Farmacologische en chirurgische behandeling van obesitas

Residentiële zorg voor ernstig obese kinderen in België

KCE reports vol. 36A

Federaal Kenniscentrum voor de gezondheidszorg
Centre fédéral d'expertise des soins de santé
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VOORWOORD

Obesitas vormt voor Amerika een grotere bedreiging dan het terrorisme, stelde de Amerikaanse minister van volksgezondheid in maart 2006. Er zijn inderdaad redenen tot bezorgdheid als men vaststelt dat de prevalentie van obesitas in Westerse landen epidemische proporties begint aan te nemen. België is daarop geen uitzondering.

Men kan zich de vraag stellen of obesitas een ziekte is. Ernstige obesitas vormt, zoals roken, een risicofactor voor toegenomen morbiditeit en mortaliteit. Een risicofactor kan echter niet worden gelijkgesteld met een ziekte. Roken bijvoorbeeld wordt nergens bestempeld als een ziekte.

Dit betreft geen semantische muggenzifterij. Het etiketteren van obesitas als een ziekte geeft het een plaats binnen het medische paradigma. De rol van de medische gemeenschap is niet langer beperkt tot het behandelen van diabetes, hypertensie, dyslipedimia of andere co-morbiditeiten verbonden aan obesitas. Er is een uitbreiding vast te stellen naar het behandelen van hun oorzaak; de oorzaak wordt de ziekte en zou moeten worden behandeld, zelfs indien er geen co-morbiditeiten aanwezig zijn. Daarom is er ook geen duidelijke begrenzing betreffendei welke graad van obesitas of overgewicht nu precies een medische indicatie betreft. Deze problematiek stak meermaals de kop op in dit HTA betreffende de behandelingen van obesitas.

De culturele idealen die momenteel in de Westerse samenlevingen heersen, leiden er bovendien toe dat de vraag naar interventies die gericht zijn op gewichtsverlies indien er medische indicaties zijn (geneesmiddelen dan wel chirurgische ingrepen) steeds meer wordt gesteld door mensen met overgewicht wiens motivatie om te vermageren voortvloeit uit esthetische redenen, afgezien van het feit of er daadwerkelijk medische indicaties zijn.

Op die manier creëert de medicalisering van obesitas een gigantische afzetmarkt. Dit zet commerciële organisaties ertoe aan om te adverteren in tijdschriften zoals bijvb. Cosmopolitan UK en op die manier de voordelen van bariatrische chirurgie in België in het licht te stellen. Vermageringsgeneesmiddelen die enkel op voorschrift verkrijgbaar zijn worden intensief gepromoot naar artsen toe.

Oplossingen voor het obesitasprobleem vallen echter buiten het medische paradigma. Zij kunnen worden gevonden in een multisectoriële benadering, nl. het verbeteren van de eetgewoonten en het aanmoedigen van fysieke activiteit. Maar - ziekte of niet - obesitas leidt tot een grote lijdensweg en de medische wereld wordt hier onvermijdelijk mee geconfronteerd. De vraag stelt zich aldus hoe effectief vermageringsgeneesmiddelen, chirurgie of intensieve interventies zoals residentiële zorg voor obese kinderen zijn? Deze onderwerpen zijn het voorwerp van onderhavig rapport.

Jean-Pierre CLOSON
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EXECUTIVE SUMMARY

Uit gezondheidsenquête van 2004 blijkt dat bijna 13 % van de Belgische volwassenen klinisch obees (Body Mass Index - BMI - >=30) en 0,9 % zwaar obees is (BMI >=40). De prevalentie van obesitas is omgekeerd evenredig aan de socio-economische status (gedefinieerd in deze enquête als het niveau van opleiding). Bovendien is obesitas een risicofactor voor verschillende gezondheidsproblemen, zoals diabetes en cardiovasculaire ziekten.

De oplossing voor dit probleem op maatschappelijk niveau kan gevonden worden in een multisectoriële benadering die erop gericht is de voeding te verbeteren en fysieke activiteit aan te moedigen. Dergelijke oplossingen vallen ver buiten het medische paradigma. Een medische behandeling is echter ook een mogelijk antwoord. Hoewel een verandering van levensstijl de belangrijkste behandeling van obesitas is en blijft, worden farmacologische en chirurgische behandelingen steeds meer toegepast. Zij vormen dan ook het voorwerp van deze studie. Er werd gebruik gemaakt van de gestandaardiseerde methodologie voor health technology assessments om de klinische effectiviteit en de kosteneffectiviteit te beoordelen om zodoende conclusies en aanbevelingen te kunnen formuleren naar de Belgische beleidsmakers toe. Onderhavig rapport bevat ook een analyse van de residentiële zorg op lange termijn voor zwaar obese kinderen in België.

Farmacologische behandeling van obesitas

Enkel de geneesmiddelen verstrekt op voorschrift in België in 2005 (orlistat en sibutramine) en rimonabant – dat weldra beschikbaar zal zijn – werden in deze studie behandeld. De behandeling met elk van deze geneesmiddelen werd – gekoppeld aan een dieet – vergeleken met een placebobehandeling bij klinisch obese patiënten in grote placebo-gecontroleerde randomised controlled trials met een looptijd van tenminste 1 jaar. Praktisch al deze studies werden gesponsord door de farmaceutische industrie en hadden een hoge uitvalratio (40 à 50 %). Een behouden gewichtsverlies van 10% van het initiële gewicht is een bescheiden, maar klinisch significante doelstelling voor elke vermageringsbehandeling. Uitgaande van deze doelstelling werd voor elk vermageringsgeneesmiddel het aantal te behandelen patiënten berekend, opdat één van hen het vooropgestelde resultaat zou bereiken en/of behouden gedurende 2 jaar (één jaar voor sibutramine), rekening houdende met de voordelen van een placebobehandeling op zich (*number needed to treat* : NNT). Statistische precisie van deze effectschatting wordt vermeld wanneer deze voorhanden was (95 % betrouwbaarheidsinterval= 95 BI). Enkel orlistat is bij kinderen getest in een randomised controlled trial gedurende één jaar.

Sibutramine (Reductil®): artsen dienen 3 tot 8 obese patiënten te behandelen, opdat één van hen een gewichtsverlies van 10% zou bereiken en/of behouden na één jaar, bovenop de voordelen van placebobehandeling (NNT: 3-8). NNT is 10 op 18 maanden, maar de producent beveelt een behandeltijd van één jaar aan omwille van veiligheidsredenen (verhoging van de bloeddruk en de hartslag).

Orlistat (Xenical®): artsen dienen 9 obese patiënten te behandelen, opdat één van hen een gewichtsverlies van 10% zou bereiken en/of behouden na 2 jaar, bovenop de voordelen van placebobehandeling (NNT: 9; 95% BI 6-17). De behandeling met orlistat gedurende vier jaar brengt geen ernstige risico's met zich mee. Bij kinderen is het gemiddelde verschil tussen de placebogroep en de groep behandeld met orlistat 1 BMI punt; de klinische significantie van een dergelijk verschil is twijfelachtig.

Rimonabant (Acomplia®): artsen dienen 11 obese patiënten te behandelen, opdat één van hen een gewichtsverlies van 10% zou bereiken en/of behouden na 2 jaar, bovenop de voordelen van placebobehandeling (NNT: 11; 95% BI 7-25). Ernstige bijwerkingen zijn frequenter in de behandelde groep (verschil in samengevoegd risico: 1%, 95 % BI 0-3 %), maar dit verschil is niet statistisch significant. Het betreft hier een nieuw geneesmiddel zodat het aantal studies en de duur ervan nog beperkt is. Zodoende kunnen geen definitieve conclusies worden getrokken betreffende de veiligheid van het geneesmiddel.

Er is geen evidentie voorhanden dat deze 3 geneesmiddelen beter zijn dan effectieve levensstijl interventies voor gewichtsverlies van patiënten met diabetes of bij de preventie van diabetes bij patiënten met een gestoorde glucosetolerantie.

Voor elk van de aangehaalde geneesmiddelen is er evidentie dat gewichtsverlies niet behouden blijft nadat de behandeling wordt stopgezet.

Er zijn nog geen gegevens gepubliceerd over de effectiviteit van deze geneesmiddelen betreffende harde eindpunten, zoals cardiovasculaire aandoeningen of globale mortaliteit, wat in feite de eindpunten bij uitstek zijn van medische behandeling. Vooraleer zulke gegevens voorhanden zijn, kunnen deze geneesmiddelen niet worden beschouwd als een chronische behandeling van obesitas.

Kosteneffectiviteitsanalyses van sibutramine en orlistat zijn allen door de farmaceutische industrie gesponsord. Hun conclusies dat deze geneesmiddelen kosteneffectief zijn, kan omwille van verschillende methodologische redenen niet als geldig worden beschouwd. Eén van de redenen is dat de veronderstelling die gemaakt is over het gewichtsbehoud na het stopzetten van de behandeling te optimistisch is en tegenstrijdig met de gepubliceerde gegevens.

De markt voor deze geneesmiddelen is potentieel gigantisch (in België werden in 2004 160.000 dozen sibutramine voorgeschreven en verkocht voor een behandeling gedurende één maand). Veiligheidsoverwegingen zijn aldus van groot belang, aangezien zeldzame, ernstige nevenwerkingen – te zeldzaam om ontdekt te worden in studies van beperkte grootte en tijdsverloop – zich kunnen voordoen in een significant aantal gevallen.

Bariatrische chirurgie

Hoewel er nog geen specifieke terugbetalingscodes en voorwaarden voor terugbetaling bestaan in het Belgische sociale zekerheidssysteem wordt bariatrische chirurgie wijdverspreid toegepast en terugbetaald. Meer dan 9000 terugbetalingen met codes waarvan men kan aannemen dat ze worden gebruikt voor bariatrische chirurgie werden door het RIZIV betaald in 2004 (+ 436 % vergeleken met 1995, + 33 % vergeleken met de cijfers van 2003). Hospitalisatie voor bariatrische chirurgie (met uitzondering van heropnames voor complicaties) kostten de sociale zekerheid minstens 15 miljoen euro in 2003.

Er is voldoende evidentie dat bariatrische chirurgie effectiever is dan een niet-chirurgische behandeling voor gewichtsverlies op lange termijn en het onder controle houden van sommige co-morbiditeiten, in het bijzonder diabetes, bij ernstig obese patiënten. Bariatrische ingrepen verschillen echter in grote mate voor wat betreft de effectiviteit op lange termijn en de veiligheid, gaande van meer invasieve en meer effectieve malabsorberende procedures (de huidige standaard is de Roux – en Y gastric bypass) tot minder effectieve en invasieve restrictieve ingrepen (zoals gastric banding). Er is een gebrek aan wetenschappelijke kennis op het vlak van bariatrische chirurgie. Belangrijke vragen, zoals wat de beste procedure is, voor welke patiënten (in overeenstemming met hun BMI, leeftijd, eetgewoonten, ...) blijven onbeantwoord. Er zijn bovendien nog geen prospectieve gegevens voorhanden betreffende de impact van bariatrische chirurgie op cardiovasculaire morbiditeit en algemene mortaliteit. Bovendien biedt bariatrische chirurgie geen genezing van het onderliggende probleem, maar blijft een langdurige chirurgische en medische follow-up alsook een levenslang dieet noodzakelijk voor het welslagen van de interventie.

Laparascopic adjustable gastric banding (LAGB) is de meest frequent toegepaste procedure in België (58 % van de terugbetalingscodes voor bariatrische chirurgie in 2004). Het is ook de minst invasieve en gemakkelijker uit te voeren dan de andere procedures. Bovendien is ze ook omkeerbaar. Toch zijn de effectiviteit en veiligheid op lange termijn van LAGB slechts summier gedocumenteerd in de wetenschappelijke literatuur en maakt de kostprijs van de band (1500-2400 euro) het een duurdere interventie. Er is geen evidentie dat LAGB op lange termijn een gunstigere risico/voordeel ratio heeft dan de meer gevestigde Roux -en-Y gastric bypass.

Het principe "primum non nocere" moet in gedachten worden gehouden, zeker als men een electieve chirurgische ingreep overweegt uit te voeren op een gezond lichaamsdeel. De risico's verbonden aan bariatrische chirurgie kunnen immers groot zijn. In bevolkingsgebaseerde studies worden één jaar na gastric bypass tot 20% heropnames en 4,6% mortaliteit vermeld, en tot 24% nutritionele tekorten op langere termijn. Ook in een aantal gevalstudies wordt een hoog percentage van heringrepen na gastric banding gesignaleerd. Voor de meeste bariatrische interventies was een uitgesproken leercurve terug te vinden, met een opmerkelijk lagere mortaliteit en morbiditeit vanaf 100 uitgevoerde operaties. In België rapporteerde 75/108 (70%) ziekenhuizen die bariatrische chirurgie uitvoeren minder dan 101 verblijven voor obesitas-chirurgie voor 2003, en 59/108 (55%) minder dan 51 verblijven.

Economische analyses ondersteunen in het algemeen de kosteneffectiviteit van bariatrische chirurgie vergeleken met een conventionele behandeling, maar zijn vaak beperkt door het gebrek aan data over de effectiviteit en veiligheid op lange termijn voor sommige procedures. Bovendien is de vergelijkingsbasis ('conventionele behandeling') vaak niet goed gedefinieerd in deze studies. Risico/voordeel ratio's van bariatrische chirurgie blijken in werkelijkheid ook minder gunstig te zijn dan in gevalstudies gevoerd door gespecialiseerde teams, wiens gegevens worden gebruikt voor het in kaart brengen van de kosteneffectiviteit.

De klinische criteria die worden teruggevonden in de meeste richtlijnen die bariatrische chirurgie aanbevelen – BMI >= 40 of BMI >= 35 + co-morbiditeiten – zijn tot op zekere hoogte arbitrair. Er is aangetoond dat bariatische chirurgie een effect heeft op vele co-morbiditeiten (afhankelijk van het type interventie; puur restrictieve interventies zoals LAGB zijn meestal minder effectief). Toch kunnen enkel ernstige co-morbiditeiten de risico's en de onzekerheden verbonden aan bariatrische chirurgie rechtvaardigen.

Bariatrische chirurgie bij patiënten onder de 18 jaar doet ethische vragen rijzen, is uiterst experimenteel en zou enkel in uitzonderlijke situaties mogen worden uitgevoerd door ervaren teams.

Er zijn geen gegevens voorhanden die het gerucht bevestigen of ontkennen dat bariatrische chirurgie in België vaak wordt uitgevoerd bij vrouwen omwille van cosmetische redenen eerder dan omwille van medische indicaties (vooral het minder invasieve gastric banding), maar het blijft een bestaand risico. Het is aan de Belgische beleidsmakers om criteria te formuleren voor de terugbetaling van bariatrische chirurgie teneinde dergelijke misbruiken tegen te gaan.

Residentiële zorg voor obese kinderen in België

Er zijn drie centra in België (het Zeepreventorium in De Haan, Clairs-Vallons in Ottignies, Porignot in Biez) die residentiële zorg bieden aan chronisch zieke kinderen. De totale capaciteit bedraagt 296 bedden, waarvan 196 (66 %) bestemd zijn voor zwaar obese kinderen van schoolleeftijd. Het gezamenlijke jaarlijkse budget van de drie centra in 2006 is 17,2 miljoen euro (meer dan 58.000 euro/bed/jaar). De gemiddelde verblijfsduur voor obese kinderen is één schooljaar.

Een precieze beschrijving van de populatie die wordt opgenomen in deze centra (graad van obesitas, comorbiditeiten, ...), van de interventies en van de uitkomsten bij vertrek is niet mogelijk omdat er geen geanalyseerde gestandaardiseerde gegevens voorhanden zijn (enkel Clairs-Vallons beschikte over één enkel rapport). Bij een niet-representatieve steekproef van 47 patiënten na ontslag uit het Zeepreventorium, was de gemiddelde aangepaste BMI (geobserveerde/ideale BMI of percentage surplus BMI) 175 % bij toelating, 121% bij vertrek en 155 % anderhalf jaar na vertrek.

Er is nood aan een klinische follow-up van patiënten die dicht bij hun thuis wordt georganiseerd en er is een gebrek aan een gestructureerd netwerk van eerste lijnszorg die kan doorverwijzen.

In het huidige financieringssysteem is de financiële toegankelijkheid van deze centra geen probleem, aangezien de kost van een verblijf van 10 maanden voor de patiënten bijna nihil is. In België is de ambulante zorg voor obesitas duurder dan de residentiële zorg.

Er zijn geen gelijkaardige bevindingen teruggevonden in de wetenschappelijke literatuur. Deze intensieve en dure benadering roept een aantal vragen op: (1) Wat is de effectiviteit op lange termijn? Wordt het gewichtsverlies behouden na ontslag? Wegen de potentiële voordelen van het weghalen van de kinderen bij hun familie en hun omgeving voor een dergelijke lange periode (intensieve zorgen, het drastisch breken met slechte gewoonten) op tegen de potentiële nadelen? (2) Levert een verblijf van 10 maanden een betere uitkomst op lange termijn dan een korter verblijf? (3) Hoe zou men residentiële zorg kunnen vergelijken met ambulante zorg, gesteld dat de financiële barrières van de ambulante zorg zouden worden opgeheven?

Legale aspecten van interventies die gericht zijn op gewichtsverlies

Vermageringsproducten en reclame: De wetgeving omtrent geneesmiddelen bevat strenge restricties voor wat betreft reclame. Ondanks de nieuwe ruimere definitie van het begrip geneesmiddel blijft het nochtans mogelijk voor allerlei vermageringsprodukten om zich te onttrekken aan de toepassing van de definitie en aldus ook de strengere reglementering betreffende reclame.

Bariatrische chirurgie: Chirurgen hebben de wettelijke verplichting de patiënt te informeren voor de operatie en patiënten hebben het recht om informatie te krijgen over de operatie vooraleer ze hun toestemming geven. Een schriftelijke toestemming is niet wettelijk verplicht, maar verschillende redenen (zoals o.a. de levenslange consequenties van de interventie) maken dat dit in het geval van bariatrische chirurgie wel aan te raden is.

De wettelijke verplichting voor chirurgen om kwaliteitsvolle nazorg te garanderen is ook van toepassing in het geval buitenlandse patiënten zich in België laten opereren. Er is echter geen precieze definitie van wat kwaliteitsvolle nazorg precies inhoudt in het geval van bariatrische chirurgie. Bovendien zijn de regels die bepalen welke wetgeving van toepassing is en welke jurisdictie er competent is in het geval van medische aansprakelijkheid onduidelijk en zijn ze sterk afhankelijk van de individuele omstandigheden. Dit dient te worden gezien in het kader van de toenemende grensoverschrijdende gezondheidszorg binnen de Europese Unie. Aanbevelingen betreffende gezondheidszorgcontracten tussen instellingen (bvb. tussen een Nederlandse verzekeraar en een Belgisch ziekenhuis) bestaan op Europees niveau, maar er is niets gereguleerd voor interventies tussen patiënten en commerciële gezondheidszorginstellingen. De toepassing van gelijkaardige aanbevelingen dient ook hier te worden aangemoedigd.

Suggesties voor verder onderzoek

In België lijkt de zorg voor obese patiënten geconcentreerd te zijn in hoog-gespecialiseerde multidisciplinaire teams in secundaire of tertiaire settings. Geografische en financiële toegankelijkheid zijn een probleem. Een analyse van de organisatie van gezondheidszorginstellingen en de financiering voor de behandeling van obesitas lag buiten het opzet van deze studie. Desalniettemin is het nodig om de mogelijkheden voor een benadering vanuit de eerste lijn te onderzoeken, om de rol van de verschillende betrokken gezondheidszorgverstrekkers na te gaan, om de rol van patiëntengroeperingen nader te bekijken en om een alternatief financieringssysteem voor te stellen.

Beleidsaanbevelingen

Farmacologische behandeling van obesitas

- De beschikbare evidentie is niet doorslaggevend genoeg om te beslissen dat sibutramine, orlistat of rimonabant zou moeten worden terugbetaald door de Sociale Zekerheid
- Sibutramine, orlistat en rimonabant zijn vermageringsgeneesmiddelen. Ze zouden niet mogen worden voorgesteld als een chronische behandeling voor obesitas.
- Artsen die deze vermageringsgeneesmiddelen voorschrijven dienen hun patiënten erover te informeren dat gewichtsverlies gewoonlijk niet behouden blijft nadat de behandeling is stopgezet.

Bariatrische chirurgie

Bariatrische chirurgie zou moeten worden terugbetaald door de Sociale Zekerheid onder bepaalde voorwaarden.

- Terugbetaling moet worden beperkt tot patiënten met een BMI >= 40 of een BMI >= 35 met gedocumenteerde, ernstige co-morbiditeiten (diabetes)
- De beslissing om te opereren moet genomen worden door een multidisciplinair team
- Het beoefenen van bariatrische chirurgie moet strikt worden beperkt tot "centres of excellence". De minimum criteria zijn:
    - Een follow-up op lange termijn met een gestandaardiseerd systeem voor het rapporteren van de resultaten. Dit zou moeten worden gerealiseerd via een verplicht register betaald met publieke middelen.
    - Een minimum activiteitsgraad rekening houdende met de bestaande studies omtrent de leercurve bij bariatrische chirurgie. Criteria zoals gehanteerd in andere landen kunnen daarbij als nuttige voorbeelden dienen.
    - Beschikbaarheid van georganiseerde en gesuperviseerde ondersteuningsgroepen
- Bariatrische chirurgie bij patiënten jonger dan 18 jaar moet worden beperkt tot één of (om redenen van geografische spreiding) maximum twee ziekenhuizen in België
- Belgische op consensus gebaseerde praktijkrichtlijnen voor bariatrische chirurgie dienen te worden uitgewerkt (aanbevelingen voor peri-operatieve zorg en klinische paden, precieze indicaties voor elk type van bariatrische interventie, aanbevelingen voor de follow-up na bariatrische chirurgie). Hierbij dienen alle betrokken zorgverleners te worden betrokken, niet alleen de chirurgen.
- De erelonen van de chirurgen dienen evenredig te zijn aan de moeilijkheidsgraad en de operatietijd van elk type van bariatrische chirurgie

Residentiële zorg voor obese kinderen

- De effectiviteit op lange termijn van residentiële zorg voor zwaar obese kinderen moet worden onderzocht via een prospectieve studie in de 3 centra. Randomisatie van patiënten voor een lange (10 maanden) of een korte behandelingsperiode (bijvb. 3 maanden) moet worden overwogen.
- Ondertussen zouden de RIZIV conventies voor residentiële zorg een verplichting moeten voorzien om een gestandaardiseerd jaarlijks rapport op te stellen. De inhoud ervan zou moeten worden vastgesteld door de centra zelf samen met experten op het vlak van obesitas.

- Een paar pilootcentra die voorzien in ambulante zorg voor zwaar obese kinderen zouden moeten worden geselecteerd en gefinancierd via een conventie, met de verplichting dat zij deel uitmaken van een onderzoeksprotocol teneinde hun effectiviteit op lange termijn te evalueren.
- Deze studies dienen te gebeuren onder de verantwoordelijkheid van een wetenschappelijk team met doorgedreven epidemiologische expertise.
- De financiering dient binnen de vijf jaar te worden geherevalueerd op basis van de resultaten van de studies.

Legale aspecten

- Specifieke wetgeving met betrekking tot reclame voor vermageringsproducten (zoals het verbod op voor – en na foto's en getuigenissen van patiënten) en meer proactieve controle van reclame is nodig.
- Voor het uitvoeren van bariatrische chirurgie dient geschreven toestemming te worden bekomen van de patiënt. De inhoud van de informatie moet worden gedefinieerd door professionele organisaties in België.
- Gezondheidszorgcontracten tussen Belgische en buitenlandse instellingen zouden de Europese aanbevelingen moeten volgen.

Verder onderzoek

- Verder onderzoek betreffende de organisatie en de financiering van gezondheidszorginstellingen voor de behandeling van obesitas, voornamelijk op het niveau van de primaire zorg, is nodig

Scientific summary

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GLOSSARY OF ACRONYMS

ABMI	Adjusted body Mass Index
AETMIS	Agence d'évaluation des technologies et des modes d'intervention en santé (Canada)
AHRQ	Agency for Health Research and Quality (USA)
AHT	Arterial hypertension
ANAES	Agence Nationale d'Accréditation et d'Evaluation en Santé (France)
APR-DRG	All Patient Refined Diagnosis Related Group
ATG	Adherence to guideline
ATP	Adult Treatment Panel
BAROS	Bariatric Analyses and Reporting System
BCBS	Blue Cross Blue Shield (USA)
BMI	Body Mass Index
BNI	British Nursing index
BPD	Bilio-Pancreatic Diversion
CBA	Cost-Benefit Analysis
CEA	Cost-efficacy Analysis
CHD	Coronary Heart Disease
CIES	Centre d'Etudes Interdisciplinaires en Economie de la Santé
CINHAL	Cumulative Index to Nursing & Allied Health
CT	Conventional Treatment
CUA	Cost-utility Analysis
DALY	Disability-Adjusted Life Years
DARE	Database of Abstracts of Reviews of Effects
DRG	Diagnosis Related Group
DS	Duodenal Switch
EBW	Excess Body Weight
EMEA	European agency for the evaluation of medicinal products
EU	European Union
Eur25	Euro for the 25 member states of the European Union
EWL	Excess weight loss
FTE	Full time equivalent
FU	Follow-up
GB	Gastric Bypass
GDP	Gross Domestic Product
GERD	Gastro-oesophageal reflux disease
GHD	General hospital Dendermonde (Belgium)
HBG	Horizontal Banded Gastroplasty
HDL	High-density lipoprotein
HIS	Health Interview Survey
HTA	Health Technology Assessment
ICD-9-CM	International Classification of Diseases, 9th revision, Clinical Modification
IDF	International Diabetes Foundation
INAHTA	International Network of Agencies for HTA
INAMI	Institut National d'Assurance Maladie Invalidité
INSERM	Institut National de la Santé et de la Recherche Médicale (France)
IOTF	International Obesity Task Force
LAGB	Laparocopic Adjustable Gastric Banding
LL-RYGB	Long-limb RYGB
LL-RYGB	Long Limb Roux-en-Y-Gastric Banding
LOCF	Last observation carried forward
LOS	Length of stay
LSA	Lifestyle advice
MAS	Medical Advisory Secretariat

MBDS	Medical basic data set
MDC	Major Diagnosis Category
MSAC	Medical Services Advisory committee (Australia)
NCEP	National Cholesterol Education Programme
NCHS	National Center for Health Statistics (USA)
NICE	National Institute for Clinical Excellence (United Kingdom)
NIH	National Institute of Health (USA)
NNT	Number needed to treat
PPP	Purchasing Power Parity
PSBH	Panel Studie Belgishe Huishouden
QALY	Quality-Adjusted Life Years
QoL	Quality of life
RCT	Randomised clinical trial
RD	Risk difference
RIZIV	Rijksinstituut voor Ziekte- en Invaliditeitsverzekerin (Belgium)
RYGB	Roux-en-Y-Gastric Banding
SCOUT	Sibutramine Cardiovascular Outcome Trial
SD	Standard Deviation
SIGN	Scottish Intercollegiate Guidelines Network
SOS	Swedish Obese Subjects
TG	Triglyceride
UCL	Université catholique de Louvain (Belgium)
UK	United Kingdom
US	United States of America
UZG	Universitair Ziekenhuis Gent (Belgium)
VBG	Vertical Banded Gastroplasty (sleeve gastrectomy)
VLCD	Very low calorie diet
WHO	World Health Organisation
WL	Weight loss
WLP	Weight loss programme
WM	Weight maintenance
WMD	Weighted Mean Difference
WMP	Weight management program

Part 1: Introduction

1 BACKGROUND

1.1 EPIDEMIOLOGY OF OBESITY

1.1.1 Definition

1.1.1.1 Adults

Obesity can be defined simply as the disease in which excess body fat has accumulated to such an extent that health can be adversely affected. However, the amount of excess fat, its distribution within the body, and the associated health consequences vary considerably between obese individuals[1].

The prevalence of overweight and obesity is commonly assessed by using body mass index (BMI), defined as the weight in kilograms divided by the square of the height in metres (kg/m2). BMI provides the most useful, albeit crude, population-level measure of obesity. The classification, proposed by WHO (see Table 1), relates BMI to the risk of disease. These markers provide common benchmarks for assessment, but the risks of disease in all populations can increase progressively from lower BMI levels[1].

Table 1. Classification of adults according to BMI[a]. From WHO[1]

Classification	BMI	Risk of comorbidities
Underweight	< 18.50	Low (but risk of other clinical problems increased)
Normal range	18.50-24.99	Average
Overweight	>= 25.00	
Pre-obese	25.00 – 29.99	Increased
Obese class 1	30.00 – 34.99	Moderate
Obese class 2	35.00 – 39.99	Severe
Obese class 3	>= 40.00	Very Severe

[a] These BMI values are age-independent and the same for both sexes. However, BMI may not correspond to the same degree of fatness in different populations due, in part, to differences in body pro,)n 2.3.2). The table shows a simplistic relationship between BMI and the risk of comorbidity, which can be affected by a range of factors, including the nature of the diet, ethnic group and activity level. The risks associated with increasing BMI are continuous and graded and begin at a BMI above 25. The interpretation of BMI gradings in relation to risk may differ for different populations. Both BMI and a measure of fat distribution (waist circumference or waist : hip ratio (WHR)) are important in calculating the risk of obesity comorbidities.

Very severe obesity is also called 'morbid obesity'.

Obesity has reached epidemic proportions globally. While genes are important in determining a person's susceptibility to weight gain, energy balance is determined by calorie intake and physical activity. Thus societal changes and worldwide nutrition transition are driving the obesity epidemic. Diets high in complex carbohydrates have been replaced by more varied diets with a higher proportion of fats, saturated fats and sugars. At the same time, moves towards less physical activity can be attributed to large shifts towards less physically demanding work, the increasing use of automated transport, technology in the home, and more passive leisure pursuits[2].

1.1.1.2 Children

For children, BMI varies from birth to adulthood, and is different between boys and girls. The interpretation of BMI values in children and young people depends on BMI population reference values, using cut-off points in the BMI distribution. There is no reference obesity values in Belgium. Therefore it is necessary to refer to the international definitions.

The American Academy of Pediatrics recommends 95th centile of BMI for age and sex as cut-off points to identify obesity. The National Center for Health Statistics (NCHS) displays BMI percentile curves by age and sex[3].

The Scottish Intercollegiate Guidelines Network (SIGN) recommends, for clinical use, the 98th centile of the UK 1990 reference chart for age and sex as BMI cut-off points to define children obesity. For epidemiological purposes, the 95th centile should be used[4].

Cut-off points for BMI have recently been proposed at international level by the International Obesity Task Force (IOTF)[5]. For wider international use, the reference population was obtained by averaging different survey results from several countries (Brazil, Great Britain, Hong Kong, the Netherlands, Singapore and the United States). This last definition was used in the Health Interview Survey and in the National Food Consumption Survey made in Belgium.

1.1.2 Morbidity and mortality associated with obesity

1.1.2.1 Adults

Overweight and obesity lead to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance.

The non-fatal, but debilitating health problems associated with obesity include respiratory difficulties, chronic musculoskeletal problems, skin problems and infertility. Chronic overweight and obesity contribute significantly to osteoarthritis, a major cause of disability in adults[2].

The more life-threatening problems fall into four main areas: cardio-vascular diseases; conditions associated with insulin resistance such as type 2 diabetes; certain types of cancers, especially the hormonally related and large-bowel cancers; and gallbladder disease. The likelihood of developing type 2 diabetes and hypertension rises steeply with increasing body fatness. Raised BMI also increases the risks of cancer of the breast, colon, prostrate, endometrium, kidney and gallbladder[2].

Various methodological issues arise when trying to estimate mortality associated with obesity, like the need to adjust for various confounders, to account for variation by age in the relation of body weight to mortality, and to account for secular trends. Several studies on obesity-associated mortality have been challenged on methodological grounds[6].

In a large, population-based study recently published, only higher levels of obesity (BMI > 35) were significantly associated with an increased mortality risk[6]. An analysis of secular trends in the United States has shown that cardiovascular risk factors have declined at all BMI levels in the US population, but, except for diabetes, the decline appears to be greater at higher BMI levels[7]. These findings are consistent with the increases in life expectancy in the United States and with the declining mortality rates from ischemic heart disease [6] – despite rising numbers of obese people.

The net result of these phenomena may be a population that is, paradoxically, 'more obese, diabetic, arthritic, disabled, and medicated, but with lower overall cardiovascular risk'[7]. Obesity appears to be more strongly related to morbidity, disability, and quality of life, than to mortality[8]. However some argue that a redefinition of obesity based on waist-to-hip ratio instead of BMI would increase the estimate of myocardial infarction attributable to obesity in most ethnic groups[9].

Metabolic syndrome: Abdominal obesity is frequently associated with a cluster of risk factors for coronary heart disease and type 2 diabetes. This cluster is named metabolic syndrome and its components are insulin resistance (with or without glucose intolerance), atherogenic dyslipidemia (raised triglycerides, low HDL-cholesterol and presence of small LDL particles), high blood pressure, and prothrombotic and proinflammatory states[10, 11]. Several definitions of the metabolic

syndrome have been proposed (NCEP-ATPIII, IDF), but all include insulinresistance, hypertension, dyslipidemia and central obesity. According to these definitions, diagnosis of metabolic syndrome is established when three or more of these risk factors are present. Although recognition of the metabolic syndrome serves undoublty to focus attention to patients at particularly high risk of heart disease and diabetes, controversy still exists about the common underlying pathological process [12-14]. Furthermore, it still unclear whether the combination of these risk factors confers a risk that is different from the sum of the each. Finally, in the absence of specific treatment, the treatment of the metabolic syndrome does not differ from the treatment of its individual components.

Table 2. NCEP-ATPIII* definition of the Metabolic Syndrome (IDF definition)**

RISK FACTOR	DEFINING LEVEL
Abdominal obesity (waist circumference) men women	 > 102 (94)* cm > 88 (80)* cm
Triglycerides	≥ 150 mg/dl
HDL-Cholesterol men women	 < 40 mg/dl < 50 mg/dl
Blood pressure	≥ 130/85 mmHg
Fasting glycemia	≥ 110 (100)* mg/dl

*National Cholesterol Education Programme-Adult Treatment Panel
** International Diabetes Federation

1.1.2.2 Children

What follows is a summary of the SIGN review[4], where detailed references and assessment of evidence levels can be found.

There is good evidence of an association between childhood obesity and **cardiovascular and other risk factors**. The main cardiovascular consequences of childhood obesity that occur during childhood are sub-clinical coronary artery disease and atherosclerosis. Several cardiovascular risk factors have been shown to be associated with childhood obesity: increased blood pressure, adverse lipid profiles, adverse changes in left ventricular mass, hyperinsulinaemia. Cardiovascular risk factors in children and adolescents are also related to central adiposity and a family history of coronary artery disease. Childhood obesity is also associated with significant 'clustering' of cardiovascular risk factors (where clustering is defined as the strong tendency for obese children to have more than one cardiovascular risk factor).

Obese children are more likely to show evidence of **psychological distress** than are non-obese children and the effect is greater for girls than boys. Obesity in childhood and adolescence is also associated with poor self-esteem, being perceived as unattractive, depression, disordered eating, bulimia and body dissatisfaction. Psychosocial distress and psychiatric disorders in children may be more associated with parental psychological/psychiatric problems than the child's own BMI, age or sex.

Obesity in childhood is associated with a number of **potential comorbidities**: the risk of developing asthma and the exacerbation of pre-existing asthma, abnormalities of foot structure and function, and increased risk of type 1 diabetes.

1.1.3 Obesity in Belgium: available data

Data of prevalence available in Belgium come mainly from the Health Interview Survey (HIS) organised by the Scientific Institute of Public Health every three years (1997-2001-2004)[15-17]. Information on health is systematically collected by interviews (without examination) of a population representative sample.

The BMI is based on self-reported weight and height. It could lead to an underestimation of the weight and an overestimation of the size and finally to a BMI underestimation.

Some other results are extracted from the National Food Consumption Survey and they present the proportion of some diseases linked to obesity[18].

Other surveys on obesity exist like the Panel Studie Belgishe Huishouden (PSBH, universiteit Antwerpen)[19], the Belstress Study (UG, ULB)[20]. The results of these studies are not presented in this report as the first study does not present precise statistics but only graphics and the second one is not representative of the Belgian population.

1.1.3.1 Obesity of the adults

Table 3 summarises data of prevalence of overweight and obesity of the adults (>18 years) coming from the Health Interview Survey (IPH). The prevalence of obesity of the adults increases slightly over the period 1997-2004. The rates, standardised in function of demographic characteristics (age and sex), increases very slightly between 1997 and 2004. Less than one percent of the population is concerned by morbid obesity. The prevalence of overweight increased between 1997 and 2001 and slightly decreased between 2001 and 2004. In 2004, about 44% of Belgians present an excess of weight.

Table 3. Prevalence of overweight and obesity (%)– Health Interview Survey – Adults (18+)– Trends 1997 to 2004

		1997	2001	2004
Nb interview		8071	9391	10318
BMI categories				
Overweight	[25 ; 30[	30.5	32.4	31.4
Obesity grade 1	[30 ; 35[	8.6	9.5	9.6
Obesity grade 2	[35 ; 40[	1.7	2.1	2.2
Morbid obesity	>= 40	0.5	0.6	0.9
Total of obesity (BMI >= 30)		10.8	12.2	12.7

Table 4 shows the distribution by age and education level.

Table 4. Prevalence BMI>=30 (%) according to sex, age and education level – Adults (18+)– Health Interview Survey 2004

	men	women	total
Total	11.9	13.3	12.7
Age categories			
18-24	1.0	5.0	2.9
25-34	4.9	8.6	6.9
35-44	13.2	9.9	11.6
45-54	14.2	15.0	14.5
55-64	21.6	20.8	21.2
65-74	15.0	21.7	18.9
>= 75	11.9	13.0	12.4
Education level			
Primary or no degree	14.2	23.1	19.1
Secondary inferior	20.0	17.1	18.5
Secondary superior	11.9	13.5	12.7
Superior education	7.8	6.9	7.3

The National Food Consumption Survey reveals that in case of obesity the proportion of cardiac disease is multiplied by 1.5, the proportion of hypertension by 4, the proportion of hypercholesterolemia by 2 and the proportion of diabetes by 7.5[18].

1.1.3.2 Obesity in childhood

Table 5 shows the prevalence of obesity among young people (2-17 years) [15-17]. The results concerning children less then 6 years old must be interpreted with caution as the number of cases is low. The increase of obesity seems more important for boys. There is less obesity among children when the parents have a higher level of education.

Table 5 . Prevalence of obesity (IOTF reference) (%)– Childhood (2-17 years) – Health Interview survey

	1997	2001	2004
N	1604	1852	1647
Total	4.7	5.0	5.4
Age categories			
2-5 years	4.8	8.8	10.6
6-12 years	6.7	6.5	5.6
13-17 years	2.3	1.9	3.3
Sex			
Boys	4.5	5.1	7.1
Girls	4.9	4.9	3.7
Highest educational level within the household			
Primary or no degree	19.1	10.3	10.4
Secondary inferior	4.4	6.5	10.2
Secondary superior	3.9	5.5	3.8
Superior education	2.6	3.2	4.7

1.2 PREVENTION OF OBESITY

Both sides of the energy balance equation must be tackled, so that people can "move a little more, eat a little less". The necessary changes are small: 90% of obesity in the United States could be abolished by walking an extra 2000 steps a day and reducing intake by 0.418MJ per day. These changes are well within the range of day to day variability in activity and diet and are potentially achievable and sustainable by large numbers people [21].

Faced with a 'global epidemic', the World Health Organisation (WHO) has proposed a 'Global strategy on diet, physical activity and health' [22]. This strategy emphasises a truly multisectoral approach to improve diet and encourage physical activity. We summarize here some of the main issues.

Education, communication and public awareness: a basis for action is provided by public knowledge and understanding of the relationship between diet, physical activity and health, of energy intake and output, and healthy choice of food items.

On the 'diet' side, this strategy recommends regulating food advertising, and food labelling. Indeed food advertising affects food choices and influences dietary habits; and consumers require clear information on the content of food items in order to make healthy choices. Food, agricultural, and fiscal policies should promote food products consistent with a healthy diet, for instance including measures to encourage the reduction of the salt content of processed foods, the use of hydrogenated oils, and the sugar content of beverages and snacks.

On the physical activity side: public policies and legislation have an impact on opportunities for physical activity, such as those concerning transport, urban planning, education, labour, social inclusion, and health-care funding related to physical activity. For instance transport policies should make available accessible and safe alternatives to motorised transport. An enabling environment with supportive infrastructure should be set up to increase access to, and use of, suitable facilities.

School policies and programmes should support the adoption of healthy diets and physical activity.

Health-care providers, especially for primary health care, but also other services (such as social services) can play an important part in prevention. Routine enquiries as to key dietary habits and physical activity, combined with simple information and skill-building to change behaviour, taking a life-course approach, can reach a large part of the population and be a cost-effective intervention.

1.3 TREATMENT OF OBESITY

The main scope of this report is the pharmacotherapy and surgical therapy of obesity. However, in order to fully understand the problem of obesity and its treatment, an overview of the literature about non drug and non surgical treatment of obesity is necessary. To evaluate the effectiveness of this treatment, it is important to establish criteria for successful treatment. Defining a clinically useful outcome might be individualized for each patient and therefore could involve a range of endpoints, such as amount of weight loss, amount of sustained weight loss, improvement in obesity-related morbidity, and improvement in quality of life. These endpoints are discussed in the first part of this chapter. Since the relation between weight loss and long term mortality is controversial, a separate part is devoted to this problem at the end of this chapter.

This rapid review of the literature was carried out by a computerized search of Medline and the Cochrane library, using "obesity", "obesity treatment", "mortality", and "weight loss" as keywords. The search was supplemented by a hand search of selected journals and consultation with experts in obesity research. Only relevant studies published between 2000 and 2006 were included. However, some pertinent studies published before 2000 were also included. Where available, only systematic reviews, randomized controlled trials, or high-quality observational studies were included.

1.3.1 Clinical endpoints for obesity treatment

1.3.1.1 Weight loss

Although body fat loss represents an obvious endpoint for obesity treatment, the available techniques to measure it, such as bioelectrical impedance, dual-energy x-ray absorptiometry, and total body water immersion, are impractical to use routinely. Therefore, surrogate markers such as decrease in body weight or body mass index (BMI) – which has a stronger correlation with the body fat mass than body weight alone – are more commonly used in clinical practice [23]. A meta-analysis showed that this correlation between percent body fat and BMI is different among different ethnic groups [24]. As a consequence, the definitions of BMI cut-off points for obesity need to be population-specific.

A reasonable and clinically significant goal for many patients is to lose 10% of body weight in the first 6 months of treatment [25]. The rationale for this initial goal – which in fact is based on international consensus – is that even moderate weight loss can significantly decrease the severity of obesity-associated risk factors [26-28].

As an alternative to weight loss, percentage of excess weight loss is a frequently used outcome measure, in particular to assess the effectiveness of bariatric surgical procedures [29]. This is calculated with the formula: percentage of excess weight loss = (weight loss/excess weight) x 100, where excess weight = body weight – ideal weight. However, no evidence was found on the correlation between excess weight and body fat mass.

1.3.1.2 Waist circumference

Observational studies demonstrated that the waist-to-hip ratio and waist circumference – both surrogate markers of the abdominal fat mass – are better predictors than BMI of obesity-related metabolic disorders [30, 31]and cardiovascular diseases [9]. It is an international consensus that men with a waist circumference greater than 102 cm and women with a waist circumference greater than 88 cm are at increased risk for metabolic diseases [25].

1.3.1.3 Weight maintenance or rate of weight regain

Once the goal of weight loss has been achieved, maintenance of this body weight becomes a major challenge. For this reason, outcome may be assessed in terms of percentage of patients maintaining 80% of their initial weight loss [32]. A decrease of 10% of body weight sustained for more than 1 year is also sometimes considered as a successful weight loss [33]. However, these outcomes are not based on solid evidence, and therefore rather arbitrary. Above this, some patients may not be able to achieve sufficient weight reduction, and prevention of weight gain then becomes a major objective.

1.3.1.4 Obesity-related morbidity

Obesity is a public health concern because of its associated comorbidities, such as diabetes, hypertension, dyslipidemia, and sleep apnea syndrome. The benefit of obesity treatment can be assessed by evaluating the improvement (i.e. decreased incidence, improved metabolic control or recovery) of these medical complications [27, 34, 33]. Because most of the obesity-related complications are cardiovascular risk factors, decrease in cardiovascular events, such as myocardial infarction or revascularisation procedures, can be relevant clinical endpoints [35].

1.3.1.5 Health-related quality of life

Health–related quality of life can be dramatically impaired depending on comorbidities, degree of obesity and disturbances in eating behaviour [36]. Standardized health-related quality of life measures, such as the SF-36 questionnaire do exist.

1.3.1.6 Conclusion

A variety of clinical endpoints can be used to measure the effects of weight loss therapy (Table 6). However, few of these endpoints are based on solid evidence.

Table 6 . Overview of clinical endpoints of obesity treatment.

End Points	Expression	Units
Weight loss	Weight loss	% (kg)
	Proportion of patients with weight loss > 10%	%
	Decrease in body mass index	kg/m2
	Percentage of excess weight loss	%
Decrease in visceral adiposity	Waist circumference	cm
Weight maintenance	Proportion of patients who have maintained 80% of the weight loss	%
	Proportion of the weight loss maintained 1 year after nadir of weight loss	%
Decrease in morbidity	Diabetes mellitus	HbA1c, incidence
	Hypertension	mmHg, incidence
	Dyslipidemia: raised triglycerides, low HDL-cholesterol	mg/dl, incidence
Health-related quality of life	SF-36 questionnaire	

1.3.2 Non pharmacological and non surgical treatment

The non pharmacological and non surgical treatment of obesity typically encompasses three cornerstones, frequently grouped by the term 'lifestyle modification': diet, exercise, and behavioural therapy. These three interventions ask for an active participation of the obese patient, and often need actions to promote compliance.

1.3.2.1 Lifestyle interventions

Dieting approach

A diet can be constituted of a calorie restriction, ranging from a moderate restriction to starvation. Above this, a diet can be characterised by a modification of its content or macronutrient composition (e.g. low-fat, low-carbohydrate, high-fat). Both are different approaches with different outcomes, and thus need a separate discussion.

Degree of caloric restriction

The classification into (moderately) low-calorie and very-low-calorie diets is rather arbitrary and heterogeneous across studies [37-39]. However, most authors agree on the fact that a diet below 800 kcal/24h is a very-low-calorie diet. For pragmatic reasons, only low-calorie and very-low-calorie diets are discussed.

(Moderately) low-calorie diets

A 500 to 1000 kcal/day deficit is needed to achieve a 0.5-1.0 kg weight loss per week [40]. Common energy levels of (moderately) low-calorie diets range from 1200 to 1800 kcal. Calories can be reduced by changing energy density and/or food portions.

The National Institutes of Health reviewed 34 randomized controlled trials to assess the efficacy of low calorie diets for lowering body weight. It was concluded that low-calorie diets can lower body weight by an average of 8% during a period of 3-12 months[40]. Ayyad et al. identified a 18% success rate – defined as maintenance of all weight (100%) initially lost (or further weight reduction) or maintenance of at least 9 to 11 kg of the initial weight loss – of conventional diet (800 – 1800 kcal/24h).

Low calorie diets that use a meal replacement strategy (1 or 2 meals substituted with a commercial fortified product containing about 200 kcal, e.g. Modifast) induced greater weight loss at 1 year (7-8%) compared with the traditional low calorie-diets without meal replacements (3-7%) [41].

Very-low-calorie diets

Clinic- or hospital-based programs sometimes use very-low calorie-diets (VLCD) requiring close medical supervision. Few randomized controlled trials compared VLCDs to control treatment [38]. The one RCT identified by Avenell et al. produced a weighted mean difference weight change of -13.4 kg at 12 months compared to control [38]. However, VLCD did not appear superior compared to conventional diet [37]. Nevertheless, in a systematic review of US studies on structured weight-loss programs, VLCDs produced significantly more weight-loss maintenance than conventional diets [42]. These findings are in contrast to those reported by Wing et al., who found a regain of 35-50% of the weight loss in the year following treatment discontinuation in patients treated with VLCDs [43]. However, caution is warranted interpreting these results, since they are of pure observational nature.

Content of diet

Numerous popular diets have been released, each with their specific macronutrient composition. The rationale of these diets is that this macronutrient composition plays a major role in inducing weight loss irrespective of the calories content. Only the low- carbohydrate and low-fat diets are discussed below since they are the most frequently studied.

Low-carbohydrate diets

Low-carbohydrate diets are characterized by a large proportion of energy intake from protein and fat. The Atkins diet – a commercial and very popular low-carbohydrate diet – was found not to be superior compared to well-balanced low-fat hypocaloric diets [44]. However, a very recent meta-analysis of randomized controlled trials found higher weight loss with low-carbohydrate diets than with low-fat diets after 6 months (weighted mean difference -3.3 kg; 95% CI -5.3 to -1.4 kg) [45]. This weight loss was accompanied by a potential unfavourable change in lipid profile.

Low-fat diets

A recent Cochrane review showed that low-fat diets are no better than calorie-restricted diets in achieving long term weight loss in obese and overweight persons [46]. However, an earlier meta-

analysis of ad libitum low-fat diets without intentional restriction of energy intake showed an increased weight loss of about 3kg compared to control intervention [47]. The same authors recently showed that a hypoenergetic low-fat diet produced similar mean weight loss compared to a hypoenergetic high-fat diet [48]. However, the low-fat diet resulted in more subjects losing >10% of initial body weight and had fewer dropouts. Similarly, a low–fat eating pattern emphasizing fruits, vegetables, and grains prevented further weight gain in postmenopausal women, according to the Women's Health Initiative Dietary Modification Trial [35]. Finally, according to a recent review of weight-reducing diets, low fat diets produced significant weight losses up to 36 months, and improved obesity-related comorbidities at 12 months [38].

Exercise

In a recent systematic review, diet associated with exercise produced a 20% greater initial weight loss than diet alone (13 kg vs. 9.9 kg, P=0.063) [49]. The combined intervention also resulted in a 20 % greater sustained weight loss after 1 year (6.7 kg vs. 4.5 kg, P=0.058). Furthermore, adding exercise to diet, or to diet and behavioural therapy, was associated with improved weight loss for up to 36 months and improvements in HDL, TGs and blood pressure [50]. However, a systematic review on the effect of physical activity on weight regain showed heterogeneous and modest results [51].

Recently, two randomized controlled trials showed that a lifestyle-modification program including an important amount of exercise therapy was able to reduce the risk of type 2 diabetes by 58% in patients with impaired glucose tolerance [27, 28]. These trials support the results of an earlier Chinese trial [52].

Behavioural Therapy

The purpose of behavioural therapy is to help patients identify and modify their eating and physical activity habits that contribute to their obesity. Adding behavioural therapy to diet, or to diet and sibutramine together, was found to improve weight loss for up to 18 months [50]. When psychological interventions, particularly behavioural and cognitive-behavioural strategies, were combined with a diet/exercise approach and compared with diet/exercise alone, the combined intervention resulted in a greater weight reduction (-4.9 kg; 95% CI –7.3 to –2.4) among overweight or obese adults [53].

1.3.2.2 Interventions to promote compliance

The ultimate goal of any diet is to maintain the weight loss at long term. In this respect, the results of all weight loss therapies have been disappointing. Most of the weight is regained after 5 years, regardless of what therapies are employed [38]. However, the literature on long term follow-up (3-14 years) of dietary treatment shows a possible adjuvant effect of group therapy, behaviour modification and active follow-up [37]. Indeed, diet combined with group therapy lead to better success rates (median 27%) than diet alone (median 15%). Active follow-up was generally associated with better success rates than passive follow-up (19% vs. 10%). Conventional diet seemed to be most efficacious in addition with group therapy, whereas VLCD apparently was most efficacious if combined with behavioural therapy and active follow-up.

Providing weight loss therapies through structured programs can add to the adherence to these therapies. A recent meta-analysis of 29 US trials of long term weight loss maintenance indicated that weight loss maintenance 4 or 5 years after a structured weight loss program averages 3.0 kg or 23% of initial weight loss, representing a sustained reduction in body weight of 3.2% [42].

With the exception of the Weight Watchers, the major commercial and self-help weight loss programs were not yet evaluated in randomized controlled trials [54]. Of 3 randomized controlled trials of Weight Watchers, the largest reported a loss of 3.2% of initial weight at 2 years.

1.3.2.3 Conclusion

Much remains to be learned about how to implement dietary, physical activity, and behavioural interventions designed to achieve weight loss and weight control in the long term. Since only few interventions showed significant effects in terms of weight maintenance and prevention of weight regain, obesity research should specifically address this problem.

1.3.3 Weight loss and long-term mortality

While many studies showed an improvement in several obesity-related risk factors with voluntary weight loss [55, 27, 28], only limited data coming from observational studies support the notion that intentional weight loss reduces total mortality [56]. This may be especially true for certain subgroups, such as individuals with diabetes [57]. However, some studies suggested an increased mortality risk associated with intentional weight loss [58, 59], while others showed no association for certain subgroups [60]. A major shortcoming in most of these observational studies is the lack of information about the weight loss method [61]. For example, it is well-known that some individuals smoke as a means of weight control. Another important drawback is the difficulty to separate intentional from unintentional weight loss due to undiagnosed or preclinical disease [62]. In fact, some authors consider the association between intentional weight loss and mortality as an inherently unobservable entity [62].

Randomized controlled trials and high-quality observational studies will be needed to resolve this controversy. Large ongoing trials, such as the SOS study [34], the Look-AHEAD trial [63], or the SCOUT study [64], probably will provide important information on the effects of surgical and non surgical obesity treatment on cardiovascular morbidity and mortality.

In conclusion, although the relationship between obesity and mortality is clear, the relation between intentional weight loss and mortality remains an unresolved controversy.

1.4 REFERENCES

1. Obesity : preventing and managing the global epidemic : report of a WHO consultation. Geneva-Switzerland: World Health Organization; 2000. Technical Report Series (894) Available from: http://whqlibdoc.who.int/trs/WHO_TRS_894.pdf
2. WHO Geneva; 2005.Obesity and overweight. WHO Global Strategy on Diet, Physical Activity and Health. Available from: http://www.who.int/dietphysicalactivity/publications/facts/obesity/en/
3. Barlow SE, Dietz WH. Obesity Evaluation and Treatment: Expert Committee Recommendations. Pediatrics. 1998;102(3):e29.
4. SIGN; 2003.Management of obesity in children and young people. Available from: http://www.sign.ac.uk/pdf/sign69.pdf
5. Cole T, Bellizzi M, Flegal K, Dietz W. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320:1-6.
6. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA. 2005;293(15):1861-7.
7. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005;293(15):1868-74.
8. Visscher TLS, Rissanen A, Seidell JC, Heliovaara M, Knekt P, Reunanen A, et al. Obesity and unhealthy life-years in adult Finns: an empirical approach. Arch Intern Med. 2004;164(13):1413-20.
9. Yusuf S, Hawken S, Ôunpuu S, Bautista L, Franzosi M, Commerford P, et al. Obesity and the risk of myocardial infarction in 27000 participants from 52 countries: a case-control study. Lancet. 2005;366(9497):1640-9.
10. Grundy SM, Brewer HB, Jr., Cleeman JI, Smith SC, Jr., Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation. 2004;109(3):433-8.
11. Grundy SM, Hansen B, Smith SC, Jr., Cleeman JI, Kahn RA. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Circulation. 2004;109(4):551-6.
12. Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2005;28(9):2289-304.
13. Grundy SM. Metabolic syndrome: connecting and reconciling cardiovascular and diabetes worlds. J Am Coll Cardiol. 2006;47(6):1093-100.
14. Pladevall M, Singal B, Williams LK, Brotons C, Guyer H, Sadurni J, et al. A single factor underlies the metabolic syndrome: a confirmatory factor analysis. Diabetes Care. 2006;29(1):113-22.
15. Demarest S, Leurquin P, Tafforeau J, Tellier V, Van der HJ, Van OH. Health Interview Survey, Belgium, 1997, Epidemiology Unit, Scientific Institute of Public Health, Brussels. In; 1998.
16. Gisle L, Buziarsist J, Van der HJ, Demarest S, Miermans PJ, Sartor F, et al. Health Interview Survey, Belgium, 2001, Epidemiology Unit, Scientific Institute of Public Health, Brussels. 2002. IPH/EPI REPORTS 2002-22 Available from: http://www.iph.fgov.be/epidemio/epifr/index4.htm
17. Bayingana K, Demarest S, Gisle L, Hesse E, Miermans PJ, Tafforeau J, et al. Health Interview Survey, Belgium, 2004, Epidemiology Unit, Scientific Institute of Public Health, Brussels. In: IPH/EPI REPORTS N› 2006; 2006.
18. Devriese S, Huybrechts I, Moreau M, Van Oyen H. National Food Consumption Survey, Belgium, 2004, Epidemiology Unit, Scientific Institute of Public Health, Brussels. 2006 2006. IPH/EPI REPORTS 2006-14 Available from: http://www.iph.fgov.be/epidemio/epifr/foodfr/table04.htm
19. Doutrelepont R, Mortelmans D. Panel Démographie Familiale - Panel Studie van Belgische Huishoudens (PSBH). Available from: http://www.psbh.ulg.ac.be/ L1 - http://www.psbh.be/index.html
20. Moreau M, Valente F, Mak R, Pelfrene E, de SP, De BG, et al. Obesity, body fat distribution and incidence of sick leave in the Belgian workforce: the Belstress study. Int J Obes Relat Metab Disord. 2004;28(4):574-82.
21. Lean ME. Prognosis in obesity. BMJ. 2005;330(7504):1339-40.
22. WHO. World Health Assembly Resolution 57/17. Global Strategy on Diet, Physical Activity and Health. Geneva: 2004 22 Mai 2004. 2005 Available from: http://www.who.int/dietphysicalactivity/goals/en/index.html
23. Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. J.Chronic.Dis. 1972;25(6):329-43.

24. Deurenberg P, Yap M, van Staveren WA. Body mass index and percent body fat: a meta analysis among different ethnic groups.[see comment]. International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity. 1998;22(12):1164-71.
25. American Gastroenterological A. American Gastroenterological Association medical position statement on Obesity. Gastroenterology. 2002;123(3):879-81.
26. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WH, Jr., Kostis JB, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA. 1998;279(11):839-46.
27. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344(18):1343-50.
28. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.
29. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292(14):1724-37.
30. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk.[see comment]. American Journal of Clinical Nutrition. 2004;79(3):379-84.
31. Wang Y, Rimm EB, Stampfer MJ, Willett WC, Hu FB. Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men.[see comment]. American Journal of Clinical Nutrition. 2005;81(3):555-63.
32. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension. 2006;47(2):296-308.
33. Despres J-P, Golay A, Sjostrom L, the Rimonabant in Obesity-Lipids Study Group. Effects of Rimonabant on Metabolic Risk Factors in Overweight Patients with Dyslipidemia. N Engl J Med. 2005;353(20):2121-34.
34. Sjostrom L, Lindroos A-K, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683-93.
35. Howard BV, Manson JE, Stefanick ML, Beresford SA, Frank G, Jones B, et al. Low-Fat Dietary Pattern and Weight Change Over 7 Years: The Women's Health Initiative Dietary Modification Trial. JAMA. 2006;295(1):39-49.
36. Kushner RF, Foster GD. Obesity and quality of life. Nutrition. 2000;16(10):947-52.
37. Ayyad C, Andersen T. Long-term efficacy of dietary treatment of obesity: a systematic review of studies published between 1931 and 1999. Obes Rev. 2000;1(2):113-9.
38. Avenell A, Brown TJ, McGee MA, Campbell MK, Grant AM, Broom J, et al. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. J Hum Nutr Diet. 2004;17(4):317-35.
39. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Long-term non-pharmacological weight loss interventions for adults with prediabetes. Cochrane Database Syst Rev. 2005(2):CD005270.
40. National Institutes o f Health, National Heart Lung and Blood Institute, North American Association for the Study of Obesity. The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Department of Health and Human Services PHS, ; 2000. (2000:00-4084.) Available from: http://www.nhlbi.nih.gov/guidelines/obesity/practgde.htm
41. Heymsfield SB, Van Mierlo CA, Van Der Knaap HC, Heo M, Frier HI. Weight management using a meal replacement strategy: meta and pooling analysis from six studies. Int.J.Obes.Relat Metab Disord. 2003;27(5):537-49.
42. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. Am.J.Clin.Nutr. 2001;74(5):579-84.
43. Wing RR, Hill JO. Successful weight loss maintenance. Annu Rev Nutr. 2001;21:323-41.
44. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, et al. A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med. 2003;348(21):2082-90.
45. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, Jr., Brehm BJ, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch.Intern Med. 2006;166(3):285-93.

46. Pirozzo S, Summerbell C, Cameron C, Glasziou P. Advice on low-fat diets for obesity. Cochrane Database Syst Rev. 2002(2):CD003640.
47. Astrup A, Ryan L, Grunwald GK, Storgaard M, Saris W, Melanson E, et al. The role of dietary fat in body fatness: evidence from a preliminary meta-analysis of ad libitum low-fat dietary intervention studies. Br.J.Nutr. 2000;83 Suppl 1:S25-S32.
48. Petersen M, Taylor MA, Saris WH, Verdich C, Toubro S, Macdonald I, et al. Randomized, multi-center trial of two hypo-energetic diets in obese subjects: high- versus low-fat content. Int.J Obes.(Lond). 2006;30(3):552-60.
49. Curioni CC, Lourenco PM. Long-term weight loss after diet and exercise: a systematic review. Int.J.Obes.(Lond). 2005;29(10):1168-74.
50. Avenell A, Brown TJ, McGee MA, Campbell MK, Grant AM, Broom J, et al. What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. J Hum Nutr Diet. 2004;17(4):293-316.
51. Fogelholm M, Kukkonen-Harjula K. Does physical activity prevent weight gain--a systematic review. Obes.Rev. 2000;1(2):95-111.
52. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care. 1997;20(4):537-44.
53. Shaw K, O'Rourke P, Del Mar C, Kenardy J. Psychological interventions for overweight or obesity. Cochrane.Database.Syst.Rev. 2005(2):CD003818.
54. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. Ann Intern Med. 2005;142(1):56-66.
55. Sjostrom CD, Peltonen M, Sjostrom L. Blood pressure and pulse pressure during long-term weight loss in the obese: the Swedish Obese Subjects (SOS) Intervention Study. Obes Res. 2001;9(3):188-95.
56. Gregg EW, Gerzoff RB, Thompson TJ, Williamson DF. Intentional weight loss and death in overweight and obese U.S. adults 35 years of age and older. Ann Intern Med. 2003;138(5):383-9.
57. Williamson DF, Thompson TJ, Thun M, Flanders D, Pamuk E, Byers T. Intentional weight loss and mortality among overweight individuals with diabetes. Diabetes Care. 2000;23(10):1499-504.
58. Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C. Prospective study of intentional weight loss and mortality in never-smoking overweight US white women aged 40-64 years. Am J Epidemiol. 1995;141(12):1128-41.
59. Yaari S, Goldbourt U. Voluntary and involuntary weight loss: associations with long term mortality in 9,228 middle-aged and elderly men. Am.J Epidemiol. 1998;148(6):546-55.
60. Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C. Prospective study of intentional weight loss and mortality in overweight white men aged 40-64 years. Am J Epidemiol. 1999;149(6):491-503.
61. Yang D, Fontaine KR, Wang C, Allison DB. Weight loss causes increased mortality: cons. Obes.Rev. 2003;4(1):9-16.
62. Coffey CS, Gadbury GL, Fontaine KR, Wang C, Weindruch R, Allison DB. The effects of intentional weight loss as a latent variable problem. Stat.Med. 2005;24(6):941-54.
63. Ryan DH, Espeland MA, Foster GD, Haffner SM, Hubbard VS, Johnson KC, et al. Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. Control Clin.Trials. 2003;24(5):610-28.
64. ClinicalTrials.gov. A Long Term Study of Sibutramine and the Role of Obesity Management in Relation to Cardiovascular Disease in Overweight and Obese Patients. In: National Institutes of Health; 2006.

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Part 2: Treatment of obesity in adults

2 OBJECTIVES AND METHODS

2.1 OBJECTIVES

The solutions to the problem of obesity at societal level are to be found in multisectorial approaches to improve diet and encourage physical activity, and fall largely outside the medical paradigm. The bio-medical paradigm applies to the medical consequences of obesity, more than to obesity itself

Nevertheless clinical treatment is also part of the response to the obesity epidemic. Lifestyle modification is and will remain the first treatment of obesity. However pharmacological and surgical approaches are increasingly used. These are the core subjects of this study. We used a standardised health technology assessment methodology to evaluate their effectiveness and cost-effectiveness, and the consequences of our findings for decision makers in Belgium. This report also includes an analysis of long-term residential care for severely obese children in Belgium.

Our objectives are:

(1) In adults:

- to conduct an health technology assessment (HTA) of the pharmaceutical treatment of obesity (limited to 2 prescription drugs licensed in Belgium, and to a third one, soon to be marketed) , and
- a HTA of the surgical treatment of obesity focusing on the more recent developments such as the gastric banding

(2) In patients under 18 year old:

- to conduct a HTA of the pharmaceutical and surgical treatment of obesity
- to document existing hospital practices in Belgium, in particular residential care for obese children

(3) to explore the consequences of our findings for political decision making in Belgium

2.2 METHODS

Standards methods for HTA developed by the KCE are described in KCE procedures, and are based on methods developed by specialised institutions such as The International Network of Agencies for Health Technology Assessment (INAHTA)[1], The National Institute for health and Clinical Excellence (NICE)[2], the Haute Autorité de santé (HAS/ formerly Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)[3]).

There is a very large body of literature on the pharmaceutical and surgical treatment of obesity, including various meta-analysis, and health technology assessment (HTA) reports, and regular updates. As an example, a simple search of the 'Health Technology Assessment' database of the Centre for Research and Dissemination (CRD)[1] , conducted in October 2005, using the term 'obesity' returned 62 hits.

The present study is mainly a 'review of reviews'. It is based on a critical reading of the most recent of these reviews, completed by an update of the scientific literature usually up to December 2005 (precise update dates are given under each section).

[1] CRD is an independent organisation whose mission is to promote the use of research-based knowledge. It maintains 3 large, continuously updated databases: DARE (Database of Abstracts of Reviews and Effects, a HTA database, and a database on economic evaluations. See http://www.york.ac.uk/inst/crd/crddatabases.htm

The studies of existing practices in Belgium are based on:

- The analysis of existing Belgian databases (billing codes, hospitals stays)
- field visits to hospitals with known expertise in the field of bariatric surgery, and multidisciplinary treatment of obesity
- field visits to the 3 centres offering residential care for the treatment of obesity in children and adolescents, and a review of the 'conventions' governing their relationship with the public funding body (INAMI/RIZIV).

2.3 REFERENCES

1. INATHA.Available from: http://www.inahta.org/
2. NICE.Available from: http://www.nice.org.uk/
3. ANAES.Available from: http://www.anaes.fr

3 CLINICAL EFFECTIVENESS OF PHARMACOLOGICAL TREATMENT OF OBESITY

3.1 DRUGS EVALUATED, AND MEASURES OF EFFECTIVENESS

We limited this review to the two prescription drugs approved for weight loss in Belgium (Sibutramine and Orlistat). We also included Rimonabant, a new drug, not yet commercialised in Belgium.

- *Sibutramine* (Reductil®), 10 or 15mg) is a combined norepinephrine and serotonin reuptake inhibitor. Its effect on weight loss is attributed to appetite suppression and increased thermogenesis.

- *Orlistat* (Xenical®) is a lipase inhibitor. It putatively aids weight loss by reversibly binding to the active centre of the enzyme lipase, preventing the digestion and absorption of some dietary fats. It inhibits approximately 30 percent of fat absorption, including the absorption of fat-soluble vitamins. The recommended dose is 3*120mg/d.

- *Rimonabant* (Acomplia®) is a selective cannabinoid-1 receptor blocker. The (newly discovered) endocannabinoid system contributes to the physiological regulation of energy balance, food intake, and lipid and glucose metabolism through both central and peripheral effects.

Primary outcomes for the effectiveness of these drugs in the treatment of obesity relate to weight loss. Secondary outcomes relate to co-morbidities (hard endpoints, such as cardio-vascular events, and/or biological markers as risk factors).

Table 7. Indicators commonly used to evaluate effectiveness of pharmacological treatment of obesity

Measure	Clinical significance
Mean weight loss (kgs) Mean decrease in BMI Mean decrease in waist circumference (cm)	Absolute measures are intuitive but difficult to relate to clinical significance. Means can conceal significant heterogeneity in responses to treatment across participants.
Mean % body weight loss	Threshold for clinical significance unclear
% > 5% weight loss	No evidence that sustained weight loss of this order is associated with improvements of co-morbidities.
% > 10 % weight loss	There is consensus-based evidence that sustained weight loss of this order is associated with improvements of co-morbidities. Most commonly used indicator.
Successful weight maintenance	Often defined as maintenance of 80% of a certain level of weight loss (>5%, or > 10%). Weight maintenance is more difficult to achieve than weight loss and is the ultimate goal of treatment.

Where possible, we have tried to express effectiveness results as a number-to-treat (NNT). NNT is the inverse of the absolute risk difference. For instance, if 20% patients achieved 10% weight loss in the intervention group and 5% in the placebo group, then the absolute risk difference is 15% and the NNT is 6.66 (1/0.15).

3.2 METHODS FOR THIS REVIEW

Several systematic reviews or meta-analysis of the pharmacological treatment of obesity have been published in the last 3 years[1-7], including one focusing on patients with diabetes[8, 9]. These are the main sources for our study. A brief description of the reviews we have used (search, inclusion criteria, last update, conclusions) can be found in annexes.

Obesity being a chronic condition, we have focused on long-term treatment (at least one year). To update our report for significant articles not included in these reviews we conducted a simple Medline search on 'sibutramine' or 'orlistat' or 'rimonabant' (free text), limiting the search to 'Randomized Clinical Trials' (RCT) published from 2003 to February 2006. We extracted studies meeting the following criteria: at least 12 month follow-up (FU), double-blind, placebo-controlled trial, intention-to-treat analysis, last-observation-carried-forward (as opposed to completers-only) analysis, not already included in one of the systematic review quoted above. These studies are discussed only when they add significantly to the conclusions of the systematic reviews on the subject.

Studies evaluating pharmacological treatment of obesity usually start with a 'run-in' phase, or weight loss period; in most cases only patients able to follow dietary advice, or meeting some criteria for weight loss, are then randomized. RCTs are classified according to their objectives, into weight reduction trials (WR) and weight maintenance trials (WM), that is weight maintenance after a desirable weight loss has been achieved. However the difference between WR and WM studies is not necessarily clear-cut. For instance one study self-identified as WM study is analysed as a WR study in 2 reviews[2, 3] because the run-in period was only 4 weeks.

3.3 SIBUTRAMINE

3.3.1 Evidence available

Between 4 and 6 studies meeting inclusion criteria are included in the systematic reviews. All are industry-funded.

Attrition rate ranges from 32% to 47%, averaging 43% in 5 studies included in the Cochrane review[1]. This is a major methodological limitation as it is difficult to compensate for such a bias in the analysis. Most studies use the 'last-observation-carried-forward' (LOCF) analysis (presented together with a 'completers only analysis'). This can affect comparisons in any direction if drop-out rates are differential (= occur at a different rate and for different reasons in the groups compared).

Weight maintenance studies offer the longer follow-up. In the STORM study[10], 605 obese patients were recruited for a 6-month period of weight reduction with Sibutramine (10 mg/day) and an individualised 600 kcal/day deficit programme. Patients with more than 5% weight loss were then randomly assigned to 10 mg/day Sibutramine (dosage could later be increased if necessary) or placebo for a further 18 months. In a Dutch study[11], 221 patients were given a 3-month very low calorie diet (VLCD). Patients with more than 10 % weight loss were then randomized to Sibutramine 10 mg/day or placebo for 18 months and all received a recommended diet and exercise programme.

One RCT does not strictly meet our inclusion criteria because it was not placebo-controlled[12]. It nevertheless provides interesting insights because of its original design and will be discussed where appropriate. Four randomized groups were compared over one year : (1) sibutramine 15 mgr plus minimal advise on diet and exercise, (2) intensive lifestyle modification alone, (3) sibutramine + intensive lifestyle modification, and (4) sibutramine + brief lifestyle modification. Compared with other trials, sample size is however rather small (+/- 50 per group).

3.3.2 Characteristics of participants and interventions

Patients are mostly healthy obese patients, their mean age ranges from 34 to 54 years and BMI 32.4 to 36.6[3]. Patients with controlled hypertension are included in most trials. One study recruited patients with hypertension[13, 14]; 1 study recruited only patients with diabetes [15].

All trials report some dietary interventions (low-calorie diet), in some cases completed by exercise[11], or behaviour modification and exercise[10]. In Wadden study[12], intensive lifestyle

modification consisted of 30 group sessions over one year. Patients were instructed to keep daily records of food intake and exercise.

3.3.3 Primary outcomes

3.3.3.1 Weight loss and maintenance

Weight loss at 12 months after randomization across 4 WR studies reviewed by Avenell[3] ranged from 4.4 kgs to 6.4 kgs in the treatment group, and from 0.5 kgs to 1.60 kgs in the control group.

The *weighted mean difference* between weight loss in treatment group vs placebo group at 12 months ranged from 4.12 kgs (95% CI: -4.97 to 3.26) to -4.45 kgs (-5.29 to 3.62) in 3 meta-analyses[1-3].

Adults taking Sibutramine for 1 year were 12% to 31% more likely to achieve 10% weight loss than those taking placebo[2]. Clinicians would have to treat between 3 and 8 patients for 1 year for one patient to achieve 10% weight loss (over the benefits provided by placebo)

In 2 weight maintenance studies with 18-month follow-up after randomization[10, 11], *successful weight maintenance* was defined as maintenance at endpoint of at least 80% of weight loss achieved at randomization.

In the STORM study[10], patients with at least 5% weight loss were randomized, successful weight maintenance after 18 months was achieved by 41% of the patients (145/350) in the treatment group, against 14% (16/114) in the placebo group. Clinicians would have to initiate treatment with Sibutramine in 4 patients having lost at least 5% body weight (95% CI: 3-5)[2] , for one of them to achieve successful weight maintenance after 18-month treatment, over the effect of placebo. Mean difference in weight between placebo and treatment group was 3.40 kgs (95% CI: -4.45 to 2.35)[3].

In the Mathus-Vliegen study, patients with at least 10% weight loss were randomized. At 18 months, successful weight maintenance was achieved by 30% in the treatment group vs 20% in the placebo group (detailed data not available for 95% CI calculation). Clinicians would have to initiate treatment with Sibutramine in 10 patients having lost at least 10% body weight, for one of them to achieve successful weight maintenance after 18-months treatment, above the benefits provided by placebo.

In Wadden study[12](not placebo-controlled), the difference in weight lost after one year was not statistically significant, between patients initially randomized to the following groups: (1) Sibutramine+minimal advise (mean 5.0 kgs), (2) Sibutramine + brief therapy (mean: 7.5 kgs); and (3) intensive lifestyle modification (mean lost: 6.7 kgs). Those assigned to the group: intensive lifestyle modification + sibutramine lost significantly more weight (12 kgs) than any other group.

3.3.3.2 Weight regain after treatment is withdrawn

Weight lost with the help of Sibutramine is regained more quickly when the drug is stopped (rebound), than weight lost without the help of Sibutramine. One study assessed weight change 3 months after the end of a 12-month treatment. Weight regain was 4.3 kgs in the group previously treated with Sibutramine, and 2.3 kgs in the group previously treated with placebo (p=0.009)[16].

In the STORM trial[10], of those patients randomized to the placebo group after 6-month run-in period with Sibutramine, less than half maintained at least 5% weight loss 18 months later.

3.3.3.3 Dose effect

No evidence of dose-effect was found in Arterburn review[2]. For all treatment durations, the summary mean difference in weight loss differed by less than 1 kg between the sibutramine, 10 and 20 mg, treatment groups.

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[2] 95% CI computed by us

[3] The STORM study compares outcomes from the beginning of the run-in period, but comparisons should strictly speaking be made from the point of randomization. Avenell[3] recalculated outcomes for the purpose of its systematic review between treatment and placebo group, from the point of randomization

3.3.4 Secondary outcomes

3.3.4.1 Hard enpoints

There are no studies directly assessing the effect of Sibutramine on reducing obesity-related morbidity and mortality.

3.3.4.2 Quality of life (QoL)

We identified only one study with at least one year follow-up specifically comparing health-related-quality-of-life in obese patients (with diabetes) treated with Sibutramine vs placebo. Despite greater weight loss at one year in the treatment group, health related QoL improved similarly in the 2 groups[17].

3.3.4.3 Metabolic outcomes

Changes in some metabolic parameters at 12 months are shown in table 2. (Outcomes at month 18 are shown in annex).

Table 8. Sibutramine + diet, vs placebo + diet at 12 months. Meta-analysis. Selected outcomes. Compiled from Avenell[18]

Outcome: Change in	N studies	n treatment /n control	Weighted mean difference 95% CI	Test for overall effect (p)
Weight (kg)	**4 WR**	**530/561**	**-4.12 (-4.97 to – 3.26)**	**< 0.00001**
Tot cholesterol (mmol/l)	**3 WR 1 WM**	**643/364**	**-0.03 (-0.17 to 0.12)**	**0.70**
LDL cholesterol (mmol/l)	**3 WR 1 WM**	**477/213**	**-0.11 (-0.23 to 0.01)**	**0.07**
HDL cholesterol (mmol/l)	**2 WR 1 WM**	**479/214**	**0.11 (0.07 to 0.15)**	**< 0.00001**
Triglycerides (mmol/l)	**4 WR 1 WM**	**724/442**	**-0.17 (-0.27 to – 0.07)**	**0.0005**
HbA_{1c}%	**1 WM**	**265/77**	**-0.07 (-0.25 to 0.11)**	**0.76**
Fasting plasma glucose (mmol/l)	**3 WR 1 WM**	**643/364**	**-0.04 (-0.22 to 0.14)**	**0.67**

WR= weight reduction study WM= weight maintenance study

In Wadden study[12] (not placebo-controlled), the differences between groups in metabolic outcomes after one year were not statistically different, but this study was not adequately powered to demonstrate such differences.

3.3.4.4 Special populations

The differences in weight loss were similar across trials that specifically recruited adults with type 2 diabetes mellitus, hypertension, and healthy obese adults[2].

A specific meta-analysis was conducted for the effect of sibutramine on obese patients with type 2 diabetes.

Table 9. Sibutramine + diet, vs placebo + diet at 12 months. Meta-analysis. Selected outcomes in type 2 diabetis patients. Compiled from Cochrane review[9]

Outcome: Change in	N studies	N treatment /N control	Weighted mean difference	p
Weight loss (kgs)	**9**	**440/423**	**-4.77 (-5.5, -3.04)**	**<0.00001**
Weight circumference (cm)	**5**	**244/231**	**-4.68 (-7.36,-1.99)**	**0.0006**
HbA1c (%)	**7**	**314/298**	**-0.54 (-1.32,0.24)**	**0.18**
Fasting glucose (mmol/l)	**5**	**218/218**	**-1.35 (-3.68, 0.99)**	**0.3**
SBP (mm Hg)	**6**	**334/339**	**-0.84 (-1.66, 0.02)**	**0.04**
DBP (mm Hg)	**4**	**238/342**	**-1.43 (0.06, 2.79)**	**0.04**
Total cholesterol (mmol/l)	**6**	**271/258**	**-0.11 (- 0.37, 0.15)**	**0.4**
HDL cholesterol (mmol/l)	**5**	**218/201**	**-0.07 (-0.03, -0.11)**	**0.00005**

Note: Random-effect model. This meta-analysis included studies regardless of length of follow-up. As treatment effect reaches its maximum between 6 months and one year, the pooled effects presented here are an overestimate of the effects observed at longer follow-up periods.

3.3.5 Adverse effects

The manufacturer of Sibutramine recommends limiting the duration of treatment to *one year*, given concerns about the safety profile of the drug, because it increases blood pressure in patients already at risk of cardio-vascular diseases. One study nevertheless reports data on 2 year-treatment[10], and the ongoing SCOUT study is designed to assess the long-term safety of Sibutramine.

Table 10. Sibutramine + diet vs placebo + diet : changes in blood pressure at 12 months. Compiled from Avenell review[3]

Outcome: **Change in**	**N studies**	**n treatment /n control**	**Weighted mean difference 95% CI**	**Test for overall effect (p)**
SBP (mm HG)	3 WR	445/375	1.16 (0.60 to 2.93)	0.20
DBP (mm HG)	3 WR	445/375	2.04 (0.89 to 3.20)	0.00005

SBP: Systolic Blood Pressure DBP: Diastolic Blood Presssure

The summary mean difference in heart rate between the treatment group and the placebo group was 3.76 beats/min (95% CI 2.7-4.82) [2].

Insomnia, nausea, dry mouth and constipation were more common in patients on Sibutramine therapy, occurring at frequency rates of 7-20%[1].

3.3.6 Predictors of treatment success

Given the large inter-individual variations in weight loss observed both in the treatment and the placebo groups of trials assessing Sibutramine, attempts have been made to identify the predictors of successful weight loss, or maintenance.

Two studies based on the STORM trial have looked at predictors of success (maintenance of 80% of initial weight loss at endpoint). Out of various pre-treatment factors analysed, only weight was found to be an independent, statistically significant, predictor of treatment success, but it explained less than 8% of the variation of body weight across patients at endpoint[19]. Weight loss after a 6-month Sibutramine treatment explained only 8% of the variation in weight at the end of the study 18 months later in multivariate analysis (while treatment group – Sibutramine vs placebo – explained only 9% of this variation)[20].

Finer re-analyzed pooled data from 7 clinical trials of at least one year duration, in order to identify the predictors of at least 5% weight loss in the Sibutramine group at 12 months[21]. A cut-off point of 4-kg weight loss after 3-month treatment with Sibutramine showed a positive predictive value of 84% (of those patients who had lost 4 kg at 3 months, 84% achieved 5% weight loss at 12 months), and a negative predictive value of 71% (of those patients who had lost less than 4 kgs at 3 months, 29% still achieved 5% weight loss at 12 months).

Unfortunately this was not controlled for any confounder, pooled analysis was done only for the Sibutramine group, and this study does not tell us whether the predictive values attached to these cut-off points were similar or different in the placebo group, and if they are, or not, independent markers of a better physiological response to Sibutramine.

Indeed many factors may be involved in successful weight maintenance, and differences in behaviour might be stronger predictors of weight regain than are differences in physiology or metabolism[22]. A positive correlation between weight maintenance and initial weight loss is likely to reflect better compliance with the treatment[20].

3.4 ORLISTAT

3.4.1 Evidence available

Orlistat is an older drug, and there is less concern than for Sibutramine concerning its safety profile. As a consequence, more studies, and with longer follow-up, are available for Orlistat than for Sibutramine. The Cochrane review found 11 studies with at least one year follow-up but limited the review to one-year outcomes[1]. Avenell[3] also presents 2 year – outcomes when available and separates results from weight reduction and weight maintenance studies..

All studies are industry-funded There are 4 studies reporting outcomes at 24 months (all weight maintenance). [23-26]. The XENDOS study (published after the latest updates of the reviews) reports outcomes at 48 months[27].

At one year drop-out rates ranged from 24 to 42% in control groups and from 15% to 36% in treatment groups[3]; at 4 year these figures were 34% and 52% respectively for the XENDOS[27] study. Drop-out rates were usually higher in the control group.

We focus on weight maintenance studies and/or studies with a longer follow-up.

3.4.2 Characteristic of participants and interventions

Most studies enrolled patients with a BMI >=30. Mean BMI ranged from 32.6 to 37.1 in Avenell review[3].

The dose of Orlistat used in all trials was 120 mg 3 x daily. Both groups were also prescribed a low-calorie diet and various degrees of lifestyle interventions.

3.4.3 Primary outcomes

3.4.3.1 Long-term weight loss and maintenance

The mean weight loss achieved after one year (8 studies[3]) ranged from 3.29 to 8.10 kgs in the treatment group and from 1.98 to 4.20 kgs in the control group.

Table 5 shows the weighted mean difference in weight between treatment and placebo groups at different lengths of follow-up.

Table 11. Orlistat 3*120 mg / day + diet vs placebo + diet : mean weight difference in kgs at 12, 24, and 48 months

N studies	n treatment /n control	Weighted mean difference in kgs (95% CI)	Test for overall effect (p)
12 months* (weight maintenance studies only)			
4	717/707	-0.85 (-1.50 to 0.19)	0.01
24 months*			
2	451/458	-3.26 (-4.15 to – 2.37)	< 0.00001
48 months[27]			
1	1640/1637	-2.8	<0.001

* Compiled from Avenell review[3]

Only 2 studies with at least 2 year follow-up[25, 26] provided a measure of the proportion of patients with at least 10% of initial weight lost at the end of follow-up[4].

Table 12. Proportion of patients achieving 10% weight loss at 2 years, and number-needed to treat

Reference	Orlistat 3*120 mg for 2 years			Placebo for 2 years			NNT
	N	Completers	10% WL (ITT)*	N	Completers	10% WL (ITT)	
Hauptmann[25]	210	56%	19%	212	43%	6,6%	8,3
Rossner [26]	244	65%	28%	243	56%	18,6%	10,4
Pooled estimate of NNT (95% CI)[5]							9 (6-17)

*WL: weight loss ITT: intention to treat ** NNT: number needed to treat; computed by us

The pooled estimate for the number-needed-to-treat (NNT) is 9 (95% CI:6-17). This means that 9 obese patients would need to be treated with Orlistat for 2 years, for one of them to achieve 10% of weight loss, over the benefits provided by placebo.

[4] Two studies[24, 27] gave these indicators only for patients completing the study, and not as an intention-to-treat analysis.

[5] See details of meta-analysis in annex.

3.4.3.2 Weight regain after treatment is stopped

In all weight maintenance trials, Orlistat proved more effective than placebo in maintaining weight lost and preventing weight regain.

On the other hand, weight lost with the help of Orlistat was regained more quickly when the drug was stopped (rebound), than weight lost without the help of Orlistat.

In one study[24], patients treated with Orlistat 360 mg during the first year, and then assigned to placebo for the second year, regained a mean of 5.63 +/- 0.42 kgs between month 12 and 24 of the study. There was no difference at the end of the second year in terms of mean weight loss, between patients having taken placebo for 2 years, and patients having taken Orlistat for one year, followed by placebo for one year.

3.4.4 Secondary outcomes

3.4.4.1 Hard enpoints

No study reports hard endpoints such as mortality, or cardio-vascular mortality. The Xendos study[27] was designed to evaluate Orlistat in the prevention of type II diabetes in obese subjects. A 4-year treatment with Orlistat decreased the incidence of type 2 diabetes in the subgroup of patients with impaired glucose tolerance at baseline, but not in the group with normal glucose tolerance at baseline (see table 7). Weight loss was comparable in both groups. In patients with impaired glucose tolerance at baseline, 17 patients would need to be treated with Orlistat for 4 years, to prevent (or delay) the onset of one case of diabetes – over the benefits provided by placebo.

Table 13. Orlistat 3*120 mgr+diet vs placebo + diet on the incidence of diabetes at 4 years. From the Xendos study[27] .

	All patients	Patients with impaired glucose tolerance at baseline
N traitement/N placebo	1650 / 1655	350 / 344
Completers(%) treatment/placebo	52 % / 34 %	NA
Cumulative incidence of diabetes (repeat test) (%) treatment / placebo	2.9% / 4.2%	8.3% / 14.2%
P (log-rank test)	0.0032	0.0171
Number-needed-to treat*	77	17

*Computed by us

3.4.4.2 Metabolic outcomes

Metabolic outcomes at 24 months are presented in table 8.

Table 14. Orlistat 360 mg + diet vs placebo + diet at 24 months N=3 studies (compiled from Avenell [3]

Outcome: Change in	n treatment /n control	Weighted mean difference 95% CI	Test for overall effect (p)
Tot cholesterol (mmol/l)	557/537	-0.21 (-0.34 to 0.09)	0.001
LDL cholesterol (mmol/l)	555/536	-0.22 (-0.31 to -0.13)	< 0.00001
HDL cholesterol (mmol/l)	557/537	-0.03 (-0.07 to 0.00)	0.07
Triglycerides (mmol/l)	557/537	0.04 (-0.07 to 0.15)	0.50
Fasting plasma glucose (mmol/l)	557/537	-0.15 (-0.24 to -0.07)	0.0005

WR= weight reduction study WM= weight maintenance study

The effect on LDL cholesterol appears to be partly independent of weight loss.

3.4.4.3 Special populations – Subgroup analysis

In the Cochrane review[1], subgroup analysis did not show any statistically significant difference in weight loss between trials enrolling high-risk groups, such as diabetic patients. Another Cochrane review specifically addressed pharmacological treatment of obesity in diabetic patients.

Table 15. Meta-analysis. Orlistat 360mg + diet, vs placebo + diet in patients with type 2 diabetes patients. Compiled from Cochrane review[9]

Outcome: Change in	N studies	N treatment /N control	Weighted mean difference	p
Weight loss (kgs)	7	710/653	-2.03 (-2.82, -1.25)	<0.00001
Weight circumference (cm)	6	579/532	-1.84 (-2.99, -0.68)	< 0.00001
HbA1c (%)	7	718/655	-0.45 (-0.58,-0.31)	< 0.0001
Fasting glucose mmol/l	8	765/693	-0.82 (-1.14, -0.50)	< 0.00001
SBP (mm Hg)	5	382/358	-2.99 (-6.29, 0.32)	0.08
DBP (mm Hg)	4	222/210	-4.21 (-7.82,-0.01)	0.02
Total cholesterol (mmol/l)	6	693/631	-0.41 (-0.52,-0.30)	< 0.00001
HDL cholesterol (mmol/l)	•	621/473	-0.02 (-0.05,0.00)	0.05

Note: Random effect model. This meta-analysis included studies regardless of length of follow-up. As treatment effect reaches its maximum between 6 months and one year, the pooled effects presented here are an overestimate of the effects observed at longer follow-up periods.

3.4.5 Adverse effects

Despite reports of cancers in several trials, the difference between the treatment and placebo group were not statistically significant in Avenell meta-analysis[3].

All the Orlistat studies reported gastro-intestinal adverse events such as oily stools and faecal incontinence, to be more frequent in the Orlistat group than in the placebo group.

3.4.6 Head-to-head comparison between Orlistat and Sibutamine

Derosa compared the effects of Sibutramine and Orlistat in diabetic[28] and hypertensive[29] obese patients. Patients were randomized to either Sibutramine, or Orlistat and followed up for 12 months. The study was double-blind. In none of these studies does any of the drug appear to be superior to the other as regards weight or metabolic parameters but sample sizes are small. Diastolic blood pressure was significantly higher at the end of follow-up in the Sibutramine group, which appears to have been generally better tolerated than Orlistat.

3.5 RIMONABANT

3.5.1 Evidence available

Three RCTs with at least one year duration have been published so far[30-32]. All are industry-funded. All suffer from high drop-out rate.

At one year, drop-out rates ranged from 40 to 50% in all 3 studies. Overall, only 50% of patients initially randomized were included in the analysis after 24 months follow-up in Pi-Sunyer study[32].

3.5.2 Characteristics of patients and interventions

Inclusion criteria were similar for Van Gaal[31] and Pi-Sunyer[32] ; indeed these studies follow the same protocol (Rimonabant-in-Obesity, RIO) [6]. Despres[30] included only patients with untreated dyslipidemia (note that the prevalence of dyslipidemia among participants of the other studies was around 60-65%).

Pi-Sunyer study[32] is the largest and reports 2-year follow-up data. After a 4-week run-in period, 3045 patients 18 year or older (mean 44 y.o) were randomized to placebo, Rimonabant 5 mg/d or Rimonabant 20 mg for one year; 88% had a BMI >= 30 and 33% had a BMI >=40. Impaired glucose tolerance was present for 3-4% participants, 1% were diabetic. Patients receiving Rimonabant were re-randomized after one year to placebo or Rimonabant (same dose as initial assignment). All participants received an individualised diet prescription and were instructed to increase their physical activity during the entire study period. At the end of the 2nd year, 1533 patients in 5 groups (50% of patients initially randomized) were included in the analysis.

3.5.3 Primary outcomes

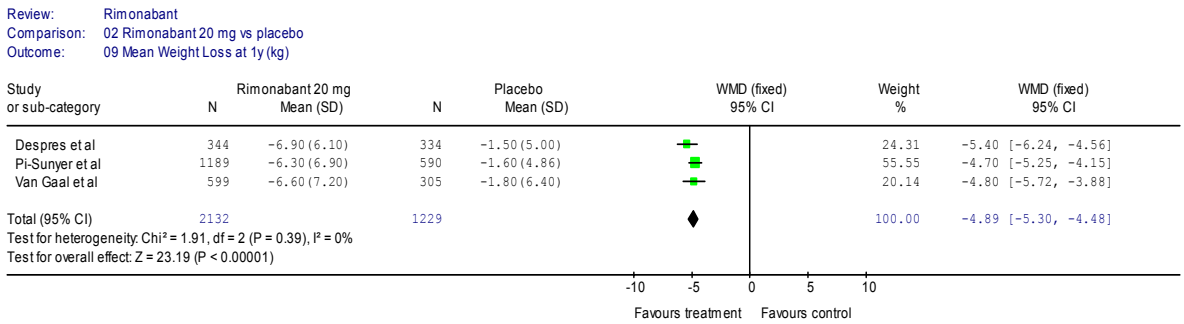
3.5.3.1 Weight loss and weight maintenance

After 1 year, mean weight difference between the placebo group and the Rimonabant-5 mgr group ranged from 1.3 kgs[32] to 1.6 kgs[30].

Pooled weight outcomes at one year for Rimonabant 20 mgr are presented in tables 10 and 11.

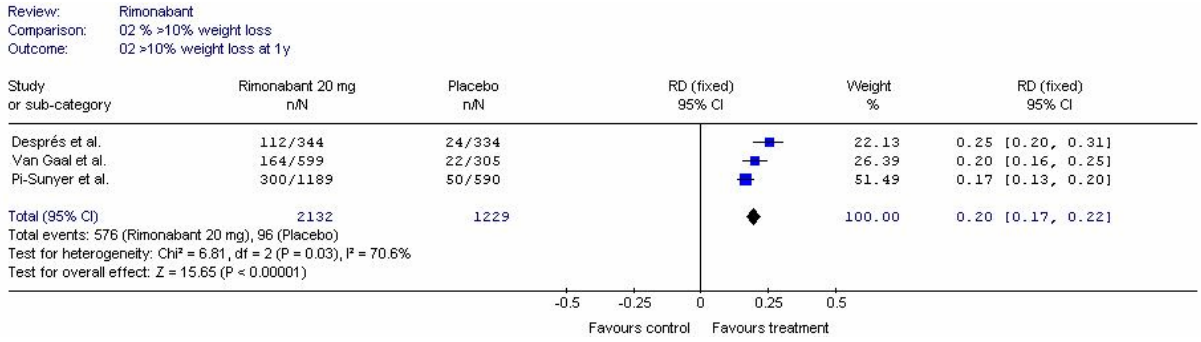
[6] When different methods of handling missing data are given, we present data computed using the last-observation-carried forward method, for reasons of comparability with results from other studies presented in this review.

Table 16. Rimonabant 20 mg + diet, against placebo + diet. Pooled estimate of weighted mean difference in weight at 1 year.



WMD: weighted mean difference

Table 17. Rimonabant 20 mg + diet, against placebo + diet. Probability to achieve 10% weight loss at one year.



RD: Risk Difference

Compared to placebo, 20% more patients achieved 10% weight loss at one year. This translates into a number-needed-to treat of 5 (95%CI: 4.5-5.9).

Outcomes **at 2 years** are shown in table 12.

Table 18. Rimonabant 5 and 20 mg + diet, against placebo + diet. Weight outcomes at 2 years[32]

	Rimonabant 5mg N=302	**Rimonabant 20 mg N=333**	**Placebo N=299**
Mean difference with placebo, kgs * (least-square mean)	-0.8 (p=0.02)	-3.6 (p<0.01)	reference-
% > 10% weight loss	na	17%	8%

The number-needed-to-treat to achieve and maintain 10% weight loss at 2 years with Rimonabant-20 mgr is 11 (95% CI: 7-25). Clinicians have to initiate treatment with Rimonabant-20 mgr for 11 patients, for one of these patients to achieve and maintain 10% weight loss after 2 year treatment, over the effects provided by placebo.

3.5.3.2 Weight loss when treatment is withdrawn

There was no difference in weight at the end of the second year between, on the one hand, patients who had taken Rimonabant 20 mg for one year, and then were randomized to placebo for the second year, and on the other hand, those patients who had taken placebo for 2 years. In other words, all the weight lost during one year treatment with Rimonabant 20mg, had been regained less than one year after the treatment was stopped.

3.5.4 Secondary outcomes

3.5.4.1 At one year

Data given in the 3 studies on LDL levels did not permit a meta-analysis, but all studies reported that changes in LDL levels were not statistically different between placebo and treatment groups.

There were no difference between outcomes in the Rimonabant-5mg group, and outcomes in the placebo group.

Selected pooled outcomes at one year for Rimonabant 20 mgr are presented in tables 13 to 16.

Table 19. Rimonabant 20 mg + diet, against placebo + diet.
One year outcomes
Ratio total cholesterol / HDL cholesterol. Placebo-subtracted change from baseline.

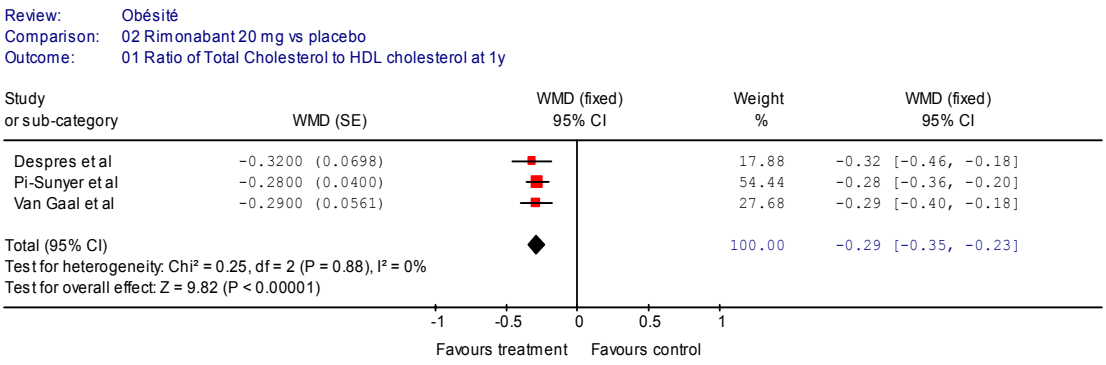
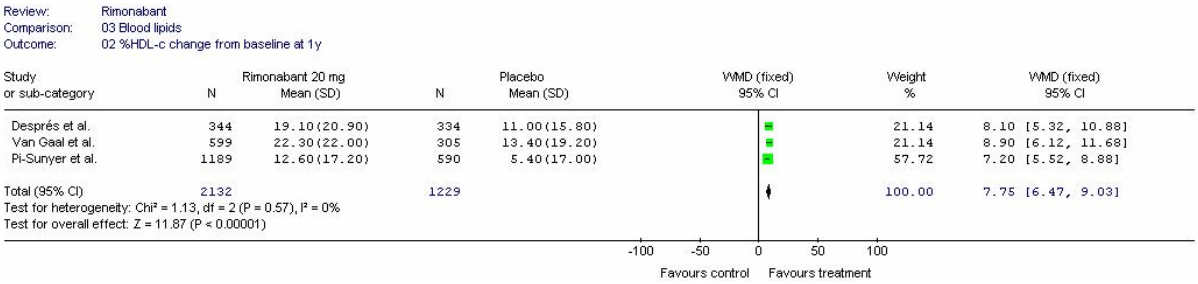


Table 20. Rimonabant 20 mg + diet, against placebo + diet.
One year outcomes.
HDL-cholesterol: change from baseline (%).



All studies noted that the effect of Rimonabant 20 mgr on reduction in HDL cholesterol appears to be partly independent of weight loss.

Table 21. Rimonabant 20 mg + diet, against placebo + diet.
One-year outcomes.
Fasting glucose. Placebo-subtracted change from baseline (mmol/l)

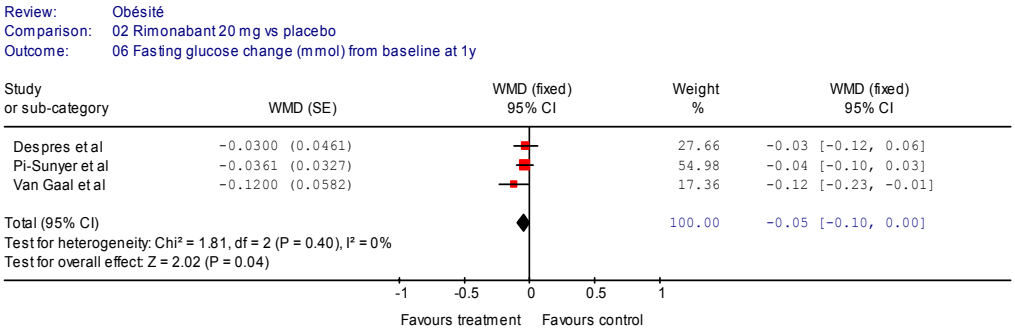
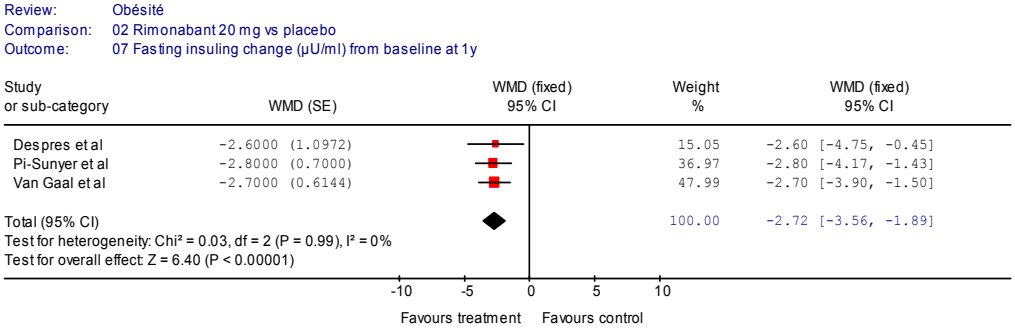


Table 22. . Rimonabant 20 mg + diet, against placebo + diet.
One year outcomes
Fasting Insulin. Placebo-subtracted change from baseline (µU/ml)



3.5.4.2 At two years

Table 23. Rimonabant 5 mg or 20 mg + diet, against placebo + diet. Selected metabolic outcomes at 2 years. Placebo-subtracted changes. From Pi-Sunyer study[32].

	Rimonabant 5 mgr	Rimonabant 20 mgr
Ratio total cholesterol to HDL cholesterol HDL cholesterol*	- 0.08 (p=0.05)	- 0.22 (p< 0.01)
Fasting glucose, mg/dl*	- 0.30 (p=0.66)	-0.82 (p=0.23)
Fasting insulin, µlU/mL*	- 1.7 (p=0.01)	-2.8 (p< 0.001)
Diastolic blood pressure, mmHg*	+ 0.7 (p=0.10)	+0.1 (p = 0.86)

* least squares mean difference

3.5.5 Adverse events

A meta-analysis of the 3 studies shows that there were slightly more serious adverse events in the Rimonabant 20 gr group, compared with the placebo group, but the difference was not statistically significant (pooled risk difference: 1 %, 95% CI: 0%-3%).

However more patients in the Rimonabant-20 mgr experienced adverse events leading to discontinuation (pooled risk difference: 6% , 95% CI 4%-8%), psychiatric and gastro-intestinal disorders seem more frequent reasons for discontinuation in the Rimonabant-20mg group than in the placebo group.

Details of meta-analysis of adverse events can be found in annex.

3.6 DISCUSSION

In placebo-controlled trials of at least one-year duration, Orlistat(3*120mg/d), Sibutramine (10-15 mg/d) and Rimonabant (20 mg/d) combined with diet, are more effective than diet alone (with placebo), in achieving weight loss in obese patients.

The overall effect is modest, and shows high heterogeneity. The mean difference in weight between the treatment and placebo group after 2-year treatment is 3.2 kgs for Orlistat and 3.6 kgs for Rimonabant 20 mgr (3.4 kgs for Sibutramine after 18 months). Improvements in metabolic risk factors are also modest. However, means reported in trials and meta-analyses fail to reveal 'the potentially complex mixture of substantial benefits for some, little benefit for many and harm for a few[33]'.

Large individual variations in weight loss are common in weight-loss drug trials. The number-needed-to treat (NNT) to achieve and maintain 10% weight loss 2 years after starting treatment is 9 (95% CI: 6-17) for Orlistat and 11 (95% CI: 7-25) for Rimonabant 20 mg (10 for Sibutramine at 18 months). These NNT seem high considering that they apply to an intermediary objective of medical treatment rather than to a hard endpoint.

Only limited research is available on predictors of response to drug-related weight loss or weight maintenance, and to our knowledge it is limited to Sibutramine. Early weight loss appears to be associated with better outcomes at endpoints, but its explanatory power as an independent variable in multivariate analysis is weak[20]. A positive correlation between weight maintenance and initial weight loss is likely to reflect better compliance with the treatment[20] rather than better physiological response to the drug.

The effect is not sustained. Weight lost with the help of these drugs is entirely regained in the year following the interruption of treatment.

Virtually all studies are industry-sponsored and tend to emphasize small benefits of their products. In the absence of direct evidence of a reduction in cardio-vascular morbidity, and overall mortality from weight loss drugs, several questions arise, such as: (1) what is the clinical significance of modest differences in weight and metabolic risk factors? (2) should long-term pharmacotherapy of obesity be seen as a treatment similar to the treatment of other chronic diseases? (3) what is the effectiveness of non-pharmacological interventions for weight loss, compared with pharmacological interventions?

3.6.1 Health benefits of modest weight loss

Modest weight loss (in the range of 10% of initial body weight) seems to result in significant health benefits[34, 35]. Risk factors such as hypertension, glucose tolerance, or lipid profile can improve quickly (for instance after one year treatment), but it is assumed that benefits in terms of reduced morbidity or mortality in the longer term relate to this weight loss being sustained overtime. Given that weight loss is rarely sustained after weight-loss drugs are withdrawn, the real question therefore relates to the duration of treatment. Some argue 'that sustained weight loss and associated favourable changes in cardiometabolic risk factors require continuous long-term treatment as seen in other chronic disorders, such as diabetes and hypertension in which treatment is effective only for as long as patients are receiving therapy'[32].

3.6.2 Can long-term pharmacotherapy of obesity be compared to the treatment of other chronic diseases?

A fundamental difference between pharmacotherapy of obesity and pharmacotherapy for other chronic conditions is that there are both medical and non-medical reasons to lose weight. In the US, 30% of patients taking prescription-only weight loss medications in 1998 reported a BMI of less than 30[36]. Patients without hypertension would not take anti-hypertensive treatment.

Weight-loss drugs being taken both for medical and non-medical reasons, their potential market is huge – probably among the largest markets for prescription drugs. In these conditions, safety becomes an even more crucial issue, because even rare adverse events, and/or adverse events associated with a low risk can translate into an important number of cases. Unusual complications, or those that occur only with long-term use, or in combination with other medications, might become apparent only when the drug is used in large populations for an extended time. Weight-loss drugs fenfluramine or dexfenfluramine, had been widely used before the adverse effect of pulmonary hypertension led to their withdrawal from the market[37].

The ultimate, medical goal of weight-loss drugs is not weight loss but relates to associated co-morbidities. Promoting weight-loss drugs for 'continuous long-term treatment as seen in other chronic disorders' requires strong evidence on their long-term safety, and effectiveness on *hard end-points* such as cardio-vascular morbidity and mortality – evidence of the kind that *is* required for drugs used for 'long-term treatment of chronic disorders' such as diabetes, hypertension, or dyslipidemia. This evidence does not yet exist for weight-loss drugs.

Finally, it might be even more difficult to achieve adherence to a chronic treatment with weight-loss drugs, than it is to achieve adherence to treatment for other chronic diseases. Rates of follow-up are much lower in RCTs evaluating weight loss drugs (40 to 50%) than in RCTs evaluating other drugs for chronic diseases. For instance the large ALLHAT trial, testing anti-hypertensive and lipid-lowering treatment, achieved an impressive 99% of expected years of follow-up, with patients followed for 4 to 8 years[38]. Adherence observed in day-to-day practice can only be lower than adherence observed in controlled conditions such as RCTs.

3.6.3 What is the effectiveness of non-pharmacological vs pharmacological treatment for weight loss?

A striking feature in the studies reviewed is the poor performance of the placebo group – that is of the diet or lifestyle intervention. This might contribute to the feeling that non-pharmacological interventions are not effective. However lifestyle modification interventions are – or can be effective. For instance, large randomized controlled trials have also demonstrated the feasibility and effectiveness of long-term lifestyle interventions to prevent the onset of type 2 diabetes in obese patients with impaired glucose tolerance[39, 40].

The authors of 2 Cochrane reviews[1, 8] conclude that weight-loss pharmacotherapy in persons with diabetes appears no more efficacious than behavioural therapy at 1 year.

3.7 CONCLUSIONS AND KEY POINTS

- In clinical trials of at least 1 year duration, Orlistat (3*120mgr) , Sibutramine (10 or 15 mgr) , and Rimonabant 20mg + diet are more effective than placebo+diet in achieving, and maintaining weight loss and improving some metabolic outcomes and risk markers/factors.
- The mean effects are modest, but mean measures conceal large variation in individual responses. Clinicians would have to initiate treatment for 9 patients (Orlistat), or 11 patients (Rimonabant 20 mgr) for one of these patients to achieve and maintain 10% weight loss after 2 years treatment, over the effect provided by placebo (corresponding number-needed-to-treat for Sibutramine at 18 months is 10).
- Before promoting weight-loss drugs for continuous long-term treatment of obesity, strong evidence is required on their long-term safety, and effectiveness on hard end-points such as cardio-vascular morbidity and mortality. Evidence of the kind that is required for any other drug promoted for the treatment of chronic disorders such as hypertension, or diabetes, is currently lacking for weight-loss drugs.
- Weight is entirely regained in the year following withdrawal of the weight-loss drug
- The current body of knowledge does not support the superiority of weight-loss drugs, as compared to effective lifestyle interventions, in the prevention of diabetes in patients with impaired glucose tolerance, or in weight loss among patient with diabetes.
- The evidence available does not support a decision to have weight-loss drugs refunded by the social security in Belgium.

3.8 REFERENCES

1. Padwal R, Li SK, Lau DCW. Long-term pharmacotherapy for obesity and overweight. Cochrane Database Syst Rev. 2003(4):CD004094.
2. Arterburn DE, Crane PK, Veenstra DL. The efficacy and safety of sibutramine for weight loss: a systematic review. Arch Intern Med. 2004;164(9):994-1003.
3. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess. 2004;8(21):iii-iv, 1-182.
4. Shekelle P, Morton S, MA M, Suttorp M, Tu W, Li S, et al. Pharmacological and Surgical Treatment of Obesity. Southern California-RAND Evidenced-Based Practice Center; 2004. Agency for Healthcare Research and Quality Evidence Reports (Evidence Report/Technology Assessment No. 103. AHRQ Publication No. 04-E028-2) Available from: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat1a.chapter.19289
5. Ioannides-Demos LL, Proietto J, McNeil JJ. Pharmacotherapy for obesity. Drugs. 2005;65(10):1391-418.
6. Li Z, Maglione M, Tu W, Mojica W, Arterburn D, Shugarman LR, et al. Meta-analysis: pharmacologic treatment of obesity. Ann Intern Med. 2005;142(7):532-46.
7. Sidhaye A, Cheskin LJ. Pharmacologic treatment of obesity. Adv Psychosom Med. 2006;27:42-52.
8. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Kim C, et al. Efficacy of pharmacotherapy for weight loss in adults with type 2 diabetes mellitus: a meta-analysis. Arch Intern Med. 2004;164(13):1395-404.
9. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2005(1):CD004096.
10. James WP, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. Lancet. 2000;356(9248):2119-25.
11. Mathus-Vliegen EMH, Balance Study G. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study. European Journal of Clinical Nutrition. 2005;59(1).
12. Wadden TA, Berkowitz RI, Womble LG, Sarwer DB, Phelan S, Cato RK, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity.[see comment]. New England Journal of Medicine. 2005;353(20):2111-20.
13. McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. Arch Intern Med. 2000;160(14):2185-91.
14. McMahon FG, Weinstein SP, Rowe E, Ernst KR, Johnson F, Fujioka K, et al. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. J Hum Hypertens. 2002;16(1):5-11.
15. McNulty SJ, Ur E, Williams G, Multicenter Sibutramine Study G. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. Diabetes Care. 2003;26(1):125-31.
16. Apfelbaum M, Vague P, Ziegler O, Hanotin C, Thomas F, Leutenegger E. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. Am J Med. 1999;106(2):179-84.
17. Kaukua JK, Pekkarinen TA, Rissanen AM. Health-related quality of life in a randomised placebo-controlled trial of sibutramine in obese patients with type II diabetes. International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity. 2004;28(4):600-5.
18. Poobalan A, Aucott L, Smith WCS, Avenell A, Jung R, Broom J, et al. Effects of weight loss in overweight/obese individuals and long-term lipid outcomes--a systematic review. Obesity Reviews. 2004;5(1):43-50.
19. Hansen D, Astrup A, Toubro S, Finer N, Kopelman P, Hilsted J, et al. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity. Results from the European multi-centre STORM trial. Sibutramine Trial of Obesity Reduction and Maintenance. Int J Obes Relat Metab Disord. 2001;25(4):496-501.
20. van Baak MA, van Mil E, Astrup AV, Finer N, Van Gaal LF, Hilsted J, et al. Leisure-time activity is an important determinant of long-term weight maintenance after weight loss in the Sibutramine Trial on

Obesity Reduction and Maintenance (STORM trial). American Journal of Clinical Nutrition. 2003;78(2):209-14.

21. Finer N, Ryan DH, Renz CL, Hewkin AC. Prediction of response to sibutramine therapy in obese non-diabetic and diabetic patients. Diabetes Obes Metab. 2006;8(2):206-13.
22. Wing RR, Hill JO. Successful weight loss maintenance. Annu Rev Nutr. 2001;21:323-41.
23. Sjostrom L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, et al. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. Lancet. 1998;352(9123):167-72.
24. Davidson MH, Hauptman J, DiGirolamo M, Foreyt JP, Halsted CH, Heber D, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized controlled trial. JAMA. 1999;281(3):235-42.
25. Hauptman J, Lucas C, Boldrin MN, Collins H, Segal KR. Orlistat in the long-term treatment of obesity in primary care settings. Arch Fam Med. 2000;9(2):160-7.
26. Rossner S, Sjostrom L, Noack R, Meinders AE, Noseda G. Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. European Orlistat Obesity Study Group. Obes Res. 2000;8(1):49-61.
27. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care. 2004;27(1):155-61.
28. Derosa G, Cicero AFG, Murdolo G, Ciccarelli L, Fogari R. Comparison of metabolic effects of orlistat and sibutramine treatment in Type 2 diabetic obese patients. Diabetes, Nutrition & Metabolism - Clinical & Experimental. 2004;17(4):222-9.
29. Derosa G, Cicero AFG, Murdolo G, Piccinni MN, Fogari E, Bertone G, et al. Efficacy and safety comparative evaluation of orlistat and sibutramine treatment in hypertensive obese patients. Diabetes, Obesity & Metabolism. 2005;7(1):47-55.
30. Despres J-P, Golay A, Sjostrom L, the Rimonabant in Obesity-Lipids Study Group. Effects of Rimonabant on Metabolic Risk Factors in Overweight Patients with Dyslipidemia. N Engl J Med. 2005;353(20):2121-34.
31. Van Gaal LF, Rissanen AM, Scheen AJ, Ziegler O, Rossner S. Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet. 2005;365(9468):1389-97.
32. Pi-Sunyer FX, Aronne LJ, Heshmati HM, Devin J, Rosenstock J, for the RIO-North America Study Group. Effect of Rimonabant, a Cannabinoid-1 Receptor Blocker, on Weight and Cardiometabolic Risk Factors in Overweight or Obese Patients: RIO-North America: A Randomized Controlled Trial. JAMA. 2006;295(7):761-75.
33. Kravitz RL, Duan N, Braslow J. Evidence-Based Medicine, Heterogeneity of Treatment Effects, and the Trouble with Averages. The Milbank Quarterly. 2004;82(4):661-87.
34. Goldstein DJ. Beneficial health effects of modest weight loss. Int J Obes Relat Metab Disord. 1992;16(6):397-415.
35. Van Gaal LF, Wauters MA, De Leeuw IH. The beneficial effects of modest weight loss on cardiovascular risk factors. Int J Obes Relat Metab Disord. 1997;21 Suppl 1:S5-9.
36. Blanck HM, Khan LK, Serdula MK. Prescription weight loss pill use among Americans: patterns of pill use and lessons learned from the fen-phen market withdrawal. Prev Med. 2004;39(6):1243-8.
37. Yanovski SZ. Pharmacotherapy for obesity--promise and uncertainty. N Engl J Med. 2005;353(20):2187-9.
38. Allhat Officers, Coordinators for the ACRGTA, Lipid-Lowering Treatment to Prevent Heart Attack T. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002;288(23):2981-97.
39. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344(18):1343-50.
40. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.

4 COST-EFFECTIVENESS OF PHARMACOLOGICAL TREATMENT

4.1 INTRODUCTION

To assess the cost-effectiveness of pharmacological treatments, we performed a systematic review of full economic evaluations. We defined the term "full economic evaluation" as an analysis that compares both costs and outcomes of at least two health care programmes (definition Drummond et al.[1]).

Two types of full economic evaluations were found: cost-effectiveness analyses and cost-utility analyses.

A cost-effectiveness analysis compares the costs and the principal outcome of different interventions. Outcomes can be defined in terms of a final endpoint such as life years gained or intermediary outcomes such as weight loss. In our analysis, we used the term of cost-efficacy analysis instead of cost-effectiveness analysis if the outcome data were based on the results of clinical trials (efficacy) and not on outcomes in daily practice (effectiveness).

A cost-utility analysis compares the costs of different interventions and the outcomes in terms of quality-adjusted life years (QALYs). Thus, this kind of analysis takes both morbidity and the mortality into account.

4.2 METHODS

4.2.1 Search strategy

Studies were sought from three sources :

- A search via "Ovid" on the following bibliographic databases: MEDLINE (1966-2006), ACP journal club (1991-2006), CINAHL (1982-2006), British Nursing Index (BNI) (1985-2006), Cochrane Library and Database of Abstracts of Reviews of effects (DARE)
- A search via the Centre for Reviews and Dissemination (CRD) on the following databases: NHS Economic Evaluation Database (NHS EED) and Health Technology Assessment (HTA) database.
- Identification of studies from the bibliography of selected studies.

The keywords used were "therapy" or "treatment" or "pharmaco*" or "medical" or "sibutramine" or "orlistat" or "rimonabant" in combination with "obes*" and with "cost" or "economic" (See Appendix).

4.2.2 Inclusion and exclusion criteria

The search was limited to papers published between January 1995 and January 2006 and written in English, Dutch or French. A first selection was based on abstracts. Only full economic evaluations which assessed a cost-effectiveness or cost-utility ratio were retained as appropriate study designs. A single economist assessed all abstracts for relevance. Full papers were obtained and assessed for all potentially relevant studies.

4.2.3 Data extraction and quality assessment

Data were extracted using a structured data extraction form (See Appendix) and quality was assessed by a single economist using a standard quality assessment checklist for economic evaluations[1] (See Appendix). The quality of studies was discussed narratively.

4.2.4 Conversion in Euro 2004

Costs were transformed into 2004 prices for each country using Gross Domestic Product (GDP) deflator. Then we applied the Purchasing Power Parities (PPP) index to obtain comparable costs in Euro among the different countries. The PPP used correspond to 2004 Euro for the 25 member states of the European Union.

4.3 RESULTS

One study[2] was not a full economic evaluation and was thus excluded from the analysis. In total, thirteen studies were eligible for inclusion in the review: nine original economic evaluations[3-11] and four reviews of economic evaluations[12-15].

4.3.1 Original economic evaluations

Among the nine original economic evaluations, three studies were cost-efficacy analyses[4, 5, 10] and six were cost-utility analyses[3, 6-9, 11]. Their quality was assessed following the quality assessment checklist and is described in Appendix. Key data extraction for each selected economic evaluation is provided in Appendix.

Orlistat was assessed in seven full economic evaluations [3-5, 7-9, 11] and Sibutramine in two full economic evaluations[6, 10].

Table 24. Economic evaluations and systematic reviews

Type of study	Type of intervention	
	Orlistat	Sibutramine
Systematic review of economic evaluations	O'Meara 2001[12], Avenell 2004[14] , Curran 2004[15]	O'Meara 2002[13], Avenell 2004[14]
Cost-efficacy analysis	Lamotte 2002[4] , Maetzel 2003[5]	Malone 2005[10]
Cost-utility analysis	Foxcroft 2000[3], Foxcroft 2005[7], Hertzman 2005[8], Lacey 2005[9] , Ruof 2005[11]	Warren 2004[6]

4.3.1.1 Cost-efficacy analysis

Orlistat

Lamotte *et al.*[4] assessed the cost-efficacy of orlistat for obese patients with type 2 diabetes and without micro- or macrovascular complications. The orlistat treatment was associated with diet and was compared with diet alone. Four patient subgroups were analysed : patients with hypercholesterolaemia, patients with arterial hypertension, patients with both complications and patients with no other complications. They used a Markov model to estimate the incremental cost-effectiveness ratio for a 10-year period. They assumed that weight was fully regained five years after termination of orlistat treatment, so seven years after the beginning of the study. As results, orlistat was shown to improve the life expectancy and this particularly for patients with both hypercholesterolaemia and arterial hypertension. The incremental costs were similar between subgroups (from €1,588 to €1,759) and the incremental cost per life-year gained ranged between €20,956 for patients with no other complications and €3,630 for patients with hypercholesterolaemia and arterial hypertension. A sensitivity analysis was performed and the highest cost per life-year gained was €29,531. Maetzel *et al.*[5] also assessed the cost-efficacy of orlistat for obese patients with type 2 diabetes and without micro- or macrovascular complications. The orlistat treatment was associated with lifestyle modifications (diet and exercises) and was compared with lifestyle modifications alone. They used a Markov model to estimate the incremental cost-effectiveness ratio for a 11-year period and assumed that weight was fully regained 3 years after termination of orlistat treatment, i.e. 4 years after the start of the study. As results, the life expectancy was a little improved with orlistat and this at an additional cost of €1,019 per patients. The incremental cost per life-year gained was €7,562. A sensitivity

analysis was performed and most results fell below a ratio of €20,000 per life-year gained, except for a change in the assumption of weight sustainability.

None of these two studies specified the cost items included in the cost calculation. Moreover, they are based on the life expectancy without assessing the quality of life.

Sensitivity analyses showed that results strongly depend on the assumption of weight sustainability after the treatment, which was, as exposed in the previous chapter, rather optimistic for pharmacological treatments of obesity in the baseline scenario.

Sibutramine

Malone *et al.*[10] investigated the cost-efficacy of sibutramine for obese patients with a BMI over 30 kg/m or a BMI of 27-29,9 kg/m with one or more obesity-related morbidities and this for a one year period. They compared a group of patients following a sibutramine treatment and a weight management programme with a group of patient following the same weight management programme but without sibutramine treatment. Patients were not blinded. They assessed direct health care costs associated with obesity.

As results, total heath care expenditure, obesity-related health care expenditure, the weight loss and the percent of weight loss were significantly higher in the sibutramine group, which results in an incremental cost-effectiveness ratio of €86 per additional percent of weight loss and of €38 per additional pound of weight loss.

The study period was too short to correctly assess the long term cost-effectiveness of sibutramine and no final outcome parameters were included in the analysis. The latter is a major weakness as the meaning of a cost per percentage of weight loss is unclear. The relative importance of percentage of weight loss can only be assessed in relationship to its consequences on final outcome parameters.

Table 24. Cost-efficacy analysis

Authors	Intervention (population)	Time frame of CEA*	Incremental efficacy		Incremental costs		Incremental cost-efficacy
			Type	Results	Type	Results**	Results**
Lamotte[4]	Orlistat + diet vs diet during 2 years (Diabetic patients)	10 years	Life-years gained		Costs (items not specified)		
Diabetic patients with no other complications				0.08		€1,686	€20,956/LY
Diabetic patients with hyper- cholesterolaemia				0.204		€1,588	€7,767/LY
Diabetic patients with AHT				0.227		€1,759	€7,747/LY
Diabetic patients with both complications				0.474		€1,721	€3,630/LY
Maetzel[5]	Orlistat + ATG care vs ATG care during 1 year (Diabetic patients)	11 years	Life-years gained	0.13	Costs (items not specified)	€1,019	€7,562/LY
Malone[10]	Sibutramine + WMP vs WMP alone during 1 year (obese patients or overweight patients with co-morbidity)	1 year	Weight loss (pound)	8.7 (p<0.01)	Obesity-related direct health care costs	€322 (p<0.01)	€38/pound WL
			% of weight loss	3.8 (p<0.01)			€86/%WL

* CEA: Cost-efficacy analysis
**Sources : GDP deflator : World Bank / PPP : Eur25 = 1 for 2004 (Eurostat)
AHT = Hypertension
ATG = Adherence to guideline
WMP = Weight management program

4.3.1.2 Cost-utility analysis

Orlistat

Foxcroft performed two studies on the cost-utility of orlistat for patients with a body mass index over 30 kg/m or over 28 kg/m with associated risk factors and who have already responded to a weight reducing regimen (weight loss of at least 2,5 kg within 4 weeks before orlistat treatment). The first study[3] was based on the EMEA (European agency for the evaluation of medicinal products) guidance, i.e. orlistat was stopped for patients who had not lost at least 5% of their weight at 3 months. The orlistat treatment was associated with diet and was compared with a placebo combined with diet. Only direct health care costs were assessed.

As results, the direct average cost for a 2-year treatment was €1,120 per patient and the number of quality-adjusted life-years gained after 2 years was 0.016 per patient. The cost per additional quality-adjusted life-year was €70,014.

In their second study[7], two different guidances were compared: the EMEA and the NICE guidance. The NICE guidance stipulates that orlistat treatment is stopped for patients who have not lost at least 5% of their weight at 3 months and at least 10% of their weight at 6 months. The orlistat treatment was associated with diet and was compared with a placebo combined with diet. Only direct health care costs were assessed.

As results, the direct average cost for a 1-year treatment was €324 per patient following the NICE criteria and €397 per patient following the EMEA criteria. The number of quality-adjusted life-years gained after one year were 0.00931 per patient following the NICE criteria and 0.01464 per patient following the EMEA criteria. The incremental cost per additional quality-adjusted life-year was thus lower in case of the EMEA guidance.

Hertzman et al.[8] assessed the cost-utility of orlistat for a 10-year period for patients with a body mass index over 30 kg/m , without diagnosed diabetes and who have already responded to a weight reducing regimen (weight loss of at least 2,5 kg within 4 weeks before orlistat treatment). The orlistat treatment was associated with diet and was compared with a placebo combined with diet. Like in the EMEA guidelines, orlistat was stopped for patients who had not lost at least 5% of their weight at 3 months. Otherwise orlistat was taking for a one year period. In their model, they assumed a period of weight sustainability of 3 years after orlistat treatment. Temporary weight loss was assumed to reduce the risk of developing diabetes and thus the expected cost of treating and controlling patients with diabetes. Only direct health care costs were assessed.

As results, the total incremental cost per patient and the incremental number of QALY gained per patient were slightly superior in the orlistat group. The incremental cost per quality-adjusted life-year gained was €11,198. Once again, the sensitivity analysis showed the important impact of the weight sustainability assumption on results.

Lacey et al.[9] performed a study similar to the study of Hertzman *et al*[8] but for a 11-year period. They also followed the EMEA guidance in their evaluation and assumed a period of weight sustainability of 3 years after orlistat treatment. Moreover, they assumed that a 10% reduction in BMI reduces the annual incidence of diabetes by 30% and that in the control group, diabetes-related savings were null. Results were similar to those of the study described above.

Ruof et al.[11] were interested in the cost-utility of orlistat over an 11-year period for overweight and obese patients with type 2 diabetes and without diabetes-related complications. Orlistat was associated with an antidiabetic drug and a weight loss programme and was compared with an antidiabetic drug and a weight loss programme alone. Once again, orlistat was stopped for patients who did not lose at least 5% of their weight at 3 months. In the cost input, they included the medication cost but also the diabetes-related complication cost, which was assumed to be reduced by the treatment-related effect on HbA1C level. This effect was assumed to be lost 3 years after treatment.

They assessed their results in two different countries: Sweden and Switzerland. The incremental cost per QALY ratios were €12,622/QALY and €10,773/QALY respectively.

Sibutramine

Warren *et al.*[6] assessed the cost-utility of sibutramine over a 5-year period for patients with a body mass index between 27 to 40 kg/m and without obesity related morbidity. At the beginning of the study, 10 mg of Sibutramine was given. Patients were assessed at 1 and 3 months. At 1 month, patients who had not lost at least 2% of their weight were considered as non responder patients. At 3 months, patients who had not lost at least 5% of their weight were also considered as non-responders. To non-responders, 15 mg of sibutramine was given and after 3 new consecutive months, treatment was stopped for patients who had not loset at least 5 % of their weight. The sibutramine treatment was associated with lifestyle modifications and was compared with lifestyle modifications alone. Cost input included drug costs, patient monitoring and savings associated with avoided coronary heart disease (CHD) and diabetes events. Other obesity-related complications were not assessed.

Results of two different countries were compared : United Kingdom and United States. The incremental cost per patient after 5 years was €458 in the US model and €425 in the UK model. The number of QALYs gained were similar in the two countries (0.05291 in the US model and 0.05895 in the UK model). The incremental cost per QALY was €8,648 in the US model and €7,198 in the UK model. Variations between the two models resulted from different discount rates and different monitoring schedules assumptions.

The models were based on a lot of assumptions and the benefits of sibutramine on cardiovascular heart disease and on diabetes should be based on the results of clinical trials rather than estimated using the model.

Table 25. Cost-utility analysis

Authors	Intervention (population)	Timeframe of the CUA*	Incremental utility		Incremental costs		Incremental cost-utility
			Type	Results**	Type	Results**	
Foxcroft 2000[3]	Orlistat + diet vs placebo + diet during 2 years (non responder criteria)	2 years	QALY	0.0160	Direct health care costs	€1,120	€70,014/QALY
Foxcroft 2005[7]	Orlistat + diet vs placebo + diet during 1 year (NICE or EMEA criteria)	1 year	QALY		Direct health care costs		
			NICE	0.00931	*NICE*	€324	€34,867/QALY
			EMEA	0.01464	*EMEA*	€397	€27,123/QALY
Hertzman[8]	Orlistat + diet vs placebo + diet during 1 year (EMEA criteria)	10 years	QALY	0.0304	Direct health care costs	€340	€11,198/QALY
Lacey[9]	Orlistat + diet vs placebo + diet during 1 year (EMEA criteria)	11 years	QALY	0.028	Direct health care costs	€420	€14,893/QALY
Ruof[11]	Orlistat + antidiabetic drug + WLP vs antidiabetic drug + WLP during 1 year (diabetic patients)	11 years	QALY	Not specified	Costs	Not specified	€12,622/QALY €10,773/QALY
Warren[6]	Sibutramine + diet and LSA vs placebo + diet and LSA during 1 year (5 years)	5 years	QALY		Direct health care costs		
			US model	0.05291	*US model*	€458	€8,648/QALY
			UK model	0.05895	*UK model*	€425	€7,198/QALY

* CUA: Cost-Utility Analysis
**Sources for conversion of national currency units to Euros for 2004: GDP deflator : World Bank / PPP : Eur25 = 1 for 2004 (Eurostat)
QALY = Quality-adjusted life-year
NICE = National Institute for Clinical Excellence
EMEA = European agency for the evaluation of medicinal products
WLP = Weight loss programme
LSA = Lifestyle advice
US = United States
UK = United Kingdom

4.3.2 Reviews of economic evaluations

Four reviews of economic evaluations were identified[12-15]). These systematic reviews were based on the economic evaluations described above or unpublished studies. Consequently, we will not further elaborate on this point.

Table 26. Review of economic evaluations

Authors	Years	Original economic evaluations included
O'Meara[12]	2001	Foxcroft[3], Roche data
O'Meara[13]	2002	BASF Pharma/Knoll
Avenell[14]	2004	O'Meara 2001[12], O'Meara 2002[13], Foxcroft[3], Lamotte[4], BASF Pharma/Knoll
Curran[15]	2004	Lamotte[4], Maetzel[5]

4.4 DISCUSSION

4.4.1 Orlistat

All the selected analyses have targeted the patients to treat and have concluded that drug treatment associated with diet or another lifestyle approach was a cost-effective alternative compared to diet or to another lifestyle approach alone.

These studies targeted the patients to show the economic advantage of reserving treatment to patients who already have lost at least 2.5 kg in one month thanks to lifestyle approaches and by stopping the treatment for patients who had not lost at least 5 kg after 3 months. This approach reduces the cost-effectiveness ratio, meaning that selective treatment is more cost-effective than treatment in all patients. The cost-effectiveness ratio is further decreased by treating only patients with diabetes or other obesity-related morbidities.

Studies with a longer timeframe (>10 years) had lower cost-utility ratios than short term studies (1 or 2 years).

However, we have major concerns regarding the validity of these studies.

Firstly, most studies had methodological weaknesses.

- Models were based on key assumptions that were not always conservative
    - Weight loss data were based on clinical trials with a follow-up of less than 2 years (1-year in most studies). To model the results on a long term period, economic evaluations assumed a weight sustainability between 3 to 5 years following the study. This assumption is not conservative because, as set out in the chapter on effectiveness of pharmacological treatments of this report, one study demonstrated that weight loss after one year with orlistat was entirely regained in the following year. As shown in the economic evaluations included in our review, results were highly sensitive to this assumption. With the assumption of weight regain after 1 year of stopping treatment, pharmacological treatment becomes much less attractive from an economic point of view.
    - Follow-up costs were also sometimes estimated using non-conservative assumptions. For example, in the study of Hertzman et al[8], the number of outpatient physician visits was assumed to be the same in the treatment and the control group, while it might be expected that follow-up will be more intensive and hence more costly in patients who are being treated.

- Studies did not compare all relevant alternatives (diet, exercise, behavioural therapy, prevention)
    - To be complete, an economic evaluation should assess all the possible alternatives, which was not the case in our selected economic evaluations. By taking into account only one alternative, known as being less effective, a bias in favour of the drug is introduced.
- Some cost items or outcomes were not included
    - The studies were often based on direct health care costs only and not on the total costs from the societal perspective.
    - Cost items included in the studies were not always specified and their accuracy could thus not be assessed.
    - Some outcomes in favour of the control group, like the loss of utility due to the treatment, were omitted.

Secondly, outcome data were often based on clinical trials (efficacy) and not on outcomes in daily practice (effectiveness). Results are thus expected to be different in real life. Patient compliance to the treatment and consequently also the effective weight loss could be lower in real life than in the clinical trials.

Thirdly, of the seven original economic evaluations on orlistat, only one study was not industry funded. Moreover, effectiveness data were generally based on clinical trials which were also industry funded. Recent studies[16-18] have highlighted the bias generated by this kind of sponsorship and showed that clinical trials and economic evaluations sponsored by the pharmaceutical industry were more likely to produce favourable results than studies funded by other sources.

Finally, only one study assessed Belgian costs[4]. The external validity of the other studies may thus be limited. Moreover, not enough studies were performed to make an evidenced-based conclusion.

4.4.2 Sibutramine

Only two economic evaluations assessed the cost-effectiveness ratio of sibutramine. The study of Malone *et al*[10] was based on a very short follow-up period (1 year). The study of Warren *et al*[6] concluded that, in a selected patient population, sibutramine was a cost-effective alternative to diet and life style for a five-year period.

However, even though these studies were based on more conservative assumptions, the same limitations than those described above apply.

In general, we conclude that the evidence base for cost-effectiveness of pharmacological treatment of obesity, be it by orlistat or sibutramine is rather weak. Relatively few studies have been performed, most of which are sponsored by the pharmaceutical industry.

Key points

According to the existing economic literature, the combination of drug treatment with diet or other lifestyle changes is a cost-effective treatment strategy for obesity compared to diet or to other lifestyle changes alone when patients are targeted.

Selective treatment in early responders or patients with obesity-related morbidity only increases the cost-effectiveness of pharmacological treatment of obesity.

The validity of the published studies may be questioned:

- Almost all studies were industry funded and were based on industry-funded clinical trials.
- All studies had methodological weaknesses (modelling assumptions were not conservative, the studies did not assess all possible alternatives and failed to include some cost or outcome items).
- Outcomes were based on efficacy data from clinical trials and not on effectiveness data from daily practice.
- Not enough studies was performed to make an evidenced-based conclusion

Due to these major weaknesses of the cost-effectiveness evaluations of pharmacological treatment for obesity, we cannot draw firm conclusions about the cost-effectiveness of this treatment strategy relative to other treatment modalities.

4.5 REFERENCES

1. Drummond M, Michael F. Methods for the economic evaluation of health care programmes. Oxford university press ed. Oxford: Oxford medical publications; 1990.
2. Rowe R, Cowx M, Poole C, McEwan P, Morgan C, Walker M. The effects of orlistat in patients with diabetes: improvement in glycaemic control and weight loss. Curr.Med.Res.Opin. 2005;21(11):1885-90.
3. Foxcroft DR, Milne R. Orlistat for the treatment of obesity: rapid review and cost-effectiveness model. Obes Rev. 2000;1(2):121-6.
4. Lamotte M, Annemans L, Lefever A, Nechelput M, Masure J. A health economic model to assess the long-term effects and cost-effectiveness of orlistat in obese type 2 diabetic patients. Diabetes Care. 2002;25(2):303-8.
5. Maetzel A, Ruof J, Covington M, Wolf A. Economic evaluation of orlistat in overweight and obese patients with type 2 diabetes mellitus. Pharmacoeconomics. 2003;21(7):501-12.
6. Warren E, Brennan A, Akehurst R. Cost-effectiveness of sibutramine in the treatment of obesity. Med Decis Making. 2004;24(1):9-19.
7. Foxcroft DR. Orlistat for the treatment of obesity: cost utility model. Obes.Rev. 2005;6(4):323-8.
8. Hertzman P. The cost effectiveness of orlistat in a 1-year weight-management programme for treating overweight and obese patients in Sweden : a treatment responder approach. Pharmacoeconomics. 2005;23(10):1007-20.
9. Lacey LA, Wolf A, O'shea D, Erny S, Ruof J. Cost-effectiveness of orlistat for the treatment of overweight and obese patients in Ireland. Int.J.Obes.(Lond). 2005;29(8):975-82.
10. Malone DC, Raebel MA, Porter JA, Lanty FA, Conner DA, Gay EC, et al. Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program. Journal of Managed Care Pharmacy. 2005;11(6):458-68.
11. Ruof J, Golay A, Berne C, Collin C, Lentz J, Maetzel A. Orlistat in responding obese type 2 diabetic patients: meta-analysis findings and cost-effectiveness as rationales for reimbursement in Sweden and Switzerland. Int.J.Obes.(Lond). 2005;29(5):517-23.
12. O'Meara S, Riemsma R, Shirran L, Mather L, ter RG. A rapid and systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity. Health Technol.Assess. 2001;5(18):1-81.
13. O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G. The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment. Health Technol Assess. 2002;6(6):1-97.
14. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess. 2004;8(21):iii-iv, 1-182.
15. Curran MP, Scott LJ. Orlistat: a review of its use in the management of patients with obesity. Drugs. 2004;64(24):2845-64.
16. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003;326(7400):1167-70.
17. Smith R. Medical journals are an extension of the marketing arm of pharmaceutical companies. PLoS Med. 2005;2(5):e138.
18. Bell CM, Urbach DR, Ray JG, Bayoumi A, Rosen AB, Greenberg D, et al. Bias in published cost effectiveness studies: systematic review. BMJ. 2006;332(7543):699-703.

5 SAFETY AND CLINICAL EFFECTIVENESS OF SURGICAL TREATMENT

5.1 BACKGROUND

Adapted from: Agency for Health Research and Quality (AHRQ) systematic review[1] and Blue Cross Blue Shield (BCBS) health technology assessment[2].

A variety of surgical procedures have been used to induce weight loss for obese patients. Procedures are classified according to the mechanisms achieving weight loss, as:

- *Restrictive procedures* : the size of the stomach is mechanically restricted thus limiting the quantity of food a patient can consume at a single meal. Main examples are adjustable gastric banding (AGB), and vertical banded gastroplasty (VBG).
- *Malabsorptive procedures*: a portion of the intestines is bypassed, thus decreasing the proportion of nutrients that are absorbed from a meal. An example is the jejuno-ileal bypass, probably the oldest surgical treatment of obesity, that has become completely obsolete.
- *Combined procedures* exert their effects by both a restrictive and a malabsorptive mechanism. These procedures include Roux-en-Y-Gastric Bypass - RYGB, and biliopancreatic diversion - BPD.

During the last several decades there has been a continued evolution in surgical techniques. Currently, laparoscopic adjustable gastric banding (LAGB) and open or laparoscopic RYGB (LRYGB) are the most commonly performed procedures worldwide, and VBG is only performed in a very small proportion of obese patients. Variations on gastric bypass (e.g., BPD, long-limb gastric bypass) are attempts to maximize weight loss in patients with super-obesity (BMI >50 kg/m2).

Care for bariatric surgery patients entails a comprehensive preoperative workup, close postoperative follow-up, and the involvement of services such as nutritional guidance and psychological support. Severe obesity is a chronic condition requiring lifelong treatment and follow-up: bariatric surgery is not a cure. Patients need to know that a commitment to permanent lifestyle changes following the operation is essential after surgery.

5.2 FOCUS AND METHODS OF THIS REVIEW

5.2.1 Research questions

This review tries to answer the following research questions :

- What is the effectiveness and safety of bariatric surgery (in general), in the treatment of severe obesity (BMI > 35, with co-morbidities; or BMI > = 40) compared with conservative treatment of obese patients?
- What is the effectiveness and safety of LAGB in the treatment of severe obesity, compared with older techniques, mainly RYGB

We focus mainly on LAGB and (L)RYGB, because these are the most frequently used in Belgium.

5.2.2 Methods

There has been in later years a large number of systematic reviews and/or health technology assessments evaluating bariatric surgery[3-5, 1, 6, 7], some specifically focusing on the relative efficacy and safety of Laparoscopic Gastric Banding procedure compared with other procedures[8-10, 2] – to mention only those published since 2004. These are the main source for this study, a description of those quoted here can be found in annex (research question, findings and conclusions).

5.3 OUTCOME MEASURES FOR BARIATRIC SURGERY

Given the variety of surgical procedures, comparisons of these outcomes between procedures are particularly important.

- Safety :
    1. Short term (30-days) and long-term (1 year) mortality
    2. Conversion from laparoscopic to open surgery (for laparoscopic procedures)
    3. Peri-operative and post-operative complications
    4. Re-operation rates
- Effectiveness
    1. Weight loss and maintenance
    2. Improvement in co-morbidities: hypertension, diabetes, sleep apnea,
    3. Quality-of-life (QoL)
    4. Nutritional status (assessment of malabsorption)
    5. Hard endpoints such as: incidence of cardio-vascular events, mortality from cardio-vascular causes, overall mortality

There are several outcome measures for weight loss.

Table 27 Different measures for weight loss and maintenance (Adapted from BCBS HTA[2]).

Measure	Definition	Comments
Decrease in weight	difference in weight, pre-and post treatment	intuitive, but the relationship to clinical outcomes is unclear, especially in morbidly obese.
Decrease in BMI	difference in BMI, pre-and post-treatment.	maybe clinically significant if change in BMI clearly leads to change in risk category
% Excess Weight Loss (EWL)	Amount of weight loss*100 / excess body weight	Most commonly used measure of weight loss in bariatric surgery. It bears some relationship with clinical significance; however threshold for this is unclear.
% patients losing > 50% of Excess Body Weight	Sometimes used as definition of e 'success' for surgery	threshold for clinical significance is arbitrary
% weight loss	(weight loss*100 / initial weight)	

EWL: excess weight loss. EBW excess body weight

Attempts are being made at standardising reporting for bariatric surgery, such as the Bariatric Analysis and Reporting System (BAROS)[11, 12] . BAROS is a scoring system incorporating excess weight loss, medical co-morbidities and quality-of-life. Points are subtracted for re-operations and defined complications. It is however very inconsistently used.

5.4 DESCRIPTION OF PROCEDURES

Adapted from AHRQ systematic review[1] and BCBS HTA[2]

5.4.1 Roux-en-Y Gastric Bypass (RYGB).

Reduction of the stomach to a small gastric pouch (30 cc) results in feelings of satiety following even small meals. This small pouch is connected to a segment of the jejunum, thus bypassing the duodenum and very proximal small intestine, and absorptive function is reduced. The "dumping syndrome," defined as abdominal symptoms and diarrhoea shortly after eating, is due to reduced transit time in the intestine, and patients must eat small meals to ameliorate these symptoms[10].

RYGB is a well established procedure and is considered in the United States as the 'reference' method, to which other, newer procedures (like laparoscopic adjustable gastric banding), should be compared[2].

Open gastric bypass is a major surgical procedure, with the risks expected with intra-peritoneal surgery. Adverse effects of gastric bypass also include complications specific to the procedure, such as leaks, obstruction at the anastomotic sites, dilatation of the pouch, staple line failure, etc. Due to the altered passage of food, patients are also at risk for a number of metabolic complications, including iron deficiency anemia, vitamin B12 deficiency, and hypocalcemia.

RYGB is now more and more performed laparoscopically (LRYGB). The mechanism by which weight loss is achieved is the same as for open RYGB, and weight loss and co-morbidity outcomes should be similar. However, different techniques can result in different types and rates of complications

Risk-adjusted in-hospital adverse outcome[13] as well as 30-days[14], are significantly lower when gastric bypass is performed by higher-volume surgeons.

Long-limb gastric bypass (LL-GBY) or distal gastric bypass, is identical to standard gastric bypass except for the length of the Roux limb. Creation of a longer Roux limb results in a greater portion of the small intestine being bypassed, thus increasing the degree of malabsorption.

5.4.2 Adjustable Gastric Banding (AGB):

The uppermost portion of the stomach is encircled by a band to create a gastric pouch with a capacity of approximately 15 to 30 cc. The band can be adjusted in the clinic by adding or removing saline via a reservoir port that is positioned beneath the skin. The size of the gastric outlet can be modified as needed, depending on the rate of a patient's weight loss. Gastric banding does not produce malabsorption. It is now almost always performed laparoscopically (LAGB). The device is expensive[7].

LAGB, unlike other bariatric procedures, involves no stapling of the stomach wall, no cutting or opening of the stomach, and no alteration of the gastrointestinal tract. It is clearly an easier laparoscopic procedure than the laparoscopic gastric bypass and it has the additional advantage of reversibility. Still LAGB is a difficult procedure that takes time and experience to carry out effectively. Many authors reported a steep learning curve effect, with markedly lower morbidities for the second 100 procedures performed[10]. Concern persists regarding the long-term efficacy of LAGB, and the long-term incidence of adverse events[10].

Short-term complications of gastric banding are expected to be low, but can occur. Possible longer-term complications include nausea and vomiting, especially if the band pressure is too high. Dilation of the pouch may occur, usually resulting in weight gain. Gastro-oesophageal reflux disease (GERD) may occur due to the increased pressure gradient introduced in the stomach. These complications may respond to adjustment of

[7] 1670 Euros excl VAT for the Swedish Band in Belgium (Source: Johnson and Johnson, personal communication). Less expensive brands are also on the market.

the band pressure. There may be slippage of the device, and over time, the device may erode through the gastric wall. Malnutrition and vitamin deficiencies may also occur as long term complications.

5.4.3 Vertical Banded Gastroplasty (VBG).

The upper part of the stomach is stapled to create a narrow gastric outlet or pouch that remains connected with the remainder of the stomach. A non-adjustable band is placed around this new inlet to prevent future enlargement of the stoma. As a result, patients experience a sense of fullness after eating small meals. Weight loss from this procedure results entirely from eating less: there is no component of malabsorption. VBG used to be one of the more common surgical procedures for weight loss because of its technical ease and low morbidity. It has been superseded since 1995 by LAGB and RYGB.

Short-term complications include those associated with upper abdominal surgery, (injuries to internal organs, or to the gastro-intestinal tract, bleeding, cardio-pulmonary complications, etc…); leaks or failure at the staple line and nausea/vomiting caused by the altered stomach physiology.

Long term complications can include persistent nausea/vomiting, gastro-oesophageal reflux disease (GERD), gastric obstructions, leaks or failure at the staple line, stenosis at the gastric outlet site, band slippage, band erosion, and dilatation of the stomach pouch. Malnutrition and vitamin deficiencies are also a long-term concern[10].

5.4.4 Biliopancreatic diversion (BPD)[8].

BPD, like RYGB, combines both the restrictive and malabsorptive strategies of obtaining weight loss. The stomach is partially resected, but the remaining capacity is generous compared to that achieved with the RYGB. As such, patients eat relatively normal-sized meals and do not need to restrict intake severely. The duodenum and jejunum) are bypassed, and substantial malabsorption occurs. This procedure is favoured by some bariatric surgery specialists. The partial biliopancreatic diversion with duodenal switch (DS) is a variant of the BPD procedure.

Short-term complications of BPD include those associated with upper abdominal surgery. Complications specific to the procedure can include gastric obstruction, leaks at the anastomotic sites, and nausea/vomiting caused by the altered stomach physiology. Anastomotic leaks are a serious complication that usually results in peritonitis and the need for an additional surgical procedure.

Long-term complications can include persistent nausea/vomiting, GERD, leaks or stenosis at the anastomotic sites, dilation of the stomach pouch. One of the most frequent complications is diarrhoea and foul smelling flatulence. This surgery is intended to cause a greater degree of malabsorption compared to gastric bypass, and the possibility of malnutrition and/or vitamin deficiencies are a greater concern.

[8] BPD has been developed by Scopinaro and is called after his name. Strictly speaking, it is a combined procedure because the stomach is partially resected, but its effects is mainly achieved through malabsorption. It can be done either as open or laparoscopic surgery. The duodenal switch modification usually includes a gastric sleeve resection (DS+GS). In Belgium BPD and DS+GS are less common than LAGB and RYGB. They are favoured by, and limited to, a few centres (Dr Hubens, personal communication).

5.5 EFFECTIVENESS OF SURGICAL TREATMENT OF OBESITY, COMPARED WITH NON-SURGICAL TREATMENT

5.5.1 Evidence available

Several systematic reviews have been published in 2005[2, 6, 7].

The AHRQ systematic review[1, 6] identified only 2 RCTs comparing surgical and non-surgical treatment. Both were conducted more than 20 years ago and assessed procedures that are not currently considered relevant (horizontal gastroplasty and jejuno-ileal bypass).

Most of the evidence for comparing surgical and non-surgical treatment comes from a large, prospective, non-randomized, intervention trial, the Swedish Obese Subjects (SOS) study[15-19]. In this study, surgically treated patients (BMI >=34 for men and >= 38 for women; most of whom were treated with vertical banded gastroplasty) were compared to a group of prospectively matched controls who underwent medical treatment. The SOS study is the only one that compares co-morbidities between surgically treated patients and a concurrent control group receiving non-surgical treatment; it is also the only one reporting on an extended follow-up (10 years) Although not randomized, this study provides the best available evidence to assess the effectiveness of bariatric surgery. However, one overall aim of this study was to address the apparent discrepancy between the effect of weight loss on risk factors, and hard endpoints (overall mortality and incidence of cardio-vasculaire events)[19], and no data have yet been published in that respect.

There are very few studies reporting on hard-endpoints. A retrospective cohort study compared overall long-term mortality between obese patients surgically treated at one hospital, and historically matched controls[20], but the information provided is insufficient to properly assess comparability of the groups. Another study used a state-wide hospital administrative discharge database to compare survival between surgically and non surgically treated obese patients[14].

Numerous case-series reporting on outcomes of bariatric surgery have also been published. However, the case series are limited by short follow-up and incomplete reporting of data that are crucial to an understanding of their validity. For instance fewer than half reported the proportion of original patients contributing data to the outcomes at follow-up[6]. Reporting on weight loss is usually better than reporting on complications, but different outcome measures make comparisons difficult.

The AHRQ meta-analysis compiled data from 147 studies[1]. Buchwald meta-analysis[4] involved compiling data from 134 studies, reporting on more than 10.000 patients (not all contributing to all outcomes).

5.5.2 Results

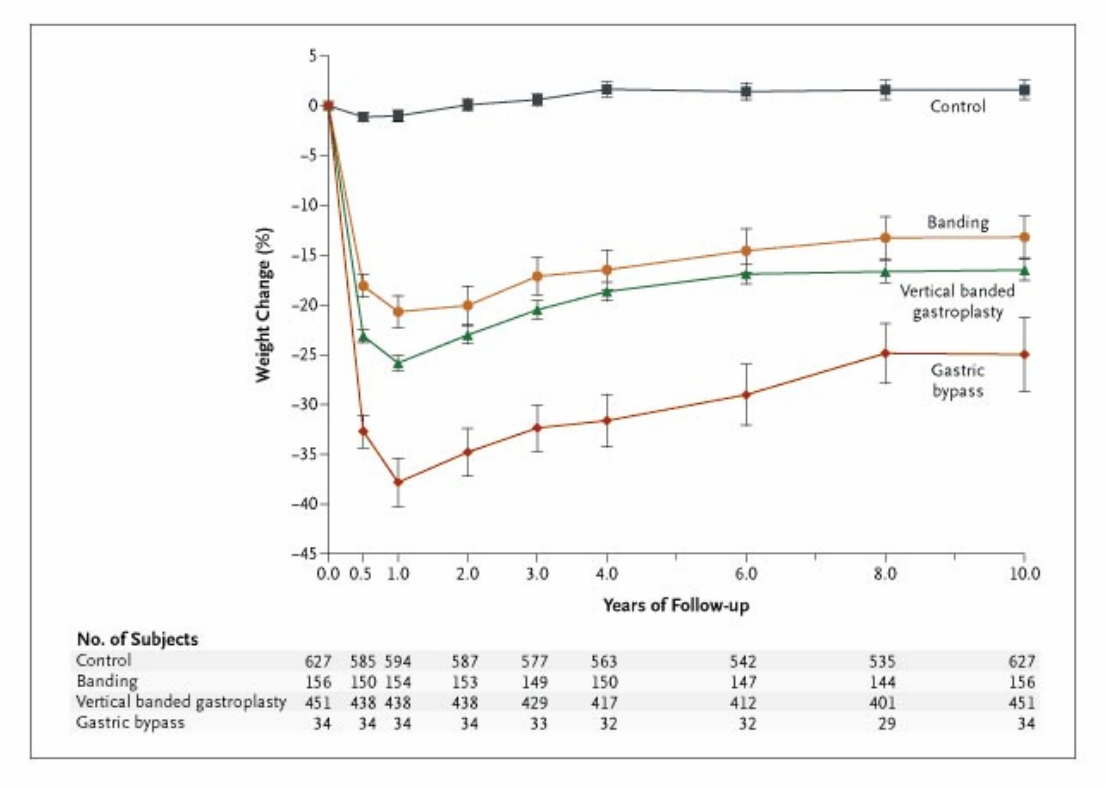
Adverse events will be analysed by procedures.

5.5.2.1 Weight loss

The average age of subjects enrolled in the SOS study was 47, about two-thirds were women, and average BMI at baseline was about 41. Procedures used were VBG (70%), RYGB (6%), and gastric banding (6%).

Weight loss in the surgically treated group was maximum 1 year after the intervention (mean=44 kgs) and there was gradual increase of weight thereafter. After 10 years[19], average weight loss was 20 kg (or 16 percent of body weight) for 641 surgically treated patients, compared with a slight increase in weight in the control group. (Loss to follow-up after 10 years was approximately 25% in each group).

Figure 1. Weight changes among subjects in the SOS study over a 10-year period[19],



In Buchwald meta-analysis[4], overall mean age of surgically treated patients was 39 years, 81% of them were women, and baseline BMI was 47 (range 32-69).

Table 28. Meta-analysis of weight outcomes of bariatric surgery, all procedures combined (from Buchwald [4])

	N patients evaluated (N treatment groups)	Weighted mean change (range of mean change)
Absolute weight loss, kg	7 588 (83)	- 40 (-70 to -9)
BMI decrease	8 232 (96)	-14 (-27 to -4)
Initial weight loss (%)	1 386 (9)	- 36% (-39% to -21%)
Excess weight loss (%)	10 172	- 65% (-93% to – 32%)

5.5.2.2 *Improvement or resolution of co-morbidities*

In the SOS study there was no statistically significant difference between the groups, ten years after surgery, as regards the incidence of hypercholesterolemia and hypertension. However surgically treated patients had a lower incidence of hypertriglyceridemia (OR 0.61, 95% CI 0.39-0.95), diabetes (OR : 0.25, 95% CI 0.17-0.38) ; and hyperuricemia (OR 0.49, 95% CI 0.34-0.71). Effect sizes after 10 years were smaller than those reported 2 years after surgery.

Additional reports from the SOS study support a substantial benefit of surgery in reducing sleep apnea, symptoms of dyspnea and chest pain[17] and improving quality of life[15]. The positive changes in quality of life after two years were related to the magnitude of weight loss, that is, the greater the weight reduction, the greater the health-related quakity of life improvements.

The AHRQ systematic review[1] assessed reports of surgery case series. These results are consistent with the statistically significant improvement reported by the SOS study for diabetes, hypertension (in the small RYGB subset), and sleep apnea, although the magnitude of benefit reported in SOS study was smaller than that reported in the case series[1].

Table 29. Systematic review of resolution or improvement of co-morbidities following bariatric surgery. Adapted from AHRQ review [1]

Co-morbidity	N studies	Resolution or improvement of co-morbidities	
		Range	Median
Diabetes	21	69% to 100 %	100%
Hypertension	18	25 % to 100 %	89%
Sleep apnea	14	95 % to 100 %	100%
Dyslipidemia	10	60% to 100%	88%

5.5.2.3 *Hard endpoints: long-term mortality*

A retrospective cohort study compared long-term mortality between 1035 surgically treated obese patients and 5746 obese controls, retrospectively matched on gender, age, and date of first diagnostic of obesity[20]. The crude relative risk for death at 5 year was 0.11 (95% CI 0.04-0.27) for surgically treated patients as compared to the control group, that is a relative risk reduction of 89%. However, apart from the matching variables, very little information is provided on the controls (for instance, their BMI was not known to the investigators), casting some doubt on their comparability with the surgically-treated patients at baseline, and only unadjusted relative risks are presented.

A large retrospective, population-based study using a state wide hospital administrative database compared long-term mortality between obese patients admitted for gastric bypass and obese patients admitted for any another cause. A modest overall survival benefit was associated with the procedure, but when survival was compared beginning one year after the procedure (whereby not taking into account 1.9% post-operative mortality) risk ratio for death, adjusted for age, sex, and some measure of co-morbidity, was 33% lower than that of non operated patients (hazard ration 0.67; 95% CI 0.54 – 0.85).

5.5.2.4 Health care costs for surgically treated vs conventionally treated obese patients

Pharmaceutical costs for patients participating to the SOS study were measured 6 years after inclusion in the study. The surgical group had lower costs for diabetes mellitus and cardiovascular disease medications but higher costs for gastrointestinal tract disorder, anemia and vitamin deficiency medications. Total costs were similar for surgically and conventionally treated obese patients[18]. No differences between groups were found either for hospitalisations costs[18].

A retrospective analysis of a large hospital database in the US, found a high rate of hospital admissions in the years following after bariatric surgery, (as compared with the rate of hospitalisations before) and concluded that 'rather than a decrease in inpatient health care utilization after RYGB, the costs associated with inpatient hospitalization may remain elevated for as many as 5 years following RYGB'[21].

5.5.2.5 Relationship between weight loss and improvement in co-morbidities following bariatric surgery for morbid obesity

One review specifically addressed the question of whether there is a threshold amount of weight loss necessary to improve health outcomes[22].

The best available evidence - from the SOS study- provides some qualitative insights into the relationship between amount of weight loss and change in health outcome measures, and the clinical significance of these changes. However, it is not possible to draw conclusions as to the relation of increment of weight loss to increment of improvement in health outcome measures. It is also not possible to identify a weight loss threshold for success of a surgical procedure[22].

5.5.2.6 Outcomes of bariatric surgery for patients with a BMI < 40

The benefits and adverse effects of bariatric surgery for non-morbidly obese (BMI < 40, with or without co-morbidity) were explored as part of the very comprehensive ECRI HTA[5]. Only one study[23] , met the inclusion criteria: (1) control group of non-surgically treated patients, or before-and-after design, (2) separate reporting of outcomes for non-morbidly obese patients. This study suffers from the usual biases small sample size, and high loss to follow-up and does not contribute much to knowledge on the subject.

5.6 COMPARISON BETWEEN BARIATRIC PROCEDURES

Under the assumption that improvement in co-morbidities is related to the amount of weight loss, comparisons between procedures will be made on weight loss (rather than co-morbidities), and short and long term adverse events.

Comparisons involve different procedures, or one procedure performed either laparoscopically or with open surgery. Because of the significant co-morbidities associated with open bariatric procedures, severely obese patients are generally at increased risk for postoperative cardiopulmonary and wound-related complications. A laparoscopic approach might be of greater benefit to this group of patients than those considered to be not clinically obese. The goals of the laparoscopic approach are to reduce the length of hospitalization and minimize the morbidity associated with open bariatric surgery.

5.6.1 Evidence available

Comparison between procedures should ideally be based on randomized controlled trials, or at least comparative studies. The most recent BCBS systematic review[2] identified few comparative studies with at least one year follow-up:

- Open Gastric Bypass (RYGB) vs

  Vertical Banded Gastroplasty (7 studies)[24-30].

  Laparoscopic Gastric Banding (1 study)[30]

Laparoscopic Gastric Bypass : one RCT[31]; another RCT with shorter FU can contribute to the analysis of short terms adverse events[32]; one non-randomized comparison of procedures is limited to adverse events[33],). All 3 were rated of poor quality[22].

Bilio-pancreatic diversion – duodenal switch: 1 study[34]

Long-limb gastric bypass[35, 29, 36-38]. A problem is that the length of the limbs being compared vary across studies.

- Laparoscopic gastric bypass vs

Laparoscopic long-limb gastric bypass: 1 study[39]

- Laparoscopic Adjustable Gastric Banding vs

Laparoscopic Gastric Bypass (3 studies)[30, 40, 41]

Vertical Banded Gastroplasty VBG[30, 42]

Currently, RYGB is presented (in the US) as the procedure of choice. The most rigorous of all comparative trials (the so-called Adelaide trial[26]) showed greater weight loss for RYGB compared with VBG and HBG, without difference in adverse events between groups. RYGB is the 'standard' procedure against which newer procedures (like LRYGB or LAGB) need to be assessed[2].

Quality of trials comparing bariatric procedures ranges from fair to poor. Such studies suffer from a number of biases, like inconsistent reporting of adverse events, short follow-up period, or high loss to follow-up, and small sample sizes.

Most of the evidence for comparing outcomes actually comes from single-arm case series. Single-arm series often have the advantage of larger numbers. However, populations at baseline are not comparable; surgical procedures are inherently prone to variability between individual surgeons, especially for procedures that are technically complex. In addition, outcomes of a surgical procedure may vary between hospitals. While reporting of weight-loss outcomes following bariatric surgery is fairly well standardized, the reporting of adverse events shows wide variability. Systematic surveillance at regularly planned intervals is generally not done[2].

It has been argued that the assessment of a new surgical procedure during the initial stages of the learning curve does not provide an accurate picture of its safety (and efficacy). Systematic reviews usually have as an inclusion criteria the reporting of a minimal number of cases which can range from 10[4, 1] to 500 (to account for the learning curve)[10].

5.6.2 Weight loss

Malabsorptive procedures seem to result in greater weight loss than restrictive procedures. There is no reason to believe that weight loss could be different if a given procedure is performed laparoscopically, as compared to open surgery. Procedure can be classified in increasing weight loss order, as: adjustable gastric banding, vertical banded gastroplasty, and Roux-en Y- gastric bypass (see Table 4).

Limited evidence, based on one comparative study and 7 single-arm studies[2], suggest that weight loss after bilio-pancreatic diversion is in the same range as weight loss after RYGB. Short term and long term adverse events seem to be less for RYGB but there are insufficient data to draw definite conclusions.

Studies reporting on Long Limb RYGB are often of poor quality. In addition the length of the limbs being compared varies across studies. The majority of comparisons do not show any significant differences in weight loss. The evidence presently available for LL RYGB is not sufficient to form conclusions on its superior efficacy compared to traditional RYGB[2].

Table 30. Comparison of bariatric surgery procedures: weight loss

RYGB*	VBG	AGB*	BPD/DS
BCBS Systematic review [2] Results from comparative studies. % Excess Weight Loss (EWL)			
N=9 studies 1 yr : median EWL 68%, range [66-71] 3 yrs: median EWL 65%, range [63-68]	7/7 trials show lesser weight loss than with RYGB. Range 19-36% less patients with > 50% EWL	(N=2 studies) %EWL range 33-39	63% (1 study)
SOS study[19] Mean weight change (weight loss*100/ initial weight) -10 years follow-up.			
-25 % (N= 34 patients)	-16.5% (N= 451 patients)	-13.2% (N=156 patients)	NA
AHRQ Meta-analysis[1] Mean weight loss, kg [95% CI] (N studies/n patients)			
1 year follow-up			
43 kg [41-43] (32/2937)	32 kg [30-34] (21/2080)	30 kg [28-32] (27/5562)	52 kg [45-59] (3/735)
36 months follow-up, or more			
41 kg [37-46] (21/1281)	32 kg [28-37] (18/1877)	35 kg [29-40] 17/3076	53 kg [48-59] (1/50)

*Open and laparoscopic procedures combined
BPD/DS : bilio-pancreatic diversion – duodenal switch

5.6.3 Adverse events: mortality

Large, retrospective, population-based studies have recently been published[14, 43]. Population-based studies reflect field reality better than case-series (often reporting outcomes from experienced surgeons); mortality is higher in these studies than in case series.

5.6.3.1 Peri-operative mortality

Definitions are often not standardised. For instance the term 'peri-operative mortality' can have different meaning (in-hospital mortality, 30-days mortality). Pooled averages are influenced by the inclusion criteria used.

Table 31 Comparison of procedures: peri-operative mortality

RYGB	LRYGB	LAGB	VBG	BPD
Systematic review of case-series > 100 cases - Range [22, 2]				
0-5% (N=11)	0-1% (N=8)			0-1.5%
Systematic review of case-series > 50 cases [44](N studies/ n patients)				
0.87% 8/2771	0.23% 10/3464	-	-	-
Systematic review, all studies [45]				
0.5% N/9258		0.05% N/5780	0.31% N/2858	
AHRQ Systematic review, studies > 10 cases [6] Early or time unspecified death % (95% CI) N studies/ n patients				
Controlled trials				
1.0% (0.5-1.9) 15/907		0.4% (0.01- 2.1) 6/268	0.2 % (0-1.4) 11/401	NR
Case series				
0.3% (0.2-0.4) 50/11590		0.02 % (0-0.78) 35/9222	0.3% (0.1-0.5) 33/4091	0.9% (0.5-1.3) 7/2808
Population-based study[14]. 30-days mortality (n deaths/N patients)				
1.9% (64/3328)		-	-	

In Flum study[14] (population-based), overall 30-day mortality of 1.9% (64/3328) for gastric bypass (open and laparoscopic combined) was higher than what is usually reported - with close to half of all early deaths occurring after hospital discharge. The odds for 30-day mortality were much higher (OR 4.7, 95% CI 1.2-18.2) for the first 19 procedures of a given surgeon, compared with the following ones[14].

Reported peri- operative mortality range from 0% to 1% for LRYGB and from 0% to 5% for RYGB[2]. Peri-operative mortality seems to favour LRYB, but definite evidence is still lacking.

5.6.3.2 Mortality at one year

In a large population study, mortality one year after bariatric surgery was 4.6% (but no breaking-up per procedure is given). Male sex, age > 64, and surgeon experience, were independently associated with a higher mortality; data also suggested an additive effect between surgeon and institutional volumes[46].

5.6.4 Adverse events: morbidity

5.6.4.1 Laparoscopic vs open procedure

Adverse events data from controlled trials comparing laparoscopic and open procedures (in general) were pooled in AHRQ systematic review[1].

There were fewer wounds, less wound infections, and more re-operations for laparoscopic vs open surgery. Data were insufficient to reach conclusions on differences for other complications.

5.6.4.2 *Laparoscopic and open gastric by-pass*

There is a lack of high-quality trials comparing RYGB and LRYGB.

Data on adverse events of open and laparoscopic RYGB are presented in appendix. A serious complication, anastomic leak, could be more frequent in LRGYB. Longer-term adverse events are less consistently reported and limited by the small number of patients reaching long-term FU.

Nutritional deficiency rates of 16% for open RYGB and 24% for LRYGB have been reported in MSAC[47] and BCBS[22] systematic review, respectively.

Risk-adjusted in-hospital adverse outcomes[13] as well as 30-days mortality[14], are significantly lower when gastric bypass is performed by higher-volume surgeons. A volume-outcome relationship has been well demonstrated for most of these procedures. A study on more than 24.000 patients showed that patients who underwent gastric bypass at high volume hospitals (> 100 admissions per year) had a shorter length of stay, lower overall complications, lower complications of medical care, lower mortality, and lower costs, as compared with hospitals with a lower volume of activities[48].

At the moment, the evidence is not sufficient to form conclusions about the relative morbidity of laparoscopic gastric bypass compared to open gastric bypass[22].

5.6.4.3 *Laparoscopic adjustable gastric banding*

Adapted from BCBS HTA[2]

Short-term adverse events for LAGB are low. Mortality in single-arm studies was rare, with a pooled average of 0.1% and a median of 0%. The most frequent short-term adverse events were conversions to open procedures (1.6%) and wound/port site infections (1.5%). (Table 6)

There were 2 trials comparing LAGB with LRGBY[40, 41], but the largest one is rated poor on quality assessment because of non-comparability of population. Data are shown in appendix.

Quality of data available to assess long-term adverse events is poor. High loss to follow-up particularly after one year is found in most studies. Average follow-up rate at 5 years was 4.9% (see table in appendix). However adverse events for LAGB can increase over the years. In a study where long-term complications were reported by year[49], the incidence of adverse events increased in years 2 through 5. For example, there were no cases of band slippage reported in year 1; but in years 2 through 4, this rate increased 1.3–1.5% per year.

The most commonly reported complications are band problems requiring intra-abdominal interventions (band intolerance, band leakage, gastric pouch problems, band slippage) and tube/port problems (leakage, breaks and misplacements).

Studies with less complete follow-up report lower rates of long-term complications compared with rates reported by studies with more complete follow-up. In several cases, these rates differ by several-fold. The rates for these long-term adverse events are on average higher than the short-term complications, and there is greater variability in the range of reported rates. For example, the range reported for re-operations (2.0–52%) and band removal (0.6–33%) is so wide that it is difficult to estimate the true rate with any degree of certainty. Some of these adverse events, such as band erosion, can be very serious and lead to significant morbidity and/or repeat procedures. However alterations in the surgical technique have been proposed, and rates of some adverse events reported in older studies may not reflect current surgical practice.

The frequency of adverse events diminishes markedly with experience (learning curve). For instance in a large case-series, the incidence of gastric pouch dilation after LAGB was the highest in centres with the lowest turn-over and 0 in the centres with the largest [50].

The 3 most recent HTA specifically assessing LAGB - the most commonly used procedure in Belgium- reached similar conclusions (Table 6):

Table 32. Conclusions of recent HTAs on LAGB

Source	Conclusions
Technology Assessment Unit (TAU) of the McGill University Health Centre, 2004[9]	LAGB is an effective procedure with an adequate safety record for up to 5 years. There is insufficient evidence on which to decide whether LAGB is a superior procedure. Given that an effective (cheaper) alternative exists (*RYGB*), it will be necessary to demonstrate clinically meaningful superiority over a longer FU before LAGB is accepted as the operation of choice
Alberta Heritage Foundation for Medical Research, 2005[10].	It is not possible to make definite conclusions on long-term safety and efficacy of LAGB because of weak evidence
Blue Cross Blue Shield, 2005 CBS[2]	LABG is a safe procedure in the short term. There is insufficient evidence to properly assess safety in the long-term. Rates for long-term adverse events are poorly documented but are likely to be higher than short-term adverse events

5.6.4.4 Vertical Banded Gastroplasty

VBG is the most common variety of gastroplasty and formerly the most commonly performed bariatric procedure in the United States. It is performed less frequently today, perhaps for the following stated reasons: (1) poor patient compliance with eating behaviour modifications, (2) dehiscence of the vertical stapled partition, (3) less effective than gastric bypass procedure for control of type 2 diabetes mellitus, (4) requirement for implantation of a foreign body (e.g., polypropylene mesh or silastic ring), (5) less sustained weight loss over time compared with RYGB procedure, and (6) side effects including gastro-esophageal reflux and solid food intolerance[10]

5.6.4.5 Bilio-pancreatic diversion

There have been numerous studies of BPD published, but there is a lack of high quality comparative trials. There is not enough evidence to support the hypothesis that BPD results in greater weight loss than RYGB[2]. In Buchwald meta-analysis[4], mean absolute weight loss was 43 kg for RYGB and 46 kgs for BPD/DS; and mean BMI decrease 17 an 18, respectively.

5.6.5 Operating time and length of stay

Table 33. Mean operating time (min) : data from RCT or comparative studies (adapted from MUHC HTA [10]

	LRYGB	LAGB	LVBG
Morino[42]		65 (range 35-120) N=49	94 (range 40-270) N=51
Weber[41]	190 (N=103)	145 (N=103)	
Mognol[51]	180 (SD 60) (N=110)	70 (SD 20) (N=179)	

Table 34. Mean length of stay (days) : data from RCT or comparative studies (adapted from MUHC HTA [10]

	LRYGB	LAGB	VBG
Morino[42]		3.7 N=49	6.6 N=51(LVBG)
Weber[41]	8.4 (N=103)	3.3 (N=103)	
Mognol[51]	8 (N=110)	2 (N=179)	
Biertho[40]	3 (SD 10.3; range 2-9) N=456	5 (SD 2.4; range 2-22) N=1261	

5.7 GUIDELINES

Numerous guidelines have been published by various scientific and professional bodies. A brief review can be found in annex. All are a variant, and refer to, the first such guidelines issued following a consensus conference organised by the US National Institute of Health (NIH)[52] . They classically recommend that bariatric surgery be considered for patients with a BMI >= 40; or a BMI >= 35 with co-morbidities. The first guideline however explicitly refers to 'life-threatening co-morbidities'.

Whereas the development of a less invasive procedures such as LAGB could potentially result in an improved risk-benefit ratio of bariatric surgery, and lead to a revision of these guidelines towards less stringent criteria, the European Association for Endoscopic Surgery decided in 2005 that its current recommendations for bariatric surgery (indications: BMI >=40; or BMI >= 35 + co-morbidities) also applied to LAGB, on the ground that there were insufficient data to properly assess its long-term adverse events and effectiveness[53].

5.8 CRITERIA FOR REFUNDING BARIATRIC SURGERY IN OTHER COUNTRIES

A detailed description can be found in appendix.

In France, criteria for refunding bariatric surgery are given per intervention. For instance, Scopinaro and BPD/DS are refunded only if the patient has a BMI > 50, and 'in exceptional cases'.

LAGB is refunded for BMI >=40, or a BMI >=35 + 'life-threatening or functional co-morbidity' such as cardiopulmonary problems, severe sleep apnoea, obesity-related heart disease. The list is non-exhaustive. There is no definition of what 'functional' could encompass. A condition for refunding is that patients have followed specialised medical treatment (diet, physical activity, psychological treatment, treatment of complications,) during at least 1 year. The device is paid fir by the social security (price of adjustable band starts at 900 Euros)

5.9 DISCUSSION

5.9.1 Risk/benefits ratio of bariatric surgery

When discussing risk/benefits ratio in bariatric surgery, it is important to remember a particular feature of bariatric surgery: it is directed at a body part which is basically **intact.** In that sense it bears similarity with cosmetic surgery.

Long term prospective, controlled trials have demonstrated that surgery is more effective than non-surgical treatment for long-term weight loss and control of some co-morbid conditions, particularly diabetes, in patients with a BMI >= 40. No prospective data are yet available on the effect of bariatric surgery on incidence of cardio-vascular events or all-cause mortality. Despite a large body of scientific literature available on bariatric surgery, all systematic reviews acknowledge the weaknesses of the available evidence base and call for better studies to be able to properly compare procedures, particularly as regards long-term adverse events and efficacy on hard endpoints such as mortality. Key questions still need to be answered such as the balance between benefits and risk in relevant patient subgroups: age, BMI, and severity of co-morbidity may influence the net benefit of surgery compared with non-surgical intervention. The major debate within the bariatric surgery community is which procedure, LAGB or RYGB (open or laparoscopic), is most appropriate for which patient group[10].

5.9.2 Risks of bariatric surgery, volume-outcome relationships, and implications for health care organisation

Risks associated with bariatric surgery can be high, and better data measuring these risks have recently been published. Data from large, longitudinal population studies on patients undergoing gastric bypass, show a mortality after 30 day, and after one year, of 2.0%, and 4,6%, respectively[43]; up to 20% of the patients were re-admitted within the year following surgery for reasons thought to relate to complications of surgery[21], up to 24% of the patients suffer from nutritional deficiencies in the long-term[22]. Adverse events related to LAGB tend to be less severe, but they are insufficiently documented, could be frequent particularly in the long-term, and LAGB is also less effective in terms of weight loss.

Many authors have reported a steep learning curve effect, with markedly lower morbidities for the second 100 procedures performed[10]. Mortality, morbidity, length of stay, and costs are closely related to the surgeon's experience[50, 13, 14, 48]. This has important implications for health care organisation.

Figure 2. Proposed criteria for becoming a Center of Excellence according to the American Society for Bariatric Surgery48

- **Institutional commitment to in-service education program**
- **Perform > 125 bariatric surgical cases per year**
- **Bariatric Medical Director in decision loop**
- **Full consultative staff and critical care services**
- **Full line of equipment and instruments for the care of bariatric surgical patients**
- **Availability of organized and supervised support groups**
- **Long-term follow-up with a system for outcome reporting**

5.9.3 Risk/benefit of bariatric surgery in patients with a BMI between 35-39 and co-morbidities

The BMI thresholds initially chosen by the 1992 consensus conference (BMI > 40, or BMI > 35 + co-morbidities) are to some extent arbitrary, but the bulk of scientific evidence available refer to patients selected according to these criteria. A complex issue in the NIH selection criteria however is the proper definition of co-morbidities which warrant obesity surgery due their seriousness and potential alleviation through weight loss[53].

Many co-morbidities have been shown to respond well to bariatric surgery, but the risk/benefit of bariatric surgery is not clear in the subgroup of patients with a BMI between 35 and 39. There are no sub-group analyses in the published literature. Could hypertension or dyslipidemia alone (for which effective, simple pharmaceutical treatment does exist) be considered as 'life-threatening co-morbidities' and justify the high risk involved and the uncertainties surrounding bariatric surgery? Only severe co-morbidities can justify the risks and uncertainties involved in bariatric surgery.

Only severe, well defined co-morbidities (for instance, diabetes) should be accepted as an indication for surgery in patients with a BMI between 35-39. The problem of course is to identify a list of such co-morbidities.

5.10 CONCLUSIONS AND KEY POINTS

- **There is sufficient evidence that bariatric surgery is more effective than non-surgical treatment for long-term weight loss and control of some co-morbid conditions, particularly diabetes. No prospective data have been published on the effect of bariatric surgery on cardio-vascular morbidity or mortality.**
- **Bariatric procedures differ widely in terms of long-term effectiveness and safety.**
- **Bariatric surgery does not cure obesity and implies a life-long commitment to diet for the intervention to be successful.**
- **Risks associated with bariatric surgery can be high. A steep learning curve has been described for most procedures**
- **Important gaps in knowledge still exist: what is the best procedure, for which patients (according to BMI, age, eating behaviour…) ?**
- **In patients with BMI between 35-39, only severe co-morbidities proven to respond well to bariatric surgery, such as diabetes can justify the risks and uncertainties associated with bariatric surgery**
- **Gastric banding is a less invasive procedure, but its long-term effectiveness and safety are not properly documented. It the current state of knowledge, it cannot be considered as superior to more established procedures such as gastric bypass.**

5.11 REFERENCES

1. Shekelle P, Morton S, MA M, Suttorp M, Tu W, Li S, et al. Pharmacological and Surgical Treatment of Obesity. Southern California-RAND Evidenced-Based Practice Center; 2004. Agency for Healthcare Research and Quality Evidence Reports (Evidence Report/Technology Assessment No. 103. AHRQ Publication No. 04-E028-2) Available from: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat1a.chapter.19289
2. Lefevre F. Newer Techniques in Bariatric Surgery for Morbid Obesity: Laparoscopic Adjustable Gastric Banding, Biliopancreatic Diversion, and Long-Limb Gastric Bypass. Technology Assessment Center. Blue Cross Blue Shield Association.; 2005 August 2005. (Volume 20, No. 5) Available from: http://www.bcbs.com/tec/vol20/20_05.html
3. Brechner RJ, Farris C, Harrison S, Tillman K, Salive M, Phurrough S. Summary of Evidence-Bariatric Surgery. Centers for Medicare and Medicaid Services; 2004 November 4, 2004. Available from: http://www.cms.hhs.gov/mcd/viewmcac.asp?where=index&mid=26
4. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292(14):1724-37.
5. ECRI (formerly Emergency Care Research Institute). Bariatric Surgery for Obesity. Plymouth Meeting,PA: 2004. Available from: http://www.ecri.org/Products_and_Services/Products/Bariatric_Resources/Default.aspx
6. Maggard MA, Shugarman LR, Suttorp M, Maglione M, Sugarman HJ, Livingston EH, et al. Meta-analysis: surgical treatment of obesity. Ann Intern Med. 2005;142(7):547-59.
7. Medical Advisory Secretariat - Ontario Ministry of Health and Long-Term Care Bariatric Surgery:Health Technology Literature Review. 2005. Available from: http://www.health.gov.on.ca/english/providers/program/mas/reviews/review_baria_0105.html
8. Chapman AE, Kiroff G, Game P, Foster B, O'Brien P, Ham J, et al. Laparoscopic adjustable gastric banding in the treatment of obesity: a systematic literature review. Surgery. 2004;135(3):326-51.
9. Chen J, McGregor M. The Gastric Banding Procedure: An Evaluation. Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC). 2004 April 27, 2004. Available from: http://www.mcgill.ca/tau/publications/2004/
10. Guo B, Harstall C. Laparoscopic Adjustable Gastric Banding for the Treatment of Clinically Severe (Morbid) Obesity in Adults: An Update. Edmonton,AB: Alberta Heritage Foundation for Medical Research.; 2005 May 2005. Information paper. HTA. Available from: http://www.ahfmr.ab.ca/publications/
11. Oria HE, Moorehead MK. Bariatric analysis and reporting outcome system (BAROS). Obes Surg. 1998;8(5):487-99.
12. Wolf AM, Falcone AR, Kortner B, Kuhlmann HW. BAROS: an effective system to evaluate the results of patients after bariatric surgery. Obes Surg. 2000;10(5):445-50.
13. Courcoulas A, Schuchert M, Gatti G, Luketich J. The relationship of surgeon and hospital volume to outcome after gastric bypass surgery in Pennsylvania: a 3-year summary. Surgery. 2003;134(4):613-21; discussion 21-3.
14. Flum DR, Dellinger EP. Impact of gastric bypass operation on survival: a population-based analysis. J Am Coll Surg. 2004;199(4):543-51.
15. Karlsson J, Sjostrom L, Sullivan M. Swedish obese subjects (SOS)--an intervention study of obesity. Two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. Int J Obes Relat Metab Disord. 1998;22(2):113-26.
16. Sjostrom CD, Lissner L, Wedel H, Sjostrom L. Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS Intervention Study. Obes Res. 1999;7(5):477-84.
17. Karason K, Lindroos AK, Stenlof K, Sjostrom L. Relief of cardiorespiratory symptoms and increased physical activity after surgically induced weight loss: results from the Swedish Obese Subjects study. Arch Intern Med. 2000;160(12):1797-802.
18. Agren G, Narbro K, Jonsson E, Naslund I, Sjostrom L, Peltonen M. Cost of in-patient care over 7 years among surgically and conventionally treated obese patients. Obes Res. 2002;10(12):1276-83.

19. Sjostrom L, Lindroos A-K, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683-93.
20. Christou NV, Sampalis JS, Liberman M, Look D, Auger S, McLean APH, et al. Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. Ann Surg. 2004;240(3):416-23; discussion 23-4.
21. Zingmond DS, McGory ML, Ko CY. Hospitalization Before and After Gastric Bypass Surgery. JAMA. 2005;294(15):1918-24.
22. Lefevre F. Special Report: The Relationship between Weight Loss and Changes in Morbidity Following Bariatric Surgery for Morbid Obesity. Technology Assessment Center. Blue Cross Blue Shield Association.; 2003. (Assessment Program Volume 18, No. 9) Available from: http://www.bcbs.com/tec/vol18/18_09.html
23. Fobi M, Lee H, Igwe D, Felahy B, James E, Stanczyk M, et al. Gastric bypass in patients with BMI < 40 but > 32 without life-threatening co-morbidities: preliminary report. Obes Surg. 2002;12(1):52-6.
24. Sugerman HJ, Starkey JV, Birkenhauer R. A randomized prospective trial of gastric bypass versus vertical banded gastroplasty for morbid obesity and their effects on sweets versus non-sweets eaters. Ann Surg. 1987;205(6):613-24.
25. Sugerman HJ, Londrey GL, Kellum JM, Wolf L, Liszka T, Engle KM, et al. Weight loss with vertical banded gastroplasty and Roux-Y gastric bypass for morbid obesity with selective versus random assignment. Am J Surg. 1989;157(1):93-102.
26. Hall JC, Watts JM, O'Brien PE, Dunstan RE, Walsh JF, Slavotinek AH, et al. Gastric surgery for morbid obesity. The Adelaide Study. Ann Surg. 1990;211(4):419-27.
27. MacLean LD, Rhode BM, Sampalis J, Forse RA. Results of the surgical treatment of obesity. Am J Surg. 1993;165(1):155-60; discussion 60-2.
28. Brolin RL, Robertson LB, Kenler HA, Cody RP. Weight loss and dietary intake after vertical banded gastroplasty and Roux-en-Y gastric bypass. Ann Surg. 1994;220(6):782-90.
29. Mason EE, Tang S, Renquist KE, Barnes DT, Cullen JJ, Doherty C, et al. A decade of change in obesity surgery. National Bariatric Surgery Registry (NBSR) Contributors. Obes Surg. 1997;7(3):189-97.
30. Hell E, Miller KA, Moorehead MK, Norman S. Evaluation of health status and quality of life after bariatric surgery: comparison of standard Roux-en-Y gastric bypass, vertical banded gastroplasty and laparoscopic adjustable silicone gastric banding. Obes Surg. 2000;10(3):214-9.
31. Westling A, Gustavsson S. Laparoscopic vs open Roux-en-Y gastric bypass: a prospective, randomized trial. Obes Surg. 2001;11(3):284-92.
32. Nguyen NT, Goldman C, Rosenquist CJ, Arango A, Cole CJ, Lee SJ, et al. Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. Ann Surg. 2001;234(3):279-89; discussion 89-91.
33. See C, Carter PL, Elliott D, Mullenix P, Eggebroten W, Porter C, et al. An institutional experience with laparoscopic gastric bypass complications seen in the first year compared with open gastric bypass complications during the same period. Am J Surg. 2002;183(5):533-8.
34. Deveney CW, MacCabee D, Marlink K, Welker K, Davis J, McConnell DB. Roux-en-Y divided gastric bypass results in the same weight loss as duodenal switch for morbid obesity. Am J Surg. 2004;187(5):655-9.
35. Freeman JB, Kotlarewsky M, Phoenix C. Weight loss after extended gastric bypass. Obes Surg. 1997;7(4):337-44.
36. MacLean LD, Rhode BM, Nohr CW. Long- or short-limb gastric bypass? J Gastrointest Surg. 2001;5(5):525-30.
37. Brolin RE, LaMarca LB, Kenler HA, Cody RP. Malabsorptive gastric bypass in patients with superobesity. J Gastrointest Surg. 2002;6(2):195-203; discussion 4-5.
38. Choban PS, Flancbaum L. The effect of Roux limb lengths on outcome after Roux-en-Y gastric bypass: a prospective, randomized clinical trial. Obes Surg. 2002;12(4):540-5.
39. Inabnet WB, Quinn T, Gagner M, Urban M, Pomp A. Laparoscopic Roux-en-Y gastric bypass in patients with BMI <50: a prospective randomized trial comparing short and long limb lengths. Obes Surg. 2005;15(1):51-7.

40. Biertho L, Steffen R, Ricklin T, Horber FF, Pomp A, Inabnet WB, et al. Laparoscopic gastric bypass versus laparoscopic adjustable gastric banding: a comparative study of 1,200 cases. J Am Coll Surg. 2003;197(4):536-44; discussion 44-5.
41. Weber M, Muller MK, Bucher T, Wildi S, Dindo D, Horber F, et al. Laparoscopic gastric bypass is superior to laparoscopic gastric banding for treatment of morbid obesity. Ann Surg. 2004;240(6):975-82; discussion 82-3.
42. Morino M, Toppino M, Bonnet G, del Genio G. Laparoscopic adjustable silicone gastric banding versus vertical banded gastroplasty in morbidly obese patients: a prospective randomized controlled clinical trial. Ann Surg. 2003;238(6):835-41; discussion 41-2.
43. Flum DR, Salem L, Broeckel Elrod JA, Dellinger EP, Cheadle A, Chan L. Early Mortality Among Medicare Beneficiaries Undergoing Bariatric Surgical Procedures. JAMA. 2005;294(15):1903-8.
44. Podnos YD, Jimenez JC, Wilson SE, Stevens CM, Nguyen NT. Complications after laparoscopic gastric bypass: a review of 3464 cases. Arch Surg. 2003;138(9):957-61.
45. Chapman A, Game P, O'Brien P, Maddern G, Kiroff G, Foster B, et al. A systematic review of laparoscopic adjustable gastric banding for the treatment of obesity (update and re-appraisal). Adelaide, SA: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S); 2002. (31) Available from: http://www.surgeons.org/Content/ContentFolders/News/ASERNIPS/Systematicreviews/Laparoscopic_Adjust.htm
46. Salem L, Jensen CC, Flum DR. Are bariatric surgical outcomes worth their cost? A systematic review. J.Am.Coll.Surg. 2005;200(2):270-8.
47. Medical Services Advisory Committee (MSAC). Laparoscopic adjustable gastric banding for morbid obesity. Canberra: 2003. (MSAC reference 14) Available from: http://www.msac.gov.au/reports.htm
48. Nguyen NT, Paya M, Stevens CM, Mavandadi S, Zainabadi K, Wilson SE. The relationship between hospital volume and outcome in bariatric surgery at academic medical centers. Ann Surg. 2004;240(4):586-93; discussion 93-4.
49. Biertho L, Steffen R, Branson R, Potoczna N, Ricklin T, Piec G, et al. Management of failed adjustable gastric banding. Surgery. 2005;137(1):33-41.
50. Angrisani L, Furbetta F, Doldi SB, Basso N, Lucchese M, Giacomelli F, et al. Lap Band adjustable gastric banding system: the Italian experience with 1863 patients operated on 6 years. Surg Endosc. 2003;17(3):409-12.
51. Mognol P, Chosidow D, Marmuse J-P. Laparoscopic gastric bypass versus laparoscopic adjustable gastric banding in the super-obese: a comparative study of 290 patients. Obes Surg. 2005;15(1):76-81.
52. Gastrointestinal surgery for severe obesity: National Institutes of Health Consensus Development Conference Statement. Am J Clin Nutr. 1992;55(2 Suppl):615S-9S.
53. Sauerland S, Angrisani L, Belachew M, Chevallier JM, Favretti F, Finer N, et al. Obesity surgery: evidence-based guidelines of the European Association for Endoscopic Surgery (EAES). Surg Endosc. 2005;19(2):200-21.

6 COST-EFFECTIVENESS OF SURGICAL TREATMENT

6.1 INTRODUCTION

To assess the cost-effectiveness of surgical treatments, we performed a systematic review of full economic evaluations. We defined the term "full economic evaluation" as an analysis which compares both costs and outcomes of at least two health care programmes (definition by Drummond et al.[1]).

Two types of full economic evaluations were found: cost-effectiveness analyses and cost-utility analyses.

A cost-effectiveness analysis compares the costs and the principal outcome of different interventions. Outcomes can be defined in terms of a final endpoint such as life years gained or intermediary outcomes such as weight loss. In our analysis, we used the term of cost-efficacy analysis instead of cost-effectiveness analysis if the outcome data were based on the results of clinical trials (efficacy) and not on outcomes in daily practice (effectiveness).

A cost-utility analysis compares the costs of different interventions and the outcomes in term of quality-adjusted life years (QALYs). Thus, this kind of analysis takes both morbidity and the mortality into account.

6.2 METHODS

6.2.1 Search strategy

- Studies were sought from three sources :
- A search via "Ovid" on the following bibliographic databases: MEDLINE (1966-2006), ACP journal club (1991-2006), CINAHL (1982-2006), British Nursing Index (BNI) (1985-2006), Cochrane Library and Database of Abstracts of Reviews of effects (DARE)
- A search via the Centre for Reviews and Dissemination (CRD) on the following databases: NHS Economic Evaluation Database (NHS EED) and Health Technology Assessment (HTA) database.
- Identification of studies from the bibliography of selected studies.

The keywords used were "surg*" and "obes*" in combination with "cost" or "economic" (See Appendix chapter 4).

6.2.2 Inclusion and exclusion criteria

The search was limited to papers published between January 1995 and January 2006 and written in English, Dutch or French. A first selection was based on abstracts. Only full economic evaluations which assessed a cost-effectiveness ratio or cost-utility ratio were retained as appropriate study designs. A single economist assessed all abstracts for relevance. Full papers were obtained and assessed for all potentially relevant studies.

6.2.3 Data extraction and quality assessment

Data were extracted using a structured data extraction form (See Appendix) and quality was assessed by a single economist using a standard quality assessment checklist for economic evaluations[1] (See Appendix). The quality of the studies was discussed narratively.

6.2.4 Conversion in Euro 2004

Costs were transformed into 2004 prices for each country using Gross Domestic Product (GDP) deflator. Then we applied the Purchasing Power Parities (PPP) index to obtain comparable costs in Euro among the different countries. The PPP used correspond to 2004 Euro for the 25 member states of the European Union. (reference for data on GDP deflator and PPP)

6.3 RESULTS

Twenty-five studies did not meet our inclusion criteria and were thus excluded from this analysis. Six studies were cost analysis and not full economic evaluations[2-7], six studies assessed the effect of bariatric surgery on pharmaceutical expenses only and did not calculate a cost-effectiveness ratio[8-13]. Finally, thirteen studies were cost-outcome descriptions, i.e. they described both costs and effects of bariatric surgery but effectiveness measures were multiple and cost-effectiveness ratios were not calculated[14-26].

In total, eleven studies[27-37] were eligible for inclusion: five original economic evaluations[27-30, 36, 37] and six reviews[28, 30-35]

6.3.1 Original economic evaluations

Among the five original economic evaluations, two studies included both a cost-utility and a cost-efficacy analysis[36, 37] and three studies were cost-utility analyses[27-30]. Their quality was assessed following the quality assessment checklist and is described in Appendix. Data extraction sheets for each selected economic evaluation are provided in appendix.

One study compared two types of surgery[37], three studies compared specific surgery to no surgery or to conventional treatment[27, 29, 36], and one study compared both different types of surgery with other surgery and with no surgery[28, 30].

Table 3 5 . Economic evaluations

Comparison	Cost-utility analysis	Cost-efficacy analysis
VBG versus LAGB	Van Mastrigt[37]	Van Mastrigt[37]
LAGB versus conventional treatment	Chevallier[36]	Chevallier[36]
LAGB versus no surgery	Clegg[28, 30]	
GB versus no surgery	Clegg[28, 30], Craig[29]	
VBG versus no surgery	Clegg[28, 30], Van Gemert[27]	
GB versus VBG	Clegg[28, 30]	
LAGB versus GB	Clegg[28, 30]	
LAGB versus VBG	Clegg[28, 30]	

VBG = Vertical banded gastroplasty
LAGB = Laparoscopic adjustable gastric banding
GB = Gastric bypass

6.3.1.1 Cost-efficacy analysis

Laparoscopic adjustable gastric banding (LAGB) versus conventional treatment (CT)Chevallier et al.[36] assessed the cost-efficacy of LAGB versus CT for three patient subgroups : patients without initial co-morbodity, patients with types 2 diabetes and patients with sleep apnea.

As results, the cumulative BMI losses after five years were higher after LAGB (incremental cumulative BMI loss after 5 years : 56.2) and were identical for each subgroup of patients due to modeling assumptions. Incremental costs were different between subgroups due to the savings generated by types 2 diabetes or sleep apnea remissions in the subgroups with initial co-morbidities. For patients without initial co-morbidity, the incremental cost was €327 and for patients with types 2 diabetes or sleep apnea, LAGB was a cost-saving

strategy (€ -2,240 and € -1,141 respectively). In conclusion, LAGB was a dominant strategy in comparison with a conventional treatment for patients with type 2 diabetes and sleep apnea because it is less costly and more effective than the CT. However, sources of data included in the model were not clear and a sensitivity analysis was not performed. Moreover, if the BMI losses for patients with type 2 diabetes and with sleep apnea were not assumed to be equal to the BMI loss for patients without co-morbidities, results could be different.

Vertical banded gastroplasty (VBG) versus laparoscopic adjustable gastric banding (LAGB)

Van Mastrigt *et al*[87] have compared laparoscopic adjustable gastric banding with open vertical banded gastroplasty for a 1-year period from a societal perspective. As results, the percentage of excess weight loss was significantly higher in the VBG group than in the LAGB group (incremental percent of weight loss : 17.82%, p-value = 0.001). Total costs were higher but the difference was not significant (incremental cost : €2,081).

The difference in the percentage of excess weight loss (%EWL) can be explained by the disparity in treatment modalities. With laparoscopic adjustable gastric banding, reaching the proper weight loss takes more time because some adjustments of the banding are needed. With a longer follow-up period, the difference in %EWL is expected to be reduced. Studies with a longer follow-up period and a larger number of patients are thus needed to make a valid conclusion.

Table 3 6 . Cost-efficacy analysis

Authors	Intervention and timeframe	Incremental efficacy		Incremental costs		Incremental cost-efficacy
		Type	Results	Type	Results*	Results*
Chevallier[36]	LAGB vs CT (5 years)	Cumulative BMI loss after 5 years	56.2	Direct health care costs		
				Patients without co-morbidity	€327	6 €/BMI point loss
				Patients with type 2 diabetes	€-2,240	Dominant strategy
				Patients with sleep apnea	€-1,141	Dominant strategy
Van Mastrigt[37]	VBG vs LAGB (1 years)	% excess weight loss	17.82 % p=0.001	Direct and indirect health care costs	€ 2,081 (not significant)	117 € / %EWL

*Sources : GDP deflator : World Bank / PPP : Eur25 = 1 for 2004 (Eurostat)

6.3.1.2 Cost-utility analysis

Laparoscopic adjustable gastric banding (LAGB) versus no surgery

The model of Clegg *et al*[28, 30] assessed the cost-utility of bariatric surgery for a 20-year period based on a systematic review of clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity. Three surgical interventions were considered : gastric bypass (GB), vertical banded gastroplasty (VBG) and silicone adjustable gastric banding (LAGB). Each intervention was compared with the other interventions and with no surgical treatment.

The only assessed co-morbidity was diabetes because long-term impact of weight-loss on other co-morbidities was considered less evident.

As results, LAGB lead to improved quality of life for an additional cost per patient of €5,769. In comparison with no surgical treatment, the cost per QALY gained for LAGB was €12,840, which was considered cost-effective (< £20,000) by the National Institute for Clinical Excellence [NICE, 2004]. The sensitivity analysis showed that the results were robust.

Gastric bypass (GB) versus no surgery

The model of Clegg *et al*[28, 30] assessed the cost-utility ratio of GB versus no surgery. In their analysis, 90% of patients undergone laparoscopic surgery and 10% open surgery.

GB led to a greater weight loss than nonsurgical treatment and improved quality of life (additional QALYs per patient : 0.45) and co-morbidity rates. In comparison with non-surgical treatment, the cost per QALY gained for GB was €9,470 which is considered cost-effective (< £20,000) by the National Institute for Clinical Excellence [NICE, 2004]. The sensitivity analysis showed that the results were robust.

The model of Craig *et al*[29] assessed the cost-utility of gastric bypass for patients with severe obesity using a deterministic decision model for a lifetime period and from a health care payer's perspective. Patients were divided in subgroups according to their age and sex.

The costs-utility ratios varied between €4,904 to €14,621 per QALY gained for women and between €9,717 and €32,330 for men.

Sensitivity analysis did not alter the conclusions for most sub-groups, except for older, less obese men, for whom the ratio increased above € 50,000 for some parameter variations.

Vertical banded gastroplasty (VBG) versus no surgery

The previously described model of Clegg *et al*[28, 30] also assessed the cost-utility ratio of VBG versus no surgery.

VBG led to improved quality of life (0.26 additional QALYs per patient) at an additional cost of €4,010. In comparison with non surgical treatment, the cost per QALY gained for VBG was €15,415 which was considered as cost-effective (< £20,000) by the National Institute for Clinical Excellence [NICE, 2004]. The parameter variations applied in the sensitivity analysis confirmed the robustness of these results.

Van Gemert *et al*[27], assessed the cost-utility of VBG in comparison with no treatment for patient with morbid obesity using a "cost-of-illness prevalence-based model" for a lifetime period and from a societal perspective. Thus, direct but also indirect costs due to the productivity losses were included. However, savings due to the reduction of co-morbidities were not included. By including these savings, the incremental cost should yet be reduced. As results, VBG in comparison with no treatment improved the quality of life at reduced costs. By taking into account a lifelong follow-up approach, VBG was thus a dominant treatment strategy. This dominance was principally due to the productivity gains, which were estimated to be $2,628 per year.

Laparoscopic adjustable gastric banding (LAGB) versus conventional treatment (CT)

The study of Chevallier *et al*[36] assessed the cost-utility ratio of LAGB in comparison with conventional treatment for two patients subgroups : patients with a BMI ≥ 40, with or without type 2 diabetes and patients with a BMI ≥ 35 with type 2 diabetes.

The quality of life for patients who had undergone a gastric banding was improved in comparison with the conventional treatment. Incremental costs were lower and this particularly for patients with type 2 diabetes, due to the savings generated by types 2 diabetes remissions. In conclusion, LAGB is a dominant strategy in comparison with conventional treatment, particularly for patients with type 2 diabetes. However, the model is based on a lot of assumptions and results could be different in reality. Moreover, a sensitivity analysis on uncertain parameters was not performed.

Laparoscopic adjustable gastric banding (LAGB), vertical banded gastroplasty (VBG) and gastric bypass (GB) comparisons

The model of Clegg *et al*[28, 30] compared the different types of bariatric interventions.

Results were in favour of gastric bypass but authors stated that no firm conclusion can be drawn due to the uncertainty in the clinical and economic evaluations.

Vertical banded gastroplasty (VBG) versus laparoscopic adjustable gastric banding (LAGB)

The study of van Mastrigt *et al*[37] found that the number of QALYs were not significantly different between VBG and LAGB and were respectively 0.76 and 0.81 for VBG and for LAGB group (-0.05 ; p = 0.138). With a cost reduction of €2,081 in the LAGB group, they concluded that this strategy was dominant. However, these differences were not significant.

Table 37. Cost-utility analysis

Authors	Intervention and timeframe	Incremental utility		Incremental costs		Incremental cost-utility*
		Type	Results	Type	Results*	
Clegg[28, 30]	LAGB vs no surgery (20 years)	QALY	0.45	Direct health care costs	€5,769	€12,840/QALY
Clegg[28, 30]	GB vs no surgery (20 years)	QALY	0.45	Direct health care costs	€4,217	€9,470/QALY
Craig [28]	GB vs no treatment (Lifetime)	QALY	Men : 0.84-2.04 Women : 1.32-2.85	Direct health care costs	Men : €19,798-€27,335 Women : €11,715-€21,523	Men : €9,717-€32,330/QALY Women : €4,904-€14,621/QALY
Clegg[28, 30]	VBG vs no surgery (20 years)	QALY	0.26	Direct health care costs	€4,010	€15,415/QALY
Van Gemert [27]	VBG vs no treatment (Lifetime)	QALY	12	Direct and indirect health care costs	From -€44,790 to -€45,656	Dominant strategy
Chevallier [36]	LAGB vs CT (5 years)	QALY		Direct health care costs		
		Patients with a BMI >=40	0.79	Patients with a BMI >=40	€-3	Dominant strategy
		Patients with a BMI >=35 and T2D	1.06	Patients with a BMI >=35 and T2D	€-2,288	Dominant strategy
Authors	Intervention and timeframe	Incremental utility		Incremental costs		Incremental cost-utility
		Type	Results	Type	Results	
Clegg[28, 30]	GB vs VBG (20 years)	QALY	0.19	Direct health care costs	€207	€1,117/QALY
Clegg[28, 30]	LAGB vs GB (20 years)	QALY	0.004	Direct health care costs	€1,552	€386,780/QALY
Clegg[28, 30]	LAGB vs VBG (20 years)	QALY	0.19	Direct health care costs	€1,759	€9,300/QALY
Van Mastrigt [37]	VBG vs LAGB (1 years)	QALY	-0.05 (p=0.138)	Direct and indirect health care costs	€ + 2,081 (ns)	LAGB dominant

*Sources : GDP deflator: World Bank / PPP : Eur25 = 1 for 2004 (Eurostat)

6.3.2 Reviews of economic evaluations

Six reviews of economic evaluations were identified[28, 30, 32-35]. These reviews were based on original studies, some of which did not meet our inclusion criteria.

Clegg *et al.*[28, 30] included four economic evaluations in their analysis but acknowledged that the only study with a good quality was the study of Van Gemert *et al*, the only study retained in our systematic review. Based on these selected studies, they conducted their proper original economic evaluation.

The study of MSAC (Medical Services Advisory committee)[31] was a health technology assessment of laparoscopic adjustable gastric banding. They assessed the cost-effectiveness of this intervention based on the study of Clegg *et al.* They estimated that in comparison with VBG, LAGB was $3,665 more costly but had a shorter stay and lower rates of revision and complications and consequently, an improved quality of life. By comparing this intervention with open RYGB, LAGB was $912 more costly with less effectiveness in terms of weight loss.

Avenell *et al.*[32] included two supplementary studies, a study of Nguyen *et al* and a study of Segal *et al.* These two studies did not meet our inclusion criteria and were thus excluded from our analysis. They converted the incremental cost-effectiveness ratios of the selected studies in UK £ and concluded that for morbidly obese patients, the incremental cost-effectiveness ratio of bariatric surgery, compared to no surgery was < £11,000 in each study, which was a ratio acceptable for the society following the NICE guidance. They also drew attention to the fact that bariatric surgery is even more cost-effective than no surgery for patients with diabetes.

Salem *et al.*[35] identified three economic evaluations which met their inclusion criteria and excluded eight studies because no cost-effectiveness ratio was determined. They concluded that these three selected studies had different perspectives, economic milieus and assumptions but that in all of them, the cost/QALY ratio of bariatric surgery, compared to no treatment or no surgery was less than $50,000 and even cost-saving in one study. They added that more complete and appropriately designed analysis should be done.

The study performed by the AETMIS (agence d'évaluation des technologies et des modes d'intervention en santé)[33] included cost-effectiveness studies but also cost analyses. They concluded that, in the current state of our knowledge, bariatric surgery improves the health and the quality of life of morbidly obese patients compared to no surgery or no treatment at an incremental cost comparable to other health programmes. Weight loss seems to reduce the prevalence of obesity-related morbidity and their associated costs and consequences. They also insisted on the necessity to have more accurate studies with a long-term follow-up.

The MAS (Medical Advisory Secretariat)[34] completed a systematic review of effectiveness and cost-effectiveness of bariatric surgery. They concluded that bariatric surgery was effective in terms of percent of weight loss and in terms of obesity-related morbidity resolving. They added that malabsorptive techniques were better than other banding procedures but that long term comparisons of these technique were not available. They identified twelve economic evaluations and two health technology assessments and have underlined the results and limits of these studies. They did not draw general conclusions from their review of economic evaluations.

Table 38. Review of economic evaluations

Authors	Years	Original economic evaluations included
Clegg *et al.*[28, 30]	2002-2003	Martin[14], Van Gemert[27], Chua[2], Sjostrom[15]
MSAC[31]	2003	Clegg[38]
Avenell *et al.*[32]	2004	Nguyen[18], Segal[39], Clegg[28], Martin[14], Van Gemert[27], Chua[2], Sjostrom[15]
Salem *et al.*[35]	2005	Clegg[28, 30], Craig[29], van Gemert[27]/ Excluded : Martin[14], Agren[19], Narbro[40, 9], Gallagher[5], Cooney[4], Nguyen[18], Naslund[41]
AETMIS[33]	2005	Monk[11], Potteiger[12], Christou[24], Sampalis[25], Snow[13], Angus[21], Gallagher[5], Agren[19, 8], Nguyen[18], Narbro[40, 9], Cooney[3, 4], Craig[29], Clegg[28], Martin[14], Van Gemert[27], Chua[2], Sjostrom[15]
MAS[34]	2005	MSAC[31], Clegg[28], Gallagher[5], Craig[29], Cooney[3, 4], Huerta[42], Narbro[9], Nguyen[18], Monk[11], Potteiger[12], Sampalis[25], Agren[19], DeMaria[20]

6.4 DISCUSSION

All the selected analyses concluded that surgical approaches are a cost-effective treatment for obesity compared to no surgery, no treatment or to a conventional treatment. While the incremental cost-effectiveness ratio for bariatric surgery is low compared to the incremental cost-effectiveness ratios of many other interventions in health care, this is in itself not a sufficient condition for reimbursement of this procedure. Health care policy makers wish to take into account other factors that are important from a societal point of view as well, such as the severity of the disease, the societal consequences of not using this particular intervention for this disease, the perceived responsibility of the patient for his or her disease, etc. Therefore, a specific threshold value for the incremental cost-effectiveness ratio does not work in practice.

These studies showed moreover the advantage of a selective treatment of patients with obesity-related complications.

Concerning the comparison between surgical strategies, GB weakly tends to be more cost-effective in comparison with VBG or LAGB but more studies are needed to confirm this trend.

The validity of these studies can be questioned for several reasons.

Firstly, most studies had methodological weaknesses.

- Models were based on key assumptions in favour of surgery
    - Assumptions on outcome data for the control group were not always conservative. In the study of Clegg *et al*[28, 30], the weight loss was assumed to be null in the non surgical group. In the study of Chevallier *et al*[36], the BMI reduction in the group following a conventional treatment was assumed to be null after 2 years.
    - Resource use estimates were mostly based on expert opinion and were not always justified.
- The studies did not compare all relevant alternatives
    - To be complete, an economic evaluation should assess all the relevant alternatives. In all economic evaluations included in our review, the alternatives assessed were not clearly described and did not compare surgical treatment with all the other possible alternatives: lifestyle changes, drug treatment, other surgical interventions, prevention measures, combinations of these measures and no intervention.

- The studies failed to include some cost or outcome items
    - Cost items included in the studies were not always specified and their accuracy could thus not be assessed.
    - Some outcomes in favour of the control group like the loss of utility due to the surgical operation and its complications were omitted in the studies.

Secondly, outcome data were often based on clinical trials (efficacy) and not on outcomes in daily practice (effectiveness). Results are thus expected to be different in real life. The weight loss could be lower in real life and patients more at risk could have more complications, which could lead to a higher cost-effectiveness ratio.

Thirdly, the only study which compared LAGB to conventional treatment[36] was industry funded. Recent studies[43-45] have highlighted the bias generated by this kind of sponsorship and showed that clinical trial and economic evaluations sponsored by the drug industry were more likely to produce results in favour of the company product than studies funded by other sources.

Finally, none of the studies assessed Belgian costs. The external validity of the studies for the Belgian situation may be limited. Moreover, not enough studies were performed to make an evidenced-based conclusion.

Key points

According to the existing economic literature, surgery is a cost-effective alternative compared to no surgery or no treatment.

Selective treatment of patients with obesity-related morbidity increases the cost-effectiveness of surgical treatment.

There is insufficient evidence to draw conclusions about the relative cost-effectiveness of different surgical procedures compared to each other.

The validity of the studies may be questioned:

- **The studies have methodological weaknesses (models were based on assumptions supporting surgery, alternatives were not clearly specified, they did not include all possible alternatives and they failed to included some cost or outcome items)**
- **Outcomes were based on efficacy data from clinical trials rather than effectiveness data from daily practice**
- **None of the studies assessed Belgian costs**
- **Not enough studies was performed to make an evidenced-based conclusion**

In comparison with the economic evaluations of pharmacological treatments for obesity, the economic evaluations of surgical interventions for obesity seem to be more valid.

6.5 REFERENCES

1. Drummond M, Michael F. Methods for the economic evaluation of health care programmes. Oxford university press ed. Oxford: Oxford medical publications; 1990.
2. Chua TY, Mendiola RM. Laparoscopic Vertical Banded Gastroplasty: The Milwaukee Experience. Obes.Surg. 1995;5(1):77-80.
3. Cooney RN, Bryant P, Haluck R, Rodgers M, Lowery M. The impact of a clinical pathway for gastric bypass surgery on resource utilization. J Surg Res. 2001;98(2):97-101.
4. Cooney RN, Haluck RS, Ku J, Bass T, MacLeod J, Brunner H, et al. Analysis of cost outliers after gastric bypass surgery: what can we learn? Obes Surg. 2003;13(1):29-36.
5. Gallagher SF, Banasiak M, Gonzalvo JP, Paoli DP, Allwood J, Morris D, et al. The impact of bariatric surgery on the Veterans Administration healthcare system: a cost analysis. Obes.Surg. 2003;13(2):245-8.
6. Muhlmann G, Klaus A, Kirchmayr W, Wykypiel H, Unger A, Holler E, et al. DaVinci robotic-assisted laparoscopic bariatric surgery: is it justified in a routine setting? Obes.Surg. 2003;13(6):848-54.
7. Livingston EH. Hospital costs associated with bariatric procedures in the United States. Am.J.Surg. 2005;190(5):816-20.
8. Agren G, Narbro K, Naslund I, Sjostrom L, Peltonen M. Long-term effects of weight loss on pharmaceutical costs in obese subjects. A report from the SOS intervention study. Int J Obes Relat Metab Disord. 2002;26(2):184-92.
9. Narbro K, Agren G, Jonsson E, Naslund I, Sjostrom L, Peltonen M. Pharmaceutical costs in obese individuals: comparison with a randomly selected population sample and long-term changes after conventional and surgical treatment: the SOS intervention study. Arch Intern Med. 2002;162(18):2061-9.
10. Gould JC, Garren MJ, Starling JR. Laparoscopic gastric bypass results in decreased prescription medication costs within 6 months. J.Gastrointest.Surg. 2004;8(8):983-7.
11. Monk JS, Jr., Dia NN, Stehr W. Pharmaceutical savings after gastric bypass surgery. 2004;14(1):13-5.
12. Potteiger CE, Paragi PR, Inverso NA, Still C, Reed MJ, Strodel W, III, et al. Bariatric surgery: shedding the monetary weight of prescription costs in the managed care arena. Obes.Surg. 2004;14(6):725-30.
13. Snow LL, Weinstein LS, Hannon JK, Lane DR, Ringold FG, Hansen PA, et al. The effect of Roux-en-Y gastric bypass on prescription drug costs. Obes.Surg. 2004;14(8):1031-5.
14. Martin LF, Tan TL, Horn JR, Bixler EO, Kauffman GL, Becker DA, et al. Comparison of the costs associated with medical and surgical treatment of obesity. Surgery. 1995;118(4):599-606; discussion -7.
15. Sjostrom L, Narbro K, Sjostrom D. Costs and benefits when treating obesity. Int J Obes Relat Metab Disord. 1995;19 Suppl 6:S9-12.
16. Gawdat K. Gastric restrictive procedures through a mini-incision: a cost-effective alternative to laparoscopic bariatric surgery in Egypt. Obes.Surg. 1999;9(5):456-8.
17. Kuhlmann HW, Falcone RA, Wolf AM. Cost-effective bariatric surgery in Germany today. Obes.Surg. 2000;10(6):549-52.
18. Nguyen NT, Goldman C, Rosenquist CJ, Arango A, Cole CJ, Lee SJ, et al. Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. Ann Surg. 2001;234(3):279-89; discussion 89-91.
19. Agren G, Narbro K, Jonsson E, Naslund I, Sjostrom L, Peltonen M. Cost of in-patient care over 7 years among surgically and conventionally treated obese patients. Obes Res. 2002;10(12):1276-83.
20. DeMaria EJ, Schweitzer MA, Kellum JM, Meador J, Wolfe L, Sugerman HJ. Hand-assisted laparoscopic gastric bypass does not improve outcome and increases costs when compared to open gastric bypass for the surgical treatment of obesity. Surg.Endosc. 2002;16(10):1452-5.
21. Angus LD, Cottam DR, Gorecki PJ, Mourello R, Ortega RE, Adamski J. DRG, costs and reimbursement following Roux-en-Y gastric bypass: an economic appraisal. Obes.Surg. 2003;13(4):591-5.
22. Chang CG, Helling TS, Dezutti B, Koenig C, Cruz S. Gastric bypass: it pays to keep military hospitals busy. Mil.Med. 2003;168(9):725-8.
23. Chen J, McGregor M. The Gastric Banding Procedure: An Evaluation. Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC). 2004 April 27, 2004. Available from: http://www.mcgill.ca/tau/publications/2004/

24. Christou NV, Sampalis JS, Liberman M, Look D, Auger S, McLean APH, et al. Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. Ann Surg. 2004;240(3):416-23; discussion 23-4.
25. Sampalis JS, Liberman M, Auger S, Christou NV. The impact of weight reduction surgery on health-care costs in morbidly obese patients. Obes Surg. 2004;14(7):939-47.
26. Paxton JH, Matthews JB. The cost effectiveness of laparoscopic versus open gastric bypass surgery. Obes.Surg. 2005;15(1):24-34.
27. van Gemert WG, Adang EM, Kop M, Vos G, Greve JW, Soeters PB. A prospective cost-effectiveness analysis of vertical banded gastroplasty for the treatment of morbid obesity. Obes.Surg. 1999;9(5):484-91.
28. Clegg AJ, Colquitt J, Sidhu MK, Royle P, Loveman E, Walker A. The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation. Health Technol Assess. 2002;6(12):1-153.
29. Craig BM, Tseng DS. Cost-effectiveness of gastric bypass for severe obesity. Am.J.Med. 2002;113(6):491-8.
30. Clegg A, Colquitt J, Sidhu M, Royle P, Walker A. Clinical and cost effectiveness of surgery for morbid obesity: a systematic review and economic evaluation. Int J Obes Relat Metab Disord. 2003;27(10):1167-77.
31. Medical Services Advisory Committee (MSAC). Laparoscopic adjustable gastric banding for morbid obesity. Canberra: 2003. (MSAC reference 14) Available from: http://www.msac.gov.au/reports.htm
32. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess. 2004;8(21):iii-iv, 1-182.
33. Hassen-Khodja R, Lance JMR. Le traitement chirurgical de l'obésité morbide. Mise à jour. Québec: Agence d'évaluation des technologies et des modes d'intervention en santé L1 - http://www.aetmis.gouv.qc.ca/site/download.php?98bb350702f0f2f90c1f602c91bc5dbd; 2005.
34. Medical Advisory Secretariat - Ontario Ministry of Health and Long-Term Care Bariatric Surgery:Health Technology Literature Review. 2005. Available from: http://www.health.gov.on.ca/english/providers/program/mas/reviews/review_baria_0105.html
35. Salem L, Jensen CC, Flum DR. Are bariatric surgical outcomes worth their cost? A systematic review. J.Am.Coll.Surg. 2005;200(2):270-8.
36. Chevallier JM, Daoud F, Szwarcensztein K, Volcot MF, Rupprecht MF. [Medicoeconomic evaluation of the treatment of morbid obesity by Swedish adjustable gastric banding (SAGB)]. Ann.Chir. 2006;131(1):12-21.
37. van Mastrigt GA, van Dielen FM, Severens JL, Voss GB, Greve JW. One-year cost-effectiveness of surgical treatment of morbid obesity: vertical banded gastroplasty versus Lap-Band. Obes.Surg. 2006;16(1):75-84.
38. Clegg A, Sidhu M, Colquitt J, Royle P, Loveman E, Walker A. Clinical and cost effectiveness of surgery for people with morbid obesity. Southampton: National Institute for Clinical Excellence; 2001.
39. Segal L, Dalton AC, Richardson J. Cost-effectiveness of the primary prevention of non-insulin dependent diabetes mellitus. Health Promotion International. 1998;13(3):197-209.
40. Narbro K, Agren G, Jonsson E, Larsson B, Naslund I, Wedel H, et al. Sick leave and disability pension before and after treatment for obesity: a report from the Swedish Obese Subjects (SOS) study. Int J Obes Relat Metab Disord. 1999;23(6):619-24.
41. Naslund I, Wickbom G, Christoffersson E, Agren G. A prospective randomized comparison of gastric bypass and gastroplasty. Complications and early results. Acta Chir Scand. 1986;152:681-9.
42. Huerta S, Heber D, Sawicki MP, Liu CD, Arthur D, Alexander P, et al. Reduced length of stay by implementation of a clinical pathway for bariatric surgery in an academic health care center. Am.Surg. 2001;67(12):1128-35.
43. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003;326(7400):1167-70.
44. Smith R. Medical journals are an extension of the marketing arm of pharmaceutical companies. PLoS Med. 2005;2(5):e138.
45. Bell CM, Urbach DR, Ray JG, Bayoumi A, Rosen AB, Greenberg D, et al. Bias in published cost effectiveness studies: systematic review. BMJ. 2006;332(7543):699-703.

7 MEDICAL AND SURGICAL TREATMENT OF OBESITY IN BELGIUM

7.1 INTRODUCTION

This chapter presents some information on treatment of obesity in Belgium. Different databases or information were consulted. Section 2 shows the evolution of drugs consumption, this concerns quasi totally the ambulatory sector. Section 3 presents the frequency of billing codes used for bariatric surgery. Information concerning hospitalisation for obesity is presented in section 4. Section 5 deals with a rough estimation of costs linked to surgical hospitalisation. The last section describes the clinical pathway of obese patients in 3 hospitals.

7.2 PRESCRIPTION DRUGS

Since October 2001, anorexiants, including norpseudoéphédrine, phendimétrazine, phentermine et propylhexédrine can no longer legally be delivered in Belgium. Two prescription drugs are authorized for obesity treatment in Belgium: sibutramine (Réductil® Abbott) and orlistat (Xénical®) Roche). These (expensive) drugs are not refunded by the Social Security. So far, a request (by the industry) to have orlistat refunded for diabetic patients has been rejected (Leo Neels, personal communication).

Figure 1 shows the evolution of drugs revenues. More details can be found in Table 1. A decrease in the consumption of orlistat is observed along with an increase consumption of sibutramine. Since 2002, total expenses linked to these drugs seem quite stable.

Figure 3. Evolution of drugs revenue in Belgium

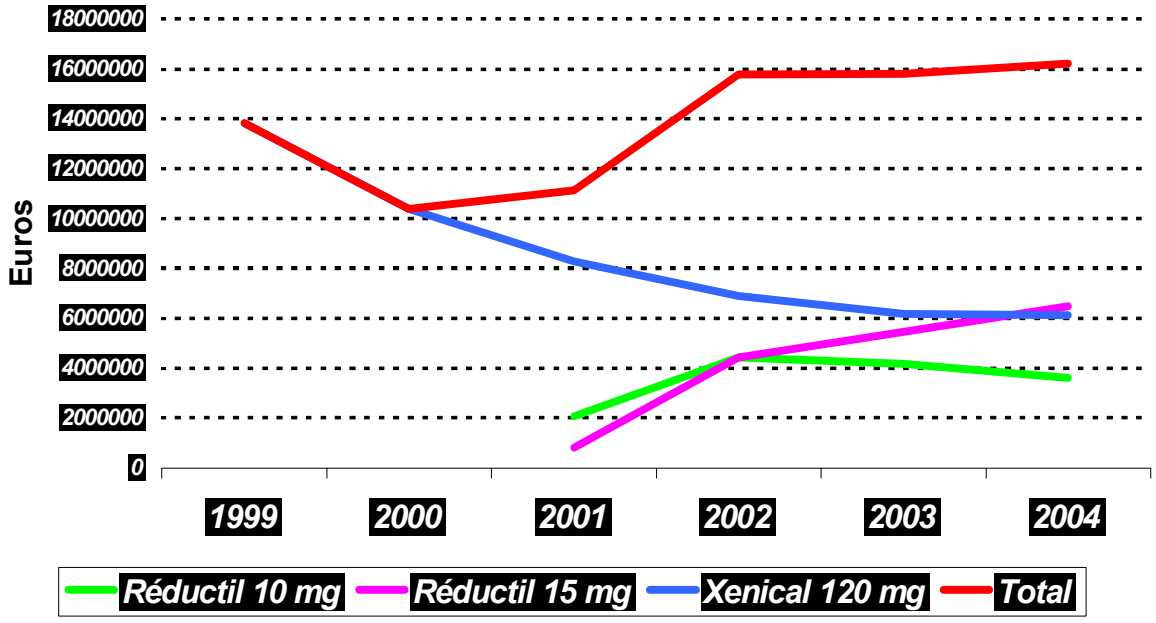


Table 39. Sibutramine and Orlistat: sales in Belgium

	Unit price (Euros)		Sales volume		Revenue (Euros)		
	Retail	Factory	Ambulatory (N boxes)	Hospital (N tabs)	Ambulatory	Hospital	Total
Reductil	10mg	28 tablets			Marketed since : July 1, 2001		
2001	65,59	52,2574	39.192	400	2.048.070	937	2.049.007
2002	65,59	52,2574	84.598	2.900	4.420.868	6.793	4.427.661
2003	76,72	62,7574	66.369	1.900	4.165.143	5.206	4.170.349
2004	76,72	62,7574	57.147	1.600	3.586.395	4.384	3.590.779
2005	76,72	62,7574					
Reductil	15mg	28 tablets			Marketed since : July 1, 2001		
2001	76,10	62,1725	13.027	200	809.921	544	810.464
2002	76,10	62,1725	71.507	500	4.445.766	1.359	4.447.125
2003	76,20	62,2668	87.336	700	5.438.133	1.905	5.440.038
2004	76,20	62,2668	104.158	700	6.485.585	1.905	6.487.490
2005	76,20	62,2668					
Xenical	120mg	84 tablets			Marketed since : 1er mars 1999		
1999	76,85	62,8800	219722	17000	13.816.119	15.553	13.831.672
2000	76,85	62,8800	164838	23000	10.365.013	21.042	10.386.056
2001	76,85	62,8800	131.087	20.200	8.242.751	18.481	8.261.231
2002	76,85	62,8800	109.458	23.000	6.882.719	21.042	6.903.761
2003	76,85	62,8800	98.112	16.200	6.169.283	14.821	6.184.104
2004	76,85	62,8800	97.119	20.400	6.106.843	18.664	6.125.506
2005	76,85	62,8800					

Source : data courtesy of M. Leo Neels, pharma.be.

7.3 BILLING CODES

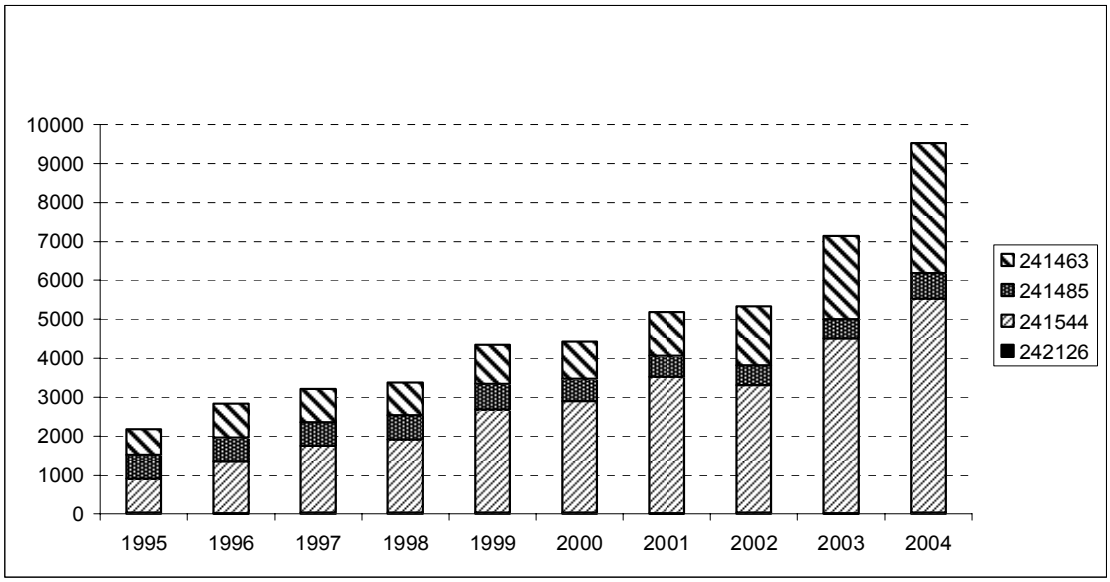
In the Belgian billing system for procedures, there is no specific code identifying bariatric surgery or more specific procedures related to bariatric surgery. These interventions are billed with codes used for the most similar interventions but performed for other pathology. Table 2 presents these codes and their signification.

Table 4 0. Codes used for bariatric surgery

Bariatric procedures	Approximated by
Gastric Banding	241544: Résection de l'estomac ou gastroplastie de réduction sans interruption de la continuité
Sleeve Gastrectomie	241485: Gastrectomie subtotale
Gastric Bypass	241463: Gastrectomie totale avec anastomose oesophagojéjunale ou gastrectomie subtotale avec restauration du transit, par interposition d'un segment intestinal
Bypass Jejuno-ileal	242126: Duodeno-jéjunostomie
Scopinaro et switch duodenal	241463: Gastrectomie totale avec anastomose oesophago-jéjunale ou gastrectomie subtotale avec restauration du transit par interposition d'un segment intestinal

Figure 2 displays at national level the evolution of the different codes presented in Table 2. In a 10 years period, the frequency of the code used for gastric banding is multiplied by 5 and the frequency of the code used for gastric bypass is multiplied by 3. The frequency of the other codes remains quite stable.

Figure 4. Evolution of INAMI codes



A study based on billing codes has been done recently by the 'Mutualités Libres'[1] to analyse use of bariatric surgery among their members. The results of this analysis are not presented here but can be consulted at the site:

http://www.mloz.be/cms/Mloz/Etude%20Obesitas%20FR%2013%20.doc.

7.4 IN-PATIENT STAYS

7.4.1 Method

Over the last decade, Belgium has developed and implemented a comprehensive data collection system covering all in-hospital stays and day-cases. Data are routinely collected by the hospitals, centralized in national database and used by Public Health Authorities for hospital funding. The MBDS (medical basic data set) contains medical information, such as main diagnosis, secondary diagnoses and procedures, from which the Major Diagnosis Category (MDC), APR-DRG (All Patient Refined Diagnosis Related Group), and a severity of illness score can be derived. It also includes administrative information such as the type of admission (e.g., emergency), readmission, transfer to another institution, discharge, death, length of stay (LOS) and demographic information, such as age and sex. The diagnoses are coded using the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM).

In this analysis, the stays are selected in function of the presence of obesity mentioned as main or secondary diagnosis. The ICD-9-CM codes retained are 278.00 Obesity, unspecified, 278.01 Morbid obesity and 278.1 Localised adiposity.

Five excel files have been given by the Ministry of Health. They are extracted from the National databases of the years 1999, 2001 and 2003. File 1 contains the number of stays, number of death, mean age and median age by year, type of hospitalisation, ICD-9-CM codes of obesity and sex. File 2 contains the number of stays and mean age by year, type of hospitalisation, ICD-9-CM code for obesity, sex and age category. File 3 contains the number of stays by year, type of hospitalisation, ICD-9-CM codes for obesity, MDC and APRDRG. File 4 contains the number of stays and the mean length of stay by year, ICD-9-CM codes of obesity, hospital, APRDRG and severity. File 5 contains the number of stays, mean age and median age, by year, ICD-9-CM code of obesity, region, APRDRG, sex, age category and hospital.

The second source of information comes from the research database of CIES-UCL containing approximately a third of Belgian in-hospital stays and day cases of 2003 in 19 hospitals. This database is used when more detailed information is needed and to estimate the expenses linked to obesity and its complications. This information will be used in next paragraph to estimate the cost of surgical treatment of obesity.

Without any specification, the results presented concern the national database.

7.4.2 Results

The total number of inpatient stays was 1.611.503 in 1999, 1.616.644 in 2001 and 1.602.846 in 2003. In 1999, obesity was the main diagnosis for 0.47% of inpatient stays and was mentioned as secondary diagnosis in 3.1% of inpatients stays. These proportions were respectively 0.56% and 3.9% in 2001; in 2003 they reached 0.79%and 5.38%. These results show an increase in the number of hospitalisations for obesity and in the number of obesity codes mentioned as secondary diagnosis while the number of inpatient stays remains quite stable during the period analysed.

Table 3 shows then evolution of the number of in-hospital stays and day-cases by sex and age category between 1999 and 2003. The number of day-cases remains quite stable during this period. But the number of in-hospital stays increases by 64% between 1999 and 2003. This increase concerns mainly people between 18 and 59 years. For people of 60 years or more, it is less important. For children, the number of in-hospital stays remains stable. The same trend is observed in Table 4 where the number of in-hospital stays is expressed in function of the number of inhabitants. Hospitalisations are more frequent among women: 85% of in-hospital stays concern women whereas the proportion of obesity in the population is the same for men and women.

Table 4 1. Number of in-hospital stays and day cases by age and sex when obesity is mentioned as main diagnosis

		1999			2001			2003	
Age	Men	Women	Total	Men	Women	Total	Men	Women	Total
Hospitalisations									
N	1164	6452	7616	1458	7703	9161	2098	10388	12486
3-11 years	24	12	36	17	21	38	35	21	56
12-17 years	44	78	122	37	72	109	25	82	107
18-49 years	805	4960	5765	1090	6025	7115	1538	8164	9702
50-59 years	175	992	1167	233	1136	1369	373	1538	1911
>= 60 years	116	410	526	81	449	530	127	583	710
Day cases									
N	43	592	635	80	668	748	78	552	630
3-11 years	2	1	3	2	3	5	5	2	7
12-17 years	1	5	6	5	5	10	5	5	10
18-49 years	32	494	526	56	515	571	58	447	505
50-59 years	7	68	75	8	104	112	9	75	84
>= 60 years	1	24	25	9	41	50	1	23	24

Table 4 2. Number of in-hospital stays per 1000 inhabitants when obesity is mentioned as main diagnosis

	2001				2003			
	Nb of hospitalisations		Nb of hospitalisation/1000 inhabitants*		Nb of hospitalisations		Nb of hospitalisation/1000 inhabitants*	
Age	Men	Women	Men	Women	Men	Women	Men	Women
18-59 years	1323	7161	0.45	2.5	1911	9702	0.64	3.3
>= 60 years	81	449	0.085	0.35	127	583	0.13	0.45

* the number of inhabitants have been found on the site http://statbel/fgov/be/figures/d21_fr.asp#3 of the SPF Economie – Direction générale Statistique et Information économique, Service Démographie

The most frequent APRDRGs are DRG 403 Procedures for obesity, DRG 421 Nutritional and miscellaneous metabolic disorders, DRG 405 Other endocrine, nutritional and metabolic procedures. They concentrate 96.3% of in-hospital stays for obesity in 1999, 97.3% in 2001 and 97.6% in 2003. The frequency of DRG 421 remains quite stable during the period analysed. But an increase of 82% is observed for DRG 403 and this increase reaches 160% for DRG 405. Table 5 shows the evolution of the number of in-hospital stays for the 3 most frequent APRDRGs.

In day cases MBDS, the main diagnosis is most frequently the code 278.1 localised adiposity. In consequence, the results are not presented here.

Table 4 3 . Most frequent APRDRGs when obesity is mentioned as main diagnosis of in-hospital stays

		1999			2001			2003	
	Obesity (278.0*)	L. adiposity (278.1)	Total	Obesity (278.0*)	L. adiposity (278.1)	Total	Obesity (278.0*)	L. adiposity (278.1)	Total
DRG 403	2725	2174	4899	4400	2122	6522	6418	2497	8915
DRG 405	494	68	562	606	61	667	1390	73	1463
DRG 421	1768	105	1873	1630	94	1724	1751	52	1803

DRG 403 Procedures for obesity
DRG 405 Other endocrine, nutritional and metabolic procedures
DRG 421 Nutritional and miscellaneous metabolic disorders

Table 6 shows the evolution of admissions for obesity and morbid obesity for in-hospital stays. An important increase of obesity codes is observed in surgical APRDRGs, particularly for morbid obesity. At this step, it is not possible to differentiate the increase due to the epidemiology of obesity from the increase due to the modification in the coding process.

Table 4 4 . Main diagnosis for APRDRGs 403, 405 and 421

	1999	2001	2003	% increase
Surgical DRGs 403 and 405				
278.00 Obesity, unspecified	318	495	680	+ 114%
278.01 Morbid obesity	2901	4511	7128	+ 146%
278.1 Localised adiposity	2242	2183	2570	+ 15%
Medical DRG 421				
278.00 Obesity, unspecified	844	512	488	-73%
278.01 Morbid obesity	924	1118	1263	+37%
278.1 Localised adiposity	105	94	52	-50%

DRG 403 Procedures for obesity
DRG 405 Other endocrine, nutritional and metabolic procedures
DRG 421 Nutritional and miscellaneous metabolic disorders

If there is a concentration of admissions for obesity in some hospitals, there is a global increase of admissions for obesity in all hospitals. Figure 3 shows the distribution of in-hospital stays among hospitals between 1999 and 2003. Table 7 displays the concentration of in-hospital stays in hospitals in 2003 when stays are classified in APRDRGs 403 or 405 and when the main diagnosis is obesity.

The distribution of bariatric surgery varies between Belgian regions: 75% of bariatric procedures are performed in Flanders.

Figure 5. Concentration of hospitalisation for obesity in hospitals

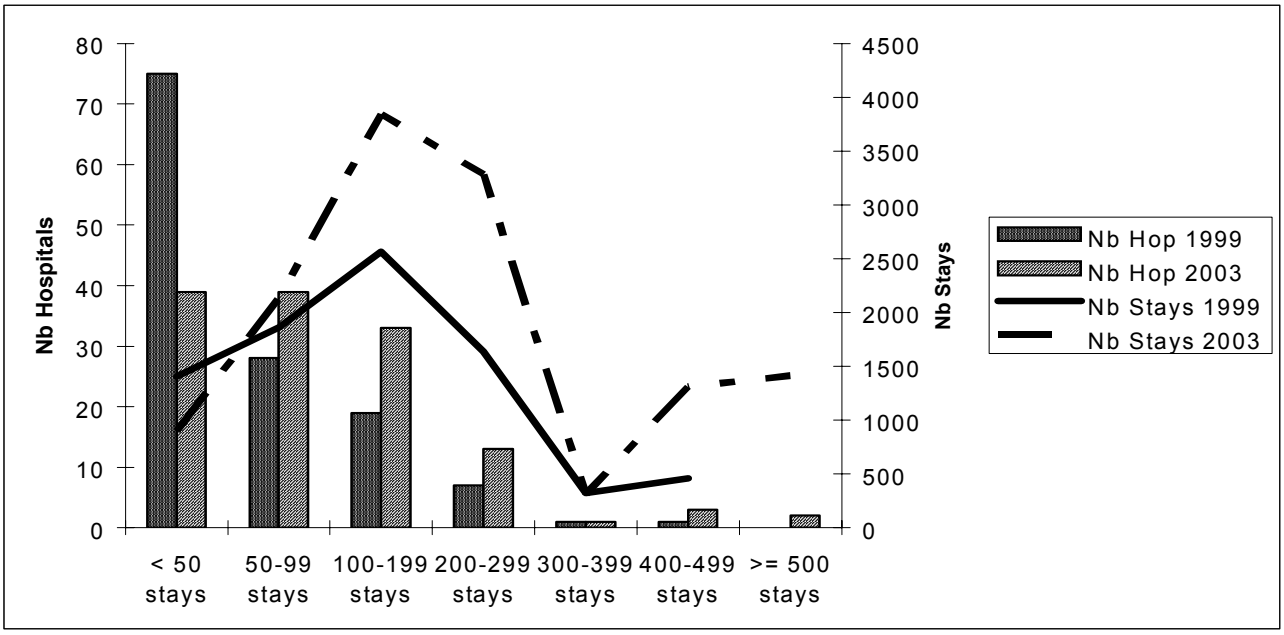


Table 4 5 . Concentration of in-hospital stays in hospitals in 2003 (APRDRGs 403 and 405, obesity as main diagnosis)

Cases	Nb Hosp	Nb Stays	% Hosp	% Stays	Sum cum Hosp	Sum cum stays
>300	4	1.703	3,7	21,6	4	1.703
201-300	5	1.180	4,6	15,0	9	2.883
101-200	16	2.168	14,8	27,5	25	5.051
51-100	24	1.621	22,2	20,5	49	6.672
1-50	59	1.218	54,6	15,4	108	7.890
Total	108	7.890	100	100	108	7.890

Five in-hospital deaths are observed in 1999 in the national database, 7 in 2001 and 7 in 2003. It represent 0.066 % in 1999, 0.076 % in 2001 and 0.056 % in 2003. It concerns in-hospital deaths of patients hospitalised for obesity. Deaths occurring after these stays are not taken into account. Available data do not allow to estimate all deaths following surgical treatment of obesity.

The research database contains 460.155 in-hospital stays where 1596 (0.35%) present an obesity code (278.0*) as main diagnosis. 70.9% of these stays are classified in APRDRG 403 'Procedures for obesity, 3.8% in APRDRG 405 'Other endocrine, nutritional and metabolic procedures' and 24.5% in APRDRG 421 'Nutritional and miscellaneous metabolic disorders'. 8.0 % of stays contain a code of dyslipidemia, 2.4% a code of coronaropathy, 20.6% a code of hypertension and 9.0% a code of diabetes.

The most frequent ICD-9-CM codes for procedures are 44.69 Other repair of stomach, 44.99 Other operations of stomach, 44.31 High gastric bypass and 43.7 Partial gastrectomy with anastomosis to jejunum, as shown in Table 8.

Table 46. Frequency of surgical procedures (research database)

	N	%
DRG 403 Procedures for obesity	1132	
44.31 High gastric bypass	209	18.5
44.39 Other gastro-enterostomy	34	3.0
44.5 Revision of gastric anastomosis	2	0.2
44.69 Other repair of stomach	546	48.2
44.99 Other operations of stomach	319	28.2
45.91 Small to small intestinal anastomosis	6	0.5
DRG 405 Other endocrine, nutritional and metabolic procedures	61	
43.7 Partial gastrectomy with anastomosis to jejunum	45	73.8
43.81 Partial gastrectomy with jejunal transposition	1	1.6
43.89 Other partial gastrectomy	2	3.3
43.99 Other total gastrectomy	1	1.6
44.66 Other procedures for creation of esophagogastric sphincteric competence	1	1.6

In the research database, 11 children stays are classified in surgical APRDRGs (403, 405). Six hospitals are concerned by this type of care but it seems to be no concentration of patients in one hospital (1, 2, or 3 children by hospital). 25 children stays are classified in the medical APRDRG of obesity. The majority of them (19/25) are hospitalised in 1 hospital for a short stay.

7.5 LENGTH OF STAY FOR BARIATRIC SURGICAL TREATMENT

We assessed the length of stay for bariatric surgical treatment from the research database described in the previous section. We selected in-hospital stays classified in APR-DRGs 403 or 405 with INAMI/RIZIV codes of bariatric surgery.

From the INAMI/RIZIV codes, we identified 4 groups of surgical interventions:

- Group 1 : Gastric banding (241544)
- Group 2 : Gastric bypass, Scopinaro or duodenal switch (241463)
- Group 3 : Sleeve gastrectomy (241485)
- Group 4 : Jejuno-ileal bypass (242126)

These groups were based on proxies (cfr Table 2) and group 2 includes more than one intervention. Because no specific code exists, we could not make more precise analyses and we could only compare groups instead of separate interventions.

In the research database, no stay for group 4 was found. Consequently, their length of stay could not be derived. This group accounts for 0.42% of surgical procedures.

The LoS was shorter for the gastric banding group than for the other groups (Table 9).

Table 47. Length of stay (days) for Gastric banding, Gastric bypass, scopinaro and duodenal switch, and Sleeve gastrectomy – 2003*

	Proxy: INAMI/RIZIV codes	Mean	Lower Quartile	Median	Upper Quartile	Minimum	Maximum
Gastric banding	241544 or 241533	3.91	2.00	3.00	5.00	1.00	24.00
Gastric bypass, scopinaro and duodenal switch	241463 or 241452	10.73	8.00	9.00	11.00	3.00	38.00
Sleeve gastrectomy	241485 or 241474	8.50	5.00	8.00	11.00	4.00	14.00

* Sources : Research database 2003 (n = 800 stays – 15 hospitals)

7.6 COST TO SOCIAL SECURITY OF BARIATRIC SURGERY IN 2003

In 2003, 7.702 hospitals stays were classified in the APR-DRG 403 (surgical interventions for obesitas), and mean cost per stay to the social security was 2521,9 Euros (source: Technische cel https://tct.fgov.be/etct/anonymous?lang=fr). It concerns in-hospital stays for which medical and financial data were available.

Assuming that 80% of these hospital stays were indeed related to bariatric surgery (based on an analysis of procedure codes associated with each stay), this translates into a total of 15.338.939 Euros.

This can only be considered as a rough estimation, and most likely underestimation of real costs. Indeed, bariatric stays in the APR-DRG 403 probably have a higher cost per stay than non-bariatric stays; on the other hand some stays for bariatric surgery are classified in APR-DRG 405 and are not included in this estimation.

7.7 DIRECT HEALTH CARE COST OF SURGERY-RELATED AMBULATORY CARE

The cost of out-patient visits before surgery and up to one year after surgery was simulated, based on expert opinions about an 'ideal' protocol for pre-operative work-up and post-operative follow-up for bariatric surgery patients without complications after surgery. So, it does not represent the real cost but rather the theoretical cost of follow-up if a patient does not present with any complication.

Because many follow-up visits are actually not reimbursed by the National Health Insurance (e.g. psychologists, dietician …), we not only simulated the costs from the perspective of the National Health Insurance Institute (RIZIV/INAMI) but also the direct health-care related out-of-pocket expenses of patients.

For non-reimbursed visits, we used unit costs charged at Saint Luc university hospital in Brussels. For reimbursed out-patient visits, 2004 official national prices of a non-accredited[9] physician were applied[10][11] (Table 10). Charges for biological analyses were not included.

Costs of complications occurring after the hospitalization for bariatric surgery and savings generated by a reduction of obesity-related morbidity were not included in this analysis because data were not available.

[9] Accredited physicians are those meeting particular requirements such as participation in continuing education programmes; they are allowed to charge higher fees.
[10] Non-accredited endocrinologist : € 25.39€ – Accredited endocrinologist : € 26.20 (2003 official national prices)
[11] Non-accredited surgeon : €15.46€ – Accredited surgeon : € 17.00€
(2003 official national prices)

The simulated cost of out-patient visits for the health care insurance for a patient who has no complication was between € 109.08 to € 118.49 per patient (2004 prices Table 10). Costs to the patients were between € 187.63 - € 293.89.

Table 48. Simulated direct cost of out-patient visits for a patient without complication*.

	Out-patient visits in preop	Follow-up (1 year)	Unit Prices (2004)	Cost to Health Care Insurance	Cost to Patient	Total cost
Surgeon	1 - 2	2	€ 15.67	28.23 - 37.64	18.78 - 25.04	47.01- 62.68
Endocrinologist	1	4	€ 25.74	80.85	47.85	128.70
Dietician	1	4	First visit : € 23 Following visits : € 12	0	71	71
Psychologist	1	1 - 5	€ 25	0	50- 150	50- 150
Direct cost of out-patient visits/patient				109.08 - 118.49	187.63 - 293.89	296.71- 412.38

* Sources : Saint-Luc practices and 2004 official national prices for a non-accredited physician.

7.8 CASE STUDIES

There is no standardised clinical pathway devoted to management of obesity in Belgium. We describe here the type of care proposed in 3 Belgian hospitals, 2 of them are university hospitals (Gent [UZG] and Brussels [UCL]) and one is a general hospital (Dendermonde [GHD]). Two surgeons were interviewed, one in UZG and one in GHD. In the other hospital, an internist (endocrinologist) was interviewed. The 2 university hospitals offer a multidisciplinary approach of obesity management whereas the general hospital offers only a surgical approach.

In case of multidisciplinary approach, the team includes a surgeon, a internist, a nutritionist and a psychologist.

At UZG, Belgian or not Belgian patients come directly to the surgical outpatient but diabetic patients are referred by the endocrinologist. Patients are seen twice by the surgeon before the operation. Their eating behaviour is assessed by a nutritionist and a psychological evaluation is done if necessary. The decision of surgical treatment is taken by the multidisciplinary team. The first follow-up consultation is planned 6 weeks after the procedure. After, the patient is seen every 6 months by the surgeon and the nutritionist.

At UCL, 50% of patients come directly to endocrinologist consultation, the other are referred by the general practitioner or by another specialist of the hospital. Patients are seen by the endocrinologist every 3 months and by the nutritionist every month. If obesity is linked to psychological problem, the patient is seen by the psychologist 2 to 6 times per year. The multidisciplinary team meets the surgeon once per month to discuss indication for surgical treatment and also once per month with the psychologist for eating disorders.

GHD offers a surgical package to patients and a third of his patients come from outside Belgium. The surgical package includes the completeness of a preoperative questionnaire. If necessary, a preoperative consultation in Belgium or in patients' country, is proposed. If the patient wants, he can be referred to the psychologist. After the surgical procedures, patients receive a diet sheet and is recommended to work with a nutritionist. Patients are seen after 1, 3, 6, 9 and 12 months, afterwards they are seen every 6 months. Foreigners are suggested to have blood test every 3 months the first year, every 6 months the second and the third years and every year after.

In each centre, patients must meet one of the following criteria to have an operation: BMI > 35 and co-morbidities or BMI > 40.

University hospitals also take care of patients hospitalised for complications of surgical procedures performed elsewhere. They raise the question of quality of care.

The complete interview of these 3 centres can be found in annex .

7.9 CONCLUSION

The results show an increase of drugs consumption until 2002 but this increase slows down after. We observed a substitution of orlistat by sibutramine.

Hospitalisations for obesity concerns mainly women whereas the population prevalence of obesity is equal between men and women.

The number of hospitalisations for surgical care of obesity has doubled between 1999 and 2003. The number of hospitals offering surgical care increases, the number of cases treated by hospital increases but there is also concentration effect in some hospitals.

There is no clinical pathway for the management of care for obesity: some hospitals offer a multidisciplinary approach, co-ordinated by a surgeon or by an internist , other hospitals offer only surgical treatment.

Even if bariatric surgery is currently not reimbursed, its practice generates an important cost to the health care system. Our rough estimation showed a total cost of 15.338.939 Euros for in-hospital stays in 2003. By taking into account the increase in the frequency of INAMI codes these last years, this cost is yet expected to double in 2007.

The length of stay was shorter for the gastric banding group than for the other groups. However, implants are not reimbursed. Their unit price ranges between 1800 to 2400€ and is totally at the charge of the patient. By taking into account the implant price, LAGB is not expected to be less expensive than other bariatric surgeries. As no specific code for bariatric surgery exists, a precise estimation of cost is not possible.

We did not assess the cost linked to complications after the hospitalization for bariatric surgery. The gains generated by bariatric surgery were also not calculated. The simulated cost of out-patient visits for the health care insurance for a patient who has no complication was between € 109.08 to € 118.49 per patient (2004 prices Table 1 0). Costs to the patients were between € 187.63 - € 293.89. Theses costs were not based on "real" data but rather on the simulation of the "ideal" practice for a patient who did not have any complication after surgery.

Key points

- **The results show an increase of pharmacological treatment.**
- **The number of hospitalisations for surgical care of obesity has doubled between 1999 and 2003.**
- **If bariatric surgery is currently not reimbursed, its practice generates an important cost to the health care system. As no specific code for bariatric surgery exists, a precise estimation of cost is not possible.**
- **There is no clinical pathway for the management of care for obesity.**

7.10 REFERENCES

1. Departement Etudes Stratégiques & Communication. Obésité : Prévention ou traitement? Le fléau de l'obésité et l'évolution dans le temps du nombre d'interventions bariatriques. Mutualites Libres, Belgique; 2005. Available from: http://www.mloz.be/cms/Mloz/Etude%20Obesitas%20FR%2013%20.doc

Part 3: Treatment of obesity in children

8 TREATMENT OF OBESITY IN CHILDREN

8.1 INTRODUCTION

This chapter has two main parts:

- a literature review on the safety and effectiveness of the pharmacological and surgical treatment of obesity in school-aged children; and particular issues raised by invasive therapies in this age-group. While acknowledging the importance, and the priority of the lifestyle interventions, these are not the subject of this chapter, and will be only briefly reviewed.
- an assessment of the residential treatment of obesity in school-aged children in Belgium. Three specialised centres in our country offer in-patient care of up to one year duration to obese children meeting definite criteria. Treatment in ambulatory care is the most important, but was beyond the scope and time limits allowed to this study, and only a brief description will be provided.

8.2 NON PHARMACOLOGICAL, NON SURGICAL TREATMENT

This section is limited to a short overview of recently published systematic reviews.

8.2.1 Methods

We searched systematic reviews that have been published since 2000 using Medline, CDR and Cochrane databases. We found three recent systematic reviews of the scientific literature and one HTA report.

We have included the three reviews:

- The Cochrane review (CR)[1]
- the National Health Services (NHS UK)[2].
- the Agency for Health Research and Quality (AHRQ USA)[3]

However, because of the weak description of the methodology in the ICSI Technology Assessment Report published in 2005 on the treatment of obesity in children and adolescent[4] (inclusion/exclusion criteria), we did not keep it in our synthesis.

Details of the content of each review are given in Table 1 We describe here the type of interventions available for children and discuss some of implications of the findings of these.

Table 4 9. Reviews on the treatment of obesity in children

	Cochrane[1]	NHS CRD[2]	AHRQ[3]
Scope	Treatment of obesity in children	Prevention and treatment of obesity in children	Screening and interventions for childhood overweight
Last search	2001	Not mentioned (update of CR published in 2002	April 2005
Inclusion criteria	Randomized controlled trials (RCTs) with a minimum of 6-month follow up	RCTs	- Fair-to-good quality research (according to predefined criteria) - 2-18 years old - for the non pharmacological/non surgical treatment: prospective cohort + RCTs with a minimum 6-month follow-up
Number of studies	18 studies	22 studies	15 studies
Main findings	Quality of evidence is poor: Very small groups Limited amount of quality data Generalisation of the evidence is limited No direct conclusions can be drawn	School-based interventions that promote physical activity, the modification of dietary intake and target sedentary behaviours may help reduce obesity particularly in girls. Family-based programmes may help reduce childhood obesity Future researches must be of good methodological quality, with a large number of participants, carried out in appropriate settings and need to be of long duration.	- Limited research available on effective generalizable interventions - No current research for 2-5 years old children. - Small number of studies - Small sample size - Short follow up - Minimal reporting of health outcomes No reporting of intention-to-treat analyses

8.2.2 Description of the interventions

All interventions aim to act on one or both sides of the energy balance equation: diet and activity.

- On the diet side:
  - Hypocaloric
  - modify the composition of the food intake in terms of nutritional input (reduce fat-, glycemic-index
  - food diversification (increase in fruit and vegetables consumption).
- On the physical activity side:
  - reducing sedentary behaviours (reduce screen-time: watching TV, video-, computer-games)
  - increasing exercise within the impact of different type of exercise (aerobic, callisthenic, etc) or intensity.

Change of diet and physical activities require behavioural change. To achieve it, multidisciplinary interventions are the more used. They consist in cooking counselling, education to healthy nutrition, stressing importance of physical activities. The means used are the information, the education, the skills development (parent's management techniques, communication), and the social support.

The targets and the actors of the interventions could be:

- children, individually or in group, obese or at risk of obesity (at least one parent obese)
- Parents, individually or in group: They are crucial in the implementation, the support and the maintenance of behavioural changes, particularly feeding habits and lifestyle such as limitation of the screen-time. Parents could be involved in the intervention as agent of change and not only as support to change
- teachers
- catering staff of the school

The interventions are conducted in:

- Clinical settings: beginning to be reported
- Non clinical settings: School-based interventions. They aim to promote healthy behaviours in all children. They therefore address every child, not only overweight or obese ones. Some interventions have a global approach: education, change of the meals at school and development and implementation of school action plan to promote healthy eating and physical activities practice. They can include a behavioural therapy component or not.

8.2.2.1 Evidence available:

Studies concern mainly school-aged children, with an over-representation of female adolescents. No trials have studied pre-school children.

All reviews agreed that there are generalized methodological flaws in the studies evaluating interventions to treat obesity in children.

No meta-analyse was done because of heterogeneity of indicators.

8.2.2.2 Outcomes of interventions

Weight-related outcomes

The effects on weight of family-based interventions are not clear[2]. When possible, Withlock et al.[3] have translated the results of different studies into BMI percentiles to compare the effectiveness of the interventions. They concluded that individual programmes using behavioural counselling show modest or no short-term results in terms of change in BMI percentiles.

For school-based programs, in terms of reducing BMI or adiposity, it appears that isolated interventions, i.e. diet or physical activity, are not sufficient to treat obesity in children. However, multifaceted interventions give encouraging results, sometimes with a statistically significant change in the BMI or in the median triceps skin fold.

Intermediary outcomes

Changes in behaviours or in functioning are intermediary outcomes. The variety of intermediary outcomes used makes it difficult to compare results across studies, i.e. change in energy intake, in physical activity, in targeted dietary component, in eating behaviour, sedentary behaviours.

For school-based programmes, multifaceted interventions give encouraging results in eating behaviours, number of hours watching television or attitude towards fitness[2].

For family-based interventions, evidence is available that they induce change in the dietary habits (daily calories, increase intake of fruit or vegetable VS decrease intake of high fat/sugar foods).

Withlock et al[3] report an improvement in depressions scores for adolescent treated girls. In a second study, they report that fewer children of 8-12 years of age in the intervention group present elevated total problems scores or elevated internalizing problem scores two years after the intervention.

The secondary type of intermediary outcomes concern physiological modifications.

No study reported immediate physiological outcomes regarding lipid level, glucose tolerance, blood pressure or physical fitness measures. Nevertheless it seems that when interventions address physical activities or sedentary behaviours, physical work capacity or physical fitness improved[5].

8.2.2.3 Safety of treatment

There is essentially no mortality directly associated with dietary, exercise and behavioural interventions. In terms of morbidity, adverse effects are not described.

All these interventions however need supervision.

8.2.3 Discussion

8.2.3.1 Prevention or treatment?

For lifestyles disease, the difference between prevention and treatment is not clear-cut. Both prevention and treatment can be the objectives of the interventions, for instance if the child is already overweight.

8.2.3.2 Medical intervention?

These reviews illustrate the fact that interventions to treat obesity in children are mainly outside the medical sphere. Nevertheless, interventions on medical settings begin to be reported in the scientific literature. Evidence is not sufficient for the moment to conclude on their efficacy.

8.2.3.3 Absence of evidence, but not evidence of absence

Finally, scarce evidence is available about the effectiveness of non pharmacological and non surgical treatment of the obesity in school-aged children.

The knowledge-base is poor resulting from different causes within:

- the small number of studies
- the methodological flaws (sample size, short follow-up) because this kind of studies are:
  - conceptually difficult to realize (lifelong process, not standardized interventions)
  - poorly funded.

However, lack of evidence of effectiveness does not mean evidence of no effectiveness and some interesting aspects of the interventions could be pointed out. For example, there are indications that family-based multifaceted interventions may help to treat the obesity in childhood, also with a key active role of the parents. In school setting, the population is not homogenous and, for example, the type of intervention (activity) addressing physical activities in schools seems to have to be sex-specific: aerobic dance give results in girls but not in boys.

There is a crucial need for longer, larger and better studies with sufficient participating subjects and with a strong methodology to assess (or not) the effectiveness of these kind of interventions.

8.2.4 Conclusion

There are indications on the efficacy of the non pharmacological and non surgical treatment for obesity in children but no clear evidence of it due to methodological flaws in existing published studies.

8.3 PHARMACOLOGICAL AND SURGICAL TREATMENT OF OBESITY IN CHILDREN

8.3.1 Methods

We found no systematic reviews of the pharmacological and surgical treatment of obesity in children. The method used for the literature search is described under each chapter. For drugs, one criterion for inclusion was a follow-up of at least 1 year.

8.3.2 Pharmacological treatment

8.3.2.1 Orlistat: evidence available and results

A Medline search on 'Orlistat' (free text) performed on March 24,2006, limited to children under 18, and to randomized controlled trials, returned 18 hits. Only 1 met our inclusion criteria in terms of study population and follow-up (at least one year)[6].

This study (industry-funded) included patients aged from 12-16 years, with a BMI >= 97Th percentile. (average: 98th percentile). Children with a BMI > 44 were excluded. Participants were prescribed hypocaloric diet, exercise, and behavioural therapy, and randomized to Orlistat, 120 mg three times daily (N=181), or placebo (N=352). Outcomes were evaluated after one year.

Drop-out was 35% in the placebo group, and 34% in the Orlistat group. Analysis was by intention to treat, using the last-observation-carried forward for drop-out patients.

Table 50: Placebo + diet vs Orlistat 360 mg + diet. Selected outcome indicators at 12 months: change from baseline. From Chanoine & al[6].

	Placebo N=181	Orlistat 3*120mg/day N=352	p
Weight-related endpoints (least square mean)			
BMI (points)	+0.31	-0.55	<0.001
Weight (kgs)	+3.14	+0.53	<.001
Secondary endpoints (least square mean, n evaluated)			
HDL cholesterol, mg/dl	- 0.31 (163)	+0.07 (323)	0.62
Fasting Glucose at 120 min, mg/dl	-10.11 (136)	-11.20 (283)	0.68

*

In the placebo group, 4.4% (8/181) lost at least 10% of their initial BMI, against 13.1% (46/352) in the Orlistat group. Clinicians would need to initiate treatment with Orlistat 3*120 mg in 12 patients (NNT: 12; 95% CI: 8-25), for one of them to achieve a loss of 10% BMI after one year treatment, over the effect achieved by placebo.

No serious safety concern emerged from this study. Mild to moderate gastro-intestinal tract adverse events occurred more frequently in the Orlistat group, such as faecal incontinence (8.8% vs 1% in the placebo group) and faecal urgency (20.7% vs 11.0%).

8.3.2.2 Sibutramine: evidence available and results

A Medline search on 'Sibutramine' (free text) performed on March 24,2006, limited to children under 18, and to randomized controlled trials, returned 25 hits. Only 1 of these reports 12-month follow-up[7].

This study (partially industry-funded) included patients aged 13-17 years, with a BMI ranging from 32 to 44. Children with a BMI > 44 were excluded. All participants were prescribed hypocaloric diet and exercise, and received comprehensive family-based behavioural weight-loss program (including parents) for one year. In addition participants were randomized to Sibutramine (n=43) or placebo (n=39) for 6 months (mo 1-6); then all received open-label Sibutramine for 6 additional months (mo 7-12). This (curious) study design does not permit to evaluate the efficacy of Sibutramine against placebo at 12 months, but only at 6 months, and therefore does not meet our inclusion criteria.

Given concerns about the safety profile of Sibutramine, this RCT gives however some information on the changes in blood pressure and pulse for those participants who took Sibutramine for 12 months. In this group, diastolic blood pressure increased from 56.8 mm Hg at baseline, to 58.7 mmHg at 12 months (difference between means: 1.9 mmHg, 95% CI: 0.27-3.53). Beats/minute increased from 79.4 at baseline to 82.7 at 12 months (difference between means: 95% CI: 0.12-6.48) [l].

8.3.2.3 Discussion and conclusions: Orlistat and Sibutramine for the treatment of obesity in children.

Published studies of Orlistat and Sibutramine in children target adolescents. There are no published data of long-term results (12 months) of Sibutramine, assessed against placebo. As regards safety, patients taking Sibutramine for one year experienced a statistically significant increase in diastolic blood pressure and pulse. A larger study with longer follow-up is under way, and results should be published in 2007 (Dr Berkowitz, personal communication).

[l] Computed by us. Differences in diastolic blood pressure between 12 mo and baseline are statistically significant, unlike differences between months 12 and 6. Only the latest are given in the article.

The Orlistat study – 12 months follow-up - suffers the same limitations as weight-loss drug studies in adults. Drop-out rate was high, and the mean difference between placebo and treatment group after one year (one BMI point), although statistically significant, is of questionable clinical significance. Weight gain was observed in both groups (less in the Orlistat group), although for severely obese children (>=97th percentile) in that age category (12-16y.o.), the objectives of treatment are clearly weight loss[8], rather than weight maintenance. Results were heterogeneous with some patients responding better than others. Identifying early those patient more likely to respond is not yet possible; in addition data are still lacking on the sustainability of weight loss attributable to Orlistat after treatment is stopped. If data in adults can be extrapolated to adolescents, weight will be quickly regained after treatment is stopped, and the real question is therefore whether this treatment should be taken forever.

In conclusion, the current knowledge base does not permit to properly assess the efficacy and safety of Sibutramine in adolescent in the long-term. The efficacy of Orlistat for one year is of questionable clinical significance, and unlikely to be sustained.

8.3.3 Surgical treatment

8.3.3.1 Evidence available and results

We searched Medline using the MeSH term *Obesity, Morbid/su [Surgery], limited to 'child' or 'adolescent', and to the years 1990-2005.

We extracted studies (any design) reporting on at least 20 cases of bariatric surgery in patients under 20 years. Only 6 studies – all case-series – were found[9-14]. We also identified consensus-based recommendations[15]:

All **case-series** reviewed suffer from one, or more, of the following problems: inconsistent reporting of outcomes, for instance failure to identify proper denominators and time-frame for outcomes, particularly adverse events; reporting not allowing assessment per surgical procedure, small numbers, particularly on long-term follow-up, loss to follow-up, etc. These studies are based on retrospective reviews of patient's files, except for Rand who collected his data through one telephone interview of former patients[9]. Detailed tables are presented in annexes. Given these methodological problems, results need to interpreted with caution.

- **Weight loss:** although large weight loss are reported, failures are frequent. In Sugerman[12] study, 20% (5/20) and 35% (5/14) of the patients evaluated 5 and 10 years respectively, after gastric bypass (or a variant) had regained all lost weight. In Angrisany study[13], excess weight loss (EWL) was less than 25% for 20% (5/25) of the patients 5 years after LAGB.
- **Co-morbidities**: data available are scarce and of poor quality. They suggest that surgery might have a positive effect on co-morbidities such as diabetes, hypertension, sleep apnea. Despite claims such as 'self-image was greatly enhanced'[12], precise data are lacking on improved self-esteem and psychological well-being after surgery .
- **Adverse events:** Re-operation is reported for 8/58 (14%) of patients after LAGB in Angrisani[13] case series. Late complication requiring additional surgery were reported in 21% of the patients in Sugerman's serie[12] (gastric bypass). Time frame in unclear in both cases. No data are presented on long-term possible adverse events on maturation or growth in this population.

A **consensus statement** has been elaborated by a group of American surgeons and paediatricians specializing in the treatment of overweight and obese children[15]. Issues addressed are:

- Eligibility criteria :

BMI should be equal or superior to 40, with co-morbidities, before considering bariatric surgery for children or adolescents. The reasons for more conservative BMI selection criteria than those used for adults are : (1) the severity of co-morbidities for the majority of obese adolescents does not warrant surgical intervention to the extent it does in adults; (2) minors cannot give their own informed consent; (3) behavioural therapy approaches to weight management might be more effective in children than in adults[16] ; (4) a proportion of obese adolescents (20-30%) may not become obese adults[17]: and (5) neuro-endocrine, skeletal, and psychosocial maturation are accelerated during adolescence and require adequate nutrition; they might be affected by bariatric surgery.

Age: a decision to operate needs to take into account both the decisional capacity of the patient, and his/her physiological maturation (sexual maturation, skeletal maturity). Based on these elements, the consensus is on a (flexible) threshold of 13 year-old for girls and 15 year-old for boys.

Other consensus criteria include for instance an evaluation of motivation, and having failed at least 6 months of organized attempts at weight loss.

- Choice of surgical procedure

RYGB and LAGB are both found acceptable, but RYGB is proposed as the most appropriate surgical option, based mainly on the results of studies in adults demonstrating higher weight loss and less surgical complications in the long-term with RYGB than with LAGB (an additional reason for this American consensus is that LAGB is not approved by the US Food and Drug Administration for use among patients under 18 years of age).

- Care of obese patients before and after surgery

There is a consensus that surgery should be performed in 'centres of excellence', and patients handled by multidisciplinary teams specialised in bariatric surgery, for assessment of eligibility, and lifelong (!) medical supervision. Supervision of adolescents who undergo bariatric procedure is essential, in particular to avoid nutritional complications.

8.3.3.2 Discussion

Responding to the epidemic of obesity in children and adolescents, use of bariatric surgery in obese patients under 18 year-old is increasing. Still it is clear from the literature that wide gaps exist in our knowledge base, and key questions are still unanswered:

- What is the ***long-term*** **efficacy** of bariatric surgery performed in young patients, not only in terms of weight loss, but also co-morbidities, psychological well-being and quality of life?
- What are the **long-term adverse events** of bariatric surgery performed in young patients whose growth is not yet complete, particularly nutritional complications?
- How to achieve **adherence** to the requirements of a life-long diet, and medical monitoring? What would be the impact of poor adherence on the efficacy and adverse events of surgery?
- What is the **best surgical procedure**? Although RYGB has proved more effective in adults, some characteristics of LAGB make it comparatively more attractive in young patients than in adults: it is less invasive, and reversible (a serious advantage when considering decisions with lifelong consequences),

and as a restrictive procedure is less prone to nutritional complications. (However restrictive procedure only might not be sufficient in severely obese, 'sweet-eaters').

- What is the **appropriate timing** for surgery? Essential elements to consider here are: (1) the ability to consent to a decision with lifelong consequences and (2) the impact on growth. Some (mainly surgeons) advocate early surgery to minimize the emotional and physical damage of morbid obesity[13], even to the point of considering surgery also for elementary school children[12]. At the other extreme are those advocating delaying surgery until adulthood when the individual may be more capable of making informed decision, and when growth is less likely to be affected.

A recent review of the evidence supporting a bariatric surgical approach to weight management in adolescents is based mainly on a review of the literature on these interventions in adults[18].

Because of the uncertainties surrounding long-term efficacy and safety of bariatric surgery in adolescents, and concerns regarding their decisional capacity, bariatric surgery is considered as the last solution: 'when all else has failed'. But what is 'all else'? Given the potential consequences of bariatric surgery, a requirement of – only - '6-month organised attempts' at loosing weight – before being eligible for bariatric surgery – seems at the same time too imprecise, and too short. In the US, for instance, programmes offering a proper alternative - behaviour-based weight management, which appear to be effective[16] are either not available, and/or too expensive[19].

8.3.3.3 Conclusions

Long-term efficacy and safety of bariatric surgery in patients under 18 remain to be properly documented and demonstrated. Optimal timing (age), eligibility criteria, and type of surgery, are not yet known. Both risks and benefits of bariatric surgery are potentially high and – unknown - in this population.

In a context of such uncertainty, the decision to use bariatric surgery in young patients requires safeguards to avoid that the decision be taken too lightly, by the patient, and /or by the surgeons. This procedure should be strictly limited to few specialised centres of excellence.

It is also an ethical duty for surgical teams operating young obese patients, to contribute to the building of the body of knowledge that is desperately needed in this area. This requires a standardised register that would allow long-term evaluation of the procedures.

8.4 ETHICAL ISSUES

8.4.1 Setting the scope: overweight, obesity, severe obesity?

The issue of prevention and treatment of severe obesity develops within the framework of more general societal issues. As has been argued in previous paragraphs, the concept of obesity is both a cultural and a statistical construct, not to be identified in absolute biomedical criteria. For the sake of a clear discussion, a conceptual difference between overweight, obesity and severe obesity is useful when discussing ethical issues in intensive treatments for children and adolescents.

There is no single cut-off point in weight index scales for this decision, to label somebody as obese. Different statistical norms should be used for different ethnic groups in order to determine a cut-off point[20]. Moreover, because adult BMI cut-off points cannot be used for assessing children and adolescents (because BMI varies throughout childhood), percentiles are used to identify extreme obesity. For the discussion in this section we use the concept of obesity for excessive weight gain with clear relationship to medical risks needing medical interventions. There is evidence to support the idea that some forms of paediatric obesity should be considered as a disease that has to be treated[5] Especially since paediatric obesity is a strong risk for

adult obesity (particularly after age 10 years) some major concerns rise. The use of intensive treatments of obese children and adolescents, in particular bariatric surgery, has to be discussed and compared to alternatives. Though at first glance it seems unacceptable even to consider surgical or other intensive treatments, needs consideration because of the emerging co-morbidities in children, similar to the ones in adults. Drastic surgery for obesity, once viewed as suitable only for adults, is more and more emerging as an option for children and adolescents. This debate needs to take into account ethical considerations.

From a societal point of view, cultural elements have an impact on defining aspects of the body. Being lean is highly valued in our current western society, and often associated with success, higher productivity, etc. Norms and values about bodies could induce a medicalisation of weight issues in general and overweight and obesity in particular. The notion of an 'obesity epidemic' can also be studied as a social construct, developed with scientific knowledge and culturally based beliefs, values and ideals. These cultural ways of thinking influence possible ways of judging individuals and social groups and, this process of giving "meaning" creates an agenda for particular policies, interventions and practices. Ethical considerations should take into account the social construction of an health issue, lifestyle issues, "*mediatisation*" leading to growing expectations of the public about medical technologies in general and leading to demands for drugs or surgical interventions in particular. As the public will acquire knowledge and develop expectations about intensive therapies, a critical assessment is needed of risks, short and longterm consequences, and aspects of medical (public) costs. Bariatric surgery for the treatment of obesity can become a trend, induced by public opinion leaders and patients obtaining their information about the surgery from the Internet. As more and more people turn to the Internet for healthcare information, the need to monitor those Web sites for accuracy and quality expands[21]

8.4.2 Ethical issues in Bariatric surgery in children and adolescents

8.4.2.1 Introduction

Is it, and under what circumstances, ethically acceptable to apply bariatric surgery in children and adolescents?.The question discussed in this paragraph is approached in a quite "instrumental" way:

In this section we try to develop a secular bioethical approach, grounded in principles of respect for the person, justice, responsibility and beneficence. We will try to focus on the consequences of the physicians work on individual patients and toward society as a whole (justice and fairness). However, it should also be noted that this "principles" approach is subject to critique, especially because of potential contradictions and theorectical inconsistencies (for example the principle of justice or fairness is potentially contrdictory to the principle of interests of the individual) (see[22]). It would go beyond the scope of this paragraph to discuss these issues.

8.4.2.2 Medical ethics[m]

One of the basic principles of medical ethics is expressed as "primum non nocere" or "at least do not harm". Especially in the case of children, long term perspectives need to be addressed, when discussing medical interventions and potential alternatives The ethical debate should focus on the ethical permissibility of practices of intensive therapies (bariatric surgery) in particular in children and adolescents. From an ethical perspective it is expected that an intervention will be benficial *on balance* for the person undergoing the intervention. Benefits and harms need to be taken into account, as well as the probabilities of the benefits and harms. In the case of bariatric surgery and based on the available knowledge, one cannot consider the intervention as an easy way out for obese people. They require a lifetime of supplementation and compliance, and little or nothing is known on the long term effect on the lives of the future adult people (see the previous paragraphs).

[m] These principles have been discussed in KCE report: "Health Technology assessment Prostate-specific antigen (KCE-report vol 31, 2006)

The principle of "at least do not harm" is related to professional responsibility and the obligation of veracity. The medical problem of obesity has to be clearly distinguished from the lifestyle and thus cultural issue. Medical professionals will anyhow have the ethical responsibility to assess whether children or adolescents have a disease. Moreover professionals are morally obliged to clearly inform the patients in a comprehensive and accurate way, adapted to the patients level of understanding.

Because of the authority position of the professional, related to its expected competence, the professional can have major impact on the choice in intervention. The more a professional encourages a patient to engage in an activity, and the more a patient engages in that activity because of that encouragement, the more responsible the professional becomes for this choice. The authorithy position does not allow to delegate decision making to the patient, without coaching. People or patients still assume that physicians would not recommend medical procedures if they do not expect them, on balance, to be good for the person. The professional's expectation is assumed to be based on knowledge, not on mere speculation. One can expect that, given the particular relationship between a physician and a patient, the concept of "patient autonomy" is not simply solved by giving information to the patient and assuming that by means of this they will have the capacity to make themselves a clear choice on different medical interventions. remaining passive or giving implicit consent by remaining silent to a requested intervention by a phycisician, under the argument of honouring "patient autonomy" is not compatible with the notion of responsibility. In other words, the physician has a responsabilty to engage children and adolescents, together with their parents into a process of shared decision making (see also chapter 9)

An ethical debate of whom is to be considered as a person is in place here.

8.4.2.3 Persons and shared decision making

In general, the ethical assumption is that a "person" is defined as moral agent who is selfconscious, rational and capable of free choice and having interests. This operationalisation leads to particular concerns when discussing about infants, children, adolescents and mentally incapable people. In this case we are discussing the issue of protection of the person and develop justifications for a category of humans who are likely to become persons[23]. The issue at stake is to accord to children or adolescents many of the rights accorded to adult persons, although these persons do not fit in the typical concept of a person. Instead of a strict sense of the person, a "social sense" of the person is used to whom similar rights of the strict person are attributed. This aspect is related to the notion of the "future" persons they can become. So, if one plans interventions on an individual, one needs to consider the impact of these interventions on the actual and future persons they will become. This means that the principle of beneficence necessarily has to take into account the long term impact of interventions on the child and adult. Moreover, in the particular case of children and adolescents, particular approaches and reflections are needed about informing this group and about and autonomous or shared decision making (together with professionals and adults).

8.4.2.4 Can one deny access to intensive therapies for children and adolescents?

In general it can be considered unethical to deny treatments and procedures that have proven effectiveness for adults, to children and adolescents, solely on the basis of age. However, this ethical principle does not exclude the need for a thorough critical examination of safety and efficacy issues[24, 20]. Bariatric surgery for morbid obesity is, even for adults, considered an intervention of last resort for patients who have attempted first-line forms of medical management, such as diet, increased physical activity, behavioural modification, and drugs. At least one can expect that bariatric surgery will not even be considered, if children or adolescents have first tried the other alternative interventions.

Since evidence is lacking on the effects of bariatric surgery on children and adolescents, Cuttler[20] suggests the need for clear statements by professional and governement agencies to address if and under what circumstances intensive obesity treatments have a place. "*The statements could address whether there is currently a place for intensive*

obesity treatments in paediatric populations; if so they could address the weight change expected by youth through life style interventions, which treatment is next if lifestyle fails, the minimal age and degree of obesity for intensive treatment, the role of comorbidities in decisions, assent and parental permission considerations, and recommend personnel/facilities for centres developing programs". An example of such an explicit statement is found[15]. The most important ethical issues when considering an adolescent for a bariatric procedure are:

- whether the patient's health is being compromised by severe obesity,
- whether the patient has failed more conservative options to meet that health need, and
- whether the patient has decisional capacity.

8.4.2.5 Who should provide bariatric surgery

Ideally, adolescents who undergo bariatric surgery should be treated an have follow-up at regional centers of excellence, with ongoing clinical data collection and targeted research. Taking into account the number of unknown elements of risks and effects of bariatric surgery, it cannot be considered a routie intervention to be performed by any centre or surgeon. Centres of excellence, taking the responsibilty of guaranteeing follow up of the young patients (maybe life long) is needed.

Moreover, the ability to make useful recommendations about the appropriate timing of bariatric surgery and optimal surgical and postoperative management depends on the collection of rigorous, high quality outcome data, and comparison with other alternative weight loss strategies.

8.4.2.6 Social justice and utilisation of resources

Justice can be interpreted as the fair, equitable and appropriate treatment of people in light of what is due or owed to persons. This latter part of the desciption is open to some interpretation. Distributive justice refers to fair, equitable and appropriate distribution. Theories of distributive justice try to connect properties of persons with morally justifiable distributions of benefits and burden[25] From a distributive point of view people need to be protected as much as possible from different forms of harm, not only the purely medical harm, but also the consequences. In particular, one has to consider the issue that some societal groups, in particular people with lower socio-economic status (SES). The lower socio-economic categories are often less insured and the health care consumption needs could potentially having major impact on further life-chances and house-hold budgets.

Bariatric surgery is a procedure with considerable risks, including the risk of death. Although bariatric procedures can result in substantial weight loss, the long-term metabolic, nutritional, and psychologic effects among adolescents are unknown. Moreover it is clear that bariatric surgery has potential life long side effects and that the patients will need lifelong follow up. Meticulous, lifelong, medical supervision of adolescent patients who undergo bariatric procedures is essential. Regular visits to the surgeon and other subspecialists with expertise in nutrition and obesity management (e.g., psychologist, dietitian, and exercise physiologist) should be provided to identify potential complications and to reinforce compliance with required eating behaviors, administration of medications and nutritional supplements, and physical activity regimens, and it is not clear to what degree the social insurance is covering for the (follow-up) interventions.

The necessity for further consumption of health care raises particular questions both for public expenditure as well as out-of pocket payments.

8.5 TREATMENT OF OBESE CHILDREN IN BELGIUM

8.5.1 Ambulatory care

This paragraph presents the organization of ambulatory care devoted to obese children in one university hospital. (UCL-St Luc) This is only one example and does not represent a global view of what is done in Belgium in this domain.

The children are cared for by a multidisciplinary team including a pediatrician specialized in endocrinology, a psychologist and a nutritionist. The treatment consists in an individual ambulatory program where the objective is to obtain a long-lasting lifestyle change. The follow-up is foreseen at least for one year or more if needed. The pediatrician consultation takes place every 3 months with the participation of the psychologist. The child is seen by the nutritionist the same day. If necessary, a consultation is organized with the physiotherapist in order to include the child in a sport program. Parents and great parents are invited to participate. The treatment ends when lifestyle changes are observed and when psychological problems are solved, whatever the weight. Some patients are referred to centers near their home.

The difficulties observed are:

- Waiting list with patients demotivation as consequence,
- Need of secretary to phone to the patient just before the consultation,
- Need of social workers to establish the link with centers near patients home,
- Lack in reimbursement of care so that a great part of the charges must be paid by the patient himself.

For more information, see appendix.

8.5.2 Residential treatment of severe obesity

Three centres are specialized in the treatment of obesity in children (< 18 year-old). They are regulated by a convention between the institution and the national sickness fund (INAMI/RIZIV). The annual total budget to finance these centres reaches almost 16 millions euros per year for 296 beds, 196 of them are dedicated for obese children. They are:

- « Zeepreventorium asthmacentrum – Medisch-Pediatrisch Centrum De Haan » (paediatric revalidation centre).
- « Centre médico-pédiatrique Clairs-Vallons » – Ottignies (paediatric revalidation centre)
- « Centre mutualiste neutre de Biez – Centre Médico-Pédiatrique L. Poriniot »

Figure 1. Location of the Belgian residential centres for the treatment of children / adolescence obesity

8.5.2.1 Methodology

We first analysed the conventions linking the centres for in-patient treatment of obesity with the INAMI/RIZIV focusing on obesity-related content.

Secondly, based on our visit to each centre and, when it exists, their activity report, we have analysed the three centres and compared them in terms of context and infrastructure, treatment programme, financing aspect and data collection.

The report of the visit of each centre is presented in appendix.

8.5.2.2 Results

Context

Background

All centres are former preventoria-sanatoria aimed to treat tuberculosis and later other pulmonary diseases. Biez and Clairs-Vallons are administrated by a sickness fund[n]. All these centres had to adjust to changing patterns of disease or care. The choice to treat obesity in children results from the own decision from the centre to develop specialized care for obese, responding to the obesity epidemic. The centres began thus to treat children mainly with severe obesity or affected by other chronic diseases.

To finance the treatments of the chronic diseases, every centre concludes an individual convention with the INAMI/RIZIV in 2000.
A convention is a contract that foresees financial and administrative relationships between contracting parties but also between the institution and the beneficiaries of the compulsory healthcare insurance. It defines:

- admission criteria for the treatment,
- revalidation programme (including the minimal human resources required),
- benefits of the revalidation,
- prices and fees of them (and the mode of payment).

All three conventions have a core approach but differ for some specific points. Each convention is directly negotiated between the centre and the INAMI. However, all will be reconverted very soon in a single generic 'convention for paediatric revalidation',

[n] Today, not every patient belongs to that fund

identical for every centre.
Conventions include but are not limited to the treatment of obesity, they finance other chronic pathologies. We will speak about the different aspect of the conventions later.

Capacity and activities of the centres

Clairs-Vallons cares not only for children with chronic disease (obesity, diabetes and HIV-positive children) but also pathologies related to the mother-child relationship and for medico-psycho-social problems (ill-treatment). The total capacity of the centre is of 80 beds, 46 are occupied by obese patients.

In De Haan as in Biez, the centres rule with only one convention (3 in Clairs-Vallons) and take in only children with chronic disease within a majority for obesity (60% (120/200 beds) in De Haan and 93% (28/30) In Biez).

There is a waiting list to be admitted in the centre of De Haan, but not for the other centres.

Geographical accessibility

Sanatoria used to be built in 'remote' locations as their objective was to isolate contagious patients.

The Zeepreventorium is easily accessible by public transport, Clairs-Vallons rather easily but L.Poriniot is not. However, isolation is not medically justified for obese children and can further exclude them from a normal life, including schooling. The difficulty to access the centre also jeopardizes the necessary parents' participation to the treatment, particularly for the disadvantaged families who do not necessary have a car.

Distribution of the children

These centres offer only residential care and no ambulatory care. Obese children are concentrated in specialised wards (pavilions) while in Biez they choose to mixed children in order to keep them integrated in a sort of 'society' and to learn them to manage their disease in an as real as possible context.

Schooling

There is a primary school in every centre (type 5). The presence of a school on site of the centre allows better planning for the treatment programme and permits a better control of the external factors that could jeopardize compliance to treatment.

The adolescents on the other centres go to regular secondary schools outside the centre. That firstly presents difficulties to find a school that supplies the type of education chosen by the student, with the right section (for vocational sections in particular). Secondly, young people receive therefore their treatment after school. To facilitate the organisation of treatment, limit the time spent in transport and to offer integrated school, Clairs-Vallons plans to implement an on-site secondary school in 2007 and the centre of Biez is discussing the appropriateness of it

Infrastructure

The infrastructure is presented in the Table 3 .

Every centre has at least one fitness room. Biez has also a swimming pool. In De Haan, the swimming pool is in rebuilding and will be used for thalassotherapy (and filled with sea water). At the moment, children walk twice or thrice a week to the municipal swimming pool.
To encourage the adoption of a healthy and sportive behaviour, even after discharge, Clairs-Vallons collaborates with a sport centre.

Table 5 1. Comparison of the (infra)structure of the centres

Centre	language	Total number of beds financed in the convention	Number of beds occupied for obesity (% total)	Repartition of the obese children in the centre	Nursery and Primary school	Secondary school	Link with a sickness fund	Fitness room	Pool	Accessibility by public transports
DeHaan	French- and Flemish-speaking	200	120 (60%)	together	Type 5	Type 5	no	yes	In rebuilding	Easy
Clairs-Vallons	French-speaking	66	46 (70%)	together	Type 5	September 2006	yes	yes	no	Easy
L.Poriniot	French-speaking	30	28 (93%)	mixed	Type 5	In discussion	yes	yes	yes	Not easy

Treatment programme

Admission

Candidates to treatment need to be referred by a medical doctor after ambulatory treatment failure, and to meet admission criteria (age under 18; BMI>= p97 or >=30; pathology criteria – see later). They meet the staff twice or thrice during the year before admission in Clairs-Vallons as in De Haan. In Biez, children first spend 3 weeks in the centre and are then evaluated by the different carers. The programme is then elaborated and after a multidisciplinary diagnostic, if the motivation is felt to be strong enough, the young patient will be admitted for one year of treatment. Some children could benefit of a second residential stay but this is rare.

Population

No systematic and standardized data are available, except for the Clairs-Vallons centre. The description of the population relies on subjective evaluation in the other centres.

Admitted obese children and adolescents are mainly female. It seems that L.Poriniot attracts more patients of low socio-economical status, what does not seem to be the case in the other centres. Clairs-Vallons has shown in its activity reports that 79% of the children present at least one co morbidity on admission; at least half of them presents more than one additional associated pathology.; 95% present associated psychological or psychiatric troubles. In 2004-2005, BMI on admission ranged from 25.77 to 55.90.

Multidisciplinary approach

Conventions explicitly require multidisciplinary treatment but do not define the details of the care package, which differs in each centre.

The programme

The final aim of the revalidation is described in the same way in the three conventions: a social, familial and school reinsertion as soon as possible. The programme has to be personalized and multidisciplinary with medical, paramedical, psychological, social and pedagogical interventions.

To two of the three conventions is annexed a detailed general programme of the treatment. The presentation of this programme seems not to be standardized. For example, the convention for the Zeepreventorium details the frequency of the physiotherapy while the one of Biez mentions only the presence of a physiotherapist in the team. There is no such a document annexed to the convention with Clairs-Vallons but the details of their activities are presented in their report.

All centres offer a mix of all or some of the following interventions (see Table 4 and appendix for details):

- Diet: to learn to eat better – targets children and/or parents
- Intensive exercise
- Individual, in group or family cognitive therapy

Each centre has elaborated its own programme and collaboration between centres is limited to discussion around the reform of the convention.

Return at home

Children return home regularly, i.e. every week-end or every other week-end depending on the centre, in order to relax from the heavy rhythm of the treatment, meet with their family and to reintegrate progressively their 'normal' live.

However, the constraints of the convention for De Haan and Biez centres limit the total number of days outside the centre (see Table 6).

Follow-up after discharge

Follow-up of the patients after discharge is not officially the responsibility of the centres.

Table 52. Comparison of the centres according to the treatment

Centre	diet (number of calories per day)	Individual psychotherapy	Psychotherapy in group	Family cognitive therapy	Physical activities	Speech therapy	Frequency of Multidisciplinary meetings per patient	Return at home	Follow up in the centre after discharge
De Haan	Standardized hypo-caloric (1600 Kcal/d)	Yes	Yes	yes	Yes	If necessary	1-2/8 weeks + informal	Every week-end	Informal: 1 consultation after 3-6 months
Clairs-Vallons	Standardized normo-caloric (2500 Kcal/d)	Yes	yes	yes	Yes	If necessary	1/week	1 week-end /2	1 consultation after 3 months
L.Poriniot	individual	yes	Yes	no	yes	If necessary	4/ year	1 week-end /2	None

Outcomes at discharge and later

Only two among the 3 centres have produced data on some outcomes of their residential treatment at discharge. In Clairs–Vallons, 2 cohorts of children were followed, i.e. 84 in total. The results at discharge concern only the 2003-04 cohort. Data from the Zeepreventorium come from scientific publication focusing on some aspect of the treatment (e.g. determinants of physical activities).

There is little information about outcomes after discharge. Researchers from Ghent University have followed patients during 6 months[26] or 1.5 years[27].

Clairs-Vallons, has data on almost 30 patients seen 3 months after discharge[28]. They focus more on the respect of the prescribed indications (physical activities, medical, dietetic or psychological follow up), and finally the weight regain.

Table 5 3. Outcomes of residential treatment

					OUTCOMES							
Centre	**Outcomes**	**Data on admission**			**At discharge**		**After 3 months**		**After 6 months**		**After 1.5 years**	
	Weight outcomes	**Age (years)**	**N analyzed/ N initially sampled**	**outcome**	**N**	**outcome**	**N**	**outcome**	**N**	**outcome**	**N**	**outcome**
De Haan	Mean BMI– 1998-2000[27]	13.5 +/- 2.1	24/30	33.5 +/- 4.8	24	24.0 +/- 4.0	-	-	24	28.1 +/- 408	-	-
	Mean ABMI– 1999-2000[o26]	13.4 +/- 2.1	47/55	175 +/- 26	47	121 +/- 17	-	-	-	-	47	155 +/- 28
	% of obese children[p26] – 1999-2000	13.4 +/- 2.1	47/55	100% (47/47)	47	8% (4/47)	-	-	-	-	47	60% (28/47)
Clairs-Vallons	Mean ABMI– 2003-2005[28]	14.0 +/- 2.5	83/86	194.86 +/- 31.2	44	140.08 +-/ 28.97	28	37.7% (10/28) of children have regained more than 5% of their initial weight	-	-	-	-
	Other outcomes											
De Haan	Mean score of Moderate or intensive physical activity[q] [27]	13.5 +/- 2.1	24/30	127.4 +/- 69.0	24	161.3 +/- 61.0	-	-	-	-	24	122.5 +/- 79.4
Clairs-Vallons	More than one co-morbidity[27]	14.0 +/- 2.5	77/86	41.6%	40	7.5%						

[o] adjusted BMI (ABMI) : report between actual BMI and ideal BMI, i.e. 50th percentile for same age and sex
[p] cut-off point from Cole, 2000[29]
[q] adapted version of the Minnesota Leisure Time Physical Activity Questionnaire

Dramatic weight loss is observed at discharge (Table 5)., but weight regain is observed after discharge. Only limited information on the outcomes of the treatment is available. Samples are very small and analyses are made in sub-sample of the population treated in the centre (no measure on the drop-out children – children with severe co-morbidity excluded, etc.). Information on physical activity is based on self-reported data.

Financing of the treatment

Admission criteria:

To be financed by the INAMI/RIZIV, children have:

- To be maximum 18 year-old,
- To suffer from a chronic affection clearly diagnosed and necessitating specific active care, with intensive multidisciplinary revalidation, not able in a hospital or ambulatory setting or by a medico-pedagogic institution.

A non-exhaustive list of chronic illness eligible for financing are listed in the convention and classified, e.g. in pneumonic diseases, immunological, endocrinal diseases and chronic infectious diseases. In this list appears severe obesity.

Obesity is established if children until 16 year-old present a BMI >= 97th percentile (according to the gender and the French INSERM curves) or if an adolescent of 17-18 year-old has a BMI>=35.

- The patient must belong to one of 4 groups for instance:
  - Children for whom staying at home is jeopardized by the chronic disease, its consequences and/or its treatment
  - Children who's family is momentarily unable to insure at home the prescribed treatment of the disease and for whom a revalidation in the centre limit a worsening of the disease and an hospitalisation

So, patients have to meet some criteria in terms of age, disease, type of necessary treatment and have to be sent in the centre on medical prescription.

Intervention of the insurance

For each patient centres receive an all-inclusive lump per patient and per day. This sum is calculated based on an annual envelope including:

- Investment charges
- Financing charges
- Functioning charges related to the programme and the cares accepted by the comity of the health care insurance
- Human resources expenses

The financing of the school (staff, use and maintenance) is excluded of the envelope.

The final intervention of the insurance per day is calculated specifically for each centre adding up the human resources costs and the general costs divided by ((365 X number of beds) X 90%). It varies from 194.21€ to 236.29€.

Only in the convention with Clairs-Vallons, a supplementary difference is made according to the severity of the pathology, i.e. moderate or severe ending up with different prices for one day of stay. The severity of the disease is for the moment assessed by the college of the medical directors of the INAMI. In the case of the obesity, severity is characterized only if there is another pathology associated, i.e. mental or somatic and after argumentation of the medical doctor of the centre. The price for the severe day of stay comes from the one applied for the revalidation centre and do not depend of the total envelope. This will be reviewed with the reform of the 'paediatric' conventions where this distinction between severe or moderate treatment will subsist and be generalized for every centre.

Parents co-payment

Parents have also to contribute for the stay. The amount vary between the centre from 1.45€ in Biez to 6.12€ per day for the Zeepreventorium. In the latter case, a part of the co-payment aims to the clothing: each resident receive the same clothes (except shoes) and the laundry is taken in charge by the centre. In Clairs-Vallons, extra could be asked to the parents to pay extra activities (i.e. excursion, some sportive activities).

Staffing

Programme of treatment depend on the qualification of the staff (more or less medical or psycho-social). The skills depend on what is requested by the team to the INAMI/RIZIV since the convention is proposed by the centre, including the staff they need.

To compare staffing across centres, we have divided the number of Full Time Equivalent (FTE) per discipline by the number of beds. This calculation does probably not reflect how resources are effectively dedicated to obese children but allows comparing the centres. Indeed, in the Zeepreventorium, 60% of the children are treated for obesity compared to Biez where 93% of the children are admitted for this treatment.

In the three centres, the nursing time is the more important followed by the physiotherapist.

Table 5 4 . Comparison of the centres according to the functioning means

Centre	Daily allowance from the INAMI/RIZIV (2006)	Differential financing for inpatient day of stay	Parents co-payment	Medical doctors (FTE per bed)[r]	Psychologist (FTE per bed)[a]	Dietician (FTE per bed)	Speech therapist (FTE per bed) [a]	Physiotherapist (FTE per bed) [a]	Nurse (FTE per bed) [a]	Social worker (FTE per bed[a]	Educator (FTE per bed) [a]	Activity report required	Number of out-patient days allowed per stay	Annual budget (INAMI/RIZIV)
DeHaan	236,29€	no	1st day: 31,91€ then: 4,64€/day + 1,48€/day for clothes	0,02	0,03	0,03	0,007	0,07	0,12	0,02	0,35	no	104 per year with a max of 14 consecutive days	11 100 977,38€ €
Clairs-Vallons	199,08€ OR 373,95€	Non-intensive OR Intensive	4,35€/day	0,04	0,05	0,04	0,03	0,07	0,18	0,05	0,27	yes	Max 14 consecutive days	4 069 784,61€ €
L.Poriniot	194,21€	no	1,45€/day	0,04	0,03	0,02	0,03	0,04	0,20	0,05	0,27	no	83 per year with a max of 14 consecutive days	1 815 025,48€ €

[r] Source INAMI/RIZIV : (FTE per skill financed by the convention/ convention bed)

Health information system: Data collection and analysis

Routine data

Apart in Clairs-Vallons, no standardized data are routinely computerized and analyzed. It allows a global evaluation of outcomes at discharge but also a description of its population in terms of

- General information on the child
- Family information
- Paediatric profile of the child
- Dietetic profile of the child
- Physiotherapist profile of the child
- Psychological profile of the child
- Follow up (3 months), in which compliance with recommended aftercare weight regain >5%

No follow up data are available to assess long term effect of the residential care after discharge.

Data collected for research purposes

Some data are collected for research purpose in collaboration with a university research team or related to a student's dissertation. Such collaborations are specific and limited. They were reported only by the De Haan and the Clairs-Vallons teams.

Activity report

Only the convention with Clairs-Vallons requires the production of an activity report describing:

- The pathologies of the beneficiaries (diagnostic and severity)
- The social, familial and educational situation of the beneficiaries
- The revalidation programmes
- The factors that have influenced the way that the revalidation have been decided (out/inpatient, severe/moderate)

In addition, they have presented data about the evolution of the patients during the stay (compliance, weight, height, BMI, associated pathologies, etc.)

Table 5 5 . Comparison of the centres according to the data collection (2006)

Centre	Systematic computerized data collection	Activity report	Collaboration with universities
DeHaan	no	no	specific
Clairs-Vallons	Yes	Yes	specific
L.Poriniot	no	no	no

8.5.2.3 Discussion

Residential or ambulatory treatment for children?

Long-term (10-month) residential treatment, as is practiced in Belgium seems to be unique in the approach of the treatment in school-aged children obesity. Indeed, we have not found published scientific literature other that the one reporting the Belgian experience. The few publications found by a 'quick and dirty' search in the scientific literature concern residential treatment of 4 to 6 weeks on camps, or studies reporting on the experience of the Zeepreventorium [30-33, 26].

Even if the published studies concern a very small number of patients, it appears that **10- month residential treatment seems to be highly effective on**, in achieving weightloss, increased physical activitiy, behaviour change, etc at discharge[34, 28].
Only one centre produced a 'one-shot' activity report. Two centres maintain close contact with academic teams from various universities. Research is conducted by the academic teams on an 'ad hoc' basis, depending on the availability of funds and students. These 2 types of sources give us indications on the efficacy of the treatment at discharge but do not allow comparisons.

If every centre was requested to collect systematic computerised and standardized data and to produce the results a standardized activity report, it would be possible to gather the results and to make a joined analysis for all the centres, to compare them (population, treatment, results) and to follow the activities.

The aim of the activity report could be multiple:

- To measure the efficacy of the treatment at discharge
- To show if financing means are sufficient or not
- To show how the public money is spend

Regarding the outcomes after discharge, there is a clear need, also expressed by the carers we met in the centres, for **long-term data follow up.** Indeed, few indications of long-term efficacy are available. In De Haan, after 1.5 year of residential treatment children have regain weight[33] and maintenance of exercise habits after discharge was not successful[27]. However, sample sizes are small. The long-term effectiveness remains therefore to be demonstrated. It is necessary to elaborate a protocol to follow the patients several months, or even years after their discharge to demonstrate effectiveness of residential treatment.

Apart from allowing intensive care, residential treatment also implies removing children from their parents, peers and sometimes school environment. '**Removing' the children from their environment might, potentially, have both advantages and disadvantages**: On one hand, this might seem an advantage because it breaks with habits helping the kids to get a new start, to change in behaviours (dietetic or sedentary). On the other hand, it also might have potential disadvantages, i.e. involvement of the parents is more difficult. Indeed, parent's participation is very important to guarantee the continuity of the habits adopted during the stay.

Regarding the occasional returns to home, the present constraints of the convention limit the number of days outside the centre. In Biez this leads to 'keeping' children in the centre during some week-end or holidays periods to guarantee the financing of these patients while it would be better to let them return home. For the discharge, this rule is also problematic because it does not allow a progressive reintegration of the child in his/her former live. This limit on the number of day should disappear in the new conventions and be replaced by a system that encourages the progressive reintegration of the children in their traditional live rather than sanction it.

After care is not 'officially' part of the residential treatment centres. Anyway, as patients come from everywhere in Belgium, a decentralized network has to be (re)created. A serious problem is therefore the lack of a specialised reference network. It is not clear

either what this 'specialised reference' should be: a multidisciplinary, hospital-based team, a dietician, a therapist trained in systemic therapy, a general practitioner, etc?

Is there an alternative to residential treatment?

In Belgium, residential treatment is in theory offered to patients who need an urgent treatment to loose weight because of the complications of morbid obesity (rapport Clairs-Vallons) or who have failed repeated ambulatory medically-supervised attempt. However, we can ask the question of 'what is succession of failures?', what has been really tried before a child or an adolescent to arrive in a centre for the treatment of obesity?

Financing of the treatment

The residential treatment is not rigorously evaluated nor is the ambulatory treatment in Belgium. Nevertheless, the first one benefits from an important financing from the government when the other has no financial help. It would be useful to evaluate the effectiveness of both treatments and to reflect on the best way to finance them.

8.5.2.4 Conclusions

Table 5 6 . Advantages and disadvantages of the residential treatment

Advantages	Disadvantage
Short term effectiveness Not expensive for the patients	Expensive for the Social Insurance Exclusion of family-based intervention in case of geographical distance Aftercare is limited by the lack of primary care reference network No after care data
Long-term effectiveness remains to be demonstrated Isolation (family, school)	

- There is a need to evaluate treatment through a standardized activity report
- There is a need to evaluate long-term effectiveness through the follow up of a cohort, for scientific purposes and to support a decision to allocate resources to this costly intervention
- Aftercare is not a mission of the residential treatment. It has to be decentralized

8.6 GENERAL CONCLUSIONS / KEY POINTS

General

- The frontier between prevention and treatment in lifestyle-related disease is unclear, particularly in the case of obesity in children
- All interventions reviewed here (surgery, medicines, residential) remain to be properly documented and evaluated as regards their long term safety and effectiveness in school-aged children
- An analysis of the organisation of care and care pathways of young obese patients in Belgium is needed.

Pharmacological treatment

- The current knowledge base is insufficient to recommend pharmacological treatment of obesity in patients < 18 year-old

Surgical treatment

- Performing an intervention with lifelong consequences, and unknown risk/benefit ratio, in patients under 18, raises serious ethical issues
- Important gaps remain in scientific knowledge, as regards the best timing for surgery, and the more appropriate surgical procedure
- Bariatric surgery in children should be strictly limited to specialised centres of excellence

Ambulatory treatment

- Ambulatory care is expensive for obese children
- A further study should explore alternative financing mechanisms to remove financial barriers to treatment

Residential treatment

- In Belgium, 3 centres offer residential treatment to obese children.
- 296 beds are occupied per year; overall budget is almost 16 millions euros, among them 196 are dedicated to the treatment of obese children.
- Long-term effectiveness of residential treatment on the long term needs to be evaluated
- Residential treatment appears to be highly effective in the short-term
- All centres need to develop and maintain a standardised, computerised, data collection system; in order for the centres to better monitor and analyse their activities.
- Every centre has its own specificities and provides a specific treatment program (dietetic and cognitive therapy) according to the staff orientation
- An analysis of the existing referral network for the medical, dietetic and psychological follow up after discharge, and how to improve it, is urgently needed.
- Residential care for obese children is less expensive for the patients than ambulatory care
- Some aspects of the conventions (such as limiting the number of days spent outside the centre) might have perverse effects

8.7 REFERENCES

1. Summerbell CD, Ashton V, Campbell KJ, Edmunds L, Kelly S, Waters E. Interventions for treating obesity in children. Cochrane Database Syst Rev. 2003(3):CD001872.
2. Summerbell C, Kelly S, Campbell K. The prevention and treatment of childhood obesity. Effective Health Care. 2002;7(6):1-12.
3. Whitlock EP, Williams SB, Gold R, Smith PR, Shipman SA. Screening and Interventions for Childhood Overweight: Evidence Synthesis. 2005. Evidence Synthesis (36) Available from: http://www.ahrq.gov/downloads/pub/prevent/pdfser/chovsyn.pdf
4. Puff A, Elias S, Hoggarth B, Schwarzenberg SJ, Sheridan K, Stang H. Treatment of obesity in children and adolescents. ICSI; 2005. Technology Assessment Report (90)
5. Whitlock EP, Williams SB, Gold R, Smith PR, Shipman SA. Screening and interventions for childhood overweight: a summary of evidence for the US Preventive Services Task Force. Pediatrics. 2005;116(1):e125-44.
6. Chanoine J-P, Hampl S, Jensen C, Boldrin M, Hauptman J. Effect of orlistat on weight and body composition in obese adolescents: a randomized controlled trial. JAMA. 2005;293(23):2873-83.
7. Berkowitz RI, Wadden TA, Tershakovec AM, Cronquist JL. Behavior therapy and sibutramine for the treatment of adolescent obesity: a randomized controlled trial. Jama. 2003;289(14):1805-12.
8. Barlow SE, Dietz WH. Obesity Evaluation and Treatment: Expert Committee Recommendations. Pediatrics. 1998;102(3):e29.
9. Rand CS, Macgregor AM. Adolescents having obesity surgery: a 6-year follow-up. Southern Medical Journal. 1994;87(12):1208-13.
10. Breaux C. Obesity Surgery in Children. Obes Surg. 1995;5(3):279-84.
11. Mason E, Scott D, Doherty C, Cullen J, Rodriguez E, Maher J, et al. Vertical Banded Gastroplasty in the Severely Obese under Age Twenty-One. Obes Surg. 1995;5(1):23-33.
12. Sugerman HJ, Sugerman EL, DeMaria EJ, Kellum JM, Kennedy C, Mowery Y, et al. Bariatric surgery for severely obese adolescents. Journal of Gastrointestinal Surgery. 2003;7(1):102-7; discussion 7-8.
13. Angrisani L, Favretti F, Furbetta F, Paganelli M, Basso N, Doldi SB, et al. Obese teenagers treated by Lap-Band System: the Italian experience. Surgery. 2005;138(5):877-81.
14. Kalra M, Inge T, Garcia V, Daniels S, Lawson L, Curti R, et al. Obstructive sleep apnea in extremely overweight adolescents undergoing bariatric surgery. Obesity Research. 2005;13(7):1175-9.
15. Inge TH, Krebs NF, Garcia VF, Skelton JA, Guice KS, Strauss RS, et al. Bariatric surgery for severely overweight adolescents: concerns and recommendations. Pediatrics. 2004;114(1):217-23.
16. Epstein LH, Valoski A, Wing RR, McCurley J. Ten-year follow-up of behavioral, family-based treatment for obese children. JAMA. 1990;264(19):2519-23.
17. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. N Engl J Med. 1997;337(13):869-73.
18. Inge TH, Zeller MH, Lawson ML, Daniels SR. A critical appraisal of evidence supporting a bariatric surgical approach to weight management for adolescents. J Pediatr. 2005;147(1):10-9.
19. Barlow SE. Bariatric surgery in adolescents: for treatment failures or health care system failures?[comment]. Pediatrics. 2004;114(1):252-3.
20. Cuttler L, Whittaker JL, Kodish ED. The overweight adolescent: clinical and ethical issues in intensive treatments for pediatric obesity. J Pediatr. 2005;146(4):559-64.

21. Nichols C, Oermann MH. An evaluation of bariatric Web sites for patient education and guidance. Gastroenterol Nurs. 2005;28(2):112-7.

22. Jonsen AR. The birth of bioethics. Oxford New York: Oxford University Press; 1998.

23. Engelhardt HT. The foundations of bioethics. New York Oxford: Oxford University Press; 1996.

24. Cuttler L, Whittaker JL, Kodish ED. Pediatric obesity policy: the danger of skepticism. Arch Pediatr Adolesc Med. 2003;157(8):722-4.

25. Beauchamp T, Childress J, editors. Principles of Biomedical Ethics. 5th edition ed. Oxford: Oxford University Press; 2001.

26. Deforche B, De Bourdeaudhuij I, Tanghe A, Debode P, Hills AP, Bouckaert J. Role of physical activity and eating behaviour in weight control after treatment in severely obese children and adolescents. Acta Paediatr. 2005;94(4):464-70.

27. Deforche B, De Bourdeaudhuij I, Tanghe A, Hills AP, De Bode P. Changes in physical activity and psychosocial determinants of physical activity in children and adolescents treated for obesity. Patient Educ Couns. 2004;55(3):407-15.

28. De Buck C, Foucart J. Convention de Rééducation fonctionnelle "maladies chroniques pédiatriques" (août 2004-juin 2005). Centre Médical Pédiatrique Clairs Vallons; 2005.

29. Cole T, Bellizzi M, Flegal K, Dietz W. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320:1-6.

30. De Bourdeaudhuij I, Crombez G, Deforche B, Vinaimont F, Debode P, Bouckaert J. Effects of distraction on treadmill running time in severely obese children and adolescents. Int J Obes Relat Metab Disord. 2002;26(8):1023-9.

31. Braet C, Tanghe A, Bode PD, Franckx H, Winckel MV. Inpatient treatment of obese children: a multicomponent programme without stringent calorie restriction. Eur J Pediatr. 2003;162(6):391-6.

32. Braet C, Tanghe A, Decaluwe V, Moens E, Rosseel Y. Inpatient treatment for children with obesity: weight loss, psychological well-being, and eating behavior. J Pediatr Psychol. 2004;29(7):519-29.

33. Deforche B, De Bourdeaudhuij I, Tanghe A, Debode P, Hills AP, Bouckaert J. Post-treatment phone contact: a weight maintenance strategy in obese youngsters. Int J Obes Relat Metab Disord. 2005;29(5):543-6.

34. Deforche B, De Bourdeaudhuij I, Debode P, Vinaimont F, Hills AP, Verstraete S, et al. Changes in fat mass, fat-free mass and aerobic fitness in severely obese children and adolescents following a residential treatment programme. European Journal of Pediatrics. 2003;162(9):616-22.

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Part 4: Legal Issues

9 LEGAL ASPECTS OF WEIGHT LOSS INTERVENTIONS

9.1 IN GENERAL

9.1.1 Liability[19]

Liability claims with regard to all different kinds of weight loss interventions are conceivable.

Patients undergoing weight loss interventions can experience different kinds of damage or injuries. Patients can claim compensation if liability of the person that caused the damage can be established. For a better understanding of the liability questions mentioned in the following text a brief overview of the different types of liability is necessary.

Civil liability aims the obtaining of compensation whereas criminal liability primarily aims a punishment. Both types of liability can be invoked simultaneously. Since patients having suffered damage with regard to bariatric surgery will particularly tend to claim compensation, civil liability will be stressed in this overview. The Belgian system of civil liability is based on the proof of the fault (negligence) of the physician by the patient (contrary to the Nordic countries where no fault has to be proven). If the proof of a fault can be established, the physician can solely be held liable if damage and a causal link between these factors can be proven.

Civil liability can be divided in contractual liability and tort liability.

9.1.1.1 Contractual liability

A contract is a binding agreement (oral or written) between two or more parties for performing, or refraining from performing, some specified act(s) in exchange for lawful consideration. Contractual liability can only be invoked if there was a contract between the patient and the person or the entity that caused the damage (for instance a physician, a hospital, an organisation,…). It is not required that there's a written contract. In the relationship between a physician and a patient the contractual relationship will mostly be oral.

The proof of a contractual fault depends on the character of what was stipulated in the contract. The contract between a patient and a physician will mostly contain an obligation to perform the best of the physician's ability (obligation of means), not to a specific result (obligation of results)[20]. There is however some discussion in Belgian jurisprudence and doctrine whether medical acts in the domain of plastic surgery can be regarded as obligations of result[21]. A contractual medical fault will therefore mostly consist of a violation of the "general standard of care". This standard of care is the level of care that can be expected from a reasonable prudent physician of the same category and in the same circumstances. When handling a liability claim the judge (or the medical expert the judge refers to) will have to judge if in the case at stake another reasonably prudent physician of the same category and in the same circumstances would have done the same. If not, there's a possible liability of the physician.

The existence of a medical contract between the patient and the physician also implies that the physician has to use safe material. There's a tendency in Belgian jurisprudence to consider the use of safe material as an obligation of results[22].

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19 For an overview on medical liability: T. Vansweevelt, *De civielrechtelijke aansprakelijkheid van de ziekenhuisgeneesheer*, Antwerpen, Maklu, 1992, 946 p.

20 Antwerpen 6 april 2000, *T.G.R.* 2000, 158; Gent 23 april 1999, *T. Gez.* 2000-01, 366, Rb. Gent 27 november 2000, *Intercontact* 2001, 6

21 Luik 18 maart 1999, *T. Gez.* 1999-00, 230; see citations by T. VANSWEEVELT, *La responsabilité civile du médecin et de l'hôpital*, Antwerpen, Maklu, 1996, 81 e.v., nrs. 110 - 113

22 Antwerpen 22 februari 1999, *A.J.T.* 1999-00, 481; *R.G.A.R.* 2000, nr. 13257, *T. Gez.* 1999-00, 285

9.1.1.2 Tort liability

The basic rule of tort liability (or extra-contractual liability) states that (in absence of a contract) when a person injures another, either intentionally or by negligence, a court may award compensation to the injured party. The fault of the physician implies there's a violation of a law (for instance: if the physician doesn't inform the patient, he violates the patients' rights act and consequently commits a fault) or a violation of the general standard of care (cfr. supra). If the proof of a fault can be established, the physician can solely be held liable if damage and a causal link between these factors can be proven.

If a contractual fault can simultaneously be regarded as a crime, one can choose to invoke tort liability or can base the claim on both systems simultaneously. This situation will often apply in medical cases since medical faults often will concur with the crime of bodily harm. Since tort liability can have some major advantages compared to contractual liability (the contract can stipulate restrictions to liability, whereas in case of tort no restrictions can be agreed[23], tort liability implies full compensation, whereas a contract can restrict compensation, etc..), it can be interesting for the patient to claim on extra-contractual basis.

9.1.2 Aftercare: The duty to supervision and the duty to post- operation information

It's generally accepted that a surgeon is also responsible for the aftercare linked to the operation[1, 24]. The duty for aftercare can be divided in two subcategories: the duty to supervision and the duty to information.

Since in the period after the operation, the possibility for complications is conceivable, the surgeon has to supervise the patient. It is allowed to delegate the supervision to a competent substitute but the surgeon is responsible for choosing a competent substitute (other surgeon, nurse,..)[25] and informing the substitute about the health status of the patient. Moreover the surgeon has got the responsibility to decide when the patient is able to leave the hospital. The patient not following the surgeon's advice is responsible for the possible damage resulting from the premature discharge[26].

After the operation the surgeon has to inform the patient about the needed aftercare. More specifically, patients having undergone bariatric surgery, should be given at the time of discharge written material that includes the information on the specific consultations and checks the patient has to undergo[27], the diet progression, appropriate food choices, information about vitamin and protein supplement and the importance of hydration. Moreover general instructions related to medication, activity, wound care, sign and symptoms to report to the physician and follow – up visits must be provided[3].

If the patient neglects to follow these indications, he/she will be responsible for the possible damage resulting from the lack of follow-up care[28].

If a surgeon neglected to provide (sufficient information on) aftercare he can be held liable if the patient can prove a fault, damage and a causal link (cfr. supra).

9.1.3 Complications: risk communication

The surgeon has to inform the patient about the normal and foreseeable risks linked to the intervention prior to the medical intervention (cfr. infra). This implies that

23 One has to note however that contractual restrictions to liability are often null according to Belgian law

24 Rb. Gent 27 november 2000, *Intercontact* 2001, 6

25 Antwerpen 14 februari 2002, T. Gez. 2001-02,107

26 T. VANSWEEVELT, o.c., 417, nr. 576

27 Gent (1e k.) 23 april 1999, *T. Gez.* 2000-01, p. 366

28 See T. Vansweevelt, *o.c.* 409, nr. 559 - 564

hypothetical or risks with a very low frequency don't have to be communicated unless they have very serious implications[29].

If a complication intrinsic to the operation occurs, there will be no fault of the surgeon as far as the physician has informed the patient about the existence of the risk of that complication. If the physician neglected to inform the patient about the risk, the patient will have to prove that he would not have consented to the operation if he had been aware of the risks[30]. If the complication however was not due to an inherent risk of the surgery but was caused by a fault of the physician, the physician can be held liable.

9.1.4 Patients' rights

The common principles generally recognised as patients' rights are the right to qualitative care, the right to information, the right to informed consent, the right to a medical record and the accessibility of it and the right to confidentiality[4, 5].

Since bariatric surgery is an act of health care and people undergoing bariatric surgery are considered as patients, the Belgian Patients' rights act is applicable. The right to qualitative care, the right to information and the right to informed consent call for deeper consideration.

9.1.4.1 Right to qualitative care

According to the patients' right act (art. 5), patients have the right to qualitative care. This implies that the surgeon has to comply with the quality standards according to the current scientific state of affairs. If surgeons fail to provide qualitative care, they can possibly be held liable if the patient can prove that the damage he/she suffered was caused by the poor care.

9.1.4.2 The right to be informed

The Patients' rights act regulates the right to information about the health status (e.g. the diagnosis, the BMI level)[31]. The right be informed about the health status has to be distinguished from the right to informed consent. Whereas the right to informed consent is linked to a decision, the right to information about the health status is not.

The patient has the right to be informed by the health care provider about all information concerning him/her that is required to understand his health status and the probable evolution. The information has to be communicated in a clear language. In principle information is given orally but the patient can request that the information will be confirmed in writing.

9.1.4.3 The right to informed consent

The right to informed consent can be derived from the right to physical integrity and to self-determination. The right to receive information prior to consent is regulated in article 8 of the Patients' rights act and concerns every medical intervention. According to the content of the information a non exhaustive list is enumerated by the law: The patient has to be informed about the nature, the purpose, the urgency, the frequency, the follow – up care of the intervention, the relevant contraindications, the risks and the side effects of the intervention, alternatives and the financial information. The explanatory memorandum[32] of the law states that consent has to be given explicitly, except when the physician, after having sufficiently informed the patient, can reasonably deduce from the behaviour of the patient that he/she consents. "Explicit" consent implies that consent can be given orally as well as written. The intention of the legislator was to promote oral consent in order to prevent the increasing use of consent forms,

29 Brussel 29 maart 1996, *T. Gez.* 1998 – 99, 32, noot D. PHILIPPE, Antwerpen, 28 juni 2001, *T. Gez.* 2003 – 04, afl. 3, 181, Rb. Antwerpen 12 mei 2004, *T. Gez.* 2005 – 06, afl. 3, 221; Rb. Antwerpen 5 november 1999, *T. Gez.* 1999 – 00, 282; Rb. Brussel 5 mei 1995, *J.L.M.B.* 1996, 431

30 Antwerpen 28 juni 2001, *T. Gez.* 2003 - 04, afl. 3, 181; Rb. Namen 30 maart 2001, *T. Gez.* 2001 – 02, 34

31 Art. 7

32 Memorie van toelichting, *Parl. St.* Kamer, 2001 – 2002, 1642/001

because of the risk of standardisation and uniformisation[33]. Patients as well as physicians however have the right to ask for a written consent form that will be added to the medical file. If the patient refuses to give a written consent, while the physician thinks that a written consent is necessary, the refusal can be noted in the patients' medical file. It has to be stressed that the signature of the patient can only be regarded as valid if the patient has inspected or could reasonably inspect the information. Extremely technical or unclear forms do not meet this condition. Moreover information has to be given in advance and timely. An informed consent form that has been signed immediately before the intervention can hardly be assumed as an informed consent[6] .

An often heard critic with regard to written consent forms is that it only serves the physician to prove that the patient consented in case of a claim in liability. Since Belgian jurisprudence however states that the patient has the burden to prove if informed consent was given to an intervention, this statement has to be put into perspective[34].

9.1.4.4 Specific content of pre-operation information with regard bariatric surgery

As the patients' rights act only sets the minimum requirements with regard to the content of the information (cfr. supra) a deeper consideration of information with regard to weight loss surgery is needed. Apart from the general information mentioned in the patients' rights act more specific information with regard to bariatric surgery has to be given to the patient.

Several categories of information have been mentioned in literature[7, 3, 8].

- Health risks associated with obesity
- Pre-surgical strategies to reduce surgical risks, including preoperative weight loss
- Alternative forms of weight loss surgery and the current understanding of respective risks and benefit, anticipated outcomes and long term effects
- The types of surgery available
- Potential complications in the postoperative period and beyond
- Common psychological adjustment issues after weight loss surgery
- Post-surgical requirements, especially those related to diet and medications
- Aftercare programs and sources of support

9.1.4.5 Informed consent and bariatric surgery: oral versus written

Since bariatric surgery is an invasive intervention with no urgency but with considerable risks to complications and long term implications explicit (>< presumed) consent is required. As stated above the patients' rights act considers written consent rather as an exception than as the general rule, mainly because of the risk of standardisation. Nevertheless there's a solid reason to recommend written consent for bariatric surgery. The invasive character of bariatric surgery and the amount of information linked to it justifies written information linked to written consent in order to allow the patient to grasp all information.

It should be noted that written consent doesn't replace the oral explanation. Oral explanation and written consent should always be complementary.

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33 Memorie van toelichting, *Parl. St.* Kamer, 2001 – 2002, 1642/001, 25

34 Cass. (1e k.) 16 december 2004, http://www.cass.be (25 januari 2005); , *NjW* 2006, afl. 140, 316, noot CALLENS, S.; , *R.W.* 2004-05, afl. 39, 1553, noot NYS, H. ; , *T. Gez.* 2004-05, afl. 4, 299, noot LIERMAN, S. .; Cass. (1e k.) 14 december 2001 http://www.cass.be (3 februari 2002); , Arr. Cass. 2001, afl. 10, 2200, concl. DU JARDIN; , *J.L.M.B.* 2002, afl. 13, 532 en http://jlmbi.larcier.be (7 februari 2003), noot LELEU, Y., GENICOT, G. ; , *J.T.* 2002, 261, noot TROUET, C. ; , *Journ. jur.* 2002, afl. 10, 6; , Juristenkrant 2002 (weergave TROUET, C.), afl. 42, 1; , *Pas.* 2001, afl. 12, 2129, concl. DU JARDIN; , *R.G.A.R.* 2002, nr. 13.494; , *T. Gez.* 2001-02, afl. 5, 239, noot FAGNART, J. ; , *T.B.B.R.* 2002, afl. 6, 328, concl. DU JARDIN, J., noot TROUET, C. .

9.1.4.6 Capacity to consent: decisional capacity and legal empowerment

Solely patients with the decisional capacity and the legal empowerment can give their informed consent to medical care or treatment. In all other situations permission for diagnosis and/or treatment of persons incapable of giving their consent will have to be provided by the parents or by a representative/ tutor.

Some specific conditions have to be fulfilled in order to conclude that a person is capable to make a decision. Literature considers as necessary conditions[9] :

- Understanding what he/she consents to: this can be tested by asking the patient to repeat and interpret the information that is given
- Choosing decisively for/against the intervention: asking the patient if he understood the consequences of the intervention, the possibility of alternatives,…
- Communicating his/her consent: one can ask the patient to react to a proposed intervention
- Accepting the need for a medical intervention: patients' refusal is presumed to be a valid exercise of his/her autonomy. In the case of a disordered patient for instance, a patients' refusal may not be a valid exercise of his/her autonomy because it is determined by its mental disorder.

Informed consent and the minor patient

Prevalence of obesity among children and adolescents continues to increase and the admissibility of minor patients for bariatric surgery can be questioned[10]. Moreover the question rises if and to what extent a minor patient (=under 18 years) has the legal empowerment to consent.

The Belgian patients' rights act

According to the Belgian law on patients' rights, the rights of minors are exercised by the parents having the custody or by their tutor (art. 12). The minor patient however has to be involved in the exercise of his rights, his age and maturity taken into account. The rights included in the act on patients rights can be exercised independently by the minor patient if the patient can be assumed to be "able to a reasonable appraisal of his/her interests". Unfortunately there's no definition in the law of the concept "able to a reasonable appraisal of his/her interests". Consequently the physician will have to judge from case to case if a minor patient can consent independently to an intervention. Factors that can be considered are the chronological age, the risks linked to the intervention, necessity and benefit of the proposed treatment and cognitive capacity for understanding treatment information[11, 12].

A special complexity can occur when the desires of the patient are different from those of the parents. If a conflict arises between the parents or the tutor and physician one can try to get a solution by de ombudsperson, if this does not work one can go to court (juvenile court or the president of first instance)[35].

Informed Consent and mentally incapable adults

Several studies report that obesity is more prevalent among individuals with mental retardation than with the general population[13-15, 12]. Persons with the Down syndrome are even 1,3 to 1,8 times more likely to be obese than people with mental retardation[16]. In this scope it is interesting to consider if and to what extent mentally disabled persons can (independently) consent to bariatric surgery.

35 Verslag kamercommissie, *Parl. St.* Kamer 2001 -2002, 1642/012, p. 95

The Belgian Patients' Rights act

A. systems of protection: the declaration of incompetence and the extended minority

If a patient is incompetent to act legally and he/she is protected by a system as the "declaration of incompetence" or the "extended minority", his/her rights will be exercised by the parents having the parental authority or a tutor[36] .

An adult that finds himself in a constant state of insanity has to be declared incompetent, even if there are intervals of lucidity. Persons that are declared incompetent cannot act independently with regard to their goods and person.

Extented minority can be applied to minors as well as to adults. A minor that is found incapable and seems to remain incapable to manage himself and his goods because of serious mental retardation can be declared as 'extended minor'. Serious mental retardation must be understood as a state of mental handicap, congenital or started during early childhood, and characterised by the undeveloped capacities of intellect, feelings and intention. Extended minority can also be adjudicated to adults that manifested the above mentioned characteristics in their minority[37] . An extended minor is subjected to parental custody or guardianship with regard to their person and goods.

According to the patients rights' act these categories of patients have to be involved as much as possible in the exercise of their rights depending on the condition they're in. An independent exercise of their rights however cannot be granted to these patients due to the severity of the incapability.

B. No system of protection

For a large group of patients the above mentioned systems of protection are not offering a solution. Think about the patients having no decisional capacity due to a disease, age, a trauma,…

The rights of this patient group are exercised by the person that has been previously designated by the patient (=the representative)[38], if and as long as the patient cannot exercise his of her rights. The designation needs to be recorded in a dated and personally signed document giving the mandate to the designated person. The mandate can be revoked any time by the patient or by the designated person. If the patient didn't designate a representative or if the representative omits to act, the rights will be exercised by the cohabiting spouse, the legally cohabiting partner or the actually cohabiting partner. If there's no such person or this person doesn't want to exercise the patients' rights, the rights will be exercised to descending order by a major child, a parent, a major brother or sister of the patient. If there's no such person, the physician will protect the interest of the patient, if necessary after consultation of a multidisciplinary team. The physician is obliged to deviate from the representatives' decision if this decision violates the patient's interest[39].

There's no specified criterion in the patients' rights act rendering patients incapable of informed consent to medical interventions. The physician will have to judge the patients' capacity to consent. It has to be noted however that it's of an utmost importance for the physician to consider the patients' decisional capacity very conscientiously because an invalid consent of the patient can cause the physicians' liability[2] (cfr. supra).

9.1.5 Advertisement on weight loss interventions

Weight-loss information and advertising on weight loss interventions (surgery, medicinal products, diets,..) is disseminated through different kinds of media: television, magazines, newspapers, e-mail, internet websites… Advertising reaches more than ever beyond

36 art. 13 patients' rights act

37 Art. 487 Civil Code

38 Art. 14 patients' rights act

39 art. 15 § 2 patients' rights act

the frontiers and is received on the territory of other Member States[40]. Patients make their decisions based, in part, on advertising. Hence, advertising that presents false or misleading information may distort patient decision making. Therefore the admissibility and the characteristics of advertisement on weight loss interventions calls for a deeper consideration.

9.1.5.1 Advertisement for bariatric surgery

General regulations on advertisement

- According to law "handelspraktijken' (trade practices)[41], any advertisement that is misleading with regard to the characteristics of a service is prohibited. 'Characteristics' has to be understood as the advantages of a service, from the point of view of the quality of the service, of the results that can be expected from the use of it, of the conditions under which the service can be obtained, such as the price,… Misleading advertisement containing facts or presentations that could mislead the consumer with regard to the identity of the seller of the service is also prohibited. Moreover it is not allowed to leave out necessary information in order to mislead the consumer[42].
- The law on the national health insurance[43] contains a general prohibition of advertising regarding the preventive and/or curative care that is reimbursed by national social security[44].
- It is forbidden for every physical person or person in law to advertise for implantable tools. It is also forbidden to advertise for acts of implanting tools[45].
- Moreover the legislation on the norms for hospitals state that it is prohibited for hospitals to advertise and to recruit patients[46]

Regulations and examples of jurisprudence on advertisement by physicians

Besides the general regulations, there are several laws specifically regulating the advertising by physicians:

- The Belgian law "Wet betreffende de misleidende en vergelijkende reclame, de onrechtmatige bedingen en de op afstand gesloten overeenkomsten inzake de vrije beroepen[47]" states that besides the application of more severe legislation, misleading advertising with regard to craft professions (such as physicians), is prohibited. Misleading advertisement is defined as any advertising which in any way, the lay-out included, misleads, can mislead and

40 In order to protect patients from misleading advertising and its unfair consequences, the European Union has laid down common rules applicable throughout the Union Policy brief: Cross-border health care in Europe: http://www.wm.tu-berlin.de/~mig/files/2005.publications/E87922.pdf
This regulatory framework has been transposed to the national legislation of the different member states. It is possible that within the frame of the European legislation there are some differences in the national legislation of the member states. Since it falls out of the scope of this report to compare all different legislations, only the Belgian legislation will be discussed

41Art. 23 Wet van 14 juli 1991 betreffende de handelspraktijken en de voorlichting en bescherming van de consumenten, *B.S.* 29 augustus 1991

42 art. 22 – 23 Wet Handelspraktijken

43 art. 127 Wet betreffende de verplichte verzekering voor geneeskundige verzorging en uitkeringen gecoördineerd op 14 juli 1994 (hierna ZIV – wet), *B.S.* 27/08/1994

44 art. 34 ZIV - wet

45 art. 70 Wet van 27 april 2005 betreffende de beheersing van de begroting van de gezondheidszorg en houdende diverse bepalingen inzake gezondheid, *B.S.* 20 mei 2005

46 Koninklijk besluit van 23 oktober 19654 tot bepaling van de normen die door de ziekenhuizen en hun diensten moeten worden nageleefd, http://www.juridat.be/cgi_loi/loi_N.pl?cn=1964102301

47 Wet 2 augustus 2002 betreffende de misleidende en vergelijkende reclame, de onrechtmatige bedingen en de op afstand gesloten overeenkomsten inzake de vrije beroepen, *B.S.* 20 november 2002

can influence the economic behaviour because of the misleading character or that causes or can cause damage to a competitor[48].

- According the Medical Deontological Code[49], physicians are allowed to advertise but the information provided by a physician has to be truthful, objective, relevant, verifiable, discreet and clear. It's prohibited for advertisement to be misleading in any way, to violate the public interest with regard to health care, to incite unnecessary examinations or treatments or to recruit patients. Note however that these regulations are not legally binding.
- Currently the Belgian national disciplinary board (Nationale raad van de Orde van Geneesheren) also published some recommendations with regard to internet sites kept by physicians[50].

Recently the highest court, Hof van Cassatie, affirmed a judgement of the appeals board of the Belgian medical disciplinary board in which a suspension of the right to practice medicine of 31 weeks was imposed on plastic surgeons for advertising on hair transplants in magazines and websites[51]. The arguments of the surgeons, stating that the right to free competition and the right to freedom of speech were violated were rejected. The court confirmed the statement of the appeals board that a similar practice conflicts with the compelling requirements of public health and that advertisement may not lead to the recruitment of patients or unnecessary treatment. Moreover the restriction to the freedom of speech was justified. According to the jurisprudence of the European Court of human rights the right to freedom of speech is violated if advertisement is accompanied by an aspect of information to the public (f.i. information on new surgical techniques)[52]. Since this was not the case, there was no violation of freedom of speech.

Application to bariatric surgery

As the band used in the method of gastric banding can be considered as an implantable tool any advertising with regard to the band or the surgical intervention linked to it is prohibited.

Moreover one can question if there's a general prohibiting for advertisement on bariatric surgery since the law prohibits advertisement on acts and materials that are reimbursed by Belgian Social Security. Today, bariatric surgery as such is not reimbursed but it can be classified as part of an existing reimbursed intervention (cfr. infra)[53]. Consequently it could be argued that advertisement for bariatric surgery is prohibited.

Advertisement on bariatric surgery is in every way prohibited if it is misleading, whether the advertiser is a hospital, a physician or a private organisation. A lot (if not all) will depend on the interpretation of the concept 'misleading' in the case at stake. Currently however, there no specific jurisprudence with regard to misleading advertisement on bariatric surgery. Nevertheless claims are very conceivable. Think about the advertisement for bariatric surgery (mostly the lap band) such as for instance in ladies' magazines (Cosmopolitan UK; cfr. infra). It could be argued that the fact that that kind of advertisement appears in non-medical magazines next to advertisement on breast enlargement misleads the patient. Bariatric surgery is presented as a non invasive intervention offering the solution for weight problems whereas it is an invasive

48 Art. 4

49 Art. 12 http://195.234.184.64/web-Ned/nl/a999/c999003n.htm

50 Aanpassing van de aanbevelingen van de Nationale Raad van 21.09.2002 en van 17.01.2004 betreffende het houden van internetsites door artsen: http://195.234.184.64/web-Ned/nl/X1bij5_2005.htm

51 Cass. 12 november 2004, met noot E. DE BOCK en E. JANSSENS, "Blijft het reclameverbod voor artsen de facto behouden?", *T. Gez*. 2005 – 2006, 208-221

52 E.H.R.M. 17 oktober 2002, Stambuk v. Duitsland, www.echr.coe.int; E.H.R.M. 25 maart 1985, Barthold v. Duitsland, Publ. Cour., Série A, nr. 90

53 A predraft of royal decree has been created with regard to the reimbursement of some bariatric surgical interventions linked to several conditions http://users.pandora.be/asgb/BijlBer05_4_051c.doc

intervention with a considerable risk to complications and a life long commitment to diets and life style changes. There has been a British case about a Belgian plastic surgeon where the British professional conduct committee (PCC=part of the General medical council and controls "fitness to practice") stated that putting misleading "before and after" pictures on a website is unacceptable practice. The PCC however found that the facts were insufficient to support a finding of serious professional misconduct[54].

In case advertisement on bariatric surgery violates the law, claims in court can be made in order to stop the misleading advertisement. Courts however are not pro-active in searching for misleading advertisement. A claim will always be needed. Since patients can't get any compensation resulting from a conviction of the advertiser, they will not tend to claim. There may however be other parties having an interest in claiming: the government regulating the medical profession, an interprofessional association or professional association with corporate personality, an association defending the interest of consumers with corporate personality, a Sick Fund, the minister(s) competent in the domain concerned[55].

There is a pro-active control by the inspectors of the "Algemene Directie controle en bemiddeling", a subsection of the ministry of Economic affairs[56]. They can a.o. start formal procedures to inform the advertiser that the advertisement is misleading and has to be adapted. Moreover they can start the procedure in court to stop the misleading advertisement. The inspectors can also act after a claim was made by any interested party[57].

The disciplinary regulations specifically applying to physicians prohibit the presentation of results of examinations or treatments, publications, conferences and other statements redundant for the patient, publication of testimonies of patients, consultations and prescriptions via the internet. It is very conceivable that some internet sites with regard to bariatric surgery don't meet these conditions. Moreover the disciplinary rules state that it is prohibited to recruit patients by means of advertisement which will often be the case for advertisement on bariatric surgery. Although the disciplinary regulations are not legally binding, they can play an important role in deontological jurisprudence.

Disciplinary claims can be made by any person having an interest. Lots of claims are made by patients having suffered from medical malpractice. Sanctions however will always be disciplinary and won't contain any compensation. Contrary to the judicial courts however, the disciplinary provincial councils can act pro-actively and have the legal empowerment to watch if physicians don't violate the disciplinary rules[58]. Unfortunately, not all violations are traced.

9.1.5.2 Advertisement for non surgical weight loss interventions

To what extent slimming products can be considered as medicinal products?

Before discussing the advertisement on medicinal products, it is necessary to clarify the definition of "medicinal products". The qualification as a medicinal product has some far-reaching consequences: preceding registration, licence for the production, specific surveillance on advertisement, the sales monopoly of pharmacists, regulation of the price by the Ministry of economic affairs, etc…

Nowadays patients-consumers are to an increasing extent confronted via different canals with 'wonder products' promising to lose weight in no time. The scientific validity and the safety of those products is often questionable. What is more, the use of such products can give patients a false safety feeling and make them miss the adequate products or methods to lose weight.

54 PCC, 22-27 juli 2004, www.gmc-uk.org

55 art. 98 Wet betreffende de Handelspraktijken

56 http://mineco.fgov.be/PROTECTION_CONSUMER/complaints/complaints_nl_003.htm

57 http://mineco.fgov.be/PROTECTION_CONSUMER/complaints/home_nl.htm

58 http://195.234.184.64/web-Ned/nl/ordewet.htm

In that scope it is interesting to analyse to what extent weight loss products can be considered as medicinal products. Although today there is some legislation and some explanatory documentation according to what can be considered as a medicinal product, there's a remaining grey zone.

Since very recently the definition on medicinal products has been enlarged it's interesting to compare the "old" definition and the new one.

The former definition on medicinal products stated that [59] :

Medicinal product is

"Every simple or composite substance, presented as possessing therapeutic or prophylactic characteristics with regard to diseases of man or animal.

or

Every simple or composite substance that is meant to be given to man of animal in order to diagnose or to cure, to improve or change organic functions."

This definition is very large and implies that a product can be defined as a medicinal product based on two criteria: the criterion of presentation (section 1) **or** the functional criterion (section 2)[17-19].

The criterion of presentation was a.o. inserted to preserve consumers from "wonder products". Even if a product doesn't have therapeutic or prophylactic characteristics, it can be considered as a medicinal product. The criterion of presentation is interpreted in a very large way by jurisprudence. If the way of presenting a product gives to a normal consumer the impression that it has therapeutic and prophylactic characteristics the product can be considered as a medicinal product[60]. If for instance in a folder a product was presented as curing obesity it can be regarded as a medicinal product. Note however that products claiming to cure "overweight" or depress the appetite don't fall into the scope of the criterion of presentation since it requires therapeutic or prophylactic characteristics with regard to a *disease*[61].

Although the definition of medicinal product allows a large interpretation, some vagueness remains with regard to some slimming products. In order to clarify the "grey zone" between what is considered as a medicinal product and what is not, an indicative list[62] of statements that can not be considered as a description of "possessing therapeutic or prophylactic characteristics" as referred to in art. 1 of the act on medicinal products has been set. With regard to weight loss and slimming products the list states that descriptions as:

- To use as supplemental nutrition when slimming (=afslanken)
- Helps to maintain your weight
- Increases the saturation point
- Support during slimming

do not meet the criterion "possessing therapeutic or prophylactic characteristics". As far as these products don't comply with the second part of the definition, those products consequently don't fall within the legal definition of a medicinal product. It has to be stressed however that it is a indicative and thus non exhaustive and non binding list. Creative (mis)use of different formulations occurs currently. Often advertisers use the word "slimming" (which changes the silhouette but not necessarily aims at losing weight; in Dutch: afslanken) instead of "losing weight" (vermageren) to escape the legislation applicable on medicinal products. The consumer is mostly not aware of this subtle use of words.

59 http://www.afigp.fgov.be/New/NL/Archief/K.B/250364.pdf

60 H.v.J. 30 november 1983, nr. C-227/82, *Jur. H.v.J.* 1983, 3883

61 C. Desmet, noot onder Antwerpen 4 december 2001, *R.W.* 1305-1308

62 http://www.afigp.fgov.be/New/NL/Archief/K.B/250364%20gezondheidsbeweringen.pdf

According to a ministerial circular anorectics and products aiming at losing weight meet the definition of a medicinal product[63]. Products having an influence on the metabolism, by blocking the enzyme, are also considered as medicinal products[64]. Products replacing a meal or changing the volume of a meal, such as for example fibres are not considered to be medicinal products.

For some specific categories of slimming products that are not considered to be medicinal products, specific legislation is applicable. The production and the commercialisation of products[65] that are composed of plants or contains plants or preparations of plants for instance is submitted to an obligatory notification. This permits to check the composition as well as the statements about the product in order to prohibit the misleading of consumers and the use of specific components in a toxic dose.

Other slimming products that cannot be considered as a medicinal product under the current legislation, are for instance low calorie food, diet food for medical use,... Food for specific purposes has to comply with strict requirements with regard to the composition: calories, proteins, fat, fibres, vitamins and minerals. Diet food for medical use is submitted to obligatory notification. Moreover there's a registration procedure at the General Food Inspection[66].

The pharmaceutical inspection can control if a particular product is a medicinal product. Unfortunately there's no pro-active control. Mostly claims are made by other competing firms. Moreover producers can ask for the preliminary advice in order to make sure which legislation will apply to their product. The advice of the pharmaceutical inspection however has no legal force.

If a producer of a medicinal product neglects to comply with the regulations of the act on medicinal product (and other legislation applicable on medicinal products), pretending that the produced product is not a medicinal product, criminal sanctions can be imposed[67].

Recently, a revision of the legislation on medicinal products has taken place in order to transpose the European legislation with regard to medicinal products[68]. The new enlarged definition of 'medicinal product' states that:

"Medicinal product" implies a substance or combination of substances -

(a) Presented as having properties for treating or preventing disease in human beings (the criterion of 'presentation')

(b) which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis' (the criterion of 'intended or actual function').

The aim of the new legislation is to clarify, from a legal point of view, the situation of certain borderline products for which there is uncertainty regarding which regulatory system should be applied. If a product clearly falls within the scope of the definition of product categories other than medicinal products, such as food, food supplements, cosmetic products the act on medicinal product is not applicable. In case of doubt, if a product falls within the definition of medicinal product as well as within the definition of another product, the law on medicinal products will have to be applied[69].

63 http://www.afigp.fgov.be/New/FR/Archives/circulaire/circ%20ozb%20280787.pdf

64 See Antwerpen 4 december 2001, *R.W.* 2002 – 03, 1303-1308 met noot C. Desmeth. t

65 koninklijk besluit van 29 augustus 1997, *B.S.* 21 november 1997 betreffende de fabricage van en de handel in voedingsmiddelen die uit planten of uit plantenbereidingen samengesteld zijn of deze bevatten

66 Wet van 24 januari 1977 betreffende de bescherming van de gezondheid van de verbruikers op het stuk van de voedingsmiddelen en andere producten; Koninklijk besluit van 18 februari 1991 betreffende voedingsmiddelen bestemd voor bijzondere voeding, *B.S.* 30 augustus 1991

67 Art. 16 and following

68 Wet van 1 mei 2006 houdende de herziening van de farmaceutische wetgeving, *B.S.* 16 mei 2006

69 To enable the application of these new regulations a "mixed commission" has been established (art. 2 § 2)

Today however it is not clear what will be the precise consequence of the new legislation on the qualification of slimming products as medicinal products. It can be presumed however that more products will fall in the scope of the definition of medicinal products.

Advertisement for medicinal products

The act on Medicinal products

Advertisement for medicinal products that are not registered[70] or that are on prescription is prohibited[71]. Governmental campaigns however are allowed[72]. Some additional regulations have been inserted by the law on the review of pharmaceutical legislation[73]

If there is a violation of the law, claims in court can be made by any party having an interest. Criminal sanctions (fines and even imprisonment) can be imposed[74].

The Royal Decree on advertisement on medicinal products

Advertisement is defined as the forms of canvassing, marketing research or stimulation, aiming at the stimulation of prescribing, delivering, selling or the use of medicinal products[75].

The Royal decree repeats the prohibition of public advertisement on non–registered medicinal products and on medicinal products on doctors' prescription. Public Advertisement for medicinal products that are not on doctors' prescription is allowed under restricted conditions. Therapeutic indications such as for instance diabetes, cancer, etc. may not be mentioned. The information mentioned in the advertisement has to correspond with the information in the scientific instruction leaflet and with the information in the file that has been accepted at the registration of the medicinal product. Moreover advertisement on medicinal products may not be misleading[76]. Advertising on medicinal products has to be verifiable, has to promote the rational use of the medicinal product, by presenting the objective without exaggerating the characteristics[77].

The "Commissie voor toezicht op de reclame van geneesmiddelen" supervises the advertisement on medicinal products[78]. Advertisement on medicinal products is submitted to a preliminary control by the minister[79]. For advertisement by means of radio or television, a permission is needed[80] . If there are violations of the royal decree, sanctions can be imposed by the Minister after the advice of the Commission. Possible sanctions are the abolition of the permission, the proof of default of the owner of the registration to change the advertisement campaign, prohibiting the continuation of the advertisement, the dissemination of a rectification[81]. Most of the regulations of the Royal decree have been inserted in the act on medicinal products in order to harmonize the pharmaceutical legislation[82]

70 art. 9 Wet 21 juni 1983 dat wijzigt art. 9 § 1 Wet van 25 maart 1964 op de geneesmiddelen, *B.S.* 17 april 1964

71 art. 7

72 art. 6.2

73 art. 19 Wet van 1 mei 2006 houdende herziening van de farmaceutische wetgeving, *B.S.* 16 mei 2006

74 art. 16 and 1

75 art. 2 § 1.3 Koninklijk besluit betreffende de voorlichting en de reclame inzake geneesmiddelen voor menselijk gebruik (hierna KB reclame geneesmiddelen,. *B S.* 12 mei 1995

76 art. 4 § 3

77 art. 4

https://portal.health.fgov.be/pls/portal/docs/PAGE/INTERNET_PG/HOMEPAGE_MENU/GENEESMIDDELEN1_MENU/HUMAANGEBRUIK1_MENU/RECLAME1_MENU/RECLAME1_DOCS/AR-KB-1995-04-07_0.PDF

78 art. 24 KB Reclame geneesmiddelen

79 art. 16 § 2

80 art. 16 § 1

81 art. 24

82 art. 19 Wet van 1 mei 2006 houdende de herziening van de farmaceutische wetgeving

The subsection "Good use of medicinal products" of the Directorate – general medicinal products assures the dissemination of relevant information and controls the advertisement on medicinal products[83]. Unfortunately there is no pro-active control.

Selfregulating bodies

Jury voor eerlijke praktijken

Patients or other persons having an interest can also appeal the "Jury voor Eerlijke Praktijken inzake reclame" but the judgements are not binding for the advertisers. The Jury can act pro-actively. Moreover preliminary non binding advices can be given to advertisers. Consequently, it will depend on the willingness of the advertiser whether or not the misleading advertisement will be adapted to the advice of the Jury[84].

The General association of the pharmaceutical industry (Pharma.be)[85]

Pharma.be stands for the Association Générale de l'Industrie du Médicament, which represents the pharmaceutical industry located in Belgium. There may be a self-regulating functioning for advertisement published by her members.

Advertisement on slimming products that cannot be considered as medicinal products

The general law: "de wet op de handelspraktijken"

As mentioned above the "Wet op de handelspraktijken" is a general law according to advertisement on products and services. This implies that this act is also applicable to slimming products that cannot be considered as medicinal products. Besides the above mentioned rule on 'misleading' information, the law also states more specifically that advertisement with regard to products or machinery that *are not medicinal products* and are wrongfully presented as improving the medical condition of the patient are prohibited[86].

Consequently for instance advertising in magazines whether or not accompanied by 'before and after' pictures reflecting men or women with an amazing loss of weight thanks to the successful use of a slimming product can be prohibited if they are misleading or are wrongfully presented as improving the medical condition of the patient.

As mentioned above claims in court can be made to stop the advertisement and a pro-active control by the inspectors of the "Algemene Directie controle en bemiddeling" is also possible. Nevertheless the majority of what could be considered as misleading advertisement slips out of the control. Moreover, even if firms are convicted a commonly used practice is to sell the same product but to give it another name .

Jury voor Eerlijke praktijken inzake reclame (cfr. supra)

With regard to slimming products a lot of claims have already been addresses to the Jury[87].

9.2 CROSS BORDER HEALTH CARE

Although people generally prefer to seek health care in their home country, there's an increasing interest to seek cross border health care. The increased patient mobility and the stream of information about better, more immediate or cheaper treatment alternatives available in other Member States urges patients to go abroad. Furthermore, growing medical specialisation combined to expensive investments often results in the

83 http://www.afigp.fgov.be/New/NL/Afdelingen/goed_gebruik_gm.htm

84 http://198.104.187.9/jep/nl_versie2/index.html

85 http://www.pharma.be/en/agim01.html

86 art. 23 – 13

87http://198.104.187.9/jep/nl_versie2/index.html;http://198.104.187.9/jep/nl_versie2/index.html;
http://198.104.187.9/jep/nl_versie2/index.html;http://198.104.187.9/jep/nl_versie2/index.html;http://198.104.187.9/jep/nl_versie2/index.html

creation of specialised centres in one member state, attracting patients from all over Europe[88].

Belgium is one of the favourite countries for foreign patients. Compared to other European countries Belgium has a large supply of health care services and it is still expanding. Hence, there are no waiting lists in Belgium. Moreover Belgian prices (= what is charged to the patient) for health care are on average lower than in our neighbour countries since prices paid by the foreign health care providers or patients don't cover the real costs. These costs are mainly funded through subsidies from the public authorities[20].

On the other hand, for hospitals too there are some financial incentives to attract foreign patients. Since hospital financing is activity – based, there are financial incentives in reaching optimal capacity. Moreover the extra income generated can contribute toward covering the costs of expensive machinery. Additional foreign patients often offer the solution to render these investments more profitable. Furthermore hospitals can get the additional experience to get specialised by attracting foreign patients for specific pathologies.

9.2.1 Cross border bariatric surgery[89]

The issue of cross border health care specifically addresses to bariatric surgery. In that scope different types of patients with specific incentives to go abroad can be distinguished.

Patients medically eligible for bariatric surgery (BMI>=40 or >=35 + comorbidities) and qualifying for reimbursement by the national social security system have an interest in going abroad to get surgery, mainly because of the long waiting lists in their home country. These patients may go abroad on their own initiative to whatever hospital they choose but reimbursement by social security can be submitted to some conditions (cfr. infra). Sometimes however sick funds (or other health care purchasers) contract with foreign hospitals to treat their patients in order to manage the mobility of patients and to fulfil their legal duties of health care (health purchase contracts).

Some obese people with a medical indication for bariatric surgery don't qualify for reimbursement, because the national sick fund doesn't reimburse bariatric surgery as such or under very strict conditions. These patients will mostly be driven to go abroad by the long waiting list in their home country and by financial incentives. Sometimes these patients will go to foreign hospitals on their own initiative. Nowadays however bariatric surgery is often arranged by (private) commercial organisations recruiting patients by advertisement, often via the internet and offering all inclusive packages, including surgery in hospitals abroad, travelling to and stay in the country where the operation will be performed[90].

Bariatric surgery is now offered in many places as a cosmetic surgery procedure, not responding to a medical problem but to an aesthetic problem. Patients looking for this kind of cosmetic bariatric surgery will not meet the criteria for reimbursement and will have to bear the cost themselves (unless they have an additional private insurance covering the costs). Mainly driven by financial incentives these patients often go abroad to undergo surgery. Patients can go abroad on their own initiative but mostly they will end up in commercial settings recruited by advertisement of private organisations.

Although patient mobility offers important benefits, some major concerns can be raised: what level of care should the patient attend, who is responsible for the aftercare, what if complications occur, what if a dispute arises, how can a patient be sure of the competence of a health care professional…Some of these issues will be discussed underneath.

88 http://www.epha.org/a/520

89 Given the limited scope of the legal part in this health technology assessment the issues regarding interventions that are performed in clinics that are not recognized as hospitals, interventions in Belgium by foreign physicians who are not registered in Belgium will not be treated.

90 http://www.obesitycare.co.uk/

9.2.2 Disputes: conflict of law and Jurisdiction

The cross border dimension of health care can be problematic if a dispute occurs with regard to the content of the contract or if tort liability of the physician is concerned (cfr. supra for the difference).

If parties reside in the same state, it is clear which court will be competent and what law will apply if a dispute arises. If for instance a British patient contracts with a British surgeon to get surgery in the UK, the law of the UK will be applicable and the court of that state will be competent to judge. If parties don't reside in the same state, for instance if a British patient contracts with a Belgian hospital, it is not that clear which law will be applicable and which court will be competent: the Belgian or the British?

It is in the patient's interest that the court of the country where he resides is competent and that the law of that country is applicable. If the patient has to take legal action in a foreign court there are some barriers that can place a heavy burden on the patient, for instance extra costs such as cost of a lawyer in a foreign country, the travel costs if the patient has to appear in court, the barrier of a foreign language…

As to the legislation, laws applicable on a contract may profoundly differ from member state to member state. A specific clause in a particular contract could be invalid according to the legislation of one country whereas it would be valid according to another one[91]. To ensure legal certainty for patients it is important to know what legislation is applicable on the contract and what court will be competent.

As to tort liability the same problems will occur, since the approach in the member states with regard to liability is not uniform. The conditions for liability (for instance definition of a fault), the limitation periods, the burden of proof, the measure of damages, etc. may be different.

In order to determine the competent court and the applicable legislation the rules of international private law will have to be applied. Since there is a diversity of cross border bariatric surgery situations which may influence the applicable regulations, it has to be stressed that the casuistic approach is the only valid one. This implies that the specificities linked to each contract or situation may lead to particular solution. The general regulatory framework and some exemplary applications to cross border bariatric surgery are elaborated in the annex linked to this chapter.

9.2.3 Aftercare and cross border bariatric surgery

A specific problem with regard to the aftercare of foreign patients rises when they return to their home country after having undergone bariatric surgery. To what extent the physician performing bariatric surgery to foreign patients is responsible for aftercare?

Since complications for bariatric surgery will often appear in the period immediately after the operation, it is necessary that the surgeon sufficiently supervises the patient. Therefore a minimum stay in the hospital after the surgery and a minimum stay in the country where the patient was operated should be provided.

As foreign patients return to their home country after the surgery has been performed most of the aftercare will happen in the patients' home country. According to the above mentioned principles the physician has the duty to inform the patient that some specific consultations and checks will be necessary. In case of bariatric surgery the aftercare program will a.o. contain regular blood checks and a (life long) diet. Consequently the physician will for instance have the duty to explain how many blood checks will be needed and the specific point in time of the blood checks. Blood checks can perfectly be

91 It has to be noted however that there is some European regulation with regard to unlawful clauses in contracts (for instance: clauses that state that a physician cannot be held liable if he/she committed a fault etc..) http://europa.eu.int/eur-lex/lex/LexUriServ/LexUriServ.do?uri=CELEX:31993L0013:EN:NOT. There has been a transposition of this directive in Belgian law: wet van 3 april 1997 betreffende oneerlijke bedingen in overeenkomsten gesloten tussen titularissen van vrije beroepen en hun cliënten, *B.S.* 30 mei 1997; For a discussion about which clauses are probited in contracts between patients and physician and the application of the law see an advice of the Belgian Nationale Orde van Geneesheren http://195.234.184.64/web-Ned/nl/a080/a080013n.htm

performed by a GP in the patients' home country. Hence, it should be recommended that the physician having performed the operation also contacts and informs the patients' GP[92]. If necessary the operating surgeon can ask to send the results of the blood check. It should be stressed that the necessary preconditions such as for instance the transfer of the medical file have to be provided.

If a patient, after sufficiently being informed about the needed aftercare, neglects to follow the instructions, the patient will be responsible for the possible damage[93]. If the physician neglected to inform the patient about the aftercare and didn't take the necessary steps to assure that sufficient aftercare was available in the home country, the physician can possibly be held liable (cfr. supra).

9.2.4 Complications and cross border bariatric surgery

As mentioned above the physician has the duty to assure sufficient aftercare which a.o. includes the supervision of the patient after surgery. Most of the complications will occur immediately or short period after the surgery. It is also possible however that complications occur once the patient gets home. Therefore the surgeon not only has to inform the patient about the risk of complications but he should also explain what to do if a complication occurs in his home country, how to recognise serious complications etc…

Local doctors may not know what surgical techniques the physician used in the initial operation, making treatment difficult or nearly impossible. Moreover revision surgeries can be more complicated than the initial operation. Therefore, in some situations it might be necessary that complications are treated in the place where the initial operation was performed. If a patient with a complication (after being informed) prefers to get treatment from another physician in his home country (not familiar with the used techniques) the physician having performed the initial surgery cannot reasonably be held liable for the possible damage resulting from the second operation.

9.3 SPECIFIC TYPES OF CROSS BORDER BARIATRIC SURGERY

As mentioned above different types of patient with divergent incentives to go abroad can be distinguished. This part of the report deals with the peculiarities of these different types of patients looking for bariatric surgery abroad.

9.3.1 Bariatric surgery reimbursed in the patients' home country

9.3.1.1 Reimbursement of costs

Rights concerning reimbursement for healthcare provided in another Member State are clarified in the *proposed* Directive on Services in the Internal Market[94] and the Regulation 1408/71 on coordination of statutory social security schemes, both reflecting the important case-law of the Court of Justice [95]. This framework improving legal certainty for both patients and social security systems reflects the following general principle according to hospital care in another member state[96]:

Any hospital care to which the patient is entitled in his own Member State he may also seek in any other Member State provided he first has the authorisation of his own system. This authorisation must be given if the system cannot provide care within a medically acceptable time limit, considering the patient's condition. The patient will be reimbursed up to at least the level of reimbursement provided by his own system.

92 Antwerpen 20 maart 1996, *T. Gez.* 1998 – 99, 385

93 T. VANSWEEVELT, o.c., p. 418, nr. 577 e.v;

94 (COM (2004) 2 final); http://europa.eu.int/comm/internal_market/services/docs/services-dir/guides/health_en.pdf; for updates see http://ec.europa.eu/internal_market/services/services-dir/index_en.htm

95 Kohl, C-155/96 of 28.04.1998, ECR 1998, p. I – 1931; Smiths and Peerbooms, C-157/99 of 12.07.2001, p. I – 05473; Vanbraekel, C-368/98 of 12.07.2001, p. I-05363, Inizan, C-56/01 of 23.10.2003; Leichtle, 8/02 of 18.03.2004,

96 http://europa.eu.int/eur-lex/en/com/cnc/2004/com2004_0301en01.pdf

There's an increasing number of patients with a medical indication and qualifying for reimbursement going abroad for bariatric surgery mostly driven by the long waiting lists in their country. Obesity guidelines recommend that bariatric surgery is medically indicated for patients with a BMI >= 40 or >= 35 with life-threatening co-morbidities. Different countries use these criteria as a basis for reimbursement of bariatric surgery. In France for example gastric banding is reimbursed for 100 % as far as certain conditions are met (BMI >= 40 or BMI >= 35 + co-morbidities, the patient has followed an at least one year program concerning diets, physical activity,…). Moreover the costs related to the used material is reimbursed.

French patients meeting these criteria can be refunded for bariatric interventions carried out in Belgium as far as they got the authorisation of their system. The authorisation must be given if the waiting lists are too long considering the condition the patient is in.

9.3.1.2 Cross border Health care purchase contracts

Countries with long waiting lists such as the Netherlands have an interest in contracting with Belgian hospitals. As mentioned above authorisation must be given by the social security system of the country of origin for hospital care if the system cannot provide care within a medically acceptable time limit, considering the condition the patient is in. To manage patient mobility, sick funds (or other health care purchasers) often contract with foreign hospitals.

To come forward to the lack of a common organisational framework with regard to cross border care some hospitals fix standardised procedures in their contracts. Recently however there have been some initiatives of a European Commission working group, the High Level Group on health services and medical care. The working group set out some key issues that should be taken into account when drawing up agreements or contracts related to purchase of health care abroad[97]. The main aim was to provide an EU level framework for cross border contracts between providers and purchasers, guaranteeing the involvement of the public authority of the home country and the country where the intervention is performed. The guidelines recommend that contracts between health care purchasers and health care providers should stipulate the applicable law and jurisdiction, the relationship between the patient and the provider of health care should be determined according to private international law or any applicable public law, commissioners of health care (for instance the national ministers of health) intend to share all information necessary, including patient information, the price of the health care should be agreed in the contract. With regard to the follow up and the contents of care some more specific quality issues are identified… e.g. special requirements, journey, frequency of controls, medication, time limits for exchange of medical records should be provided.

There are some Belgian hospitals that have special agreements with foreign health care purchasers (mostly Sickness Funds) for bariatric surgery (with regard to patients that meet the criteria for reimbursement in their home country). An example: From May to December 2004 the CZ Dutch Sick Fund gave authorisation to 121 patients to undergo bariatric surgery in a Belgian hospital.[98]

9.3.2 Bariatric surgery in commercial settings

A minority of the population comes to Belgium to undergo bariatric surgery in the scope of a health purchase contract. Mostly however patients come on their own initiative and end up in commercial settings. A common practice with regard to bariatric surgery in commercial settings are the all inclusive packages containing surgery, transport, hotel stay in the country where surgery is performed… Since those packages are often offered by private (read profit) organisations there is a non-negligible risk to low quality of care. A specific problem addresses to the aftercare provided in the scope

97 "high level group on health services and medical care"
http://www.europa.eu.int/comm/health/ph_overview/Documents/key_level_002_en.pdf

98 http://www.ose.be/files/health/BelgianCaseStudy_ForPrint.pdf, p 85.xd

of an organised package contract. Such packages often limit aftercare to a minimum to minimise the length of stay in the hospital and consequently to reduce the costs. Some organisations even offer separate packages for aftercare which implies that the patient can decide what kind of aftercare he will enjoy depending on the price he's willing/able to pay[99]. Since the patient mostly has contracted with the organisation that has determined the modalities of the aftercare, one could question to what extent the surgeon is responsible for the aftercare in such circumstances. Notwithstanding the existence of a contract between a patient and an organisation limiting the necessary aftercare to an unacceptable minimum the physician cannot be discharged of his liability. According to the medical treatment agreement the physician has to provide care as long as the health status of the patient demands and as long as the patient wishes[l]. Consequently the surgeon will have to inform the patient that and what aftercare is needed. If he neglects to warn the patient that for instance the proposed aftercare is insufficient, he could be held liable. If the patient however chooses to have the insufficient aftercare and neglects the advice of the surgeon, the patient will be responsible for the possible damage resulting from it.

It should be remarked that as mentioned above in the general principles the patient has the right to qualitative care (art. 5 Belgian patient's rights act). Consequently liability of hospitals or surgeons offering poor care is conceivable if it can be proven that the damage resulted from the poor care. The right to qualitative care is integrated in the Belgian patients' rights act and in many other patients' rights acts of different European countries. In the last few years patients' rights have been the object of many national Patient rights acts. Although common principles are shared by the member states, the implementation however was very divergent. Some form of European charter of patients' rights would be helpful to express the shared principles and values of all EU health systems in a way that would give patients increased confidence in seeking care throughout the EU[100].

9.3.3 "Cosmetic" bariatric surgery?

9.3.3.1 The concept

Obesity is a medical disease to the extent that it affects health, because of associated morbidities (hypertension, diabetes, arthritis, sleep apnea…). The standard cut off point of BMI superior to 30 to define obesity is to a certain degree arbitrary, because the relationship between an increase in BMI and the incidence of co-morbidities is a more complex one (compounded for instance by several factors such as age, gender or ethnicity). Still this cut-off point provides a convenient benchmark for assessment. This report is assessing medical and surgical treatment for obesity using this standard definition. Numerous guidelines recommend that surgery should be considered for patients with a BMI>= 40 or a BMI >= 35 with life-threatening co-morbidities (cfr. clinical part). However, bariatric surgery – and in particular the less invasive laparoscopic adjustable gastric banding technique – is now offered in many places as a cosmetic surgery procedure, not responding to a medical problem but to an aesthetic problem. Driven by culturally determined ideals of beauty there's a pressure that mostly affects women to lose weigh even if there's no medical indication at all. In response to this tendency women are encouraged to undergo bariatric surgery by advertisement in women's magazines (for instance Cosmopolitan UK) include gastric banding, liposuction and breast enlargement in the same list of possible services.

The question rises to what extent patients undergoing bariatric surgery without meeting the criteria for medically indicated surgery can be considered as cosmetic surgery. Notwithstanding the above mentioned cut-off points the limit between what can be considered as cosmetic bariatric surgery and bariatric surgery for medical indication is not clear. There's a so – called grey zone. For instance, people having a BMI >30 are obese but will not qualify for bariatric surgery based on a medical indication. To some extent the cut-off points for bariatric surgery are arbitrary since it

99 http://www.obesitycare.co.uk/

100 Policy brief: Cross-border health care in Europe: http://www.wm.tu-berlin.de/~mig/files/2005.publications/E87922.pdf

is not based on evidence but on a consensus obtained in 1992. Since 1992 methods and materials have become more safe. This considerations taken into account, it is unclear if bariatric surgery performed on these patients has to be considered as cosmetic bariatric surgery.

9.3.3.2 Legal admissibility of "cosmetic" bariatric surgery

The fact that cosmetic bariatric surgery is performed on (physically) healthy patients raises some important issues. Is "cosmetic" bariatric surgery legally allowed? Does the sole fact of informed consent of the patient justify the surgery? To what extent can the physician performing "cosmetic" bariatric surgery be held liable if damage occurs?

It is generally accepted that a medical intervention is solely allowed if the risks are proportional to the benefits or the aim of the intervention[1, 2]. The violation of physical integrity of the patient can only be justified by a higher value, the promotion of health. Nowadays the interpretation of "health" does not have to be limited to 'physical health' but can be understood in a broad sense, namely the status of general physical, psychological and social wellness[101]. Taking into account this definition of health the negative influence of physical characteristics such as overweight can place a heavy burden on men's (psychological) health. Consequently cosmetic bariatric surgery can be justified if there's a balance (proportionality) between the risks (the risks linked to the invention) and the benefits for health (psychological health, social wellness,..).

The problem in balancing risks and benefits for health is however that today risks and benefits are not easily measurable. At first sight gastric banding for instance is less invasive and it is a reversible intervention. On the other hand however the long term effects of the intervention are not clear.

Nowadays there's no jurisprudence on the legal character of bariatric surgery not meeting the criteria for medical indications. In every way it will be up to the judge (or the judicial expert) to determine if there was a disproportion. If there's a disproportion the surgeon commits a fault by having performed the operation. It can be argued however that in this hypothesis the patient can also be held liable. By consenting to an irresponsible medical intervention the patient commits a fault towards himself[21, 22]f. It is obvious that this argumentation only applies as far as the patient was informed about the risks linked to the surgery. Hence the importance of correct and clear information given by the physician should be stressed (cfr. Supra).

Besides the rule of proportionality, an aesthetic intervention is only allowed if informed consent was given (cfr. infra). Some authors argue that written consent is needed for interventions with a weakly curative character[23-25]. Since "cosmetic" bariatric surgery could be regarded as weakly curative, one could recommend a written consent.

101 Cass. 16 december 1948, *J.T.* 1949, 84 met noot R. Salvatier

9.4 KEY POINTS AND RECOMMENDATIONS

General

- For all types of bariatric surgery an written informed consent is required. A complementary oral explanation however is necessary. The contents has to be defined by the society of bariatric surgery and information should be standardised. Moreover the written consent form has to provide a clause that the patient agrees to be included in a national registry.
- The surgeon has the duty to sufficiently provide the patient of pre – en and post-operation information on the surgical intervention.
- The patient rights act stipulates that the patient has right to qualitatively good care. If the patient can prove that the surgeon didn't offer sufficiently qualitative care, he could be held liable if the patient can prove the causal link between the damage and the poor care.

Cross border bariatric surgery

- The surgeon should assure qualitative aftercare in the patient's home country. In that scope networking with hospitals and/or physicians in the patients home country is a practice that should be encouraged.

Slimming products and advertisement

- Producers of non – medicinal slimming products misuse the gaps in the legislation on medicinal products to escape the severe regulations applicable on medicinal products. Although the enlarged definition of medicinal products in the new legislation on medicinal products probably will imply that more slimming products are considered as medicinal products, interpretation and consequently misuse remains possible. Therefore more specific legislation is needed with regard to what slimming products can be regarded as medicinal products. Moreover more proactive control on medicinal products is needed.
- There's a lack of control for advertisement on slimming products that cannot be considered as slimming products. Therefore a more effective and pro-active control should be organised. Nowadays it primarily depends on the courts' interpretation of what is misleading advertisement on slimming products. In order to clarify what can be regarded as misleading advertisement with regard to non-medicinal slimming products, specific legislation on advertisement prohibiting before and after pictures and patient's testimonies could offer a solution.

"Cosmetic bariatric surgery"

- Cosmetic bariatric surgery can be defined as bariatric surgery solely performed for aesthetic reasons. Actually surgeons cannot reasonably be held liable for performing "cosmetic bariatric surgery" as such if the patient consent to the intervention after being sufficiently informed and qualitative care was offered.

9.5 REFERENCES

1. Vansweevelt T. De civielrechtelijke aansprakelijkheid van de geneesheer en het ziekenhuis. Antwerpen: Maklu; 1992.
2. Nys H. Geneeskunde. Recht en medisch handelen. Mechelen: Kluwer; 2005.
3. Garza S. Bariatric weight loss surgery: patient education, preparation and follow-up. Critical care nursing. 2003;26:101-4.
4. Trouet C, Dreezen, I. Rechtsbescherming van de patiënt. De wet van 22 augustus 2002 betreffende de rechten van de patiënt. Nieuw Juridisch Weekblad. 2003(16):2-12.
5. X. De wet patiëntenrechten. Tijdschrift voor Gezondheidsrecht. 2003(2):65-159.
6. Dijckhoffz. Deel III. Het recht op informatie en geïnformeerde toestemming. Tijdschrift voor gezondheidsrecht. 2003 - 2004:115-6.
7. Mason EE, Hesson WW. Informed consent for obesity surgery. Obes Surg. 1998;8(4):419-28.
8. Sabin J, Fanelli R, Flaherty H, Istfan N, Mariner W, Barnes JN, et al. Best practice guidelines on informed consent for weight loss surgery patients. Obesity Research. 2005;13(2):250-3.
9. Appelbaum PS, Grisso T. Assessing patients' capacities to consent to treatment.[erratum appears in N Engl J Med 1989 Mar 16;320(11):748]. New England Journal of Medicine. 1988;319(25):1635-8.
10. Wittgrove AC, Buchwald H, Sugerman H, Pories W, American Society for Bariatric S. Surgery for severely obese adolescents: further insight from the American Society for Bariatric Surgery.[comment]. Pediatrics. 2004;114(1):253-4.
11. Feierman L, Chu. Reproductive rights project. Teenagers, health care and the law: a guide to the laws on minors' rights in New York. 1997.
12. Moran R, Drane W, McDermott S, Dasari S, Scurry JB, Platt T. Obesity among people with and without mental retardation across adulthood. Obesity Research. 2005;13(2):342-9.
13. Bell AJ, Bhate MS. Prevalence of overweight and obesity in Down's syndrome and other mentally handicapped adults living in the community. Journal of Intellectual Disability Research. 1992;36(Pt 4):359-64.
14. Prasher VP. Overweight and obesity amongst Down's syndrome adults. Journal of Intellectual Disability Research. 1995;39(Pt 5):437-41.
15. Melville CA, Cooper SA, McGrother CW, Thorp CF, Collacott R. Obesity in adults with Down syndrome: a case-control study. J Intellect Disabil Res. 2005;49(Pt 2):125-33.
16. Rubin SS, Rimmer JH, Chicoine B, Braddock D, McGuire DE. Overweight prevalence in persons with Down syndrome. Mental Retardation. 1998;36(3):175-81.
17. Callens S, editor. De definitie van het geneesmiddel in het Europees en Belgisch recht. Gent: Mys en Breesch; 1998.
18. Callens S. De definitie van het geneesmiddel. Tijdschrift voor gezondheidsrecht. 1998-1999:24-6.
19. Callens S, Peers, J. Organisatie van de gezondheidszorg. Antwerpen: Intersentia; 2003.
20. Glinos IA, Boffin, N, Baeten, R. Contracting cross-border care in Belgian hospitals: an analysis of Belgian, Dutch and English stakeholders perspectives. 2005. Available from: www.europe4patients.org
21. Dabin J. Faute envers soi-même et responsabilité à l'égard des proches. Annals de droit. 1965:p. 123.
22. Kruithof R. L'obligation de la partie lésée de restreindre le dommage. R.C.J.B. 1989:24-5.
23. Delva WD, R. Enkele civielrechtelijke aspecten van contraceptie, sterilisatie en kunstmatige inseminatie. Tijdschrift voor privaatrecht. 1974:482.
24. Andre R. Les responsabilités. Brussel; 1981.
25. Leenen HJJ. Handboek gezondheidsrecht. Alphen aan de Rijn: Samson H.D. Tjeenk Willink; 1994.

Part 5: Conclusions and recommendations

10 GENERAL CONCLUSIONS AND CONSEQUENCES FOR DECISION MAKING

Almost 13% percent of Belgians adults have a BMI >=30; and 0.9% a BMI >=40 (2004 data). Because of associated co-morbidities, obesity is a major and increasing public health problem in our country.

The most important aspects of obesity prevention (for instance school policies and programmes), and treatment (lifestyle modifications) fall largely outside the clinical, bio-medical paradigm. However, medical approaches to treatment (weight loss drugs and surgery) are part of the response to the obesity epidemic. Belgium also appears to be a pioneer in offering long-term residential care for obese children. These medical approaches are the core subjects of this health technology assessment.

10.1 PRESCRIPTION DRUGS FOR WEIGHT LOSS

10.1.1 Discussion

Two prescription weight-loss drugs – orlistat (Xenical®) and sibutramine (Reductil®) are presently available on the market in Belgium. A third one – rimonabant (Accomplia®) should be available soon. These drugs are proposed as an adjunct to the multidisciplinary treatment of obese patients (BMI >= 30, or in some cases, BMI >=27, if co-morbidities are present).

Large randomized, placebo-controlled clinical trials are available, providing data on safety and effectiveness on weight loss, and some metabolic parameters, for up to 4 years for orlistat, and 2 years for sibutramine and rimonabant. All these trials have important drop-out rates (40-50%). Given in conjunction with diet and/or lifestyle intervention, all drugs proved more effective than placebo as regards weight loss and improvement of some metabolic parameters such as lipid profile. However, the overall effect of weight-loss drugs is modest: more or less 10 patients need to initiate treatment, for one of them to achieve and maintain 10% weight loss after 2 years, over the effect provided by placebo. Mean difference in weight between placebo and treatment group after 2 year-treatment is of the order of 3-4 kgs. The effect is not sustained after treatment is withdrawn.

Before promoting weight-loss drugs as the chronic, long-term treatment of obesity, more data are required on their long-term safety, and effectiveness on hard-endpoints - such as cardio-vascular events which are the ultimate goal of treatment. Such data - of the kind that are required for other drugs used in the treatment of chronic diseases (hypertension, dyslipidemia) - do not yet exist for weight-loss drugs. Due to concerns with the safety profile of Sibutramine, the manufacturer himself recommends to limit treatment to one year (studies evaluating long-term safety are underway), and long-term treatment is not even an option at the moment. Still more than 160.000 boxes of Sibutramine have been prescribed, and sold in Belgium in 2004 (one box=one month treatment).

A fundamental difference between weight-loss drugs, and drugs for the treatment of other chronic diseases, is that weight-loss drugs will be taken both for medical and non-medical reasons (even if licensed as prescription-only); and the potential market is huge. Safety then becomes an even more important issue, because of the large number of persons likely to take these drugs. Even infrequent, but serious adverse events, too rare to be detected in the clinical trials of current size and duration (for instance, psychiatric side effects for rimonabant), might translate into a significant number of cases.

Assumptions used in cost-effectiveness analyses on the sustainability of weight loss after treatment is withdrawn, are too optimistic and contradict published data.

10.1.2 Recommendations

- The evidence available on the effectiveness of weight-loss drugs in the treatment of obesity does not support a decision to have sibutramine, orlistat, or rimonabant refunded by the social security.
- Weight-loss drugs should not be promoted as a chronic treatment for obesity.
- Clinicians prescribing weight-loss drugs need to inform their patients that weight-loss is usually not sustained after treatment is withdrawn.

10.2 BARIATRIC SURGERY

10.2.1 Discussion

Although specific billing codes and conditions for refunding do not yet exist within the Belgian social security system, bariatric surgery is widely practised, and refunded: more than 9000 bills with codes assumed to be used for bariatric surgery were paid by the third party payer (INAMI/RIZIV) in 2004 (+ 33% as compared to 2003, + 436% as compared to 1995). Hospitalisation for bariatric surgery (excluding re-hospitalisations for complications) cost the social security at least 15 millions Euros in 2003.

There is sufficient evidence that bariatric surgery is more effective than non-surgical treatment for long-term weight loss and control of some co-morbid conditions, particularly diabetes, in severely obese patients. However bariatric procedures differ widely in terms of long-term effectiveness and safety, from more invasive and more effective malabsorptive procedures (the current standard being the Roux-en-Y gastric bypass), to less effective and less invasive restrictive procedures (such as gastric banding). Important gaps in scientific knowledge exist in the field of bariatric surgery. Key questions, such as what is the best procedure, for which patients (according to BMI, age, eating behaviour…) still need to be answered. No prospective data have yet been published on the impact of bariatric surgery on cardio-vascular morbidity, and overall mortality. In addition, **bariatric surgery is not a cure**, and long-term surgical, and medical follow-up are needed, as well as a life-long commitment to diet, for the intervention to be successful.

Laparascopic Adjustable Gastric Banding (LAGB) is the most frequent procedure in Belgium (58% of billing codes used for bariatric surgery in 2004), probably because it is less invasive, easier to perform than other procedures and reversible. Nevertheless long-term effectiveness and safety of LAGB are poorly documented in the scientific literature, and the cost of the device (1500-2400 Euros) makes it a more expensive intervention. There is no evidence that in the long-term, LAGB has a better risk/benefit ratio than the more established Roux-en-Y gastric bypass.

The principle 'primum non nocere' has to be kept in mind, particularly for an elective surgical intervention involving an undamaged body part. Risks associated with bariatric surgery can be high: up to 20% of re-hospitalisations one year after gastric bypass have been described in population-based studies; high rates of re-operation after gastric banding have also been described in some case-series. A **steep learning curve** effect has been described for most of bariatric procedures, with markedly lower mortality and morbidity associated with surgery for the second 100 procedures performed. In Belgium, 75/108 (70%) of hospitals practising bariatric surgery in 2003 reported less than 101 stays for obesity surgery this year, 59/108 (55%) reported less than 51 stays.

Clinical criteria found in most guidelines recommending bariatric surgery - BMI >= 40, or BMI >= 35 + co-morbidities are to some extent arbitrary, and which co-morbidities do qualify as an indication are subject to debate. Many co-morbidities have been shown to respond well to bariatric surgery (depending also of the type of technique used; purely restrictive procedure such as gastric banding being usually less effective) – but should, for instance hypertension or dyslipidemia alone (for which effective, simple pharmacological treatment does exist) justify bariatric surgery? Some guidelines

introduce the concept of 'life-threatening' or 'severe' co-morbidities, and include a non-exhaustive list of these co-morbidities. However concepts such as 'obesity-induced physical problem interfering with lifestyle' are vague. Only severe co-morbidities can justify the risks and uncertainties associated with bariatric surgery.

As rumour has it, bariatric surgery in general, and the less invasive LAGB in particular, are often performed in patients, mostly women, not meeting medical indications, and requesting the intervention largely for cosmetic reasons. There are no hard data that could permit to confirm or disprove this, but the risk does exist. The challenge for decision-makers in Belgium, is to establish criteria for refunding bariatric surgery that would prevent such abuses. Criteria that would simply include 'BMI >= 35 , and co-morbidities' might still leave room for abuses because they are too vague. On the other hand, it is not possible to propose an exhaustive, and exclusive list of co-morbidities that would justify bariatric surgery in the sub-group of patients with a BMI between 35 and 39. Hard choices have to be made here, when establishing criteria for refunding bariatric surgery in this group.

10.2.2 Recommendations :

There is enough evidence that bariatric surgery is a cost-effective intervention, but associated risks can be high. These interventions should be refunded by the social security, under strict criteria of quality assurance and conditions for patient selection.

Clinical criteria

Limiting interventions to patients with a BMI >=40 seems too restrictive, in view of the guidelines and criteria applied elsewhere. Bariatric should be refunded also for patients with a BMI >= 35, with a documented, severe co-morbid condition, such as diabetes (as evidenced by a measure of HbA1c).

Conditions imposed on patients

Patients with a BMI > = 40 are largely regarded as being unlikely to respond to lifestyle modification or medical treatment. Imposing one year of medically-supervised multidisciplinary medical treatment before bariatric surgery in these patients, seems excessive. However, because of associated co-morbidities, all patients should be assessed by an internal medicine specialist, and the decision to operate should be made by a multidisciplinary team.

Written, informed consent is highly recommended. (see later, 'legal issues')

Coverage of refunding

For patients eligible for bariatric surgery according to the criteria defined above, refunding should include the medical device used (such as the gastric band)

Conditions imposed on hospitals practising bariatric surgery

Because of the important implications of volume-outcome relationship for quality of care, practice of bariatric surgery should be strictly limited to experienced centres of excellence. The American Association for Bariatric Surgery (AABS) has defined criteria to qualify as a 'centre for excellence' ; these criteria could be adapted to Belgium. AABS criteria include:

- Long term follow-up with a system for outcome monitoring. In Belgium this implies the compulsory, standardised, preferentially computerized, registration of each patient undergoing bariatric surgery. As a tool to monitor and improve quality of care, this register has to be **publicly** funded
- At least 125 cases of bariatric surgery per year. In Belgium, identifying a minimum volume of cases should take into account the results of studies on volume-outcomes relationship in the field of bariatric surgery.
- Availability of organized and supervised support groups

Bariatric surgery in patients under 18 year-old

Bariatric surgery in patients under 18 year-old raises serious ethical issues, should be performed only in rare circumstances, and requires highly specialised multidisciplinary teams. Taking into consideration the number of eligible children, it can be limited to one, or (for reasons of geographic coverage) maximum, 2 hospitals in Belgium, selected on the basis of their specific experience, possibilities of long and complete follow-up, and multidisciplinary approach. Bariatric surgery in patients under < 18 year old. is highly experimental, and care need to be taken that this experience contributes to the body of scientific knowledge in this field.

Good clinical practice

Good clinical practice guidelines for bariatric surgery are urgently needed. These should include:

- Guidelines for peri-operative care and clinical pathways
- Precise indications for each type of bariatric surgery procedures
- Guidelines for follow-up after bariatric surgery

Given the current state of knowledge, these guidelines will be mainly consensus-based. Consensus development should include all professionals involved in the decision to operate and follow-up (for instance, gastro-enterologists, who have to deal with complications related to malabsorption, and general practitioners, who are involved in follow-up), and not only surgeons.

Billing codes for bariatric surgery

Surgeon fees need to be adjusted to the difficulty and operating time needed for each type of bariatric procedure. For instance, gastric bypass is a longer and more difficult procedure than LAGB. This difference is not adequately reflected in the billing codes developed for various bariatric procedures in the Royal Decree awaiting approval.

10.3 RESIDENTIAL CARE FOR OBESE CHILDREN IN BELGIUM

10.3.1 Discussion

Three centres in Belgium offer residential care to chronically ill children; 196/296 beds (66%) are dedicated to severely obese, school aged children. The combined annual budget of these 3 centres in 2006 is 17,2 millions Euros (more than 58.000 Euros/ bed/year). Average length of stay for obese children is one school year.

The demand is high. Waiting list in the largest centre – Zee Preventorium - is one year.

A precise description of the population admitted in these centres (severity of obesity, co-morbidities…), of the processes, and of the outcomes at discharge, is not possible, because no standardised data are being routinely computerised and analysed. After 10-month residential treatment, most children appear to have lost weight, and improved in various other respects. On a sub-sample of 47 patients retrieved after discharge from the Zee Preventorium, mean adjusted BMI (observed/ideal BMI, or percent excess BMI) was 175% on admission, 121% at discharge, and 155% one year and half after discharge.

Several questions do arise.

Are the benefits observed at discharge maintained in the long term? Do the potential advantages of removing children from their family and environment for such a long period time (intensive care, breaking drastically with poor habits) overcome the potential disadvantages (less family involvement for instance)? Regular visits to the Zee Preventorium might be difficult for families living on the other side of the country. One centre is not accessible by public transportation. Would long-term outcomes really be different if length of stay was reduced to 3 months, for instance? Is this very intensive and expensive type of care, if at all effective in the long term, superior to an intensive multidisciplinary approach in primary care? To our knowledge, no similar experience is

described in the scientific literature. This resource-intensive approach needs to be urgently evaluated scientifically.

Only one centre (Clairs-Vallons), has produced a one-shot report using standardised indicators. Such data are not available in the other centres. For instance it is not possible to know for each cohort the proportion of failures, or the improvement of co-morbidities. A routine data collection system standardised across centres is needed, so that centres could monitor their results, and outcomes be compared between centres.

Should the mission of these centres extend to, and their financing include, clinical follow-up of patients after discharge? Clinical follow-up of patients after discharge need to be available close to home, and is the responsibility of the primary care network. There is however a problem, in that no structured reference network is yet available, and it is not clear where the patient need to be referred to (specialised obesity team, general practitioner, behavioural therapist?).

Do proper alternatives to residential treatment of severely obese children exist in Belgium? A few specialised teams, mainly in teaching hospitals, offer ambulatory care to obese children. However, apart from a problem of unequal geographical distribution of these services, ambulatory care also entails higher cost for the patients than residential care. This is a serious barrier to the utilisation of these services (even more so for a disease disproportionately affecting less privileged social classes), and provides a perverse incentive to the utilization of residential care.

It was beyond the scope of this study to explore in detail issues such as the distribution, quality, and financing of ambulatory care for severely obese children. A further study is needed to provide practical recommendations in these respects.

Should the capacity of these centres be increased, to meet demand and reduce waiting time? Recent media exposure might have increase demand and pressure on policy makers. However, as long as the long term effectiveness of residential centres and superiority over ambulatory primary and secondary care approaches has not been demonstrated, a further increase in capacity and additional resources cannot be defended by rational arguments.

Another reason is that there is a striking imbalance between resources allocated to ambulatory care, and resources allocated to residential care of severely obese children. On the other hand, the effectiveness of intensive, multidisciplinary care for severely obese children it not known either. We suggest identifying a limited number of pilot projects, to be funded through a convention. These would be evaluated with a clear and validated research methodology, in parallel with the residential approach.

10.3.2 Recommendations

- Long-term effectiveness of residential care for severely obese children needs to be assessed through a prospective study involving all 3 centres. Randomization of patients to long (10-month) or short (for instance, 3-month) treatment should be considered. Long-term studies imply additional costs, but these should be weighted against the large budget presently allocated to these centres
- In the mean time, INAMI/RIZIV-conventions should include the obligation to produce a standardised annual report. This report can be limited to the more meaningful indicators. Precise contents should be identified by obesity experts and the centres themselves
- A few pilot centres providing ambulatory care for severely obese children, should be selected and funded through a convention, under the obligation to be included in a research protocol evaluating their long-term effectiveness.
- These studies need to be under the responsibility of a scientific team with high epidemiological expertise, in order to insure validity, and maximize scientific output.
- Funding should be re-evaluated in 5 year time, pending the results of these studies.
- Clinical follow-up of patients after discharge should be the responsibility of the primary care network, and not of these centres. A further study should analyse the strengths and weaknesses of the existing primary care network, and develop recommendations to improve it.

10.4 LEGAL ISSUES: KEY POINTS AND RECOMMENDATIONS

10.4.1 General

- The surgeon has a legal obligation to provide sufficient information to the patient before the intervention. A written informed consent is not a legal obligation but is highly recommended before all types of bariatric surgery, in particular because of the life-long consequences of the intervention. A complementary oral explanation is necessary. Contents have to be defined by professional bodies (for instance, the SOBS – Section of Obesity Surgery in Belgium within the Belgian Society for Surgery). The written consent form has to provide a clause that the patient agrees to be included in a national registry.
- The patient has a legal right to quality care. If the patient can prove that the surgeon didn't offer good quality care, the surgeon could be held liable if the patient can prove the causal link between the damage and sub-standard care.

10.4.2 Cross border bariatric surgery

- The surgeon should insure good quality aftercare in the patient's home country. In that scope networking with hospitals and/or physicians in the patients home country is a practice that should be encouraged. European guidelines as regards health care purchase contracts between a Belgian and a foreign institution (for instance, a Dutch insurer and a Belgian hospital), should be followed.

10.4.3 Slimming products and advertisement

- Producers of non–medicinal slimming products misuse the gaps in the legislation on medicinal products to escape the severe regulations applicable on medicinal products. The enlarged definition of what a medicinal product is in the new legislation on medicinal products probably will imply that more 'slimming products' are considered as medicinal products, but interpretation and consequently misuse remains possible. More specific regulation is needed with regard to what slimming products can be regarded as medicinal products. Moreover more proactive control on medicinal products is needed.
- There's a lack of control for advertisement on slimming products that cannot be considered as slimming products. Therefore, a more effective and pro-active control on slimming products should be organised. Today it primarily depends on the courts' interpretation of what is misleading advertisement on slimming products. In order to clarify what can be regarded as misleading advertisement with regard to non-medicinal slimming products, specific legislation on advertisement prohibiting before and after pictures and patient's testimonies could offer a solution.

10.4.4 "Cosmetic bariatric surgery"

- Surgeons cannot reasonably be held liable for performing "cosmetic bariatric surgery" (bariatric surgery solely performed for aesthetic reasons) if the patient consented to the intervention after being sufficiently informed and good quality care was offered.

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Wettelijk depot : D/2006/10.273/28

KCE reports

1. Effectiviteit en kosten-effectiviteit van behandelingen voor rookstop. D/2004/10.273/1.
2. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase 1). D/2004/10.273/2.
3. Antibioticagebruik in ziekenhuizen bij acute pyelonefritis. D/2004/10.273/5.
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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.
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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.
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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.
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