual intervention considered for funding. This approach requires a more flexible budget, as the budget will have to be adapted to the societal WTP for the health outcomes generated by each new intervention that is considered worthwhile. Therefore, it is more difficult to apply this approach in an NHS based system. The advantage of re-defining a WTP for each intervention is that it allows taking all objectives of health care policy into account. Moreover, it does not require the additional theoretical assumptions of the ICER threshold value approach that have proven to be problematic in real life. The price of this increased flexibility is a potential reduction in transparency. The more room there is left for deviation from some kind of 'rule of thumb', the less transparent decisions become.

2.8.2 Comparison with past decisions

One suggested way to identify the societal WTP for a QALY is to look at the ICERs of interventions for which a decision has already been made in the past. This leads to a kind of restricted league table that could be used to determine the relative position of interventions towards previously accepted or rejected interventions. However, as decisions are rarely made on the basis of cost-effectiveness considerations alone,[98] ICERs of interventions for which a positive or negative decision has been made in the past should always be considered along with all their arguments for the positive or negative recommendation if they are used for comparative purposes in current decision making processes. This evaluation might lead to the conclusion that the decision made at that moment was actually not the optimal decision and would maybe not have been made currently. This complicates even further the feasibility of comparison with past decisions. Moreover, comparison with ICERs calculated in the past is only warranted if the ICERs are obtained in the same way, i.e. using the same methodology, and under the same conditions, i.e. costs, existing technologies, experience etc. Conditions change, however, as a consequence of which this requirement is rarely fulfilled.

2.8.3 Weighing the ICER against other decision criteria in the decision making process

Policy decisions about health care technologies are not taken without consideration of elements and aspects beyond cost-effectiveness. There are different ways to deal with this:

1. either the additional elements are made explicit, measured or objectified and explicitly weighed in the decision making process,[8, 57, 65, 102-105] or
2. the additional elements are taken implicitly into account in the decision making process.[67]

The first approach assumes that all elements *can* be measured or objectified. The subsequent weighing of the elements in the decision making process can be done in different degrees of explicitness. One extreme is to remain implicit about the actual weight of each of the additional elements and let the result depend on the discussions between policy makers about the different elements and their relative importance.[105] Another extreme is to determine the weights a priori,[103, 104] reducing the need for discussion between health policy makers and/or stakeholders.

Whatever the approach chosen for weighing the additional elements, the main objective is to increase transparency in the elements that are considered in the decision making process and at least make them explicit.[s]

One of the elements could be the ICER and its relation to a predefined ICER threshold value. This is one way to consider the economic value of an intervention in the decision making process. Other possibilities exist, however. For example, economic considerations can also be introduced in this approach by looking at the economic elements (cost, budget impact, general health outcome) in a disaggregated form,[77] and weighing these separate elements explicitly in the decision making process. We elaborate on this in section 2.8.6. In summary, being explicit about the decision criteria offers added value and does not depend on whether one accepts the idea of an ICER threshold value or ICERs as such.

In the case where the additional elements are taken implicitly into account in the decision making process, it is unlikely that a single threshold value can be identified that fits all policy decisions about all health technologies.[64] This ultimately boils down to the less transparent situation described earlier where the societal WTP for a QALY differs for every single intervention.

With the ICER being one of the many considerations in health care policy making, the probability of rejecting an intervention increases as its ICER increases. If cost-effectiveness considerations are taken into account in the decision making process, the general idea is that interventions with a relatively low ICER would be accepted more easily than interventions with a relatively high ICER. How much 'more easily' depends on the other considerations, characteristics and societal concerns taken into account when taking the decision.[67]

The level of uncertainty around the ICER may also be an important determinant in the decision to reimburse an intervention. For instance, procedures with little evidence on effectiveness will typically be characterised by large credibility intervals around the ICER. It seems logical that, given the uncertainty about the effectiveness of a procedure, policy makers will be more reluctant to reimburse the procedure. In such a case, the risk of taking a 'premature' decision might have to be assessed.

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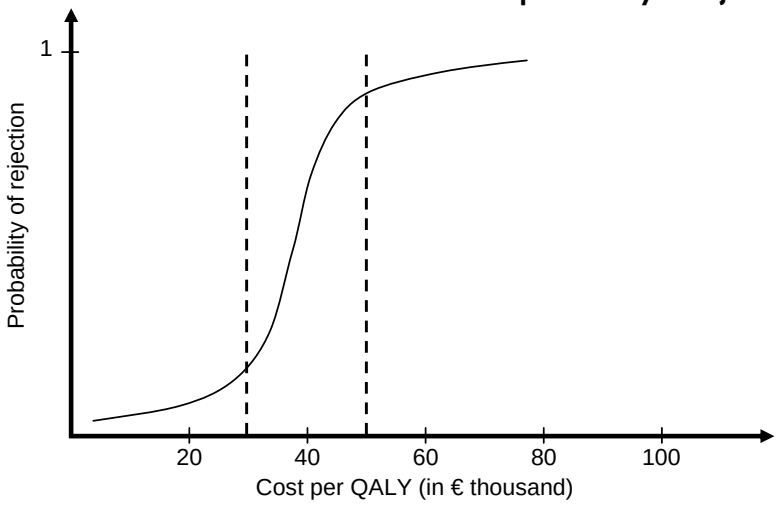
s In this context it is worth noting that NICE makes a distinction between "assessment" and "appraisal". Assessment refers to the scientific review of the evidence about how well a group of similar treatments work, and whether they offer value for money. The assessment report forms the basis for the appraisal. Appraisal refers to the formal assessment of the quality of research evidence and its relevance to the clinical question or guideline under consideration, according to predetermined criteria. The Appraisal Committee develops NICE's guidance about using drugs or treatments in the NHS (see http://www.nice.org.uk/website/glossary)

For example, is the decision to wait for more evidence socially acceptable or would this decision be harmful.

A 'cost-effectiveness probability of rejection' curve reflects the likelihood of an intervention being rejected depending on the value of its ICER (Figure 5).[67] This is a theoretical curve as the probability of rejection may be different for different types of interventions. Moreover, as it is impossible to quantify the precise impact of all other policy considerations and policy considerations will differ across interventions, it will in practice be impossible to calculate the probability of rejection.

Figure 5: The relation between the ICER and probability of rejection



2.8.4 The average GDP per capita as a threshold value for the average cost-effectiveness ratio

According to Williams[99] it makes sense to allow each citizen the average Gross Domestic Product (GDP) per capita, as a reflection of each citizen's 'fair share' of a nation's wealth. Therefore, the average per capita GDP might be used as a threshold value for the *average* cost-effectiveness ratio in the evaluation of an intervention's cost-effectiveness. The same reasoning was followed by the World Health Organisation's Commission on Macroeconomics and Health, be it with 'Disability Adjusted Life Years (DALYs) averted' as the generic health outcome measure instead of QALYs or LYG.[t] The Commission specifies that averting one DALY for less than the average per capita income is very cost-effective, averting one DALY for less than three times the average per capita income is still cost-effective and averting one DALY for more than this amount is not cost-effective. The construct and meaning of DALYs is fundamentally different from that of QALYs. The similarity between the WHO criteria and the criterion suggested by Williams in 2004 is therefore highly misleading.

Independent from this specific caveat, the suggested ICER threshold value of one time the average GDP per capita is problematic in different ways. First, the approach actually proposes a threshold value for the *average* cost-effectiveness ratio and not for the *incremental* cost-effectiveness ratio. It can, therefore, not be considered an appropriate threshold value for ICERs. Moreover, it is inappropriate to base decisions on average cost-effectiveness ratios because this would mean that the cost and health effects of the alternative treatment are both zero. Even in cases where there is no alternative treatment and the relative comparator is 'doing nothing', this will not be the case. Resource allocation based on average cost-effectiveness ratios will therefore not maximise health with the given budget. Second, the approach implicitly assumes society is willing to devote its entire GDP to health care.[5]

t The number of DALYs of a disease reflects the number of healthy life-years lost in a population due to the disease. Four aspects of disease are taken into account in the DALY measure: the number of patients suffering from the disease, the severity of the disease, mortality and the age at death.

The entire GDP might not even be enough if citizens require combinations of treatments whose total average cost-per-QALY exceeds the average GDP per capita. Therefore, this approach is not feasible and conflicts with the efficiency evaluation objective of economic evaluation.

2.8.5 The opportunity costs approach

Gafni and Birch have argued that CEA and ICERs may not be very useful in real life decision making contexts, even for maximizing health from a given budget, simply because the basic conditions for using ICERs for this purpose are not and can never be fulfilled.[50, 68] Either ICERs would be interpreted as in the theoretical ICER threshold value approach, which is inappropriate given that the baseline conditions are not fulfilled (see 2.7). Or, alternatively, the ICER threshold value would be defined as a value for the societal WTP per QALY (or LYG), in which case the threshold approach would inevitably lead to budget expansions.[98] There is evidence from Ontario (Canada), England and Australia that the adoption of the ICER threshold value approach has indeed been associated with substantial unplanned increases in healthcare expenditures without any evidence of any increase in total health benefit.[62, 64]

The suggested alternative to the use of ICERs and CEA in a decision making context characterized by fixed budgets is to present the real opportunity costs of the implementation of the programme under consideration.[63, 98] The opportunity costs of the programme are equal to the health benefits foregone in other programmes that have to be downgraded or abolished to finance the new one. It implies the notion of choice between desirable but mutually exclusive outcomes. If the benefits foregone from the cancelled programme are higher than the benefits generated by the new programme, the new programme should not be funded from the limited budget (unless there are other non health-economic arguments to fund it).

As such, the additional resource requirements are identified and the implications of cancelling other interventions are made explicit.[46] This increases the transparency of the decision making process.

The implementation of this approach on a national level might be problematic for different reasons. It is difficult to know precisely which activities will be displaced to be able to implement a new intervention. As a result, only accepting new technologies if the source of the resources is made explicit could paralyse the system. Other decision problems might appear. For example, what happens if in a decentralised reimbursement decision system decision makers think to find the resources for two different interventions from disinvestment in the same third intervention? Furthermore, interventions with a large budget impact will probably be more problematic to implement than projects with a smaller budget impact, even if they may be more cost-effective, since they will need to identify relatively more projects to sacrifice.

On a local or institutional level, their may be more possibilities to use the opportunity cost approach. For example, hospitals that have to decide on buying a new device or implementing a new health care programme, might consider the savings they will have to realize elsewhere in their organization to free resources for the new investments.

Despite the potential practical problems, the opportunity cost approach makes the important point that disinvestments are always needed in a system with a fixed budget. First candidates for disinvestment should be interventions that have become obsolete or are no longer considered worth their costs. In a mixed public-private financing system, the opportunity cost approach might become even more complex, because every decision to reduce public financing of an intervention (in order to contain costs from the perspective of the public payer) has a potential impact on both health and income inequalities.

2.8.6 Cost-consequences analysis

Many authors have suggested that ICERs and CEA may have a limited meaning to health care policy makers.[77, 106-112] Coast (2004)[77] sees three reasons for this:

1. health policy makers might not have the same objectives as presumed by economic evaluations
2. the ICER might not provide sufficient information about the efficiency of an intervention from the health care policy makers' point of view
3. the presentation of and methods used in economic evaluations might not be meaningful to decision makers.

The danger arising from this situation is that either economic evaluations become marginalised in the decision making process, or, more worrying, that economic evaluations are used without careful thought about what is behind them and consequently serve as a basis for decisions that do not reflect society's objectives.

An alternative to ICERs and ICER thresholds is to present the separate elements of economic evaluations that *do* make sense to decision makers in disaggregated form,[77] such as costs per patient, costs for the entire population, outcomes in terms of life years gained, impact on quality of life, disease severity etc.

In health economics, this is called cost-consequences analysis.[2, 4] These elements can then be weighed –implicitly or explicitly- by policy makers in the decision making process. The major advantage of this approach is that -in contrast to the ICER- the separate elements make sense to policy makers. The ICER, being a ratio, masks important aspects of an intervention. The absolute values of the numerator and denominator are lost when only looking at the value of the ICER, while these absolute values *are* important. For example, an intervention offering 0.001 additional QALY per patient for an additional cost of €80 has the same ICER as an intervention offering 10 QALYs for an additional cost of €800 000 per patient. If for the latter intervention only 3 patients are eligible and for the former 100 000, both interventions may nevertheless be perceived differently by policy makers. Moreover, it allows more than the other alternatives, to take uncertainty in the economic elements into account. The disadvantage of the approach is that, in the absence of an ICER, it is impossible to assess the efficiency of an intervention.

While efficiency in resource allocation is clearly not the only concern of health care policy makers, it cannot be denied that it *is* a concern. Ignoring cost-effectiveness is as unethical as using cost-effectiveness as the sole criterion for resource allocation decisions.[113, 114]

Key points

Alternatives to the theoretical ICER threshold value in a fixed budget setting have been suggested, differing in the extent to which they support the notion of an ICER threshold value as a guiding resource allocation rule:

- **Instead of defining the ICER threshold value as the ICER of the least cost-effective intervention still financed, the ICER threshold value could be defined in terms of societal willingness to pay for a (weighted) QALY (or LYG). This requires a flexible health care budget.**
- **A second suggested alternative is to derive the ICER threshold value from past reimbursement decisions.**
- **A third suggested alternative is to consider the ICER as one element in the decision making process that has to be weighed against other elements. This weighing can be explicit or implicit.**
- **A fourth suggested alternative is to define a threshold value for the *average* cost-effectiveness ratio as the average GDP per capita, reflecting the citizens' 'fair share' of a nation's wealth.**
- **A fifth suggested alternative abandons the idea of an ICER to guide decisions and argues that the real opportunity costs of financing an intervention should be made explicit and compared to its benefits in terms of better health outcomes.**
- **A last suggested alternative is to present all economic elements that are relevant for decision making in disaggregated form, in order to allow the decision maker to weigh the economic elements against other elements.**
- **Each alternative has its practical weaknesses: either there is a lack of data to implement the approach, or there are unresolved measurement problems, or in practice they do not really increase the transparency of decisions. They all have in common that they look for ways for making economic considerations explicit in the health care decision making context.**

3 THE ROLE OF ECONOMIC EVALUATIONS IN HEALTH CARE DECISION MAKING

3.1 DECISION MAKING PROCESSES

Major efforts are being devoted in many countries to develop tools and methods to create processes of "research-informed" decision making. Rational and informed decision making is implicitly put forward as part of the emerging evidence-based and health technology assessment movements. The use of ICERs and ICER threshold values is part of this development. However, a purely instrumentalist approach to decision making in health care is to be avoided. Decision making in health care is not to be reduced to well-informed and technical, rational assessment of problems upon which best solutions are formulated.[115]

The study of decision making processes is not recent. Different models have been identified and discussed in the history of social sciences. Some of the basics of decision making theories will help to understand why decisions on health care technologies or interventions cannot be solely based on economic and clinical (technical-rational) considerations.

- The Rational Decision Making model focuses on reasoned (rational and logical) decisions. It is based on an axiomatic approach that decisions are (or should be) the result of rational weighing of alternatives before selecting a choice. The rational model assumes, stated in a simplified manner, that it is possible to select one single and best solution to a problem. It is based on the assumption that the problem is well known and identified, that clear assessment rules are available to judge possible solutions and that solutions for a problem are chosen based on these assessment rules. It also presupposes that all possible options or approaches to solving the problem under study are identified and that (in political decisions) the costs and benefits of each option are assessed and compared and that the best intervention is selected. The underlying assumptions of this rational decision making have been criticised. It has been argued that not all knowledge is readily available to make clear assessments of a situation, be it on one solution or on possible alternatives; that cognitive capacities of decision makers are limited; that preferences are not always clear or that preferences do not remain stable over time.
- The "bounded rationality model", an adapted form of the rational model, tries to deal with these criticisms. This model assumes that a certain extent of rationality in decision making is possible, be it that different cognitive (e.g. capacity to deal with information) and circumstantial factors (availability and timeliness of information on the solutions and alternatives at the time of decision making) inhibit total rational assessments of a problem. The bounded rationality model assumes that "as rational as possible" decisions can be taken. Variants of the bounded rationality model refer to "procedural rationality" in which decisions are developed within the procedural constraints of the agencies or actors responsible for taking decisions.

Moreover, people rarely adhere to logical models of choice. Other decision making theories, using a completely different perspective, have documented that decision making is primarily an interactive process rather than a rational and well thought-through process of assessing a problem.

- The "incrementalism" or "muddling through" decision making model argues that goals are set as politically feasible goals in which people strive for acceptable rather than theoretical best solutions.[116-118] Other, more psychological decision making theories, have highlighted the importance of schemata in determining how people interpret new information based on

their pre-existing beliefs and cultural values. "Attribution theories" have argued that people use heuristics, rules to test their vision on a problem (schemata) and facilitate the processing of information. The decision making process produces decisions only marginally different from past practice as incremental decision making deals with selective issues as they arise. Problems or issues are dealt with ad hoc, using whatever analysis is close at hand, without any comprehensive review of all the associated issues. The incremental decision making model stresses that objectives are seldom explicitly specified, that remedial action (rather than rational analysis) is taken when it becomes essential, and more important decisions are dependent on the power struggles between interest groups.

- Related models have documented that decision making processes are political in nature. Decisions can be explained from a "political rationality" point of view, in which actors take decisions as a result of power plays, bargaining, coalitions, public acceptance of decisions, etc. The political models recognize the process of reconciling the interests of different stakeholders within a variety of internal and external constraints, rather than a purely rational assessment of all ins and outs of a (health care) problem.

We limited ourselves to a *very* rudimentary sketch of the complex field of decision making theories. This sketch allows arguing that decision making in daily practice is determined by a complexity of factors, and certainly not only a rational instrumental consideration and balancing of available alternatives. Decision making is in essence an interactive process in which different factors affect the outcome, the decision.

What we do see in the current time frame of health care decision making, is that major efforts are being made to "rationalise" decision making as much as possible offering information collected and analysed using scientific methodological principles (evidence, economic evaluation,…) where possible. It is one of the necessary steps to make decision making processes more transparent. The development and use of scientific knowledge is however only one of the components of real-life decision making.

Key points

- **Decision making is a far more complex process than an informed rational assessment of problems, weighing of alternatives and the formulation of best solutions.**
- **Different decision making models learn that rationality -if any- is bounded, that decisions are developed incrementally and that decision making processes are political in nature.**
- **Efforts are made to 'rationalise' health care decision making by offering information and knowledge gathered on a methodological sound basis, and to make decision making processes more transparent.**

3.2 INFORMED POLICY DECISION MAKING

A particular field of study related to decision making evolves around supporting decision makers with the necessary (scientific) information. The use of scientific information in decision making processes is a very complex process. It has been argued that for policy makers, any form of information that supports a decision is often considered as relevant knowledge. Decisions are thus in most of the cases not taken on the basis of scientific or technical information only, but on a mix of information sources.[119-121]

Issues on the use of research utilization have been discussed in literature on knowledge brokering and information dissemination between researchers and decision makers. We will not elaborate much, but quote insights from two systematic reviews.

One systematic review discusses the facilitators of and barriers to the use of research evidence by policy makers.[122]

- The most commonly mentioned facilitators were: personal contact between researchers and policymakers; timeliness and relevance of the research; research that included a summary and clear recommendations; research that confirmed current policy or endorsed self-interest; community or client demand for the research; and research that included effectiveness data.
- The most commonly mentioned barriers were: absence of personal contact between researchers and policy makers; lack of timeliness or relevance of research; mutual mistrust; power and budget struggles; poor-quality research and political instability or high turnover of policymaking staff.

The review also clarifies that "Use" of research can be viewed in three different ways: 1) direct use (research directly affects the decision); 2) selective use (research is selected to legitimate pre-determined positions); and 3) enlightening use (research helps to set new benchmarks for what is possible and deepens understanding).

Lavis et al.[123] distinguish four broad categories or models for developing evidence-based policy making. These models are presented as a typology, but can be applied either alone or in combination.

- Enhancing push factors (Model A) - "Push" efforts are generally led by researchers, or communications staff of research institutes and aim to increase awareness of research evidence among policy makers and civil society. Such efforts are well suited to situations where the potential research users are unaware they should be considering a particular message or in some cases would prefer to continue to disregard evidence. HTA and evidence based research agencies operate most of the time within this model.
- Enhancing pull factors (Model B) - User-pull and/or demand for research evidence are critical for research evidence uptake. It occurs when policy and decision makers identify an information gap and request evidence or commission research to fill this gap. These kinds of demands are often handled by policy advisory units within Ministries of Health and/or other policy making or technical support units (sometimes also applied research by universities or research institutes)
- Supporting exchange efforts (Model C) - Exchange efforts occur when producers and users of research work in partnerships and establish links.
- Supporting implementation of an integrated model (Model D) - integrated models combine elements of the three models described above.

Key points

- **Decisions are in most of the cases not taken on the basis of scientific or technical information only, but on a mix of information sources.**
- **Several barriers and facilitators have been identified for developing scientifically informed decision making.**
- **Knowledge and research evidence can be used by decision makers in three different ways: direct, selective and enlightening.**
- **Knowledge brokering is an important topic to be further explored in order to support decision makers.**
- **The process of 'knowledge brokering' for policy makers can be summarized in four models: an information push model, an information pull model, an exchange model and an integrated model.**

3.3 EMPIRICAL EVIDENCE ON THE USE OF ECONOMIC EVALUATIONS IN HEALTH CARE DECISION MAKING

"…, the results of rigorous clinical trials and sensitive modelling techniques tell us little about how data on clinical and cost effectiveness are interpreted at the level of national policy formulation".[124]

It has been repeatedly argued in this report that health care decision making is assumed, in an ideal situation, to be focussing on an optimal allocation of available resources with the purpose of maximising health. Decision makers are expected to focus on interventions that provide the most health gains for a given expenditure of resources.[114] Moreover, a systematic approach is expected to increase transparency and consistency in the decisions taken.[125]

A particular branch of empirical research has been studying the impact of economic evaluation studies on the policy making processes. The successful application of cost-effectiveness principles has been documented as being a problem in different health care systems.[114, 126-128] Several barriers to the use of the results of economic evaluations have been observed.[129] The barriers have been summarized as issues of *accessibility* of research evidence and (scientific, structural/institutional and ethical/political) *acceptability* of research evidence.[17]

A systematic review on the use of economic evaluations in the UK revealed that a number of features of the decision making process hamper the use of cost-effectiveness analysis, such as capacity to understand economic analysis, attitudes to economic evaluations including concerns on the basis of analysis and its use, the scope of the research questions and the scope of the policy question.[130] A survey in nine European countries documents that decision makers use different sources of economic information, but that many decision makers also believe that a lot of the information obtained can be biased through sponsorship.[112] Despite the widespread use of modelling and cost-effectiveness ratios for health care decision support, there are concerns with regard to the quality of the models:[131] concerns exist about the transparency and validity of the models, the lack of high level clinical data, possible bias when observational data are used and difficulties with extrapolation.

In order to deal with these perceptions and increase the legitimacy of research findings major efforts are being devoted to the development of guidelines on how to perform economic evaluation. Moreover, decision makers do not fully understand health economics outcomes statements such as in particular incremental cost-effectiveness ratios, willingness to pay, QALYs etc.[77] *or* consider them to be irrelevant.[132]

Decision makers are convinced that although economic evaluations can be useful in principle, in practice their usefulness is considered limited as the studies do not always apply to the particular decision making context.[133-136] Economic evaluations seldom take contextual factors into consideration[137] although health care systems and health insurance regimes differ, and particular cultural, social, economic and political conditions are important background variables to understand decision making procedures. A recent comparison of drug reimbursement decisions between the UK, Australia and New Zealand concluded that different factors might drive reimbursement decisions in different countries.[138] Drugs that have the potential to save lives (e.g. leukaemia) or alleviate particularly complex diseases (e.g. multiple sclerosis) were reimbursed in all three countries. For other drugs, severity of the disease becomes important in the elements considered during the decision making process. Perceptions of disease severity might differ between countries. Raftery (2008) suggests that *"the perception of 'dread' diseases depends on social factors, such as patient lobbying and public perceptions. Decisions on which drugs to fund, in the final analysis, depend on their political and social acceptability".*[138]

Timeliness of information is a particular issue. Cost-effectiveness analyses crucially depend on evidence of effectiveness and therefore always come later in the life cycle of a technology. Healthcare decisions, however, are frequently needed in the early stages of a technology's life cycle.

As a consequence, decision makers are sometimes in a position of having to take decisions without having adequate cost-effectiveness data at their disposal.[139]

Moreover, clinical effectiveness and cost-effectiveness are only two of many considerations in making policy choices. Valuing different types of outcomes is inherently value-laden, where economic evidence needs to be combined with stakeholder deliberation.[114]

Key points

- **Barriers in the use of economic evaluation studies have been summarized as issues of *accessibility* of research evidence and *acceptability* of research evidence**
- **The capacity to understand economic analysis, attitudes to economic evaluations (including concerns about the basis of the analyses and their use), the scope of the research questions and the scope of the policy question, hamper the use of cost-effectiveness analysis in decision making**
- **Effectiveness and cost-effectiveness are only two of many considerations in making policy choices. Economic evidence needs to be combined with stakeholder deliberation.**

3.4 COST-EFFECTIVENESS ANALYSIS, ICER THRESHOLD VALUES AND DECISION MAKING

Internationally there is an ongoing methodological debate on what could be the role of CEA and ICERs in health care decision making. International agencies such as the World Health Organization[u] and the World Bank[v] promote the use of CEA. Eichler and colleagues[125] predict "*CE thresholds will gradually become a reality, irrespective of whether local decision makers welcome them or remain critical, because it is meaningless to perform CE-studies in the absence of an acceptance threshold […] neither theory nor empiric evidence supports the expectation that CE thresholds will evolve as the sole decision criterion" (p525)*

Although some scholars are convinced about the pervasiveness of the use of ICERs, there still is fundamental methodological debate on the foundations for using an ICER threshold value in decision making. The methodological issues have been discussed extensively previously in this report. Some authors have documented that currently accepted thresholds are determined rather arbitrarily, and that further methodological debate is needed.[47, 48, 140] A large number of factors might be expected to generate variation in the cost-effectiveness of healthcare interventions across locations.[137] Arguments have been developed that differential threshold values are needed for diverse disease and treatment characteristics (e.g. higher thresholds for life-saving treatments), age, gender and race factors, and arguments are being developed to develop equity adjustment procedures to cost-effectiveness thresholds.[141]

The main message of the critiques is that in real world decision making some of the theoretical assumptions of ICER threshold values do not hold (see 2.7) and considerations of cost-effectiveness are insufficient to inform decision makers. Moreover there remains the issue of implicit and explicit threshold values. Many countries do not use explicit thresholds for coverage decisions (see also 3.5), while some countries use an implicit ICER threshold value, above which the decision would usually be negative (e.g. Australia, New Zealand and Canada).

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u The "Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis" seeks to provide analysts with a method of assessing whether the current as well as proposed mix of interventions is efficient. It also seeks to maximize the generalizability of results across settings. http://www.who.int/choice/en/index.html

v The World development report 1993 "Investing in health" proposed a universal method to set health priorities for all countries based on the central idea that priority in allocating means and resources should go to problems that cause a large disease burden and with cost-effective interventions that are available.

The most extensive discussion on the use of ICER threshold values by government agencies can be found in the UK. In the UK, arguments have been developed why it is improper to apply a specific threshold.[61] For a number of reasons, NICE formally rejects the use of an absolute ICER threshold value for judging the level of acceptability of a technology:[67]

"Firstly, there is no clear empirical basis for deciding at what value a threshold should be set. Secondly, there may be circumstances, as discussed below, in which the Institute would want to ignore a threshold even if one could be defined. Thirdly, to set a threshold would imply, unreasonably, that efficiency (health maximisation) had an absolute priority over other objectives (particularly equity or fairness). Fourthly, many of the supply industries whose products are appraised by the Institute are monopolies or oligopolies with high R&D costs but low production costs. Consequently, there are natural tendencies towards monopoly pricing and a threshold would provide an incentive to set prices to achieve an ICER just below the threshold and discourage price competition"[w]. *In the same discussion context, NICE adopted a formal standpoint on the use of scientific and social values*[x] *"Social value judgements are equally necessary but are concerned with the societal values embodied, explicitly or implicitly, in the Institute's advice. The need for judgements of this kind is independent of the scientific or empirical validity of the evidence, and is concerned with what should be considered to be appropriate for the NHS"*

Therefore, judgments about whether ICERs can be considered 'reasonable' are made by independent members of NICE's advisory committees (particularly the *appraisal*[y] committee) and the guideline development groups. Moreover, decision makers have to judge anyway whether an ICER represents good value by following a 'rule of thumb' rather than looking formally at opportunity cost (see for more details in 3.5.2). Decision makers have a very imperfect idea of the costs and benefits of current health care interventions which have not always been systematically documented. Therefore, it is not always clear whether existing interventions or alternatives should (continue to) be reimbursed.

Based on an analysis of cost-effectiveness research in US public health policy, Grosse et al (2007, p. 382)[114] conclude that "*although CEA methods pose ethical challenges, excluding cost-effectiveness as a consideration is also ethically problematic. Ultimately cost is an issue of fairness as well as of efficiency. CEA findings should be used as inputs in a deliberative evidence based decision making process that considers the viewpoints and values of multiple stakeholders."*

The use of ICER threshold values is paradoxical. On the one hand it appears to be an easy way to communicate about the complex issue of efficient use of public means. On the other hand the methodological problems associated with defining the value of the ICER threshold are an argument for decision makers to maintain the deliberation and negotiation process.

Economic evaluation (CEA or ICERs) cannot provide a blue-print solution for decision making. At best, it supports the process of a more rationalised decision making process. Multiple criteria have to be discussed for setting priorities in the allocation of constrained resources.

The observation that in priority setting multiple criteria play a role and that decisions are the result of complex processes has led to the exploration of multi-criteria decision analysis (MCDA) techniques. Baltussen and Niessen[103, 142] argue that MCDA may be an important tool towards a more rational priority setting process in health care, promoting the use of quantitative rather than qualitative analysis.

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w http://www.gserve.nice.org.uk/niceMedia/Pdf/boardmeeting/brdmay04item6.pdf

x http://www.gserve.nice.org.uk/niceMedia/Pdf/boardmeeting/brdmay04item6.pdf

y NICE clearly distinguishes 'assessment' from 'appraisal'. Assessment refers to the review of the evidence about how well a group of similar treatments work, and whether they offer value for money. The assessment report forms the basis for the appraisal. Appraisal refers to the formal assessment of the quality of research evidence and its relevance to the clinical question or guideline under consideration, according to predetermined criteria. The Appraisal Committee develops NICE's guidance about using drugs or treatments in the NHS (see http://www.nice.org.uk/website/glossary/).

But they also pay attention to the role of advisory panels in the definition of the relevant criteria and their relative importance for priority setting, and in making recommendations for reallocating resources on the basis of MCDA results.

Daniels (often in collaboration with Sabin) has made some ethical reflections on the decision making process within health care grounded in democratic and social justice theory. The basic principle in Daniels' reflection[143-148] is that a fair process is needed to establish legitimacy for critical resource allocation decisions. This process, labeled as "accountability for reasonableness", is based on deliberative processes (or democracy) at different decision making levels. It puts forward four conditions for fair rationing that would enable to break open the black box of health care decision making:

- Publicity: decisions and the rationales for decisions must be accessible. This principle implies that careful consideration should be given by decision makers to the arguments for the choices they make. Publicity would lead to transparency and coherence in the giving of reasons.
- Relevance: The grounds for decisions must be ones that people, who seek to cooperate with others on terms that are mutually justifiable, can accept as relevant to meet citizens or patients needs fairly under resource constraints. This is particularly relevant when claims are made that treatments or technologies "cost too much" to be reimbursed, especially in situations where information is lacking to make these claims. In such cases it is of particular importance for the "legitimacy" of the democratic process to be explicit about the procedures to take decisions and develop arguments underlying the (moral) reasons to take decisions. Decision makers should be made "accountable for the reasonableness".
- Appeals: there must be mechanisms to challenge and resolve limit-setting decisions to revise and improve policies in the light of new evidence or argument.
- Regulation: there must be some form of regulation to ensure that the previous conditions are met. These regulations could come through governmental regulation or through voluntary auto-regulation (but Daniels pleads for an accreditation of this latter governance model)

Elaborating further on the notion of accountability for reasonableness, Gruskin and Daniels (2008) propose a human rights approach.[149] A human rights approach sets out a process that requires analyzing which rights and which populations would be positively or negatively affected by each intervention. Specific attention must be paid to who would benefit most, and in what ways, from each intervention, and who would be left out.

Key points

- **In real world decision making, economic evaluations alone are not sufficient to inform policy makers.**
- **Neither theory nor empirical evidence supports the expectation that ICER threshold values will evolve as the sole decision criterion. CEA findings should be used as inputs in a deliberative evidence based decision making process that considers the viewpoints and values of multiple stakeholders.**
- **Ensuring 'accountability for reasonableness' requires opening the black box of health care decision making. Four conditions contribute to the 'accountability for reasonableness': publicity, relevance, appeals and regulation.**

3.5 THE USE OF ICER THRESHOLD VALUES IN OTHER COUNTRIES

Decisions that influence the diffusion and uptake of technologies can be influenced by many different factors such as available (public) resources, reimbursement mechanisms, regulatory frameworks and cultural and social determinants (e.g. attitudes towards technological innovations). It is therefore reasonable to expect that threshold values will not be identical in different countries,[125] as budgets and preferences (might) differ.

Decision makers may use implicit or explicit threshold values. Explicit threshold values means that decision makers have formally adopted and made public a threshold by which their decisions on resource allocation will be bound. By contrast, implicit thresholds are not official or public, but may be inferred retrospectively by analysis of the decision making pattern in a given health-care system.[125] In this section we examine to what extent explicit ICER threshold values are used in health care policy decisions in a selection of countries.

3.5.1 Methodology

We searched for existing written material about the use of economic considerations in health policy. Written documents, often grey literature retrieved through the Internet, were scrutinized to find clues about the existence and the use of ICER threshold values in health policy. We started by consulting the ISPOR website[z] to see whether pharmacoeconomic guidelines were published for the selected countries and which organization was the author of the guidelines (HTA agencies or others). Those guidelines and the website of the authors' organization were scrutinized for the use of ICER threshold values. In a next step, the websites of the health departments of the national (or local) governments and the websites of the national (or local) bodies responsible for decision making and reimbursement decisions about pharmaceuticals were consulted for further relevant information.

A summary of the findings for each country included in our review is provided in Table 3.

3.5.2 England and Wales[aa]

NICE, the National Institute for Health and Clinical Excellence in the UK, set an explicit threshold value as from 2002.[150]

NICE's "Guide to the Methods of Technology Appraisal 2004",[151] mentioned two threshold values: £20 000 and £30 000 per QALY gained. In November 2007, NICE issued a new draft "guide to the methods of technology appraisal" for consultation.[152] The consultation process continued until 29 February 2008. The updated guide was published in June 2008.[153]

With respect to the threshold values, the guide states:

"The Appraisal Committee does not use a precise ICER threshold above which a technology would automatically be defined as not cost effective or below which it would. Given the fixed budget of the NHS, the appropriate threshold to be considered is that of the opportunity cost of programmes displaced by new, more costly technologies. Therefore, the Appraisal Committee judges cost effectiveness in relation to the cost effectiveness of interventions currently funded by the NHS and those previously agreed by the Committee to be cost ineffective. Consideration of the cost effectiveness of a technology is a necessary, but is not the sole, basis for decision making. Consequently, the Institute considers technologies in relation to a threshold range, between which other factors have an increasing influence upon the decision to recommend a technology."

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z ("Pharmacoeconomic Guidelines around the World" http://www.ispor.org/PEguidelines/index.asp/

aa Website consulted, accessed autumn 2008: National Institute for Health and Clinical Excellence (http://www.nice.org.uk)

In this paragraph, it is stated that no precise ICER threshold value is used for decision making but that rather a threshold range is defined, based on the ICERs of currently funded health interventions.

This means that, while the Appraisal Committee is clear about not wanting to use a single threshold value for funding decisions, it nevertheless chooses to follow a certain guiding principle with respect to decisions about interventions in relation to their ICERs.

The guiding principles are as follows:

- For interventions with an ICER < £20 000/QALY gained, decisions will primarily be guided by cost-effectiveness considerations. In principle, the recommendation will be to provide this intervention, unless there are major doubts about the plausibility of and/or certainty around the estimated ICER. Thus, account is taken of the results of the sensitivity analysis and potential limitations to the generalizability of the findings regarding effectiveness.
- For interventions with an ICER between £20 000/QALY gained and £30 000/QALY gained, NICE takes account of the following factors:
  - The degree of (un)certainty about the ICER.
  - Whether there are strong reasons to indicate that the assessment of the HRQoL has inadequately captured, and may therefore misrepresent, the health utility gained.
  - The innovative nature of the technology, specifically where the innovation adds benefits of a substantial nature compared with available alternatives which may not have been captured in the QALY measure.
- For interventions with an ICER > £30 000/QALY gained the same factors will be taken into account. A stronger case is needed on these factors to approve such interventions.

These guiding principles suggest that 'additional elements', are only explicitly considered in the decision making process by the Appraisal Committee if the ICER exceeds £20 000/QALY. For interventions with ICERs below £20 000/QALY the only additional element considered is the uncertainty around the estimate of the ICER.

Recently, a report has been published on the relative societal value of health gains (QALYs) to different population groups in the UK.[44] The study identified attributes that determine societal preferences for the allocation of health gains and estimated equity weights for QALYs based on data from 688 interviews in people from the general public.[bb]

3.5.3 Canada[cc]

In Canada, cost-effectiveness data are formally required for all new outpatient medications since 1996.[94] Given this long-standing requirement for economic evidence in Canada, it might be expected that the role of ICERs and ICER threshold values is well established in that country.

Despite the formal requirement for cost-effectiveness evidence from the Canadian Agency for Drugs and Technologies in Health (CADTH), no information was found on how this economic evidence is used for decision making, neither from the CADTH published guidelines[154], nor from the other websites consulted.

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bb Before the interviews in the general public were performed, relevant attributes for societal preferences were identified through focus groups with 57 members of the general public and from a survey of 172 NHS employees.

cc Website consulted, accessed autumn 2008: the Canadian Agency for Drugs and Technologies in Health (http://www.cadth.ca), including the Common Drug Review that conducts rigorous reviews of the clinical and cost effectiveness of drugs, and provides formulary listing recommendations to the publicly funded drug plans in Canada (except Québec).

In the Canadian literature, Laupacis et al.[155] suggested in 1992 that evidence for adoption of a new intervention in Canada was strong with an ICER below CAN$20 000/QALY (CAN$ of the year 1990), moderate with an ICER between CAN$20 000/QALY gained and CAN$100 000/QALY gained, and weak if the ICER exceeds CAN$100 000/QALY gained. Laupacis et al.[155] acknowledged however that these lower and upper boundaries were arbitrary.

Furthermore, there is no formal evidence that any of these boundaries has been accepted or used by any Canadian decision making institution.[94]

Recently, Rocchi et al.[94] reviewed the published (September 2003 to March 2007) drug reimbursement recommendations generated by the advisory board of the Common Drug Review (CEDAC – Canadian Expert Drug Advisory Committee) in order to identify the role of economic evaluations and indicate whether an implicit threshold was used. Of the 62 files reviewed, ICERs were considered in less than half of the cases (40%, 25 files), including 12 negative recommendations and 13 positive recommendations. Medications with a positive recommendation ranged from dominant to CAN$80 000/QALY. Medications with a negative recommendation ranged from CAN$32 000/QALY gained to CAN$137 000/QALY gained. From this, Rocchi et al.[94] concluded that these implicit thresholds did not act as a clear demarcation line, because the ICER range for medications with a positive recommendation overlapped with the ICER range for medications with a negative recommendation. They also suggested that the resulting inconsistency in which ICERs lead to a positive recommendation may be due to the fact that other factors are considered in the context of a specific review.

3.5.4 The Netherlands[dd]

The Dutch Health care Insurance Board (CVZ, College voor Zorgverzekeringen) examines the basic package of care to which all Dutch patients have access. They provide the Ministry of Health, Welfare and Sport (VWS, Volksgezondheid Welzijn en Sport,) with advice about what care should be added or removed. The Pharmaceutical Aid Committee is an expert committee within the CVZ that assists in assessing whether new medicines need to be included in the basic package and be reimbursed. To be considered for reimbursement, manufacturers are formally required to provide cost-effectiveness data of all new drugs for which they claim an added-value. With this respect, CVZ has edited the "Dutch Guidelines for Pharmacoeconomic Research" since 1999, with an updated version published in April 2006.[16] Those guidelines do not mention how the pharmacoeconomic information is used for making decisions about the reimbursement of drugs in the Drug Reimbursement System.

The Council for Public Health and Health Care (Raad voor de Volksgezondheid en Zorg) is an independent body advising the government on public health and health care. At the end of June 2006, the Council published the report "Zinnige en Duurzame Zorg" ("Sensible and Sustainable Care") that addresses issues such as which criteria should be applied in order to identify priorities for the funding of care from collective resources. The Council divides the process of deciding which forms of care should or should not be funded from collective resources into four phases:

- Agenda-setting (scoping): defining the priorities for the decision making process (urgency principle)
- Assessment (quantifiable criteria): disease burden, efficacy and cost-effectiveness
- Appraisal (non-quantifiable criteria): community review of the outcome of the assessment phase, principles of fairness and solidarity
- Implementation: ensuring the forms of care that have been identified as warranting funding from collective resources are indeed funded in this way, and that other forms of care are not

dd Websites consulted, accessed autumn 2008: the Health Care Insurance Board (http://www.cvz.nl/), Ministry of Health, Welfare and Sport (http://www.minvws.nl/en/), the Council for Public Health and Health Care (http://www.rvz.net/)

The Council specifies that, for this decision making process to function optimally, the Minister must define an acceptable limit for some parameters, such as the disease burden and the cost-effectiveness value. The Council believes that it is not entitled to define such threshold values and that a democratic discussion has to determine the limit. In order to foster the discussion about this topic, the Council suggests an absolute maximum ICER threshold value of €80 000/QALY gained, provided that the disease severity index exceeds a specific threshold value.[156]

The index reflecting disease severity is obtained following the guidelines from the Dutch Health Insurance Board.[157] The measure reflects the health-related quality of life associated with a specific condition and is based on the number of QALYs lost due to the disease relative to the number of QALYs expected without the disease.

Therefore, although ICERs are considered in the decision making process of the Council, no explicit ICER threshold value has been defined so far in The Netherlands. Other factors also play an important role in this process.

3.5.5 USA[ee]

In the USA, the figure of US$50 000/QALY gained has frequently been quoted for many years as being the cost-effectiveness threshold value.[125, 140] Hirth et al.[158] report that this number was originally based on the supposed annual cost per QALY for the Medicare program for patients with chronic renal failure, but they further argue that this standard might have been based on a considerable underestimation of the chronic renal failure program's true costs.

Recently, Braithwaite et al.[96] investigated whether the advocated $50 000/QALY rule is consistent with current resource allocation decisions in the US. They estimated a lower bound for the societal WTP per LYG by calculating the incremental benefits of all medical advances since 1950 in terms of mortality reduction and the associated incremental costs. They simulated the costs and health outcomes in a US birth cohort without the medical advances and the health outcomes and costs with the medical advances. Major assumptions about the mortality reduction and costs attributable to medical advances had to be made. Based on the simulation, they estimated the ICER for 'modern' health care. From the empirical observation that most individuals in the US favour expanding the health care budget, they inferred that society's WTP for health care must exceed the ICER of modern health care and therefore the ICER threshold value must be higher than the estimated lower bound.

The estimate of the upper bound for the societal WTP for a LYG was based on observed people's decisions not to buy unsubsidized insurance even if they are not insured otherwise. The approach assumes that individual's unwillingness to get insured (even when income is sufficiently high) implies societal unwillingness to pay. The costs and benefits associated with and without unsubsidized insurance are simulated and used to obtain an ICER for insurance. According to Braithwaite et al. the preference not to get insured may point towards an upper-bound estimate for the societal WTP. The base case analysis suggests $183 000/LYG and $264 000/LYG as plausible lower and upper bounds for the ICER threshold value. When both quantity and quality of life were considered, in their sensitivity analysis, the lower and upper bounds became $109 000/QALY and $297 000/QALY respectively. Braithwaite et al.[96] conclude that an ICER threshold value of $50 000/QALY is not consistent with current allocation decisions in the US. As the plausible lower and upper bounds for the ICER are substantially higher than $50 000/QALY, it is very unlikely that this ICER threshold value is consistent with societal preferences in the United States.

Despite the existence of such thresholds published in the US literature, so far, the Centers for Medicare and Medicaid Services have avoided the explicit use of cost-effectiveness criteria in their coverage decisions and it is unclear to what degree cost-effectiveness is used to guide coverage decisions in the private sector.[140]

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ee Website consulted, accessed autumn 2008: the Centers for Medicare & Medicaid Services (http://www.cms.hhs.gov/), the Academy of Managed Care Pharmacy (http://www.amcp.org/)

In their recent editorial, Weinstein[140] adds that because economic evaluations are not used in any systematic or consistent way in the United States, it should not be surprising that there is no consensus as to the appropriate value of the cost per QALY that should guide health care decisions and policies.[140] Further, in the Format for Formulary Submissions (the suggested template for performing pharmacoeconomic evaluations in the US) published by the Academy of Managed Care Pharmacy in 2005, we found no information about the formal existence of an explicit ICER threshold value.

3.5.6 Australia[ff]

The role of the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia is to recommend to the Minister for Health which drugs and medicinal preparations should be subsidised by the Australian Government under the Pharmaceutical Benefits Scheme. It further advises the Minister and the Pharmaceutical Benefits Pricing Authority about the cost-effectiveness ('value for money') of a proposed drug compared with other drugs already listed in the Pharmaceutical Benefits Scheme for the same, or similar, indications.

The PBAC has edited Guidelines for Preparing Submissions to the Pharmaceutical Benefits Advisory Committee whose aim is to provide practical information (including guidance for economic evaluations) to the pharmaceutical industry for making a submission to PBAC.[14] The guidelines are also intended to help PBAC assess submissions. When making choices between competing therapeutic modalities, the factors considered by PBAC are cost-effectiveness, but also other important factors which include uncertainty, equity, extent of use and total costs. A threshold under which an ICER is considered attractive by the PBAC is not explicitly specified in the guidelines.

Although the PBAC does not appear to work with an explicit threshold value, Henry et al.[95] report that observation of the decisions of the PBAC between 1994 and 2003 point to an apparent threshold of AU$69 900/QALY gained above which reimbursement has been found to be unlikely. There is however no evidence that this implicit threshold is effectively used to guide PBAC's decisions.

3.5.7 New Zealand[gg]

The role of the Pharmaceutical Management Agency (PHARMAC) in New Zealand is to manage the pharmaceutical budget on behalf of the District Health Boards, and to decide which medicines are funded by the Government. Recently, PHARMAC published an updated version of The Prescription for Pharmacoeconomic Analysis (June 2007) which describes how PHARMAC undertakes its economic evaluations and how it interprets ICERs.[159]

As stated in their 'Prescription for Pharmacoeconomic Analysis'-report, PHARMAC decided not to define an explicit threshold value below which a pharmaceutical is considered 'cost-effective'.[160] Their justification for this is as follows:

- The main reason for this is that cost-effectiveness is only one decision criterion used by PHARMAC. One proposal may be more cost-effective than another but rate poorly on other decision criteria and therefore may not be funded (hence, on 'successfulness grounds', it will not be considered cost-effective).

ff Websites consulted, accessed autumn 2008: Pharmaceutical Benefits Advisory Committee (http://www.health.gov.au/internet/main/publishing.nsf/Content/Pharmaceutical%20Benefits%20Scheme%20(PBS)-1), the Australian Government, Department of Health and Ageing.

gg Website consulted, accessed autumn 2008: the Pharmaceutical Management Agency in New Zealand (http://www.pharmac.govt.nz/)

- Another reason for not having a fixed ICER threshold value is that the spending on community pharmaceuticals is required to be kept within a fixed budget within a given year. Given the binding nature of this constraint and all things being equal, what is and is not considered 'cost-effective' varies with the amount of funding available (not just in terms of the total budget each year, but the available budget at any point in time, as explained in 2.5.3: a fixed budget requires a variable ICER threshold value).

Pritchard et al.[93] speculated that PHARMAC's decisions are broadly consistent with an implicit threshold of NZ$20 000/QALY (NZ$ of the year 2000). The authors did not, however, perform a systematic analysis of PHARMAC's decision reports.

3.5.8 Finland[hh]

The Finnish 'guidelines for preparing a health economic evaluation' are published as an annex to the Decree by the Ministry of Social Affairs and Health on applications for a reasonable wholesale price, on special reimbursement status for a medicinal product, and on the documentation to be attached to the application (decree 1111/2005).

Despite the formal requirement to provide health economic evaluations for new chemical entities in Finland, we could not identify the use of any explicit ICER threshold value, neither from the websites consulted (including the legislation of the institutions), nor from the Finnish pharmacoeconomic guidelines.

3.5.9 Sweden[ii]

In 2003, the Swedish Pharmaceutical Benefits Board published general guidelines for conducting economic evaluations.[161] The English version of those guidelines does not contain information about the use of an ICER threshold value for decision making.

The main task of the Pharmaceutical Benefits Board in Sweden is to ascertain if a pharmaceutical or medical device is to be included in the pharmaceutical benefits scheme and be reimbursed by society. The Pharmaceutical Benefits Board weighs three criteria ('principles') when making its decisions:

- The human value principle; which underlines the respect for equality of all human beings and the integrity of every individual.
- The need and solidarity principle; which says that those in greatest need take precedence when it comes to reimbursing pharmaceuticals. In other words, people with more severe diseases are prioritised over people with less severe conditions.
- The cost-effectiveness principle; which states that the cost for using a medicine should be reasonable from a medical, humanitarian and social-economic perspective.

Cost-effectiveness thus appears to be a central concern in the Swedish reimbursement system,[162] but a threshold value under which a treatment is considered cost-effective does not appear to be explicitly stated. Other factors, besides cost-effectiveness, are also weighed in the decision making process of the Pharmaceutical Benefit Board.

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hh Websites consulted, accessed autumn 2008: the Finnish Office for Health Technology Assessment (http://finohta.stakes.fi), the Finnish Ministry of Social Affairs and Health (http://www.stm.fi), the Pharmaceuticals Pricing Board (the body responsible for pricing decision and operating under the control of the Ministry of Social Affairs and Health), the Social Insurance Institution (the body responsible for the reimbursement of pharmaceuticals, http://www.kela.fi).

ii Websites consulted, accessed autumn 2008: the Swedish Council on Technology Assessment in Health Care (http://www.sbu.se), the Centre for Medical Technology Assessment (http://www.cmt.liu.se), the Swedish Pharmaceutical Benefits Board (http://www.lfn.se/), the National Centre for Priority Setting in Health Care (http://e.lio.se/prioriteringscentrum)

3.5.10 Norway[jj]

The Norwegian Medicines Agency approves medicines and monitors their use, and ensures efficient, effective and well-documented use of medicines. On its website, the Norwegian Medicines Agency has published guidelines for pharmacoeconomic analysis in connection with applications for reimbursement in 2005.[163] Those guidelines do not inform on when an intervention is considered cost-effective.

From the websites consulted, no explicit threshold value could be identified in Norway.

3.5.11 Denmark[kk]

The Health Technology Assessment Handbook published in 2007 reports the views of DACEHTA (the Danish Centre for Health Technology Assessment) on when to consider a technology cost-effective.[164] They state that when two technologies do not dominate one another and an incremental cost-effectiveness ratio (ICER) is calculated for those two interventions, whether we should accept the new (or old) technology as being cost-effective ultimately depend upon the maximum price that the decision maker is willing to pay for the extra effect. DACEHTA further reports that there are no generally applicable limits concerning what can be considered a reasonable QALY price.

Table 3: Explicit, implicit and assumed ICER threshold values in other countries

Country	Authors	ICER threshold
Explicit ICER threshold range		
UK	NICE[151]	£20 000 - £30 000 per QALY
Implicit ICER threshold values or ranges based on past allocation decisions		
Australia	Henry et al. and the PBAC[95]	AU$69 900 per QALY
New Zealand	Pritchard et al. and PHARMAC[93]	NZ$20 000 per QALY
Canada	Rocchi et al. and the CDR[94]	Range of acceptance: dominant to CAN$80 000 per QALY Range of rejection: CAN$31 000 to CAN$137 000 per QALY
ICER threshold values or ranges proposed by individuals or institutions		
USA	Weinstein[140]	$50 000 per QALY
USA	Braithwaite et al.[96]	$109 000 - $297 000 per QALY
The Netherlands	The Council for Public Health and Health Care[156]	€80 000 per QALY
Canada	Laupacis et al. [155]	CAN$20 000 to CAN$100 000 per QALY
No ICER threshold values or ranges identified		
Finland, Sweden, Norway, Denmark		

CDR: Common Drug Review; NICE: National Institute for Health and Clinical Excellence; PBAC: Pharmaceutical Benefits Advisory Committee; PHARMAC: Pharmaceutical Management Agency.

jj Websites consulted, accessed autumn 2008: The Norwegian Medicines Agency (http://www.legemiddelverket.no), the Norwegian Knowledge Centre for the Health Services (http://www.nokc.no, this website is in Norwegian only), The Ministry of Health and Care Services (http://www.regjeringen.no/), The Norwegian Labour and Welfare Organisation (responsible for reimbursement and medical benefits, http://www.nav.no).

kk Websites consulted, accessed autumn 2008: the Danish Centre for Evaluation and Health Technology Assessment (http://www.dacehta.dk), the Danish Institute for Health Services Research (http://www.dsi.dk), the Danish medicine agency (http://www.dkma.dk/)

Key points

- **In the UK, a discussion is ongoing on the use of ICER threshold values. Currently the UK uses an explicit threshold range of £20 000 to £30 000 per QALY gained.**
- **Implicit threshold values based on past allocation decisions were published in Australia (AU$69 900 / QALY gained), New Zealand (NZ$20 000 / QALY gained) and Canada (range of acceptance: dominant to $80 000 per QALY gained, range of rejection: $31 000 to $137 000 per QALY gained).**
- **Thresholds values or ranges proposed by individuals or institutions were found in the USA (50 000$/QALY), in the Netherlands (€80 000 per QALY gained) and in Canada (20 000 - 100 000$/QALY).**
- **The lower and upper limit for the social WTP for a QALY in the US was estimated to be 109 000$/QALY and 297 000$/QALY respectively.**
- **With the exception of the UK, no explicit ICER threshold value (or range) is used in the countries examined.**
- **In all countries decision making is not solely based on cost-effectiveness considerations. The technology is assessed based on the threshold range together with other criteria. In the presence of high ICERs, those other criteria become more important.**
- **In most countries it appears that interventions with a low ICER are more likely to become accepted than interventions with a high ICER.**

3.6 THE USE OF ICER THRESHOLD VALUES IN BELGIUM

Additional to the international comparison a limited field study explored the use of cost-effectiveness evaluations in health care reimbursement decisions in Belgium. We focused on two committees: the Drug Reimbursement Committee (DRC or CTG/CRM) and the Technical Committee for Implants (TCI or TRI/CTI), both having an important role in reimbursement decisions.

3.6.1 Background on DRC and TCI

The decision to reimburse pharmaceutical products and devices in Belgium is taken by the Minister of Social Affairs after consultation with the Minister of Budget, but the Minister is advised on these matters by the DRC and the TCI respectively. Both committees are organised within the NIHDI but their structure, working procedures and place in the decision making process are different.

The DRC advises the Minister of Social Affairs directly. Although the advice is not strictly binding, the Minister can only deviate from the advice formulated by the DRC for social or budgetary reasons. The composition of the DRC and the procedures for formulating a reimbursement proposal for a pharmaceutical product are stipulated in two Royal Decrees, approved on 21/12/2001.[165, 166] The DRC is composed of representatives of sickness funds (the *mutualities*), universities, medical doctors and pharmacists. Representatives of the pharmaceutical industry, the Ministry of Economic Affairs, the Ministry of Budget, the Ministry of Social Affairs, the Ministry of Public Health and the NIHDI can attend the meetings and participate in the discussions but have no voting rights. The DRC has to formulate an advice within strict time limits: the decision to reimburse a pharmaceutical product has to be taken within 180 days after the submission of a reimbursement request file by a pharmaceutical company. The advice of the DRC with respect to reimbursement has to reach the Minister of Social Affairs at day 150 at the latest.

According to the European Transparency Directive[167] any decision not to reimburse a pharmaceutical product must contain a statement of the reasons *"based upon objective and verifiable criteria, including, if appropriate, any expert opinions or recommendations on which the decision is based"*.[II]

The TCI does not provide direct advice to the Minister of Social Affairs. The TCI is embedded in the historically developed NIHDI structures for reimbursement decisions, where an advice of the TCI is typically first discussed in a convention or agreement commission (*overeenkomsten- en akkoordencommissie / commission de conventions ou d'accords*) before it is sent to the Insurance Committee (*Verzekeringscomité/Comité de l'assurance soins de santé*) and the Commission for Budgetary Control (*Commissie voor begrotingscontrole / Commission du contrôle budgétaire*). Its composition and procedures are stipulated in the 'Sickness and Invalidity Insurance law'[169] and a Royal Decree stipulating the practical working procedures within the TCI.[170] The TCI is composed of representatives of sickness funds, universities and hospital pharmacists. Representatives of the Ministry of Social Affairs and the Ministry of Public Health can attend the discussions but have no voting rights when it comes to formulating the final advice of the TCI. As from 2009, the TCI will be reformed and an "Implants and Medical Devices Reimbursement Committee" will be established.[171] The structure and working procedures will from then be similar but not identical to those of the DRC. For example, the committee will also advise the Minister of Social Affairs directly but will not be subject to the same strict deadlines as the DRC.

3.6.2 Aims and methods of the field study

The purpose of the field research is to better understand whether and how cost-effectiveness issues (ICERs) are considered and discussed in those two advisory committees within the NIHDI. The purpose of this field study is purely explorative. We tried to better understand how clinical effectiveness is balanced against cost-effectiveness and other criteria. Furthermore -if relevant- we tried to grasp whether specific explicit or implicit ICER threshold values are used and what the opinions of decision makers in these committees are on the (potential) advantages and disadvantages of CEA and ICER threshold values.

We conducted two group-interviews with respectively members of DRC and TCI. The interview with members of the DRC was done with members of the "bureau" (president, secretary and two staff members of the NIHDI). The interview with TCI took place as part of a formal meeting of the TCI: 11 persons participated in the interview (excluding the NIHDI administrative staff members who were present but did not actively participate in the interview).

To prepare for the group discussions, the researchers studied the formal procedures of each of the committees.

Each interview was conducted by one moderator (not the same for the two committees), who used a checklist of topics to be discussed: Three researchers took notes. The interviews were reported in a written common raw data document (no transcripts) developed by all of the researchers.

A thematic content analysis was done collectively by the researchers based on these notes.

II The criteria which are taken into account by the DRC in deciding whether or not to reimburse a product are included in the Royal Decree of 21/12/2001.168 They include the therapeutic value (taking into account the efficacy, effectiveness, side effects, applicability and user-friendliness of the product), the market price and the requested reimbursement price, the clinical effectiveness and likely impact of the product (taking into account therapeutic and social needs), the budget impact for the NIHDI and for Class I products (drugs for which the company claims added therapeutic value compared to existing drugs) the cost-effectiveness of the product from the NIHDI perspective.

3.6.3 Results of the field study

The results in this section reflect the researchers' summary of what has been said during the interviews based on the notes taken during the interviews. This description does *not* necessarily reflect the official position of the full committees and should not be interpreted as such.

3.6.3.1 Drug Reimbursement Committee

As described previously, the DRC has to work according to a very formal and time-limited procedure to assess a reimbursement request and advise the minister on the reimbursement of a pharmaceutical product. This formal procedure has a major impact on the information used and the preparation of the decision making agenda within the committee. Especially the particular time constraints have an influence on the decision making process. For Class I pharmaceutical products[mm] the reimbursement request file submitted by the pharmaceutical company must contain a pharmacoeconomic evaluation. Therefore, according to the bureau, cost-effectiveness of pharmaceuticals is an essential issue in the decision making process. Internal NIHDI experts scrutinize the reimbursement request: they can ask the company to provide the electronic economic model to verify the model in-depth and search additional literature and verify the literature review. The experts prepare an evaluation file which is presented to all DRC members and discussed during a meeting.

It is repeatedly underlined that the formal procedures and time constraints put a lot of pressure on the handling of reimbursement dossiers. This simple procedural fact makes the work of the committee members, and the NIHDI experts sometimes stressful. The expected pace of handling dossiers also impacts on the decision making process. The preparatory work of the NIHDI experts is fundamental to the decision making process itself: members heavily rely on this preparatory work (without necessarily always agreeing with or following the evaluation of the NIHDI experts).

The current organisation of the decision making process is recognised to "rationalize" the decision making process. Especially since the committee has to clearly justify its decision. Although the factual decision making process is not free of emotional and other factors, rational arguments are seen as an essential part. It was mentioned during the interview that for instance media can increase the societal pressure on (members of) the committee. Moreover within the committee different stakeholders are represented, leading to situations where members also try to defend specific interests.

The formal preparatory stage requires a clear pre-assessment of cost-effectiveness issues of a pharmaceutical product. The interviewees recognise that it is not always entirely clear whether high level clinical evidence is readily available based on the submitted dossiers: it often lacks information on "hard" outcomes. It is said that, when evidence on hard outcomes is lacking, the NIHDI experts doing the pre-assessment are more inclined to question the validity of the economic evaluation. Sometimes it is even perceived that ICERs are used in the dossiers to conceal the lack of clear clinical evidence.

The available budget is judged as being a far more important criterion for taking decisions on pharmaceuticals than ICERs. This does however not mean that this criterion is decisive: the budget impact is approached in a flexible way. It is clear for the respondents that budget impact remains a fundamental criterion in the ultimate voting outcome. The number of patients that can be served within the budget constraints is an additional consideration.

The decision making process and the criteria used are clearly different when the patient population are children. The committee tends to be more tolerant for children, and tries to understand what a product would mean for the future of the child.

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mm Class I pharmaceutical products are so-called innovative products for which the company claims an added therapeutic value compared to existing drugs.

ICERs are used tentatively, as one of different criteria. Moreover, the DRC does not use a formal ICER threshold value when assessing pharmaceutical products: one interviewee even opposes the use of an "absolute" threshold value in the decision making process, as each pharmaceutical product has its own particularities.[nn] In answer to the question whether the committee makes a difference between outcome measures (LYG or QALY) used in the ICER, the answer was negative.[oo]

The perceived therapeutic need and the perceived therapeutic added value are the factual and informal decision criteria used during the deliberation. Additional criteria such as "is it a true innovation" or an adaptation or alternative of already available product,[pp] has an impact on the assessment of medical necessity.

In case of a revision of a product (revision of reimbursement decision after the product has been on the market for some time), the committee expects in principle more information (more real life data both on clinical and cost-effectiveness) about the product, since it is then also more feasible for the industry to present more and better data.

It is also recognised by the interviewees that the interpretation of cost-effectiveness studies within the decision making process in the committee had to go hand in hand with a learning process of the members. For example, it took a gradual process to make clear to the members that cost-effectiveness is not the same as cost-saving. Moreover, it is not clear whether all members of the committee truly understand the methodological background of an ICER, but nevertheless the use of an ICER leads to expressions as "€80 000 per QALY is high".

In other words, our respondents recognise that the decision making process within the DRC, although being rationalized and substantiated with clinical and economic data, remains a deliberation process of people, in which different formal and informal criteria are used.

3.6.3.2 Technical Council for Implants

Although the working and decision making procedure of the TCI will be modified in 2009, the current process of assessing a technology within TCI is less formally defined than in DRC. It is recognized that in the future the need for more objectified criteria in the decision making process will be needed. Therefore, it has been decided to work more along the lines of the DRC procedures from 2009 onwards, with the establishment of the 'Implants and Medical Devices Reimbursement Committee'.

The committee makes a difference between so-called 'me too' demands or demands for reimbursement of 'new technologies'. Demands for the latter have to be substantiated by the industry with clinical studies, which are often not available for implants and medical devices. Often experts from the field are invited and heard by the committee to substantiate the existing knowledge and the information on the clinical effectiveness of a new device.

The members of the TCI say that they consider cost-effectiveness as a decision criterion. Members of the committee report to be aware of the relevance of cost-effectiveness of implants, but simultaneously state that CEAs or publications are not assessed on a systematic basis for decisions within the committee.

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nn Nevertheless, we found an example of a threshold value of 30 000 €/LYG in a motivation document for a reimbursement decision of the Minister of Social Affairs (http://www.riziv.fgov.be/inami_prd/SSP/CNS2/Pages/MinisterialDecisionDet.asp?qs_SpcCod=00642119&qs_EffDat=20071101&qs_MdId=5023).

oo In the evaluation reports prepared by the evaluators of the NIHDI the distinction is nevertheless sometimes made and retained by the Minister of Social Affairs in his motivation for reimbursement (for example http://www.riziv.fgov.be/inami_prd/SSP/CNS2/Pages/MinisterialDecisionDet.asp?qs_SpcCod=00581188&qs_EffDat=20070301&qs_MdId=6175)

pp 1.5 to 3 years after the initial reimbursement request and a positive reimbursement decision for a class I pharmaceutical product, companies have to submit a revision file. This file should contain evidence on the effectiveness and cost-effectiveness of the product in real life situations.

As implants are often presented for reimbursement in early stages of use, feasibility to find and use scientific (clinical and economic) information is seen as a major problem. Moreover the available studies are not always considered relevant, especially if they come from large organisations or centres of excellence.

The deliberation and decision making process is to a large extent negotiated and expert opinion based. The role of the staff members of the NIHDI is less extensive than in the DRC. The preliminary work is done by the working groups, specialised in specific domains (e.g. cardiovascular implants, orthopaedic implants etc). The working groups prepare an advice, which is afterwards discussed in the plenary TCI meetings. Advice can be typified as sometimes supported by available (economic) studies, rather than systematically based on CEA or economic evaluations. ICERs are not used in the decision making process.

Decision makers focus mainly on the available budget. These budgetary constraints form the framework within which decisions on reimbursement are taken. The procedural particularity of the decision making process of the committee is that budgets have to be set and prepared almost one year in advance of the following working year. A budget has to be reserved for the following year, but estimations of the budget needed are not always accurate, sometimes leading to specific problems.

In the answers of the committee members it became clear that cost issues (in terms of reimbursement) and cost saving issues are considered more than cost-effectiveness issues. Costs are not always estimated or calculated, they are approached rather intuitively and experience-based. They stressed that it is often rather obvious to demonstrate the added value of a product.

Besides this economic element it is stressed that quality of life (not expressed as a QALY) is a relevant criterion to steer the decision making process.

One of the members of the committee explicitly refers to the difference between a theoretical and a political ratio in reimbursement decision making processes. The difference implies that other criteria than clinical effectiveness or cost effectiveness have to be considered. Cost effectiveness analysis can be of value but cannot be considered as the sole criterion to base reimbursement decisions upon for implants. Moreover, it is mentioned that the committee also has to consider other interests and has to work in a context of societal and media pressure.

3.6.3.3 Summary

The ways in which the two selected committees operate illustrate the growing awareness of the potential relevance of clinical evidence and economic evaluation studies. However, factors described in decision making literature are equally affecting the decision making process. Efforts are made to "rationalise" the decision making process and substantiate demands for reimbursement with scientific evidence. It helps to make the decision making criteria more transparent. But it also has to be stressed that the decision making process remains an interactive deliberation process, which is certainly not to be reduced to the technocratic rational application of scientific (clinical and economic) findings: decisions on reimbursement are negotiated and can only be understood taking into account circumstantial factors.

The DRC is clearly going through a learning curve in the use of cost-effectiveness knowledge in their decision making process. Clinical effectiveness and cost effectiveness (including ICERs) are becoming criteria to be documented by the firms and are actively considered, be it with the necessary critical attitude. It is stressed that decisions on reimbursement are affected by a lot more criteria and by the nature of the decision making process.

The TCI has been reflecting and working on procedures to make their decision making process more rational and procedural. The TCI will move towards a more formal (legal) description of working practices such as the DRC's, but currently both committees' processes are still clearly distinct. Currently the decision making process is not systematically substantiated yet by scientific clinical evidence and economic evaluation studies. The use of cost-effectiveness analyses has not yet pervaded the decision making process.

Key points

- **Although efforts are made to 'rationalise' the decision making process and substantiate reimbursement requests with scientific evidence, decision making processes in Belgium remain mainly an interactive deliberation process.**
- **Clinical effectiveness is the most important scientific criterion used in the decision making process of both the DRC and the TCI.**
- **Cost-effectiveness is sometimes considered in the DRC but rarely in the TCI.**
- **Budget impact is by both committees considered more important than the ICER.**

4 GENERAL DISCUSSION

4.1 ECONOMIC EVALUATION AND ICERS

The aim of this report was to provide an introduction to economic evaluation and ICERs for non-health economists and summarize the potential strengths and weaknesses of the use of ICERs and ICER threshold values in health care decision making.

One important caveat for using health economic evidence is the comparability of the methodologies used to obtain the ICER estimate. ICERs are useful for health care policy makers only in as far as they are comparable between interventions. It is thus considered of utmost importance to critically analyse the context for which ICERs have been calculated. Moreover solutions have to be sought for the existing methodological variability. Guidance for economic evaluations in health care can reduce methodological variability. The Belgian pharmacoeconomic guidelines[18] were developed as a response to this request for standardisation.

However, guidance is a necessary but not a sufficient condition. Economic evaluations and more specifically economic models[qq] often remain black boxes. Without offering policy makers the possibility to 'play' with an economic model, it is unlikely that they will trust the ICERs resulting from them. The Belgian pharmacoeconomic guidelines therefore demand that the DRC can ask for the electronic version of the pharmacoeconomic model presented by the pharmaceutical company in its drug reimbursement request, if so desired.

Furthermore, methodological standardization and control does not make the ICER a blue-print solution for policy making. Although it is generally accepted that economic efficiency is important and should be considered in resource allocation decisions, other elements than efficiency are taken into consideration in a decision making process. Many countries use the ICER to inform decision makers about interventions' relative value for money but there is still debate about whether an ICER and more specifically the ICER threshold value is the most appropriate way to introduce efficiency considerations in the decision making process.

The advantages of an explicit ICER threshold value would be an improved transparency and consistency of decisions, at least if methodological issues can be dealt with in a satisfactory manner. The drawbacks of using an explicit ICER threshold value might be the creation of an excessively mechanical decision making process, without consideration of other relevant variables or a tendency of companies to price up to the ICER threshold value or manipulate economic models to stay below the ICER threshold value.[rr]

4.2 WAYS TO INTRODUCE EFFICIENCY CONSIDERATIONS IN HEALTH CARE DECISION MAKING

Approaches for bringing efficiency considerations into the health care decision making process vary in the extent to which they accept the ICER and the ICER threshold value. Most of the approaches remain rather theoretical, due to the practical problems associated with implementing them.

The ICER threshold value is generally perceived as a fixed value against which the ICERs of interventions can be compared with to decide whether the new intervention is cost-effective. Besides the methodological problems mentioned before, this perception also ignores the difference between fixed and flexible budget situations.

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qq Note that all economic evaluations of health interventions are based on modelling to some degree. Models are used for different reasons, e.g. extension of time horizons, extrapolation of intermediate outcome parameters to final outcome parameters, simulation of effectiveness as compared to efficacy.18

rr NICE has introduced the distinction between 'assessment' and 'appraisal' to reduce this risk (see 3.4).

- A fixed ICER threshold value is incompatible with a fixed health care budget. A fixed budget requires the revision of the ICER threshold value every time a positive reimbursement decision is taken.
- In a flexible budget context, the ICER threshold value can be defined as the maximum societal willingness to pay for a QALY (or LYG). At first sight this approach looks appealing because it seems to take social values better into account. The implementation of this approach requires however:
  - that the societal willingness to pay for a generic QALY can be measured. Measurement of societal WTP for *a* QALY (or LYG) is methodologically impossible because the value of a QALY is always context-dependent.
  - that the societal WTP adequately reflects the value of the health care sector relative to other sectors. The use of societal WTP for a QALY (or LYG) as a fixed ICER threshold value will ultimately determine (the expansion of) the health care budget. The maximum societal WTP for a QALY will have to be revised regularly to make sure that the health care budget keeps reflecting the relative societal value of the health care sector.

Because of these requirements, no country uses the maximum societal WTP for a (generic) QALY (or LYG) as an ICER threshold value.

Some researchers have tried to derive the societal WTP from past decisions. As explained in the report, this is an invalid approach, as decisions are never made independent from additional considerations (e.g. equity, valuing patient or intervention characteristics).

Three approaches identified in literature suggest to forget about the ICER threshold value and to focus on other variables: the ICER of interventions as such (in comparison with ICERs of other interventions but without reference to an ICER threshold value), the opportunity costs of interventions or the disaggregated outcomes of the economic evaluation.

- The first approach argues that the ICER is to be compared to the ICER of another intervention without reference to an ICER threshold value. The in-between comparison of ICERs allows policy makers to draw conclusions on the relative cost-effectiveness of interventions, but does not give a yes or no answer to the question of whether the intervention increases the health care sector's efficiency. Neither does it allow policy makers to draw conclusions about the intervention's *value for money*, as this requires the inclusion of other considerations, such as equity, in the decision making process. The advantage of the approach is that it contributes to 'objectifying' the economic efficiency element in the decision making process.
- The opportunity cost approach states that ICERs are not the right vehicle for making resource allocation decisions. It requires making explicit where the resources for financing a new intervention in a fixed budget context must come from. This may be difficult in practice, especially in systems where decisions are typically taken within sub-budgets of the total health care budget and transfers between sub-budgets are not necessarily considered (as is the case in Belgium).
- The cost-consequences approach refers to the disentangling of economic evaluations into concrete elements and (economic) outcomes, enabling an explicit weighting of the separate elements in the decision making process.

A combination of the different approaches will probably offer better support to decision makers to assess the economic efficiency of interventions. For example presenting the ICER as well as the disaggregated results of an economic evaluation will allow future research in the ICER value above which an intervention does never obtain a positive decision (irrespective of their 'score' on other criteria) but below which a decision can still be negative

(= an implied ICER threshold, reflecting the absolute maximum society is willing to pay for an additional QALY or LYG). It will moreover familiarize policy makers with the ICER even if they do not wish to give a high weight to the ICER in decisions about specific technologies. This will eventually lead to a reference set in the minds of health care policy makers, against which they can value the ICER of new interventions. This is obviously a long-term and gradual process.

4.3 HEALTH CARE DECISION MAKING CONTEXTS

This report also briefly discussed the use of economic evaluations in health care decision making. The most important insight from this overview is that decision making processes cannot be reduced to a purely technocratic and rational assessment. From a social justice perspective on decision making, there are good arguments to pursue to clarify on and make the argumentative logic more transparent. More reflection and rationality in health care decision making is certainly worth pursuing. The principle that decisions should be substantiated with well documented, transparently brought scientific and other knowledge is increasingly accepted.

Health technology assessment is becoming a very useful methodology to support this ambition. Economic evaluation is part of any HTA and neglecting economic arguments would be unethical. As resources cannot be consumed twice, choices are inevitable. Consuming health care resources for one intervention implies denying these resources to another intervention. And precisely these choices need deliberation. Besides economic and clinical research based arguments, social justice considerations remain a core element in the decision making process. The question on the allocation of limited resources to obtain optimal outcomes is therefore not a technical "neutral" issue but also an issue of societal values. These values develop within political, social and economic contexts. The economic efficiency argument will weigh differently in decision making processes. Economic (technical rational) criteria will be given another meaning e.g. according to the health care field (e.g. preventive, curative, long term care, end-of life care) or the population addressed with the intervention (e.g. children). This is one of the reasons why decision makers should not solely rely on seemingly simple tools such as ICERs and ICER threshold values. In order to make more optimal use of economic analyses in health care decision making, researchers and analysts should become more aware that decisions on the use of health interventions are likely to be influenced by a range of social, financial and institutional factors. Taking better into account this knowledge would bring us closer to the core aims of HTA.

4.4 SUGGESTIONS FOR FURTHER RESEARCH

We need more research on the appropriateness of the theoretical foundations of the ICER and ICER threshold value for different health care systems. In particular, the difference between social security-based systems and NHS-based systems is relevant for at least two reasons: on the one hand the budgetary context (fixed or flexible), on the other hand the characteristics of the decision making processes. The literature currently relies on the assumption of a universally applicable theory of CEA, but arguments can be made in favour of a more context-sensitive analysis:

- First, much of the literature on ICERs and ICER threshold values implicitly assumes a Beveridge-type health care model or -if not- simply ignores the specificities of the health care system. Health care systems do for instance not all operate within a fixed budget approach (e.g. we argued why a fixed ICER threshold value is incompatible with a fixed budget (a NHS-based system) and why it would be more, yet not completely, compatible with a social security system). We need further theoretical and methodological elaboration of CEA taking the health care system characteristics into account.

- Second, political decision making structures and cultures diverge. The role and place of stakeholder deliberation processes and the importance given to technocratic analysis is different between countries. Moreover, the societal context (e.g. values of the welfare state, political preferences, …) potentially impacts on the criteria considered and on health care decision making processes and outcomes. The differences between the systems and the place of economic evaluations in decision making processes within these systems merit further exploration, in order to open the "black box" of decision making on health technologies.

A first practical step should aim at a better understanding of the decision making criteria on health technologies. It is an ethical principle that these criteria should be transparent and debatable within a democratic welfare state. The criteria used when taking decisions about a technology have to be identified in a scientific manner. This requires multidisciplinary scientific research (economics, medical science, ethics, and social science). A clearer definition of the criteria policy makers wish to take into account when taking decisions on health interventions would allow the HTA community to increase the value of its assessments for policy makers.

Key points

- **There is a consensus that economic efficiency should be one of the decision making criteria. There are different ways to introduce efficiency considerations in the decision making process.**
- **Using ICERs in combination with an ICER threshold value is one possibility.**
- **Methodological variability in economic evaluations reduces the value of ICERs for assessing interventions' cost-effectiveness. Compliance with the guidelines for economic evaluations and control of the economic evaluations is needed if ICERs are to inform health care policy makers.**
- **The ICER threshold value is generally perceived as a fixed value against which the ICERs of other interventions can be compared to decide whether the new intervention is cost-effective. In real life, however, the ICER threshold value can never be a fixed value over a long period of time.**
- **Alternative approaches are the in-between comparison of ICERs without reference to an ICER threshold value, the opportunity cost approach and the cost-consequences approach. Combinations of different alternatives are probably the most valuable.**
- **Although the weight of economic considerations might differ between decisions, ignoring economic efficiency in health care decision making is unethical.**
- **Besides economic and clinical research based arguments, social justice considerations remain a core element in the decision making process. The question on the allocation of limited resources to obtain optimal outcomes is therefore not a technical "neutral" issue but also an issue of societal values.**
- **More research is needed on the applicability of theoretical foundations for CEA in different health care systems and on the place of CEA in different political decision making structures and cultures.**
- **Research is also needed on the decision criteria deemed relevant in the Belgian context.**

5 CONCLUSION

The aim of this report is to provide a reference document for non-health economists on economic evaluation in health care, its basic concepts and its potential value for health care policy making. The report explains why ICER threshold values, defined in their neo-classical welfarist sense and under a fixed budget constraint, have a theoretical basis that is, however, untenable in daily practice because basic assumptions are not fulfilled. This raises the question about whether we still need ICERs, since, according to theory, they should be compared with an ICER threshold value.

ICERs can be valuable in two ways:

- define the ICER threshold value as the maximum societal WTP for a unit of health effect. This option requires a flexible budget and the measurement of the maximum societal WTP for a generic QALY.
- determine the acceptability of an ICER on a case-by-case basis by evaluating the societal WTP for a unit of health effect for each intervention separately. This option does not require the identification of an ICER threshold value but derives interventions' relative cost-effectiveness by means of in-between comparisons of ICERs. Other considerations are weighed against the efficiency criteria once the relative position of the intervention's ICER compared to other interventions' ICERs is determined.

Other options, *not* using the ICER, to inform health policy makers about the efficiency of interventions are:

- the opportunity cost approach
- the cost-consequences approach.

Clearly, each of these approaches has its merits and weaknesses. The budgetary context is an important determinant for the applicability of the alternatives but also methodological issues may impede the application of an approach. Because it is unethical to ignore economic efficiency in the decision making process, a combination of approaches will probably offer the best result in terms of informing health care policy makers.

No single country included in our review used a single ICER threshold value. Either an 'acceptable' range is defined as in the UK, or no explicit ICER threshold values are used at all. In most countries, it appears that interventions with a low ICER are more likely to become accepted than interventions with a high ICER. In the presence of high ICERs, other assessment elements may become more important.

In Belgium decision making remains mainly an interactive deliberation process, although efforts are made to 'rationalise' the decision making and substantiate reimbursement requests with scientific evidence. In contrast to clinical effectiveness, cost-effectiveness is sometimes considered in the decision making process by the DRC but rarely by the TCI.

A key message we derive from this work is the importance of transparency about the criteria and social values that are weighed in a health policy making process. Therefore it is important that the information presented to health care policy makers makes sense to them, e.g. by presenting the information in disaggregated form in addition to 'composite' ICERs.

6 RECOMMENDATIONS

- Cost-effectiveness should be a criterion in the decision making process, as ignoring economic efficiency is unethical. Dossiers submitted to support policy makers should therefore always include an economic evaluation.
- Economic models should be reported in a transparent way, presenting all information used in the model in a way that allows the policy makers to verify the assumptions, view the uncertainties and weigh the importance of the assumptions and uncertainties for the decision. Transparency and control of economic models is crucial to increase their credibility.
- The results of economic evaluations should be presented in disaggregated form. This includes "unpacking" the ICER but also presenting other economically relevant outcome parameters that can be derived from the economic evaluation but that are not necessarily visible in the ICER estimate.
- Alongside the disaggregated presentation of economically important elements, also the ICER should continue to be presented, calculated following standard methodological guidelines.
- Scientific research should continue to be used in the decision making processes on the allocation of health care resources. It will allow policy makers to back up arguments in favour of or against a particular decision by scientific evidence.
- Decision makers should be more transparent in their decision making criteria and the relative importance of the different criteria in each decision.

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KCE reports

1. Effectiviteit en kosten-effectiviteit van behandelingen voor rookstop. D/2004/10.273/1.
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3. Antibioticagebruik in ziekenhuizen bij acute pyelonefritis. D/2004/10.273/5.
4. Leukoreductie. Een mogelijke maatregel in het kader van een nationaal beleid voor bloedtransfusieveiligheid. D/2004/10.273/7.
5. Het preoperatief onderzoek. D/2004/10.273/9.
6. Validatie van het rapport van de Onderzoekscommissie over de onderfinanciering van de ziekenhuizen. D/2004/10.273/11.
7. Nationale richtlijn prenatale zorg. Een basis voor een klinisch pad voor de opvolging van zwangerschappen. D/2004/10.273/13.
8. Financieringssystemen van ziekenhuisgeneesmiddelen: een beschrijvende studie van een aantal Europese landen en Canada. D/2004/10.273/15.
9. Feedback: onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport: deel 1. D/2005/10.273/01.
10. De kost van tandprothesen. D/2005/10.273/03.
11. Borstkankerscreening. D/2005/10.273/05.
12. Studie naar een alternatieve financiering van bloed en labiele bloedderivaten in de ziekenhuizen. D/2005/10.273/07.
13. Endovasculaire behandeling van Carotisstenose. D/2005/10.273/09.
14. Variaties in de ziekenhuispraktijk bij acuut myocardinfarct in België. D/2005/10.273/11.
15. Evolutie van de uitgaven voor gezondheidszorg. D/2005/10.273/13.
16. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid. Fase II : ontwikkeling van een actuarieel model en eerste schattingen. D/2005/10.273/15.
17. Evaluatie van de referentiebedragen. D/2005/10.273/17.
18. Prospectief bepalen van de honoraria van ziekenhuisartsen op basis van klinische paden en guidelines: makkelijker gezegd dan gedaan.. D/2005/10.273/19.
19. Evaluatie van forfaitaire persoonlijk bijdrage op het gebruik van spoedgevallendienst. D/2005/10.273/21.
20. HTA Moleculaire Diagnostiek in België. D/2005/10.273/23, D/2005/10.273/25.
21. HTA Stomamateriaal in België. D/2005/10.273/27.
22. HTA Positronen Emissie Tomografie in België. D/2005/10.273/29.
23. HTA De electieve endovasculaire behandeling van het abdominale aorta aneurysma (AAA). D/2005/10.273/32.
24. Het gebruik van natriuretische peptides in de diagnostische aanpak van patiënten met vermoeden van hartfalen. D/2005/10.273/34.
25. Capsule endoscopie. D/2006/10.273/01.
26. Medico–legale aspecten van klinische praktijkrichtlijnen. D2006/10.273/05.
27. De kwaliteit en de organisatie van type 2 diabeteszorg. D2006/10.273/07.
28. Voorlopige richtlijnen voor farmaco-economisch onderzoek in België. D2006/10.273/10.
29. Nationale Richtlijnen College voor Oncologie: A. algemeen kader oncologisch kwaliteitshandboek B. wetenschappelijke basis voor klinische paden voor diagnose en behandeling colorectale kanker en testiskanker. D2006/10.273/12.
30. Inventaris van databanken gezondheidszorg. D2006/10.273/14.
31. Health Technology Assessment prostate-specific-antigen (PSA) voor prostaatkankerscreening. D2006/10.273/17.
32. Feedback : onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport : deel II. D/2006/10.273/19.
33. Effecten en kosten van de vaccinatie van Belgische kinderen met geconjugeerd pneumokokkenvaccin. D/2006/10.273/21.
34. Trastuzumab bij vroegtijdige stadia van borstkanker. D/2006/10.273/23.
35. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase III)- precisering van de kostenraming. D/2006/10.273/26.
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41. Klinische kwaliteitsindicatoren. D/2006/10.273/43.
42. Studie naar praktijkverschillen bij electieve chirurgische ingrepen in België. D/2006/10.273/45.
43. Herziening bestaande praktijkrichtlijnen. D/2006/10.273/48.
44. Een procedure voor de beoordeling van nieuwe medische hulpmiddelen. D/2006/10.273/50.
45. HTA Colorectale Kankerscreening: wetenschappelijke stand van zaken en budgetimpact voor België. D/2006/10.273/53.
46. Health Technology Assessment. Polysomnografie en thuismonitoring van zuigelingen voor de preventie van wiegendood. D/2006/10.273/59.
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49. Antivirale middelen bij seizoensgriep en grieppandemie. Literatuurstudie en ontwikkeling van praktijkrichtlijnen. D/2006/10.273/65.
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52. Rapid Assessment: Cardiovasculaire Primaire Preventie in de Belgische Huisartspraktijk. D/2007/10.273/03.
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57. Organisatie en Financiering van Musculoskeletale en Neurologische Revalidatie in België. D/2007/10.273/18.
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61. Vacuümgeassisteerde Wondbehandeling: een Rapid Assessment. D/2007/10.273/30
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63. Wetenschappelijke ondersteuning van het College voor Oncologie: een nationale praktijkrichtlijn voor de aanpak van borstkanker. D/2007/10.273/35.
64. HPV Vaccinatie ter Preventie van Baarmoederhalskanker in België: Health Technology Assessment. D/2007/10.273/41.
65. Organisatie en financiering van genetische diagnostiek in België. D/2007/10.273/44.
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67. Hadrontherapie. D/2007/10.273/50.
68. Vergoeding van schade als gevolg van gezondheidszorg – Fase IV : Verdeelsleutel tussen het Fonds en de verzekeraars. D/2007/10.273/52.
69. Kwaliteit van rectale kankerzorg – Fase 1: een praktijkrichtlijn voor rectale kanker D/2007/10.273/54.
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76. Kwaliteitsbevordering in de huisartsenpraktijk in België: status quo of quo vadis? D/2008/10.273/18.
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78. Richtlijnen voor farmaco-economische evaluaties in België. D/2008/10.273/23.
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80. Evaluatie van de effecten van de maximumfactuur op de consumptie en financiële toegankelijkheid van gezondheidszorg. D/2008/10.273/35.
81. Kwaliteit van rectale kankerzorg – phase 2: ontwikkeling en test van een set van kwaliteitsindicatoren. D/2008/10.273/38
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86. Functiedifferentiatie in de verpleegkundige zorg: mogelijkheden en beperkingen. D/2008/10.273/52.
87. Het gebruik van kinesitherapie en van fysische geneeskunde en revalidatie in België. D/2008/10.273/54.
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