CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Controversies in Obesity Management

Public Meeting

July 14, 2015

Agenda

- **Public Meeting Convened, Topic Overview** | 9:30 am
- **Presentation of the Evidence and Economic Modeling, Q&A** | 9:35 – 10:40 am (Dr. Dan Ollendorf)
- **Public Comments** | 10:40 – 11:30 am
- **Lunch** | 11:30 – 12:00 pm
- **CTAF Q&A with Experts / Deliberation and Votes** | 12:00 – 1:15 pm
- **Break** | 1:15 – 1:30 pm
- **Barriers and Potential Solutions, Policy Roundtable Discussion, Best Practice/Policy Recommendations** | 1:30 – 3:05 pm
- **Reflections from CTAF Panel** | 3:05 – 3:25 pm
- **Summary and Closing Remarks** | 3:25 – 3:30 pm
- **Meeting Adjourned** | 3:30 pm
  - **Download meeting materials: http://tinyurl.com/CTAF-OM**

CTAF Overview

- Core program of the Institute for Clinical and Economic Review (ICER), an independent non-profit research organization that evaluates scientific evidence on the clinical effectiveness and cost implications of medical interventions
- Goal: Help patients, clinicians, insurers, and policymakers apply evidence to improve the quality and value of health care
- Deliberation and voting by CTAF Panel – independent clinicians, methodologists, and leaders in patient engagement and advocacy
- Supported by grants from the Blue Shield of California Foundation and the California HealthCare Foundation

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Evidence Review

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July 14, 2015

I have no conflicts of interest.

Background

- Two-thirds of Americans overweight or obese
- Bariatric surgery: commonly employed for class 3 (BMI 40+) or class 2 (BMI 35-39.9) obesity
  - Uncertainties: long-term effectiveness and safety, best practices for patient selection and follow-up, outcomes in patients with BMI <35
- Newer treatment options:
  - Devices: vagus nerve block, temporary intragastric balloons, GI liner system
  - Drugs: liraglutide, lorcaserin, naltrexone/bupropion, phentermine/topiramate

Objective

- Evaluate evidence on comparative clinical effectiveness and comparative value of bariatric surgery, devices, and drugs vs. conventional weight-loss management (combinations of diet, exercise, and/or behavioral/ lifestyle interventions)
  - Universal comparator in nearly all RCTs and cohort studies
  - Indirect comparisons between intervention types problematic due to marked differences in baseline characteristics and clinical comorbidity

Methods

- *Target population*: adults (18+) and adolescents (12-17) who are overweight or obese (BMI 25+)
- *Interventions:*
  - Surgery: Roux-en-y gastric bypass (RYGB), vertical sleeve gastrectomy (VSG), laparoscopic adjustable gastric banding (LAGB), biliopancreatic diversion with or without duodenal switch (BPD±DS)
  - Devices: Maestro®, EndoBarrier®, various balloons
  - Drugs: BELVIQ®, Contrave®, Qsymia®, Saxenda®

Methods (2)

- *Comparators:*
  - Conventional weight-loss management
  - Head-to-head comparisons (most commonly between surgical approaches)
- *Outcomes:*
  - Mortality
  - Weight loss
  - Resolution of obesity-linked comorbidities
  - Quality-of-life (QoL) and functional outcomes
  - Complications and other adverse effects

Study Selection

- Primary focus on good- and fair-quality RCTs and prospective comparative cohort studies
- Retrospective comparative cohort data assessed separately from RCTs and prospective cohorts
- Case series data generally reserved for information on longer-term (>2 years) outcomes and evaluated separately:
  - Exception: devices, where follow-up terminates at balloon or DJBL removal (typically 6 months)

Level of Certainty in Evidence by BMI Class and Intervention Type

BMI	<30		30-34.9		35-39.99	≥40
T2DM	Yes	No	Yes	No	---	---
Bariatric Surgery						
BPD						
LAGB						
RYGB						
VSG						
Devices						
IGB						
DJBL						
vBloc						
Drugs						
Liraglutide						
Lorcaserin						
N/B						
P/T						

Key
No evidence
Low certainty
Moderate certainty
High certainty

BPD: biliopancreatic diversion; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-y gastric bypass; VSG: vertical sleeve gastrectomy; IGB: intragastric balloon; DJBL: dudoneal-jejunal bypass liner; vBloc: vagus nerve blocking device; N/B: naltrexone/bupropion; P/T: phentermine/topiramate

BARIATRIC SURGERY

Surgery vs. Conventional Weight-Loss Management

- Mortality:
  - 20-40% reductions in rate of all-cause mortality at 7-15 years of follow-up
  - Some data concerns (e.g., independent effects of weight loss, health status of controls)
- Weight loss:
  - Meta-analysis: in patients with BMI ≥35, pooled mean difference of 7.4 kg/m^2 lost vs. conventional management (95% CI: 6.2, 8.6; range: 5-14)

Surgery vs. Conventional Weight-Loss Management (2)

- Comorbidity Resolution:
  - Type 2 diabetes most frequently studied by far
  - Nearly all studies of RYGB or LAGB in patients with BMI 30-34.9
  - Meta-analysis: surgical patients nearly 4 times more likely to achieve resolution (log OR 3.6; 95% CI 2.5, 4.7; range: 2.0-7.0)
  - Hypertension and hyperlipidemia also frequently tracked in diabetic populations
  - Very limited comparative evidence on comorbidity resolution other than diabetes (e.g., asthma, arthritis, sleep apnea)

Surgery vs. Conventional Weight-Loss Management (3)

- Adolescents:
  - Single RCT of 50 patients, age 14-18 (mean BMI 41), undergoing LAGB or lifestyle intervention*
  - Difference of ~12 kg/m^2 lost in favor of LAGB
- Long-term outcomes (other than mortality):
  - Challenged by attrition, survivor bias, and crossover
  - <3% of more than 1,000 long-term studies had 80% or better sample retention after 2 years**
  - Best available data suggest 5-10% weight regain and 30-40% comorbidity relapse beyond 2 years of follow-up

*O'Brien et al., JAMA 2010;303(6):519-526.
**Puzziferri et al., JAMA 2014;312(9):934-942

Head-to-Head Evidence Comparing Variants of Bariatric Surgery

- Total of 24 good- and fair-quality studies comparing bariatric surgical procedures
- Meta-analysis of BMI change only feasible for RYGB vs. VSG
- No statistically-significant differences in BMI change between these two procedures in any individual study or overall

Harms of Bariatric Surgery

Prospective Studies

Procedure	# of Studies	# of Patients	Follow-Up; Range, Median (Months)	Complication Rate; Range, Median (%)*	Reoperation Rate; Range, Median (%)	# of Deaths
BPD	7	189	12-60, 18	17-79, 31.6	3-45, 13.0	0
LAGB	14	13,005	12-120, 24	3-61, 17.9	1-33, 14.8	11
RYGB	26	15,830	1-120, 16	0-78, 19.4	0-33, 6.0	62
VSG	12	2,613	12-36, 12	1-80, 9.5	0-17, 2.0	2

Retrospective Studies

Procedure	# of Studies	# of Patients	Follow-Up; Range, Median (Months)	Complication Rate; Range, Median (%)*	Reoperation Rate; Range, Median (%)	Mortality Rate; Range, Median (%)
BPD	9	2,659	3-63 (24)	8-83, 26.9	0-30, 3.6	0-2.9, 1.40
LAGB	17	16,335	3-72 (29)	0-53, 10.1	0-44, 7.4	0-2.0, 0.15
RYGB	23	840,895	2-72 (29)	0-78, 9.2	0-22, 5.8	0-4.3, 1.94
VSG	11	16,574	2-63 (23)	0-80, 8.8	0-17, 3.9	0-3.9, 0.07

* Complication rate may include reoperations in some studies

Bariatric Surgery: Summary

- BMI of 35 or greater:
  - 20-40% lower rates of all-cause mortality vs. conventional weight-loss management over 7-15 yrs of follow-up
  - Reductions in body weight of 6-9 kg/m^2 over 1-2 yrs of follow-up
  - Moderate certainty of substantial net health benefit
- BMI of 30-34.9 and Type 2 diabetes
  - Nearly four-fold greater likelihood of resolution vs. conventional management over 1-2 yrs of follow-up (36-100% vs. 0-6%)
  - Suggestion of relatively high rates of relapse at 3-4 years
  - Moderate certainty of small or moderate net health benefit
- Insufficient evidence for BMI 30-34.9 without Type 2 diabetes

Bariatric Surgery: Summary (2)

- Head-to-head study:
  - RYGB vs. VSG: moderate certainty of comparable net health benefit
  - Limited comparative data for other procedures, and trends in the field suggest above comparison is the most relevant
- Insufficient evidence:
  - Adolescent populations
  - BMI <30

DEVICES

Maestro vBloc Device

- Only device of interest with FDA approval
- 2 RCTs, but only one of current-generation device*
  - N=239 (84% female; mean age 47; mean BMI 41)
  - Published data available for 12 months of follow-up; sham-controlled study
  - Excess weight loss (EWL): 24.4% vs. 15.9% for sham (p=.002)
    - Total weight loss: 10.9 kg vs. 7.3 kg for sham
  - Serious complications occurred in 6 (3.7%) device patients; 5 (3.1%) required device removal

*Ikramuddin et al., *JAMA* 2014;312(9):915-922.

Maestro vBloc Device: Summary

- Single RCT of current-generation device
- Modest improvement in excess weight loss vs. sham device, primary efficacy endpoint (10% greater EWL) not met
- Uncertainty regarding longer-term effectiveness and safety
- Low certainty of a small or comparable net health benefit

*Ikramuddin et al., *JAMA* 2014;312(9):915-922.

Intragastric Balloons

- No currently-approved balloon systems in US
- 7 studies (5 RCTs) but problematic evidence base:
  - Variability in balloon duration and # of placements
  - Inconsistent data on weight trends and follow-up after balloon removal
  - Early removal in up to 20% of patients
- Judgment: low certainty of comparable net benefit vs. conventional weight-loss management

EndoBarrier Device

- Not approved in US
- Two RCTs (n=114):
  - Mixed evidence on weight loss
  - Complications led to early device removal in majority of patients in one RCT
  - Ongoing RCT halted due to infection concerns
- Judgment: insufficient evidence on net health benefit vs. conventional weight-loss management

MEDICATIONS

Medications

- No head-to-head comparisons
- Most studies limited to 1 year of follow-up; some crossover data available at 2 years
- Network meta-analysis: no material differences in effectiveness or discontinuation due to adverse events (AEs)

Medications (2)

- Liraglutide (Saxenda):
  - 3 RCTs (n=~4,700*) showed 5-6% incremental weight loss vs. placebo or orlistat at 1-2 years of follow-up
  - Liraglutide 2-4 times more likely to achieve 5% or 10% weight loss than comparators (placebo or orlistat with lifestyle intervention)
  - GI distress most common side effect; discontinuation due to AEs in 7-9% of patients
- Lorcaserin (BELVIQ):
  - 3 RCTs (n=~4,600) showed 3-4% incremental weight loss vs. placebo/lifestyle intervention at 1 year
  - Lorcaserin 2-3 times more likely to achieve 5% or 10% weight loss than lifestyle intervention alone
  - Discontinuation due to AEs in 4-9% of patients

*with addition of Pi-Sunyer et al., NEJM 7/2/15

Medications (3)

- Naltrexone/Bupropion (N/B) (Contrave):
  - 4 RCTs (n=~4,500) showed 3-4% incremental weight loss vs. placebo at 56 weeks of follow-up
  - N/B 2-3 times more likely to achieve 5% and 10% weight loss than lifestyle intervention alone
  - Discontinuation due to AEs in 20-30% of patients
- Phentermine/Topiramate (P/T) (Qsymia):
  - 5 RCTs (n=~4,500) showed 6-7% incremental weight loss vs. placebo/lifestyle intervention at 6-12 months (8-10% for higher dose)
  - P/T 2-4 times more likely to achieve 5% or 10% weight loss than lifestyle intervention alone
  - Discontinuation due to AEs in 12-16% of patients (larger studies)

Medications: Summary

- Data from 14 RCTs across 4 medications
- All 4 drugs result in greater weight loss than lifestyle intervention alone, but benefits modest
  - Indicated for BMI 30+ or 27+ with obesity-linked comorbidities
  - Studies conducted in adults only
- Discontinuation due to AEs variable but not inconsequential
- Summary judgment: small net benefit, moderate certainty for all medications

Public Comments Received

- Goal of review should be to expand the treatment armamentarium
- Obesity is a chronic, relapsing, and remitting condition, and treatment should be evaluated in this light
- Variety of unpublished studies provided
- Clarity around BMI classes studied for each intervention of interest

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Economic and Health-System Value Analysis

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July 14, 2015

Economic Analysis Components

- Incremental costs per outcomes: ICER simulation model of 1- and 10-year costs and outcomes of:
  - Each bariatric surgical procedure
  - N/B pharmacotherapy (largest evidence base at recommended dose)
  - vBloc therapy (only FDA-approved device)
  - Drug/device used in sequence with surgery
- Health System Value:
  - Potential budgetary impact of extending bariatric surgery to a) all patients with BMI 30-34.9, and b) patients in this BMI class with diabetes

Incremental Cost per Outcomes: Methods

- All BMI ≥30 and broken down by class
- Universal comparator: conventional weight-loss management
- Outcome: Quality-adjusted life years (QALYs)
- Effectiveness driven by BMI reductions:
  - Mortality: changes driven by BMI reductions
    - 1-yr data from RCTs; further trajectory modeled using observational study data
    - Reduction in mortality with bariatric surgery: 30%
- QoL and costs based on data linked to BMI class
- Other costs (e.g., intervention, complications) from published sources

Incremental Costs per Outcomes: 1-Year Findings, BMI ≥30

Outcome/Cost	Standard Care	N/B	vBloc	RYGB	VSG	LAGB	BPD±DS
BMI ≥30							
Clinical Outcome							
BMI loss (mean)	1.4	3.0	3.8	10.4	9.8	7.8	12.5
Death (%)	1%	1%	1%	2%	2%	2%	2%
Reoperation (%)	0%	0%	6%**	6%	3%	12%	7%
Medical complication (%)	0%	0%	4%	11%	13%	2%	21%
Costs ($)							
Procedure	$0	$1,645	$17,500	$24,277	$18,788	$15,987	$36,160
Reoperation	$0	$0	$710	$787	$402	$1,478	$893
Other Complications*	$3,710	$3,710	$4,364	$5,035	$5,167	$4,570	$5,925
TOTAL	$3,710	$5,355	$22,574	$30,099	$24,357	$22,035	$42,979

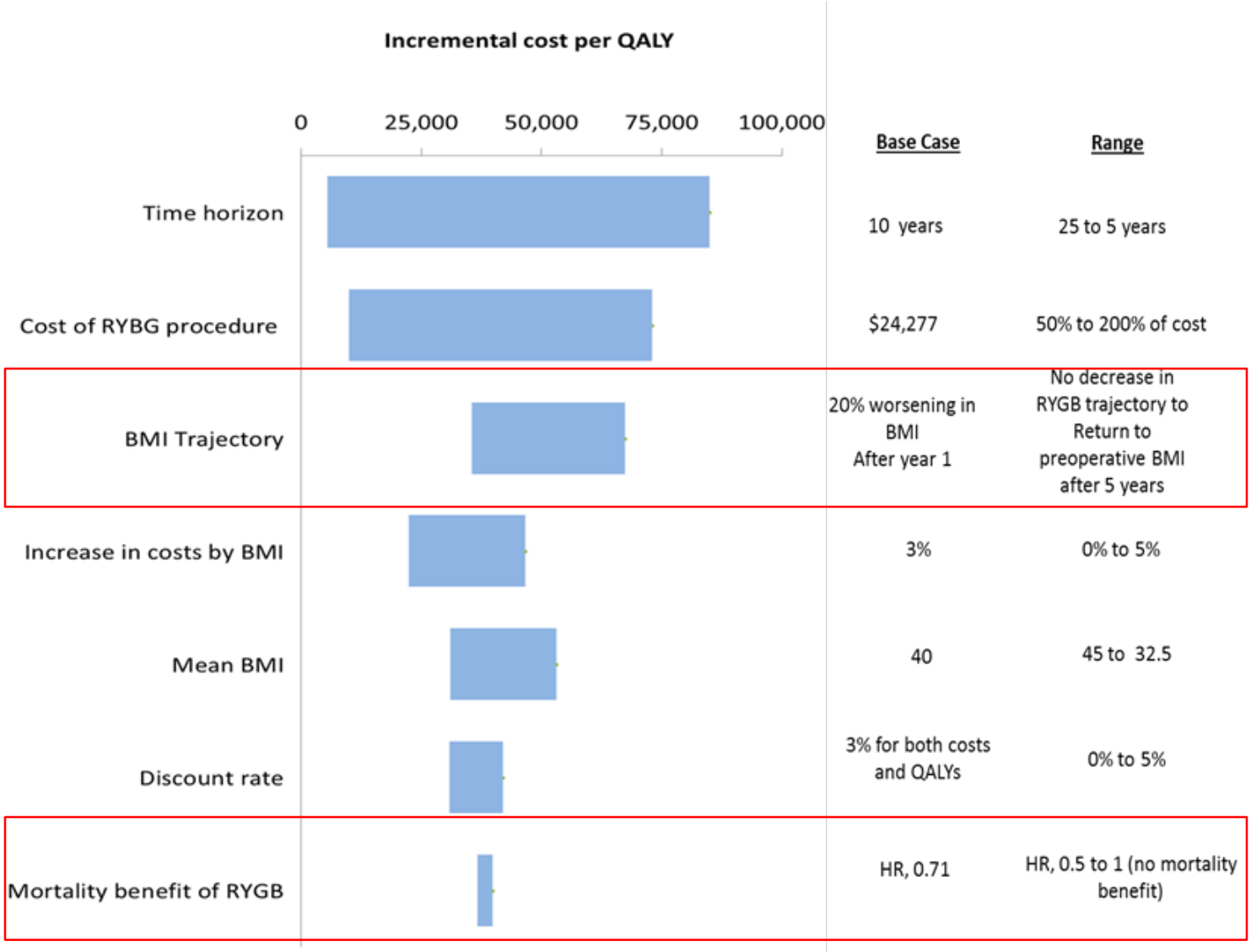
* Includes age-related background health care costs for obesity derived from Østbye 2014

** 5.6% of vBloc patients assumed to have the device removed

Incremental Cost/QALY: 10-Year Findings, BMI ≥30

BMI Level/Procedure	Cost ($)	Effectiveness (QALYs)	Cost-effectiveness ($/QALY gained)	
			vs. standard care	vs. RYGB
BMI≥30				
Standard care	$34,923	7.5680	N/A	Less expensive & less effective
N/B	$47,732	7.6656	$131,250	Less expensive & less effective
vBloc	$51,471	7.7191	$109,543	Less expensive & less effective
RYGB	$54,110	8.0807	$37,423	N/A
VSG	$48,702	8.0417	$29,087	Less expensive & less effective
LAGB	$47,668	7.9252	$35,680	Less expensive & less effective
BPD±DS	$65,741	8.2307	$46,508	$77,574

Sensitivity Analyses: RYGB vs. Conventional Weight-Loss Management



Treatment Sequencing

- Incremental cost-effectiveness of N/B continuation for patients achieving 5% or 10% weight loss, switch to RYGB for all others:
  - $41,000 - $44,000 per QALY gained vs. conventional weight-loss management (vs. >$130,000 for N/B alone)
- Incremental cost-effectiveness of vBloc continuation for patients achieving 10% weight loss, switch to RYGB for all others:
  - $104,000 per QALY gained (vs. $109,000 for vBloc alone)

Health-System Value: Methods

- Prevalence of BMI 30-34.9 in Medicaid: ~28%
  - 11% of these patients have diagnosed or undiagnosed diabetes
- Applied proportions to estimated number of adults enrolled in Medi-Cal: ~6.6 million
- One-year budgetary impact of adopting surgery based on difference in one-year costs between VSG (least expensive common surgical procedure) and conventional weight-loss management: ~$21,000
- Applied to varying assumed percentages of surgical adoption, also included 10-year offsets

Health-System Value: Results

Measure	All Enrollees (11.7 million)	Adults with BMI 30-34.9 (25% Receive Surgery)	Adults with BMI 30-34.9 and diabetes (25% receive surgery)
One-Year Costs*			
Total Expenditures	$77,500,800,000	$9,325,884,204	$1,025,847,262
PMPM	$552	$66.42	$7.31
% Increase	---	12.03%	1.32%
One-Year Costs with Offset **			
Total Expenditures	$77,500,800,000	$7,420,688,730	$816,275,760
PMPM	$552	$52.85	$5.81
% Increase	---	9.57%	1.05%

*Assumed one-year difference in cost between VSG and standard care of $20,554
**Adjusted one-year difference for downstream cost offsets of $16,355

Insurance PMPM increase if 10% of candidate population receives surgery:

- 4.8% for all patients with BMI 30-34.9
- 0.5% for patients with diabetes and BMI 30-34.9

Public Comments Received: Model

- “Dollars per pound lost” measures have no place in critical analyses
- Consider FDA-approved labeling for model assumptions (e.g., discontinue medication if 5% weight loss not achieved)
- Incorporate adherence assumptions into model
- Many fewer patients opt for obesity treatment than assumed in health-system value analysis
- Include costs of lifetime follow-up care post-surgery

Summary

- Findings from incremental cost per outcomes analysis similar to other published models for bariatric surgery
  - Surgery falls within generally-accepted cost-effectiveness thresholds vs. conventional weight-loss management
  - Most favorable results seen in highest BMI class
- Incremental costs per outcomes of medication-based treatment most favorable when assessed in sequence with surgery
- Potential budgetary impact of expanding bariatric surgery to all patients with BMI 30-34.9 is substantial but less pronounced when limited to patients in this class with diabetes

CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Controversies in Obesity Management

Questions for Deliberation

July 14, 2015

Comparative *Clinical Effectiveness* Example Question

Is the evidence "**adequate**" to demonstrate that "**intervention A**" is superior to "**comparator B**" for patients with "**condition X**"?

Yes

No

Care Value Example Question

From the perspective of a Medicaid program, what is the care value of "**intervention A**" vs "**comparator B**"?

A. **Low**

B. **Intermediate**

C. **High**

Health System Value Example Question

Assuming baseline pricing and payment mechanisms, what would be the **health system value** of "**intervention A**" for a state Medicaid program?

A. **Low**

B. **Intermediate**

C. **High**

Practice Question

What is your favorite professional basketball team?

A. **Cleveland Cavaliers**

B. **Cleveland Cavaliers**

C. **Cleveland Cavaliers**

D. **Golden State Warriors**

Bariatric Surgery: BMI 30.0-34.9, T2DM

Q1. For adult patients with a BMI of 30.0-34.9 and Type 2 diabetes, is the evidence adequate to demonstrate that the net health benefit of *bariatric surgery* is greater than that of *conventional weight-loss management*?

Yes

No

Bariatric Surgery: BMI 30.0-34.9

Q2. For adult patients with a BMI of 30.0-34.9 who do not have Type 2 diabetes, is the evidence adequate to demonstrate that the net health benefit of *bariatric surgery* is greater than that of *conventional weight-loss management*?

Yes

No

RYBG and VSG: BMI ≥35

Q3. For adult patients with a BMI ≥35, is the evidence adequate to demonstrate that *RYGB* and *VSG* have a comparable net health benefit?

Yes

No

Maestro vBloc: BMI ≥35

Q4. For adult patients with a BMI ≥35, is the evidence adequate to demonstrate that the net health benefit of *the Maestro vBloc system* is greater than *that of conventional weight-loss management*?

Yes

No

Drugs: BMI ≥30 or BMI ≥27 w/ comorbidity

Q5. For adult patients with a BMI ≥30 or BMI ≥27 with an obesity-related comorbidity, is the evidence adequate to distinguish the net health benefit among the four drugs reviewed?

Yes

No

Care Value:
Bariatric Surgery, BMI 30.0-34.9, T2DM

Q6. [If yes to question 1– adult patients with a BMI 30.0-34.9, and Type 2 diabetes] Given the available evidence, what is the care value of bariatric surgery vs. conventional weight-loss management?

A. **Low**

B. **Intermediate**

C. **High**

Health System Value: Bariatric Surgery, BMI 30.0-34.9, T2DM

Q7. [If yes to question 1] Given the available evidence, what is the overall health system value of bariatric surgery for a state Medicaid program?

A. **Low**

B. **Intermediate**

C. **High**

Care Value: Bariatric Surgery, BMI 30.0-34.9

Q8. **[If yes to question 2 – adult patients with a BMI 30.0-34.9, who do not have Type 2 diabetes] Given the available evidence, what is the care value of bariatric surgery vs. conventional weight-loss management?**

A. **Low**

B. **Intermediate**

C. **High**

Health System Value: Bariatric Surgery, BMI 30.0-34.9

Q9. [If yes to question 2] Given the available evidence, what is the overall health system value of bariatric surgery for a state Medicaid program?

A. **Low**

B. **Intermediate**

C. **High**

Care Value:
Maestro vBloc, BMI ≥35

Q10. [If yes to question 4 – adult patients with a BMI ≥35] Given the available evidence, what is the care value of the Maestro vBloc system vs. conventional weight-loss management?

A. **Low**

B. **Intermediate**

C. **High**

Health System Value: Maestro vBloc, BMI ≥35

Q11. [If yes to question 4] Given the available evidence, what is the overall health system value of the Maestro vBloc system for a state Medicaid program?

A. **Low**

B. **Intermediate**

C. **High**

Policy Roundtable Participants

- **Joel Brill, MD, FACP,** Medical Director, FAIR Health Inc., Chief Medical Officer, Predictive Health, LLC
- **Alexander Li, MD,** Deputy Director, Care Transitions, Los Angeles Department of Health Services
- **John Morton, MD, MPH, FACS, FASMBS,** Chief of Bariatric and Minimally Invasive Surgery, Stanford University School of Medicine; President, American Society for Metabolic and Bariatric Surgery
- **Sameer Murali, MD, MSHS,** Bariatric/Internal Medicine, Southern California Permanente Medical Group
- **Philippe Jean Quilici, MD, FACS,** Attending Physician, Department of Surgery, Providence St. Joseph Medical Center and Cedars-Sinai Medical Center
- **Michelle Vicari,** Patient Advocate
- **John Yao, MD, MBA, MPH, MPA, FACP,** Staff Vice President of Medical Policy, Anthem