AMCP Florida Day of Education

April 22, 2023

NSU Florida College of Pharmacy NOVA SOUTHEASTERN UNIVERSITY

AMCP Florida

AMCP Florida

Mission

The Florida AMCP Affiliate seeks to serve the AMCP membership in the state of Florida in three primary areas; networking, education, and advocacy.

www.amcp.org/Florida-AMCP

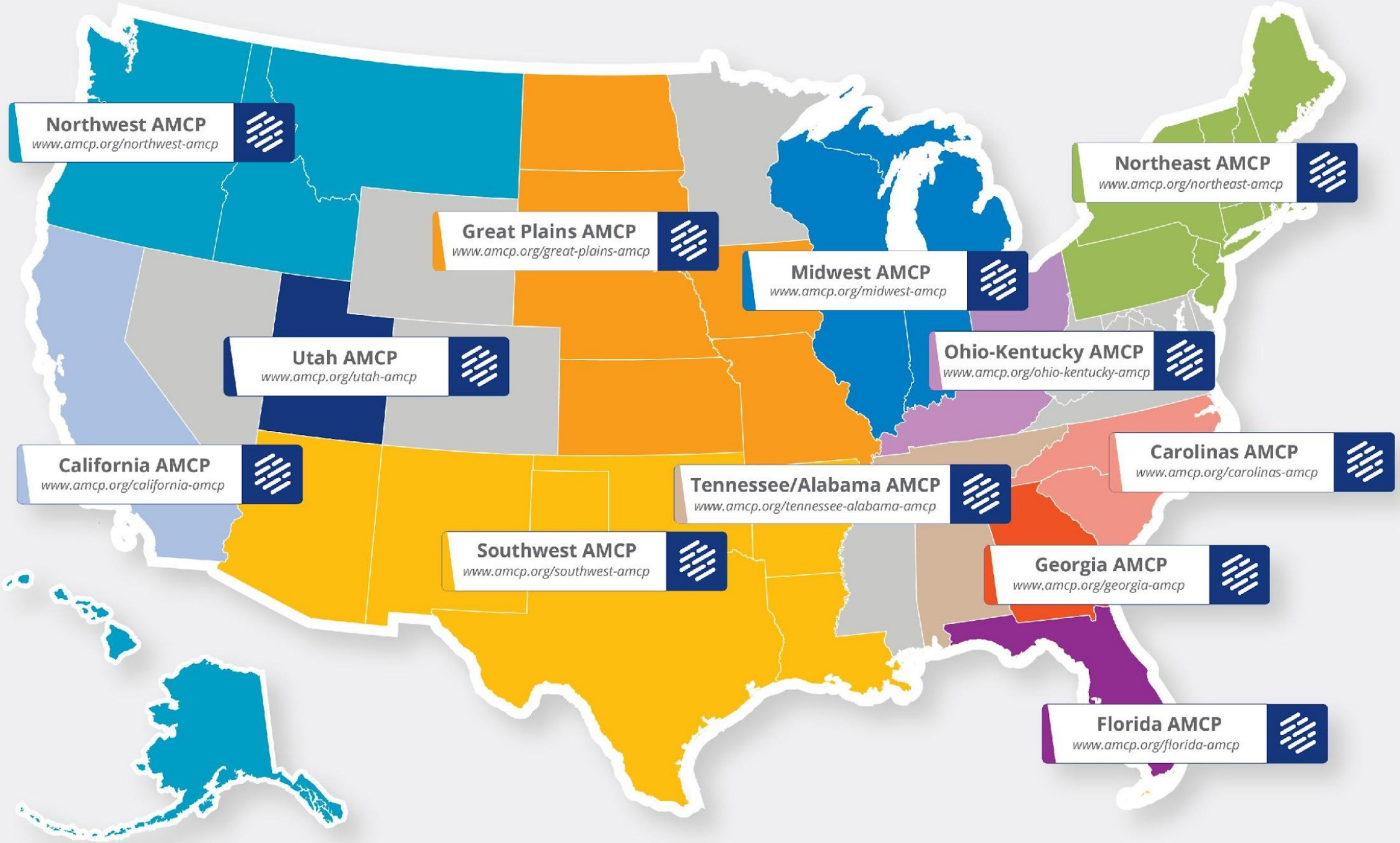
AMCP

Optimizing medicine.
Improving lives.

Mission

To improve patient health by ensuring access to high-quality, cost-effective medications and other therapies.

AMCP AFFILIATES



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Day of Education

Saturday, April 22, 2023

NSU Florida College of Pharmacy NOVA SOUTHEASTERN UNIVERSITY

Agenda

8:00AM-8:30AM **CHECK-IN / REGISTRATION, EXHIBITS/NETWORKING & BREAKFAST**

8:30AM-8:45AM **WELCOME / REVIEW AGENDA / GAME**

8:45AM-9:45AM **Obesity (*CE*)**
Cynthia Moreau, PharmD, CPH, BCACP, CDCES, ChenMed, Clinical Pharmacist

9:45AM-10:45AM **Value Framework Assessment Overview (*CE*)**
Cynthia Miller, MD, MPH, FACP, Precision Value, VP Medical Director-Access Experience

10:45AM-11:15AM. **BREAK / EXHIBITS / NETWORKING/SNACK**

11:15AM-12:30PM **Federal Legislative Update: Inflation Reduction Act & Panel Discussion (*CE*)**
Moderated by: Jennifer Mathieu, MA, AMCP, Vice President, Policy and Government Relations

Panel Participants:
- Cynthia Griffin, PharmD, Florida Blue, Vice President, Medicare Pharmacy Programs
- Shawn Barger, PharmD, Aetna, Director of Medicare Formulary Strategy, Compliance & Operations
- Ashley Peterson, MHA, Artia, Medicaid Pharmacy Director, Contracting & Analytics (Former Administrator, Bureau of Medicaid, Pharmacy Policy)
- Javier Gonzalez, PharmD, Abarca Health, Chief Growth & Commercial Officer
- Jonathan Hickman, PharmD, Genentech, Medical Executive Director

12:30PM-1:30PM **LUNCH / EXHIBITS / NETWORKING**

1:30PM-2:30PM **The Evolving Biosimilars Landscape Panel Discussion (*CE*)**
Moderated by: Wendy Bailey, Rh, BSPharm, MSPharm, MBA, Centene, Vice President of Health Plan Pharmacy Strategy

Panel Participants:
- David Fox, PharmD, Florida Healthcare Plan, Clinical Pharmacy Director
- Jorge Garcia, PharmD, MS, MHA, MBA, FACHE, Baptist Health South Florida, Assistant Vice President-System Oncology Pharmacy Service Line
- Jennifer Miles, PharmD, BCACP, BCMTMS, Jackson Health Ambulatory Care, Assistant Director of Ambulatory Clinical Pharmacy Services
- Richard Gourash, R.Ph., MBA, BioPlus, VP Oncology

2:30PM-3:30PM **Health Disparities in Healthcare (*CE*)**
Shanada Monestime, PharmD, BCOP, GO2 for Lung Cancer, Director, Community Engaged Research

3:30PM-4:30PM **Oncology Accelerated Drug Approvals that Lack Confirmatory Trials (*CE*)**
Presented by: Laura Bobolts, PharmD, BCOP, Onco Health, Senior Vice President, Clinical Strategy & Growth

4:30PM-5:00PM **EXHIBITS / NETWORKING**

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Kahoot Game

https://create.kahoot.it/share/amcp-day-of-education-2023-kahoot-1/797fce56-e783-4f7e-8ce6-273294e62283

Management of Obesity

Cynthia Moreau, PharmD, CPh, BCACP, CDCES
Clinical Pharmacist
ChenMed
cynthia.moreau@chenmed.com

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Objectives

- Review and compare available pharmacological options for management of obesity
- Understand which patients are candidates for pharmacotherapy for weight loss
- Develop an individualized treatment plan for weight loss given based on patient characteristics
- Describe considerations in managed care for management of obesity

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Adult Obesity Prevalence

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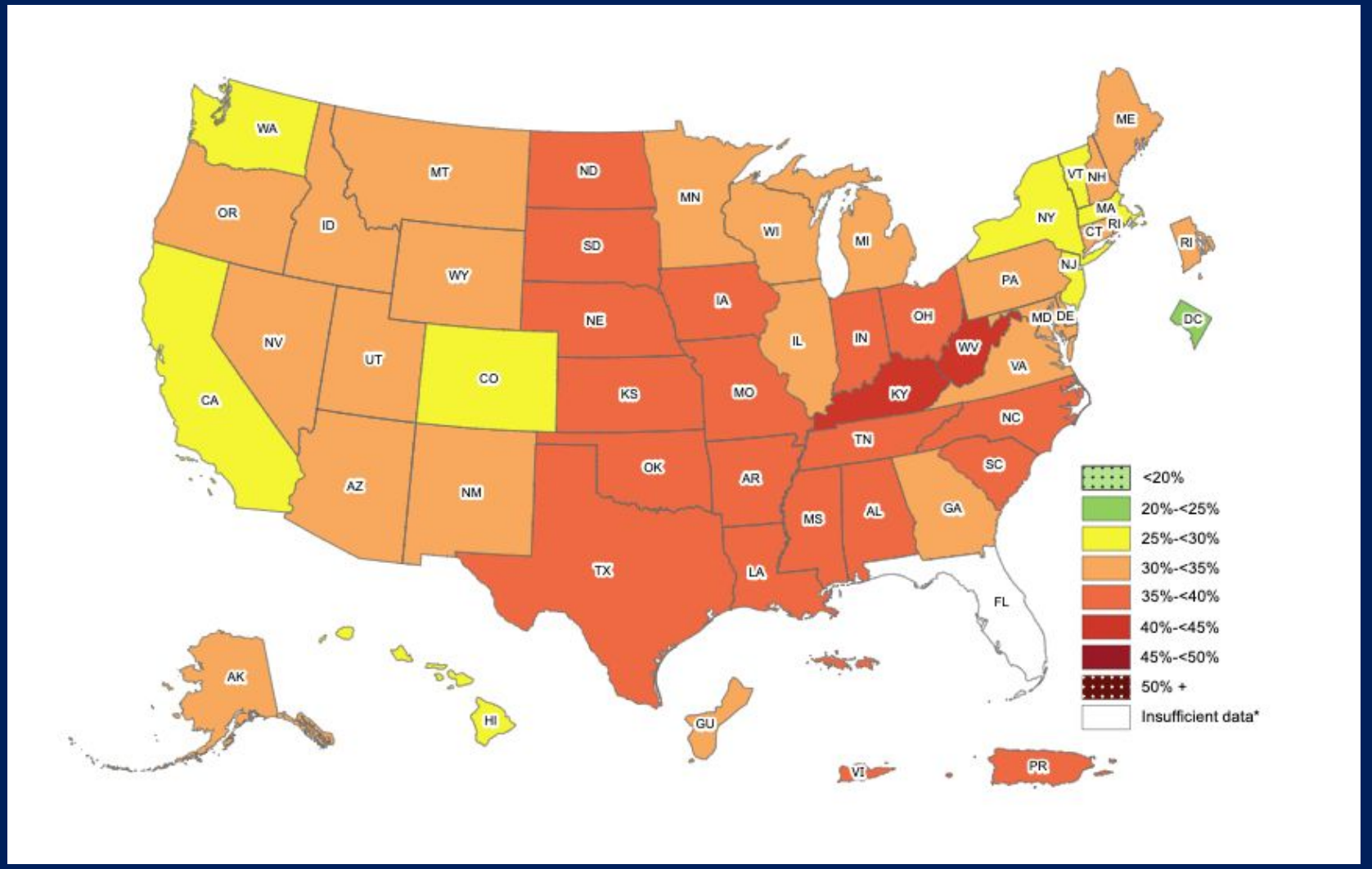

https://www.cdc.gov/obesity/data/prevalence-maps.html#overall

Etiology

- Genetic
- Behavioral
- Environmental
- Cultural
- Medications

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Defining Obesity

- Body Mass Index (BMI)
  - Measure of body weight (kilograms) adjusted for height (meters^2)
  - Most useful population-level measurement of overweight and obesity

$$\text{BMI} = \frac{(\text{weight in kilograms})}{\text{height in meters}^2}$$

Classification	BMI
Underweight	< 18.5 kg/m^2
Normal weight	≥ 18.5 to 24.9 kg/m^2
Overweight	≥ 25.0 to 29.9 kg/m^2
Obesity	≥ 30 kg/m^2
Class I Obesity	30.0 – 34.9 kg/m^2
Class II Obesity	35.0 – 39.9 kg/m^2
Class III Obesity	≥ 40.0 kg/m^2 (extreme obesity)

Waist Circumference

- BMI limitations
  - Does not distinguish body fat distribution determinant of metabolic risk

- Waist circumference (WC)
  - Measure of excess abdominal fat
  - Most useful in BMI < 35 kg/m^2
  - High-risk WC:

    Men: > 40 inches

    Women: > 35 inches

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Obesity and Disease

Type 2 Diabetes Mellitus	Cancer	Heart Disease	Obstructive Sleep Apnea	Hepatobiliary	Osteoarthritis
• Central adiposity	• Males – colon, rectum, prostate • Females – breast, endometrial, gallbladder	• Hypertension • Atrial fibrillation • Heart failure • Dyslipidemia • Coronary artery disease	• Males > females • May be life-threatening • Reduced nocturnal oxygen saturation • Excess daytime sleepiness	• Gallbladder disease • Fatty liver disease	• Knees, ankles

Bray GA. *Endocr Rev*. 2018;39(2):79-132.

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Management of Patients with Obesity

Lifestyle interventions

Pharmacotherapy

Surgical approaches/Medical Devices

Comprehensive Lifestyle Intervention

- Initial goal: loss of 5-10% from baseline weight within 6 months
  - Clinically significant improvements in BP, lipids, glycemic control
- Calorie-reduced diet
  - Energy deficit ~500 kcal/day

    Women: 1200-1500 kcal/day

    Men: 1500-1800 kcal/day

Comprehensive Lifestyle Intervention

- No diet type superior in producing sustainable weight loss
  - Best predictor of success = adherence (patient preference)
- Physical activity:
  - Aerobic physical activity ≥ 150 minutes per week
  - 200-300 minutes per week to maintain long-term weight loss

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Management of Patients with Obesity

Lifestyle interventions

Pharmacotherapy

Surgical approaches/Medical Devices

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Approved Medications for Weight LOSS

Long-Term Use

Orlistat (Xenical®, Alli®)

Phentermine/Topiramate ER (Qsymia®)

Naltrexone SR/Bupropion ER (Contrave®)

Liraglutide (Saxenda®)

Semaglutide (Wegovy®)

Short-Term Use

≤ 12 weeks

Phentermine (Adipex-P®, Lomaira®)

Diethylpropion (Tenuate®)

Benzphetamine (Regimex®)

Phendimetrazine (Bontril®)

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History of Weight Loss Medications

Gadde KM. *Clinical Chem*. 2018;64(1):118-129.

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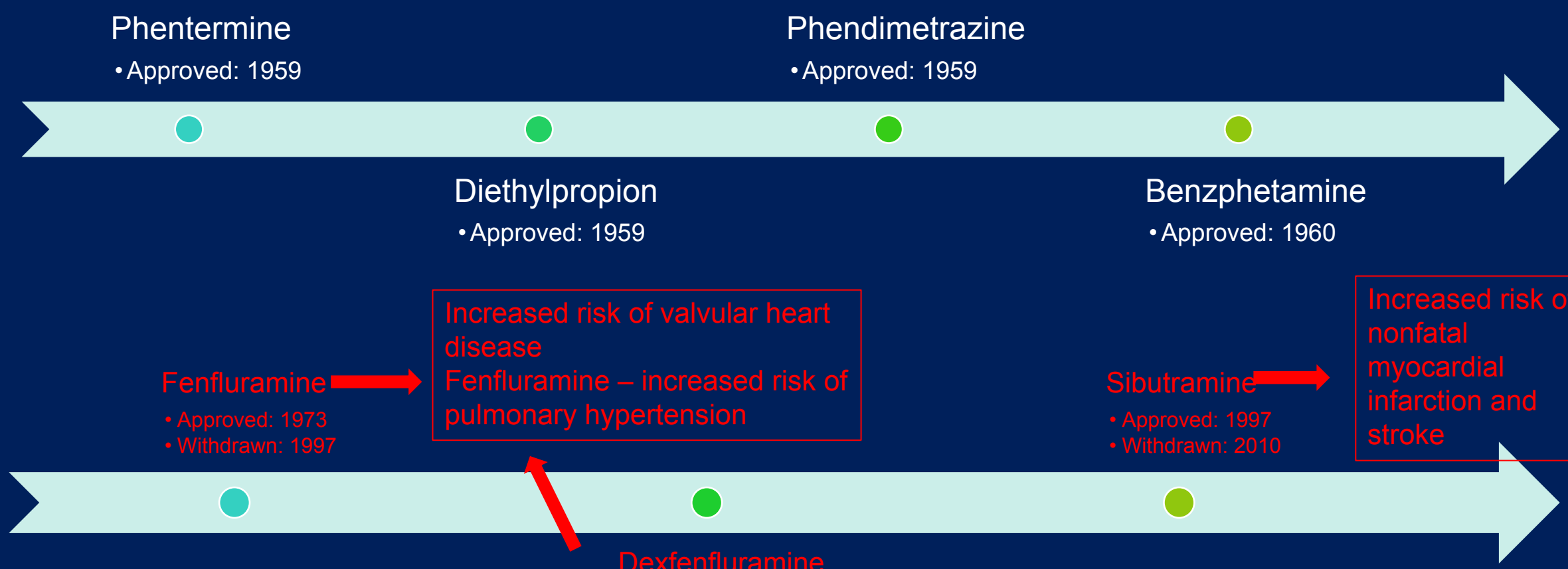
History of Weight Loss Medications



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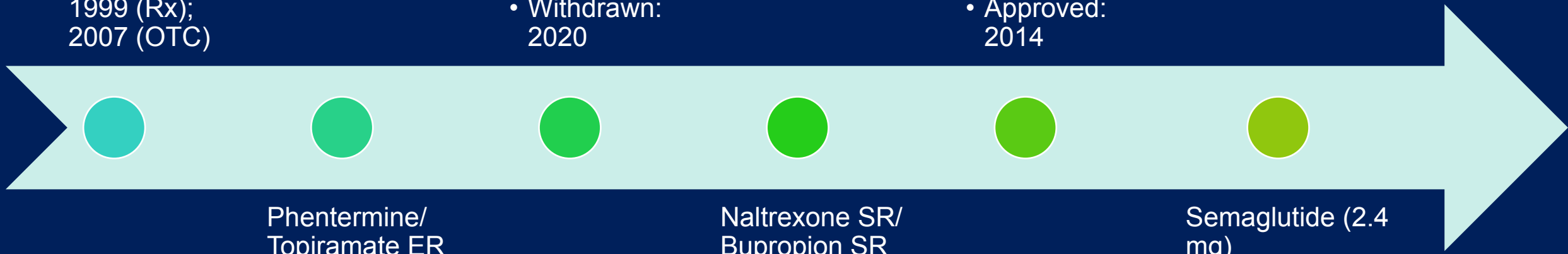

Orlistat
- Approved: 1999 (Rx); 2007 (OTC)

Phentermine/ Topiramate ER
- Approved: 2012

Lorcaserin
- Approved: 2012
- Withdrawn: 2020

Naltrexone SR/ Bupropion SR
- Approved: 2014

Liraglutide (3 mg)
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Semaglutide (2.4 mg)
- Approved: 2021

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History of Weight Loss Medications

Potential cancer risk > benefits

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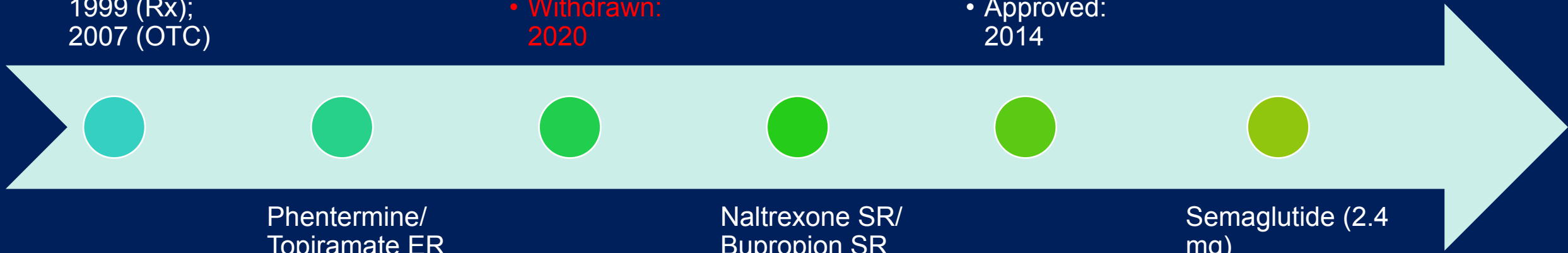

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Question

- Which of the following patients is an appropriate candidate for pharmacotherapy for weight loss according to clinical guidelines?

A. A 45-year-old female with a BMI of 25 and type 2 diabetes

B. A 29-year-old female with a BMI of 27 and glaucoma

C. A 30-year-old male with a BMI of 32 and no other health conditions

D. A 36-year-old male with a BMI of 28 and hypertension

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Candidates for Pharmacotherapy for Weight Loss

BMI $\geq$ 30 kg/m^2

BMI $\geq$ 27 kg/m^2 + $\geq$ 1 comorbidity

Jensen MD. *J Am Coll Cardiol*. 2014;63(25):2985-3023.

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Candidates for Pharmacotherapy for Weight Loss

BMI $\geq$ 27 kg/m^2 +
$\geq$ 1 comorbidity

- Obesity-related comorbidities:
  - Dyslipidemia
  - Hypertension
  - Type 2 diabetes
  - Obstructive sleep apnea
  - Metabolic syndrome
  - Knee osteoarthritis
  - Asthma or COPD
  - Nonalcoholic fatty live disease
  - Polycystic ovarian syndrome
  - Coronary artery disease

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History of Weight Loss Medications

Gadde KM. *Clinical Chem*. 2018;64(1):118-129.

Orlistat (Xenical®, Alli®)

Mechanism of action

- Inhibits gastric and pancreatic lipase inhibits intestinal fat absorption

Dosing

- Xenical (Rx): 120 mg three times daily before meals
- Alli (OTC): 60 mg three times daily before meals
- Take during or up to 1 hour after fat-containing meal

DEA Schedule

- Not scheduled

Orlistat (Xenical®, Alli®)

Contraindications/Warnings

- Pregnancy
- Cholestasis

Adverse Effects

- Gastrointestinal - abdominal pain, bowel urgency, steatorrhea, fecal incontinence (limit fat intake to < 30% of daily calories)
- Liver failure (rate)
- Gallbladder disease
- Increased urine oxalate (monitor renal function) (caution in hx of kidney stones)
- Decreased absorption of fat-soluble vitamins supplement with multivitamin

Drug Interactions

- Warfarin, amiodarone, cyclosporine, levothyroxine

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Phentermine/Topiramate ER (Qsymia®)

Mechanism of action

- Phentermine: reduces appetite through increase in norepinephrine levels in hypothalamus
- Topiramate: may reduce appetite through effect on GABA receptors

Dosing

- 3.75/23 mg once daily x 14 days **7.5/46 mg once daily**
- If weight loss < 3% after 12 weeks 11.25/69 mg once daily x 14 days **15/92 mg once daily**

DEA Schedule

- IV

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Phentermine/Topiramate ER (Qsymia®)

Contraindications/Warnings

- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAO inhibitor within 14 days

Adverse Effects

- Paresthesia
- Dizziness
- Insomnia
- Altered taste
- Constipation
- Dry mouth
- Increased heart rate

Drug Interactions

- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)

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Phentermine/Topiramate ER (Qsymia®)

Contraindications/Warnings

- Pregnancy
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- Constipation
- Dry mouth
- Increased heart rate

Topiramate – increased risk of oral clefts

- Available under Risk Evaluation and Mitigation Strategy (REMS) program – requires negative pregnancy test before treatment and monthly during

Drug Interactions

- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)

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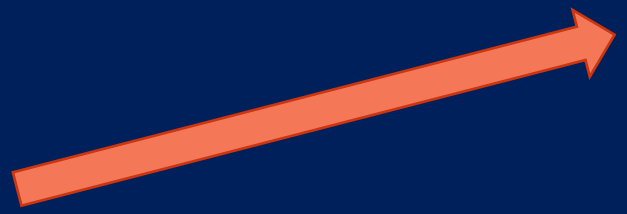

Monitor heart rate; use with caution in cardiovascular disease

Drug Interactions

- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)

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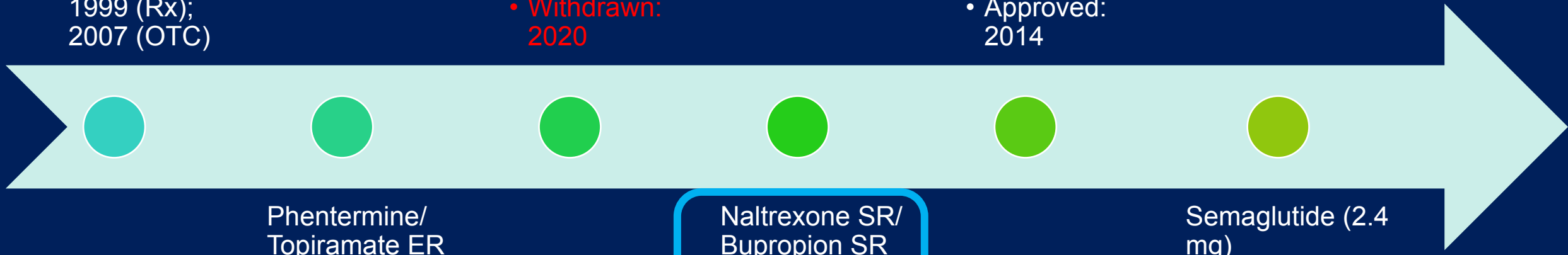
History of Weight Loss Medications



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Naltrexone SR/Bupropion SR (Contrave®)

Mechanism of action

- Bupropion: dopamine and norepinephrine reuptake inhibitor in hypothalamus
- Naltrexone: mu opioid receptor antagonist
- Effect on hypothalamus (appetite) and mesolimbic dopamine circuit (reward system) reduced food intake

Dosing

- 8/90 mg 1 tablet once daily x 1 week 8/90 mg 1 tablet twice daily x 1 week 8/90 mg 2 tablets AM + 1 tablet PM x 1 week **8/90 mg 2 tablets twice daily**

DEA Schedule

- Not scheduled

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Naltrexone SR/Bupropion SR (Contrave®)

Contraindications/Warnings

- Pregnancy
- Uncontrolled hypertension
- Seizure disorder
- Eating disorder (anorexia/bulimia)
- Chronic opioid use/acute opioid withdrawal
- MAO inhibitor within 14 days

Adverse effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Headache
- Dizziness
- Insomnia
- Dry mouth
- May increase HR

Drug Interactions

- Opioids, bupropion-containing products, CYP2B6/CYP2D6 inhibitors

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Naltrexone SR/Bupropion SR (Contrave®)

Contraindications/Warnings

- Pregnancy
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- Chronic opioid use/acute opioid withdrawal
- MAO inhibitor within 14 days

Adverse effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Headache
- Dizziness
- Insomnia
- Dry mouth
- May increase HR

Caution in cardiovascular disease/do not use in uncontrolled hypertension

Drug Interactions

- Opioids, bupropion-containing products, CYP2B6/CYP2D6 inhibitors

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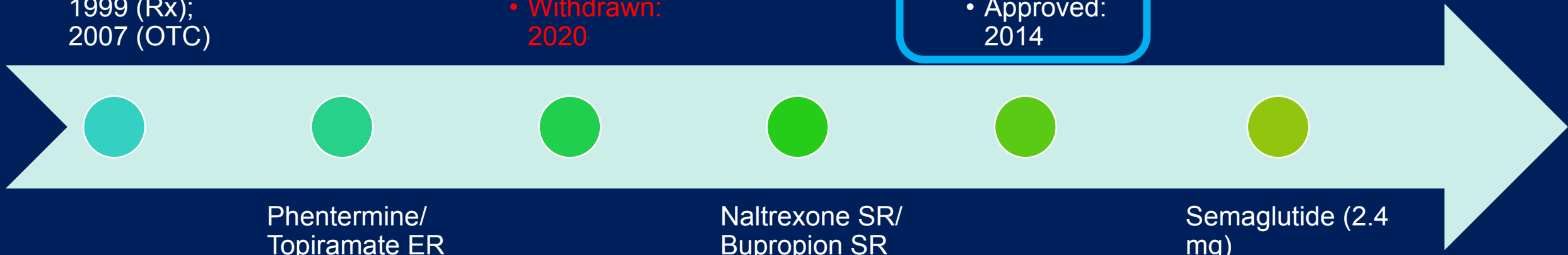
History of Weight Loss Medications



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- Approved: 2021

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Liraglutide = Victoza® (diabetes management)

Liraglutide (Saxenda®)

Mechanism of action

- Glucagon-like peptide-1 (GLP-1) receptor agonist – stimulates glucose-dependent insulin release, slows gastric emptying, reduces food

Dosing

- 0.6 mg SC daily x 1 week 1.2 mg SC daily x 1 week 1.8 mg SC daily x 1 week 2.4 mg SC daily x 1 week **3 mg SC daily**

DEA Schedule

- Not scheduled

Liraglutide = Victoza® (diabetes management)

Liraglutide (Saxenda®)

Contraindications/Warnings

- Pregnancy
- Personal/family history medullary thyroid cancer [Boxed warning]
- Moderate/severe renal impairment
- History of pancreatitis

Adverse Effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Acute pancreatitis
- Gallbladder disease
- Hypoglycemia

Drug Interactions

- Other hypoglycemic agents

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Semaglutide = Ozempic®
Rybelsus® (diabetes management)

Semaglutide (Wegovy®)

Mechanism of action

- Glucagon-like peptide-1 (GLP-1) receptor agonist – stimulates glucose-dependent insulin release, slows gastric emptying, reduces food

Dosing

- 0.25 mg SC once weekly x 4 weeks 0.5 mg SC once weekly x 4 weeks 1 mg SC once weekly x 4 weeks 1.7 mg SC once weekly x 4 weeks **2.4 mg SC once weekly**

DEA Schedule

- Not scheduled

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Semaglutide = Ozempic®
Rybelsus® (diabetes management)

Semaglutide (Wegovy®)

Contraindications/Warnings

- Pregnancy
- Personal/family history medullary thyroid cancer [Boxed warning]
- Moderate/severe renal impairment
- History of pancreatitis

Adverse Effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Acute pancreatitis
- Gallbladder disease
- Hypoglycemia

Drug Interactions

- Other hypoglycemic agents

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History of Weight Loss Medications

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Phentermine (Adipex-P®, Lomaira®)

Mechanism of action

- Amphetamine analog: Stimulates release of norepinephrine in hypothalamus reduced appetite

Dosing

- 15, 30, or 37.5 mg daily (1-2 doses daily)
  - Adipex-P = 37.5 mg; Generic = 15, 30, 37.5 mg
- Lomaira: 8 mg three times daily before meals

DEA Schedule

- IV

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Phentermine (Adipex-P®, Lomaira®)

Contraindications/Warnings

- Pregnancy
- Hyperthyroidism
- Glaucoma
- MAO inhibitor within 14 days

Adverse Effects

- Nervousness
- Dry mouth
- Insomnia
- Increased heart rate/blood pressure

Drug Interactions

- MAO inhibitors

Phentermine (Adipex-P®, Lomaira®)

Contraindications/Warnings

- Pregnancy
- Hyperthyroidism
- Glaucoma
- MAO inhibitor within 14 days

Adverse Effects

- Nervousness
- Dry mouth
- Insomnia
- Increased heart rate/blood pressure

Caution in cardiovascular disease/do not use in uncontrolled hypertension

Drug Interactions

- MAO inhibitors

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Choosing a Medication

- No head-to-head comparison studies of approved medications
- Meta-analysis of 28 RCTs (n=29,018)

Medication	Mean weight loss versus placebo	≥ 5% weight loss (OR)	≥ 10% weight loss (OR)	Discontinuation due to adverse event (OR)
Phentermine/topiramate	-8.80 kg	9.22	11.40	2.29
Liraglutide	-5.24 kg	5.54	4.99	2.95
Naltrexone/bupropion	-4.95 kg	3.96	4.19	2.64
Orlistat	-2.63 kg	2.70	2.42	1.84

Meta-analysis completed in 2016; Semaglutide not yet approved for weight loss

VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity.

Choosing a Medication

Medication	Glycemic measures	Blood pressure	Lipids
Phentermine/topiramate	+++	++	++
Liraglutide	++++	++	++
Naltrexone/bupropion	++	Unfavorable	+
Orlistat	+++	++	++

Gadde KM et al. *Clinical Chemistry*. 2018;64(1):118-129.

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Choosing a Medication

- Semaglutide (Wegovy®) – STEP 1 Study
  - n=1,961 adults (BMI ≥ 30 or ≥ 27 + comorbidity) WITHOUT diabetes
  - 68 weeks of treatment with once-weekly SC semaglutide 2.4 mg or placebo

Endpoint	Semaglutide	Placebo
Percentage mean change in body weight from baseline	-14.9%	-2.4%
	Treatment difference: -12.4% (95% CI -13.4 to -11.5, p<0.001)	
Change in body weight	-15.3 kg	-2.6 kg
≥ 5% weight loss	86.4%	31.5%
≥ 10% weight loss	69.1%	12%

- Semaglutide – improvement in cardiometabolic risk factors
- Most common adverse events – nausea, diarrhea (more patients discontinued semaglutide vs. placebo)

Wilding JPH, et al. *N Engl J Med*. 2021;384:989-1002.

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Choosing a Medication

- Clinical guidelines:
  - Agents approved for long-term use preferred
  - No agent preferred over another
- Individualized approach
  - Side effects
  - Cautions/contraindications
  - Drug interactions
  - Weight-related complications and medical history

Wilding JPH, et al. *N Engl J Med*. 2021;384:989-1002.

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Choosing a Medication

	Orlistat	Phentermine/ Topiramate	Naltrexone/ Bupropion	Liraglutide	Semaglutide	Phentermine
Type 2 Diabetes				★	★	
Hypertension			Contraindicated in uncontrolled HTN			
Cardiovascular disease (CAD)				★	★	
Arrhythmia		May increase HR	May increase HR			May increase HR
Seizure disorder			Lowers seizure threshold			
Opioid use		Caution in hx of drug abuse	Opioid antagonist			Caution in hx of drug abuse
Hyperthyroidism/ Glaucoma		Contraindicated	May trigger angle closure glaucoma			Contraindicated
Thyroid cancer				Contraindicated	Contraindicated	
Pregnancy		REMS program				

Key: Green = safe to use; Yellow = use with caution; Red = contraindicated

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Choosing a Medication

- Renal and hepatic impairment
  - May require dosage adjustments
  - Limited data in severe impairment
- Gallbladder disease
  - Orlistat, liraglutide, and semaglutide
- Pancreatitis
  - Avoid liraglutide and semaglutide

Wilding JPH, et al. *N Engl J Med*. 2021;384:989-1002.

Monitoring of Therapy

- Medication-specific parameters
- Weight loss

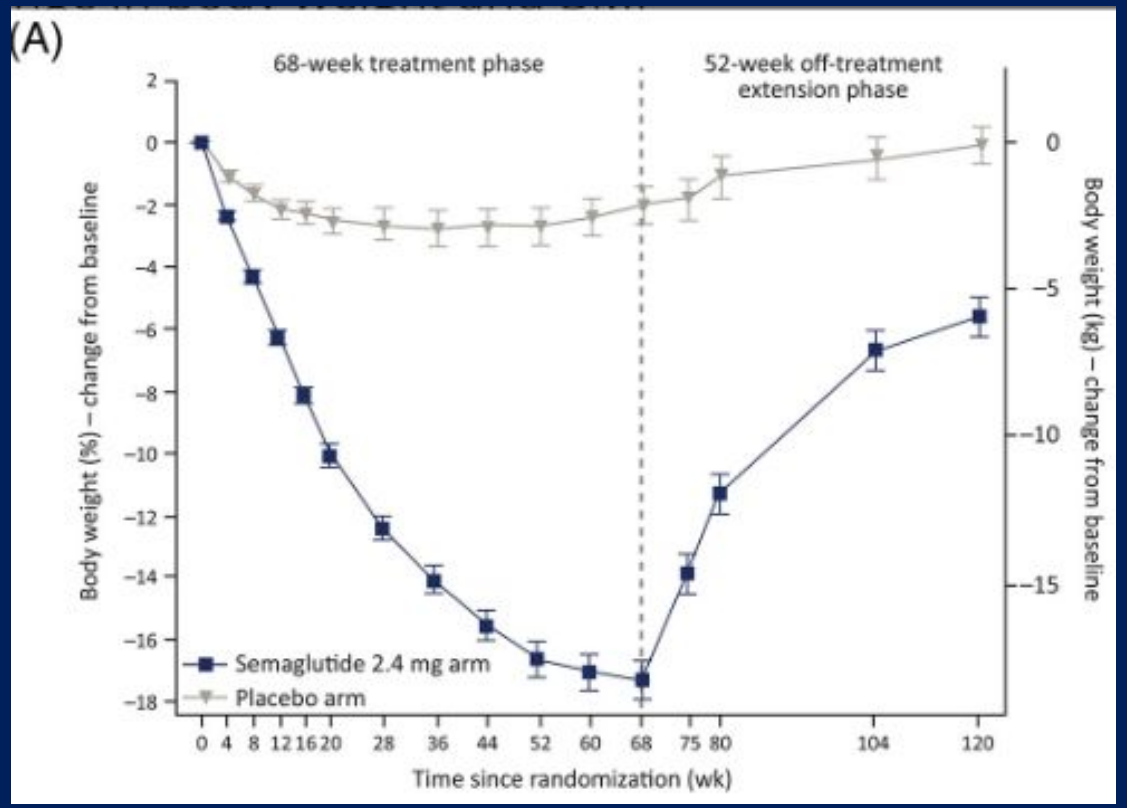
  Assess patients monthly x 3 months, then at least every 3 months

Orlistat, Qsymia, Contrave, Wegovy	Saxenda
• Discontinue if < 5% weight loss at 12 weeks	• Discontinue if < 4% weight loss at 16 weeks

Remember: Phentermine (Adipex-P®, Lomaira®) not recommended for use beyond 12 weeks.

Weight Regain

- STEP 1 Trial Extension
  - STEP 1 Study
    - n=1,961 adults (BMI ≥ 30 or ≥ 27 + comorbidity) WITHOUT diabetes
    - 68 weeks of treatment with once-weekly SC semaglutide 2.4 mg or placebo
  - Extension: 327 patients followed for additional 52 weeks off-treatment
    228 – semaglutide; 99 - placebo



Wilding JPH, et al. *Diabetes Obes Metab*. 2022;24:1553-1564

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New Drug Poised to Take Weight-Loss Throne

Eli Lilly's Mounjaro is outperforming Ozempic in clinical trials

By Steve Huff, Newser Staff
Posted Apr 9, 2023 2:25 PM CDT

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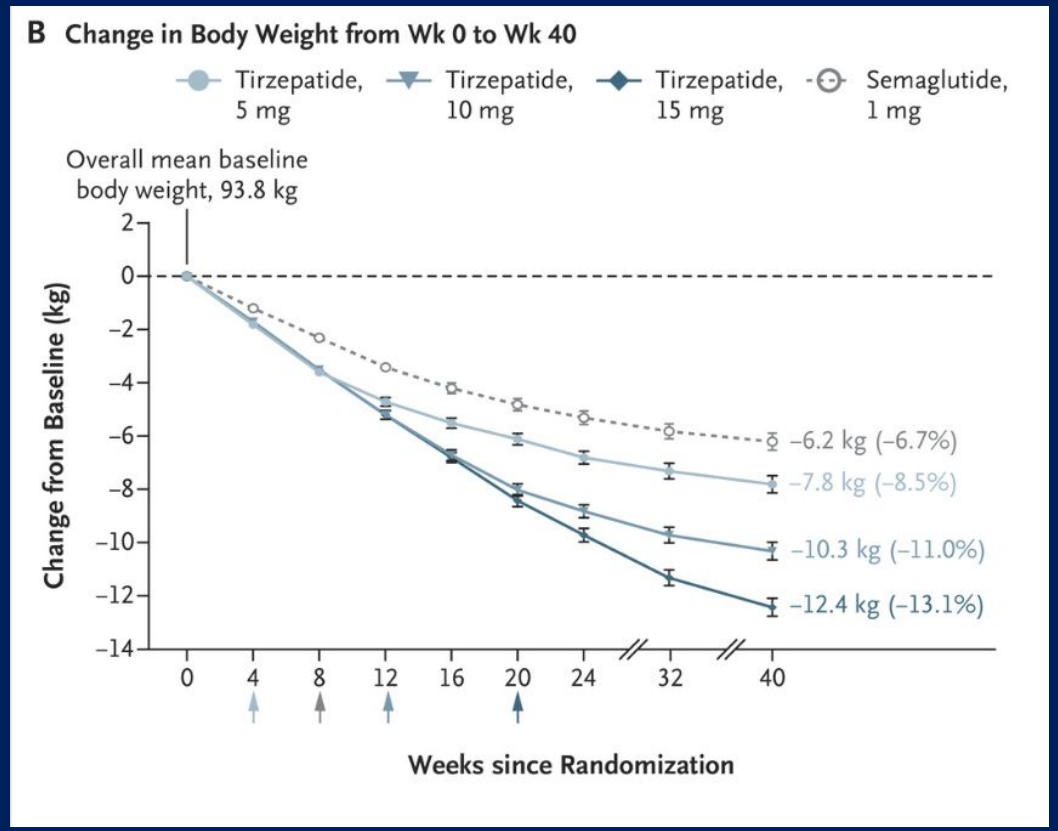
Tirzepatide (Mounjaro®)

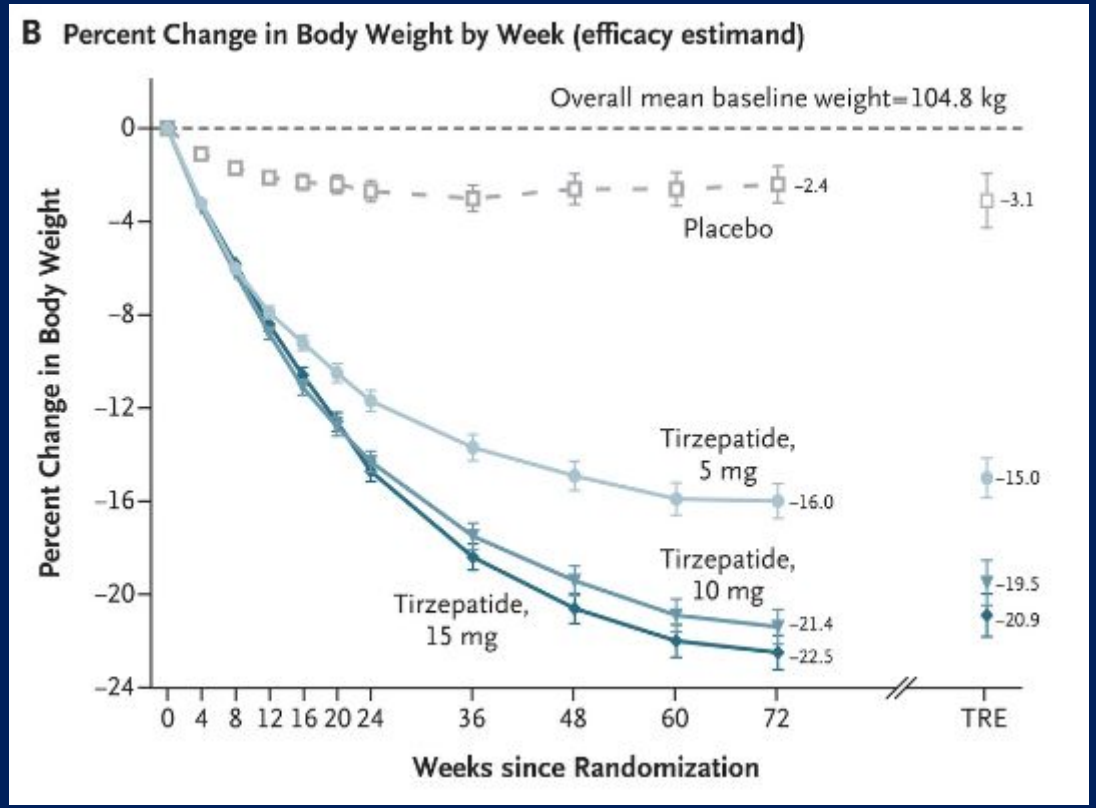
- GLP-1/GIP receptor agonist
- Once-weekly subcutaneous injection
- SURPASS-2 trial:
  - Tirzepatide vs. semaglutide 1 mg
  - 1800 patients with type 2 diabetes
  - Primary end point: change in A1C from baseline to 40 weeks
  - A1C reduction: tirzepatide (2.3%) > semaglutide (1.86%)
  - Weight reduction: tirzepatide > semaglutide



Frias JP, et al. *N Engl J Med*. 2021; 385:503-515.

Tirzepatide (Mounjaro®)

- SURMOUNT-1:
  - Tirzepatide vs. placebo
  - 2539 patients withOUT diabetes
  - Primary end points (72 weeks):
    (1) % change in weight from baseline
    (2) weight reduction of 5% or more



Jastreboff AM,, et al. *N Engl J Med*. 2022; 387:205-216.

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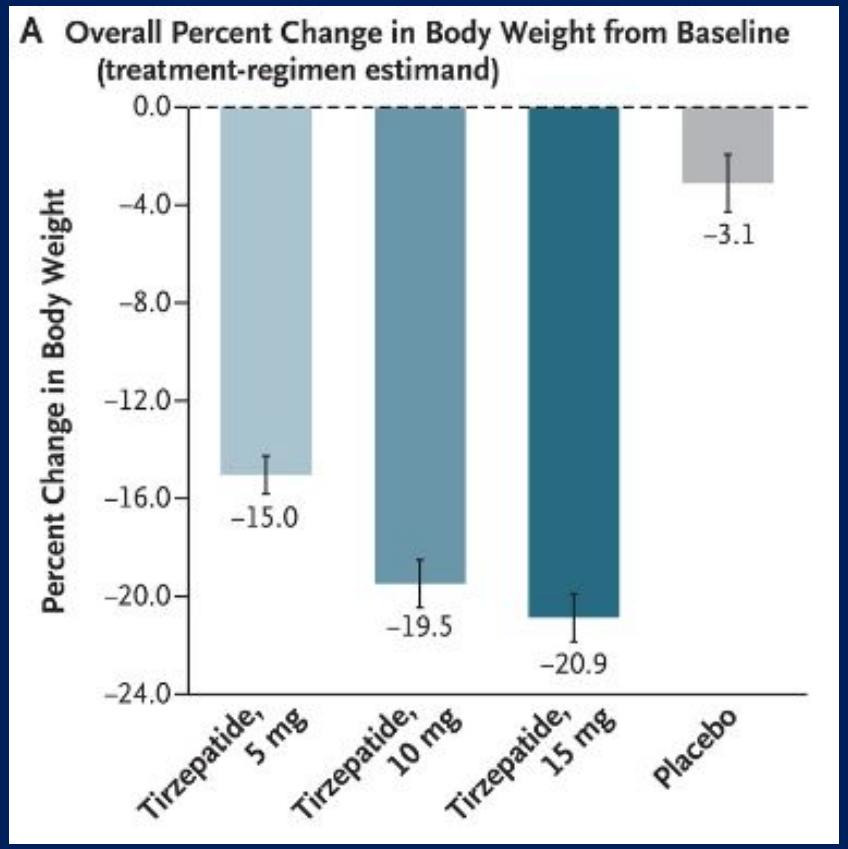
Tirzepatide (Mounjaro®)



Jastreboff AM,, et al. *N Engl J Med*. 2022; 387:205-216.

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Tirzepatide (Mounjaro®)

- SURMOUNT-2: *estimated completion April 2023*
  - Tirzepatide vs. placebo
  - 900 patients with type 2 diabetes
  - Primary end points (72 weeks):
    (1) % change in weight from baseline
    (2) weight reduction of 5% or more

- October 2022: FDA granted Fast Track designation for weight loss

https://investor.lilly.com/news-releases/news-release-details/lilly-receives-us-fda-fast-track-designation-tirzepatide

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Pharmacists' Roles

- Outpatient settings
  - Patient assessment & design of individualized treatment plans (nonpharmacological and pharmacological)
  - Risk-benefit analysis for pharmacological interventions
  - Appropriate use of pharmacotherapy
- Inpatient settings
  - Medication reconciliation
  - Medication management for patients undergoing bariatric surgery
  - Patient education & transitions of care

Clements JN, et al. *JACCP.* 2021; 11:1469-1484

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Considerations in Managed Care

- Patient & provider perceptions
- Patient access
- Adherence
- Clinical burden of obesity

Amaro A, Kaplan M, Massie DC. *Am J Manag Care*. 2022;S307-S318.

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Considerations in Managed Care

Popularity of Ozempic, Mounjaro, similar drugs may be driving shortages for people with diabetes, obesity

Doctors say too many people are obtaining the drugs despite not being obese.

By Lizann Robinson, Mack Muldofsky, Claire Pedersen, and Ivan Pereira
February 23, 2023, 11:59 AM

https://abcnews.go.com/Health/popularity-ozempic-mounjaro-similar-drugs-driving-shortages-people/story?id=97356709

Considerations in Managed Care

- Coverage of pharmacotherapy
  - Medicare
    - Medications for weight management excluded from Part D
    - Medicare Advantage plans may offer expanded coverage for weight loss treatment plans
  - Medicaid
    - Optional coverage, varies from state to state
  - Private
    - Varies
    - Requirements – prior authorization, step therapy, etc

Amaro A, Kaplan M, Massie DC. *Am J Manag Care*. 2022;S307-S318.

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Quality Measures in Obesity

- Centers for Medicare & Medicaid Services (CMS)
  - Preventive Care and Screening: BMI Screening and Follow-Up Plan

    Percentage of patients with BMI documented within previous 12 months AND had a follow-up plan documented (if BMI was outside normal parameters)
  - Increased screening increasing diagnosis increased action plans reduced health care costs

Amaro A, Kaplan M, Massie DC. *Am J Manag Care*. 2022;S307-S318.

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Health Care Costs

- Retrospective analysis of 15,000 patients (2012-2018):
  - Significant health care cost savings for patients achieving clinically meaningful weight loss (lifestyle interventions and pharmacotherapy)
- Modeling studies:
  - Moderate/extensive expansion of coverage for lifestyle intervention with or without pharmacotherapy increased treatment utilization ~$20 billion in savings over 10 years
  - 100% uptake of pharmacotherapy by Medicare/Medicaid ~$200 billion savings over 75 years

Amaro A, Kaplan M, Massie DC. *Am J Manag Care*. 2022;S307-S318.

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Summary

- Obesity can predispose patients to a number of comorbidities
- Lifestyle intervention is the foundation of effective weight management initiatives
- Several medications are FDA-approved for management of obesity
- Several barriers pose a challenge to widespread obesity treatment

Management of Obesity

Cynthia Moreau, PharmD, CPh, BCACP, CDCES
Clinical Pharmacist
ChenMed
cynthia.moreau@chenmed.com

Value Framework Assessments

How Health Care Systems and Payers Can Use Data to Inform Decision-Making

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Learning Objectives

1. Understand the need for value framework assessments
2. Describe the different types of value framework assessments in the U.S.
3. Discuss how U.S. payers will utilize value framework assessments in the future

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Faculty Disclosure

Dr. Cynthia Miller does not have any conflicts of interest associated with this presentation.

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Pretest Question 1

U.S. spend drivers include all of the following except:

a. More chronic conditions

b. New therapies and technologies

c. An aging population

d. Health inequities

e. A higher number of uninsured

Pretest Question 2

All of the following are true, except:

a. ICER uses QALYs as part of its framework

b. The AHA/ACA conducts their own trials for cost-effectiveness

c. NCCN is designed to be used in shared decision making between the patient and provider

d. Real world evidence allows us to address the evidence-efficacy gap

Pretest Question 3

Which of the following are ways that the U.S. is moving towards a more value focused assessment:

a. The Inflation Reduction Act
b. FDA requirement for Patient Reported Outcomes in trials
c. FDA focus on real world evidence generation
d. Both A and C
e. A, B and C

Do we really have a spending problem?

Higher Spend ≠ Better Outcomes[1,2]

Spend and Resources

- Higher spend percent of GDP, per person
- Lowest rate of practicing physicians and hospital beds

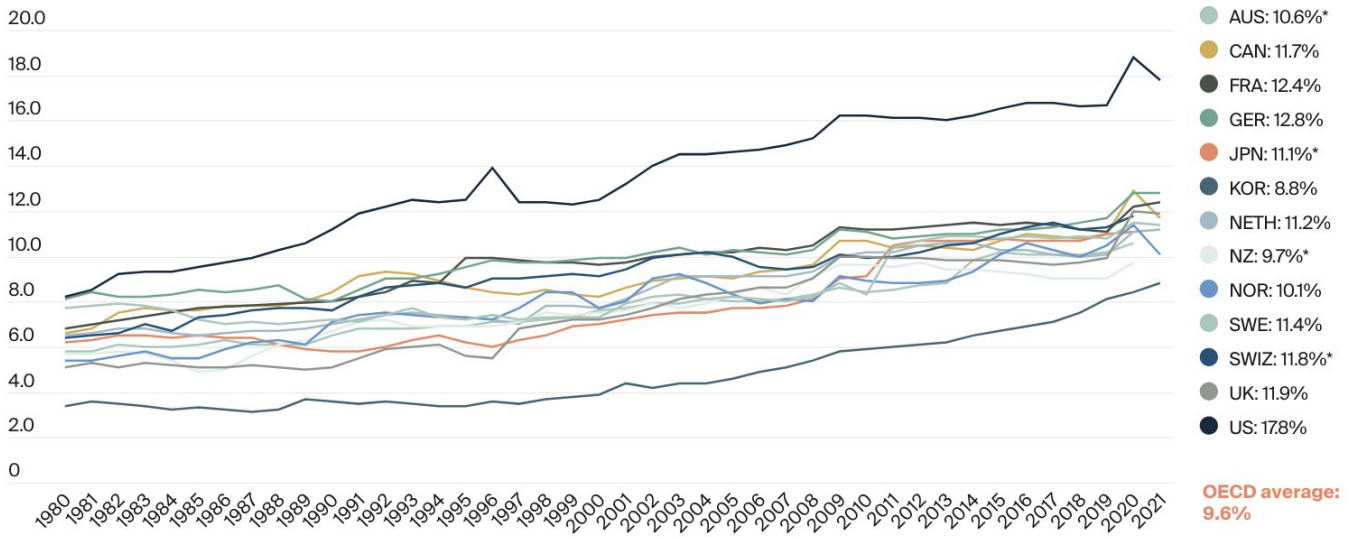
Outcomes

- Lowest life expectancy at birth
- Highest death rate for avoidable/treatable conditions
- Highest infant and infant mortality
- Highest rate chronic conditions

[1]

The U.S. is a world outlier when it comes to health care spending.

*Percent of GDP spent on health, 1980–2021**



Download data

Notes: * 2020 data. Current expenditures on health for all functions by all providers for all financing schemes. Data points reflect share of gross domestic product. Based on System of Health Accounts methodology, with some differences between country methodologies. GDP = gross domestic product. OECD average reflects the average of 38 OECD member countries, including ones not shown here.

Data: OECD Health Statistics 2022.

Source: Munira Z. Gunja, Evan D. Gumas, and Reginald D. Williams II, *U.S. Health Care from a Global Perspective, 2022: Accelerating Spending, Worsening Outcomes* (Commonwealth Fund, Jan. 2023). https://doi.org/10.26099/8ejy-yc74

We are not getting the same value and the outcomes for the amount spent as other countries

What is behind rising costs?[4,5]

Cost drivers =

Increased use of services:

- Aging population, more insured, more chronic conditions

+ Intensity of services:

- New therapies and technologies

44% increase in the number of adults aged 65 and older from 2020-2040

50% of American adults have at least one chronic disease

Case Study: Accelerated approval and the FDA[8]

A rise in spend has highlighted potential need for reform in approval processes

Health inequities are leading to higher spend[12]

- $320 billion annual health care spend
- In 2040, $1 trillion annual health care spend (if unaddressed; $11.8 trillion of total spend)
- $42 billion in lost productivity per year
- Late diagnosis, delayed care, poor access, income disparities, limited access to scientific advances and prevention

Risk for COVID-19 Infection, Hospitalization, and Death by Race/Ethnicity[17]

Rate ratios compared to White, Non-Hispanic persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
Cases[1]	1.5x	0.8x	1.1x	1.5x
Hospitalization[2]	2.5x	0.7x	2.1x	1.9x
Death[3, 4]	2.1x	0.8x	1.6x	1.7x

Race and ethnicity are risk markers for other underlying conditions that affect health, including socioeconomic status, access to health care, and exposure to the virus related to occupation, e.g., frontline, essential, and critical infrastructure workers.

Note: Adjusting by age is important because risk of infection, hospitalization, and death is different by age, and age distribution differs by racial and ethnic group. If the effect of age is not accounted for, racial and ethnic disparities can be underestimated or overestimated.

Addressing health inequities may mitigate rising spend

1.

The Quintuple Aim: A Solution?[20,21]

- Pay-for-performance (P4P) and value-based contracts are becoming more common
  - Key quality measures reported publicly
  - Emphasis and rewards (internally and externally)
- Many systems are struggling to succeed in this newly incentivized and rapidly changing environment
- Value-based programs are exposing high-cost areas in the health care system and increasing transparency

Focusing on quality, costs, and health equity through value-based arrangements may help solve the spending problem

How are we doing? Not so great [23,24]

Comparison	2017	2022
Fee for Service	41%	40.5%
FFS + Quality	25.4%	19.5%
APM	29.8%	32.6%
Population health	3.8%	7.4%

Savings:

- ACO* 0.4%-6.1%
- Bundled payments: $453-$1166 per episode
- Capitated: Full risk savings: $161 pmpy** or 3.6% lower than no risk

https://www.healthaffairs.org/do/10.1377/hpb20221014.526546/

Most surveyed payers believe that the number of advanced payment models will increase and drive practice transformation efforts, resulting in better quality and more affordable care

*ACO = Accountable Care Organization; **pmpy = per member per year

How might we translate this to drug pricing?[25]

A new model based on value rather than volume may upend the rebate-based system

Value Assessment Frameworks

US and ex-US

What is a Value Framework Assessment?[2,26]

Health Technology Assessment (HTA)[27]

"Health technology assessment is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system." – ISPOR

Value Framework Assessment

Frameworks that inform discussions about how to define and assess value at various levels of the US health care system

Some terms:

Opportunity cost

Cost-benefit/cost-effectiveness

Societal perspective

Patient-centered outcomes

Quality Adjusted Life Years (QALY)

Cost-effectiveness ratio

Incremental cost–effectiveness ratio

HTAs are commonly used in Europe to determine coverage based on pricing

What do US payers do today to assess value?[28] Survey says:

How payers assess value (P&T* Pharmacy committee)

- Expected cost and clinical benefits
- Medical necessity
- Appropriate use
- Therapeutic alternatives
- Treatment class

How payers implement value assessments (“Value” Committee)

- Noncoverage
- Tiering
- Step therapy
- Prior authorization
- Preferred products

US payers rely on utilization management rather than a government entity to determine coverage and utilization

*P&T = Pharmacy and Therapeutics

Value-based pricing models do exist in the US[30]

Image above taken from Avalere Health LLC. [34]

While US payers have implemented some value-based pricing, these pricing constructs are difficult to scale, are fragmented, and remain proprietary

Value Framework Assessments (VFAs) in the US[31]

Non-oncology

- CMS (Centers for Medicare and Medicaid Services)
- ACC/AHA (American College of Cardiology/American Heart Association)
- ICER (Institute for Clinical and Economic Research)

Oncology

- ASCO (American Society of Clinical Oncology)
- MSKCC (Memorial Sloan Kettering Cancer Center)
- NCCN (National Comprehensive Cancer Network)

Although these are the major recognized VFAs in the US, there are additional models

CMS as a Value Framework Assessment Entity:
The Inflation Reduction Act[32,33]

Value Assessment Provisions

- HHS secretary negotiates maximum prices for select brand-name drugs covered under Part B and Part D
- Manufacturers submit product information (manufacturing, government support, patent)

  AND

  supporting evidence (comparative data and effectiveness, unmet need)

What is new?

- Supply side vs demand side
- Research and development costs
- Production and distribution costs

Value assessment across the life cycle

Implementation of the Inflation Reduction Act is expected to reduce innovation in the long term. The Congressional Budget Office estimates that there will be a reduction of new drugs by 1% over 30 years[33]

Institute for Clinical and Economic Review (ICER)[34]

Framework

- Cost-effectiveness analysis
- QALYs
- Population level

Orientation

- Coverage
- Reimbursement
- Affordability
- Limitations
  - Not at the individual level
  - Concern about transparency

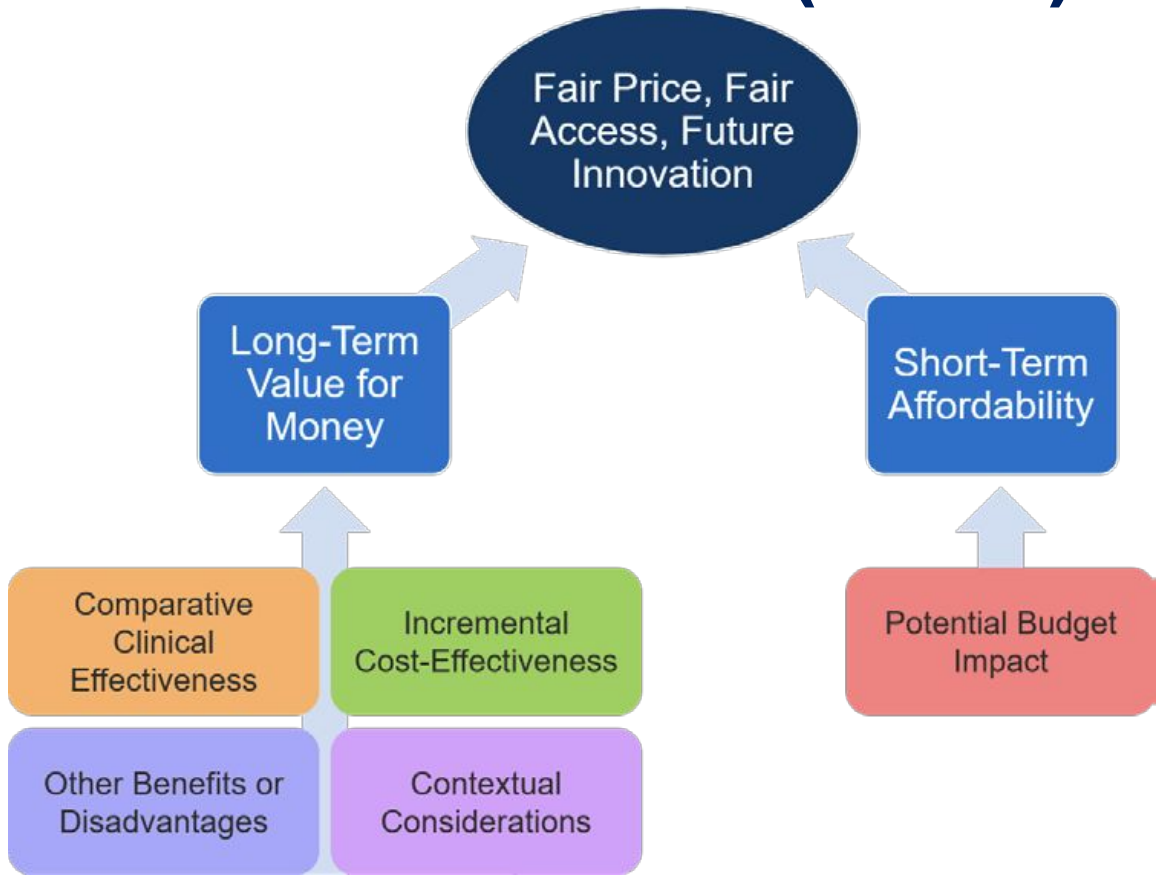


Image above taken from ICER[35]

While ICER often identifies a cost-effective price, this has not led to price reductions

ICER Example: Product X for Disease A

Disease A affects large part of US population and does not have a cure

Product X

- $80,000/year treatment
- incremental cost-effectiveness ratio $20,000
- Incremental QALYs 0.6
- Delays disease progression

Cost comparison

- Product X TCOC $400,000
- SOC TCOC $420,000

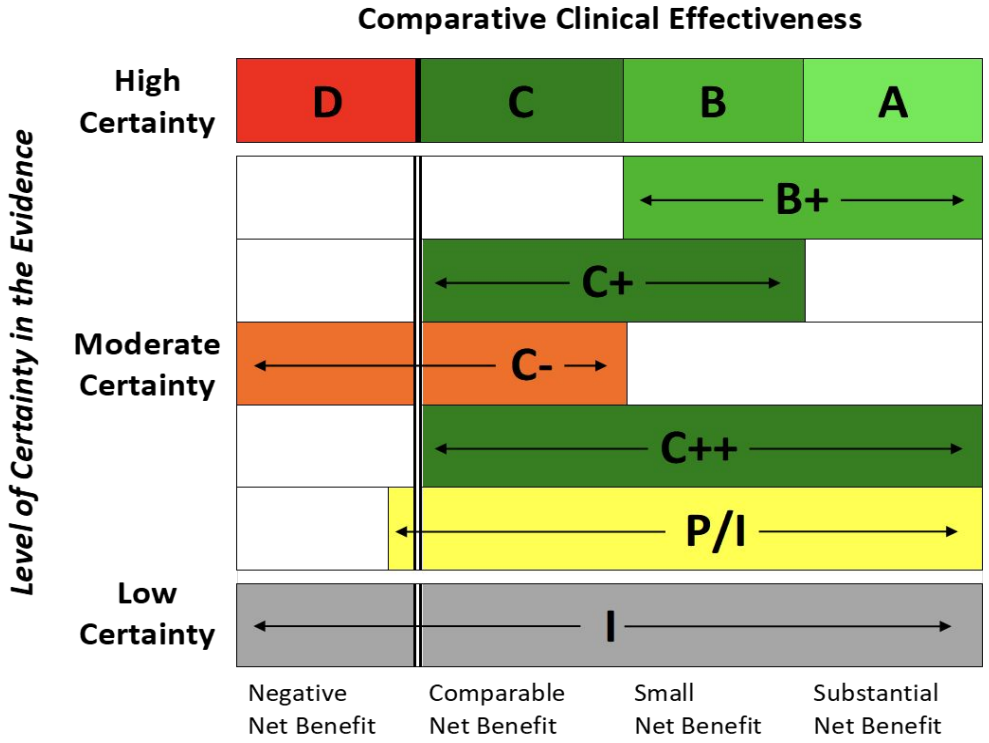
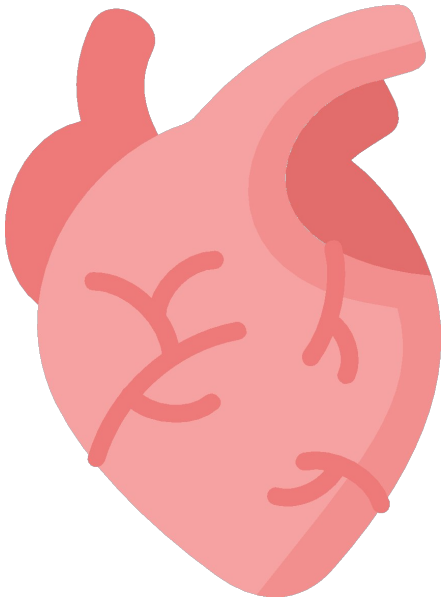


Image above taken from ICER[35]

TERMS: QALYs = quality-adjusted life years; SOC = standard of care; TCOC = total cost of care

QALYs incorporate both the delay of disease progression and any side effects that may detract from quality of life

American College of Cardiology/ American Heart Association[2]



Framework

– Cost-effectiveness analysis

– Assign “level of value”

- QALYs
- Level of evidence

– Population-level

Orientation

– Clinical pathways

– Guidelines

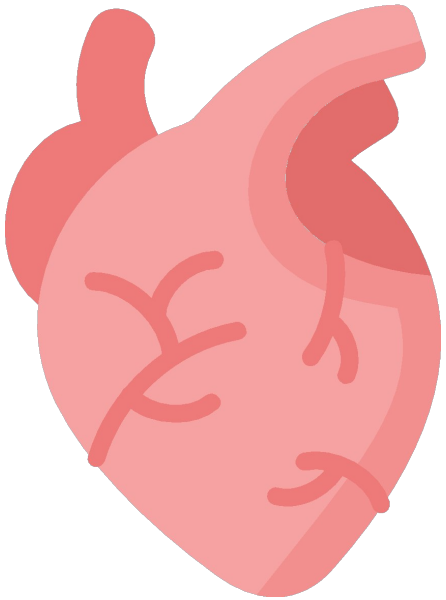
Limitations

– Rely on published cost-effectiveness studies

– Limited to specific focus around cardiology

The ACC/AHA model has assisted in writing guidelines and pathways that are most cost-effective in the area of cardiology for not only medications but also procedures

ACC/AHA Example[36]



2022 Heart Failure Guidelines

"In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value"[36]

- Based on 7 cost-effectiveness trials
- Rated as "high" in the table entitled "Value Statements"

The ACC/AHA model may incorporate findings from multiple cost-effectiveness studies to create a value statement

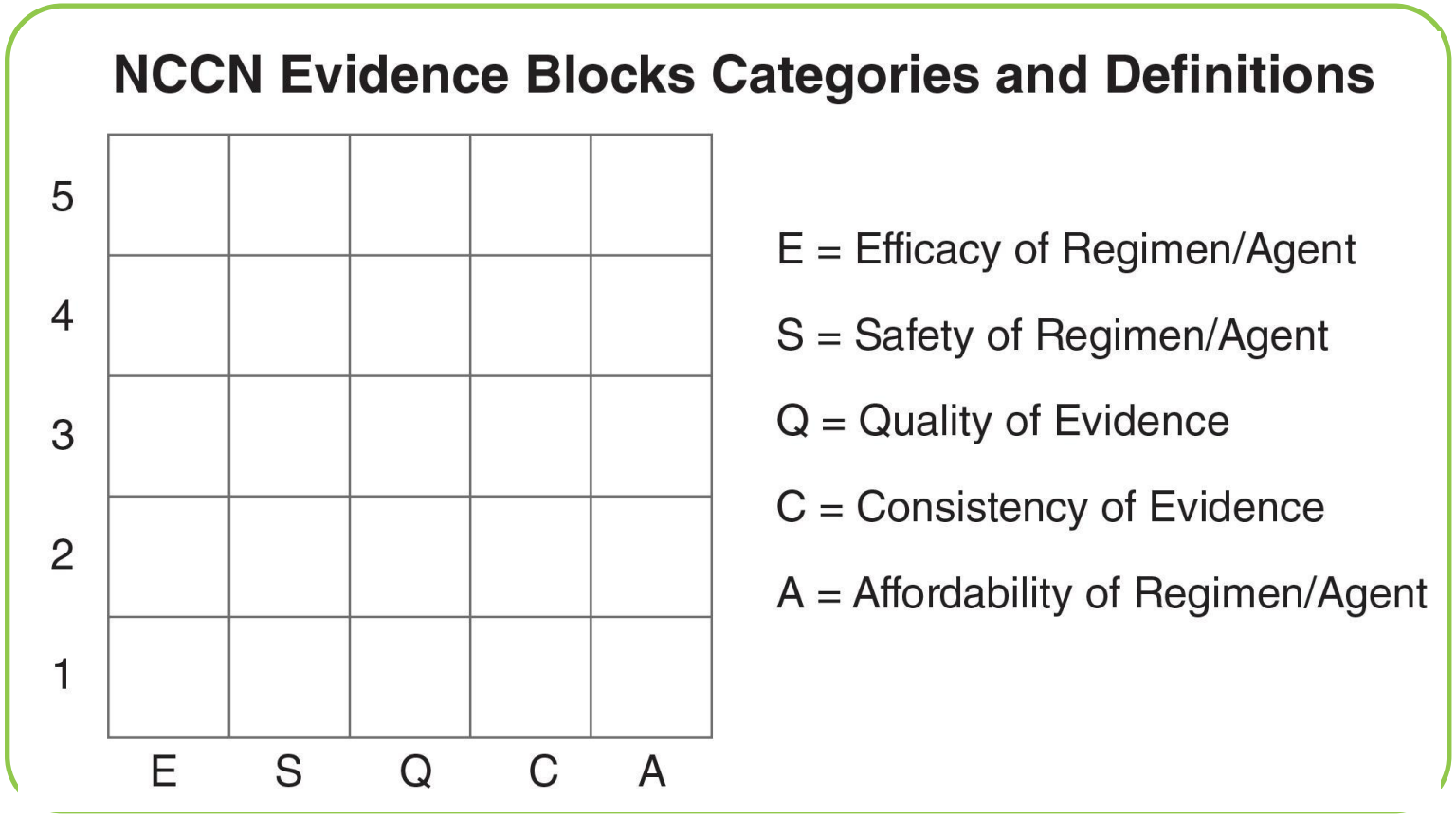
Oncology Frameworks[37,38,39,40]

ASCO/NCCN

- Benefits and harms
- Shared decision-making
- Drug costs from provider/patient perspective

MSKCC

- DrugAbacus calculator
- Policymakers
- Willingness to pay vs innovation and development



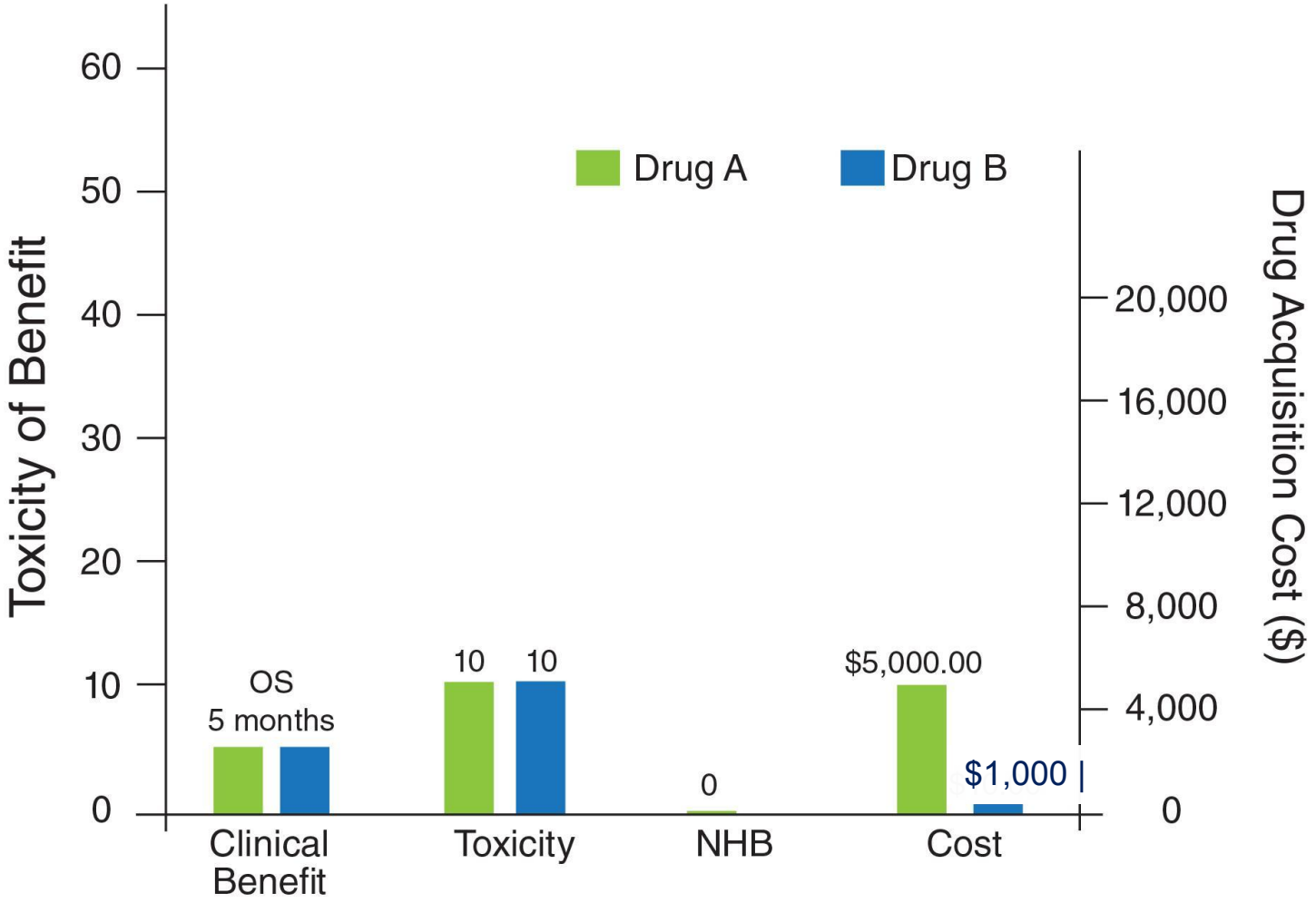
Oncology frameworks are used to make individual-level decisions and to inform clinical pathways

ASCO Example[38]

Case:

Drug A is the standard of care for Disease X.

Drug B was testing in a clinical trial against Drug A. The two drugs showed equal overall survival and toxicity levels.



ASCO's HTA is limited to drugs with head-to-head clinical trials

How do they compare?

	Stakeholders	Methods	Purpose
CMS	Pharma, PBMs	Price setting, negotiation	Drug Pricing
ICER	Payers, Pharma	Internal Cost-Effectiveness model	Coverage/Reimbursement
ACC/AHA	Physicians	Evaluate published cost-effectiveness trials to establish value statement	Inform Clinical Pathways/Guidelines
ASCO	Physicians, Patients	Evaluation Head-to-Head Trials	Shared Decision Making
NCCN	Physicians/, Patients	Expert Panel Literature review	Shared Decision Making
MSKCC	Policymakers	Abacus calculator	Drug Pricing

When using VFAs, it is important to recognize their intended purpose and limitations

Ex-US Models[41]

- France
  - Commission for Transparency
- Germany
  - Institute for Quality and Efficiency in Health Care
- Switzerland
  - Federal Office for Public Health
- England
  - National Institute for Health and Care Excellence (NICE)

Ex-US HTA evaluation can lead to pricing negotiations or coverage decisions that differ from the US

41. Vokinger KN, Naci H. Negotiating drug prices in the US—lessons from Europe. *JAMA Health Forum*. 2022;3(12):e224801.

The Future of VFA: Real-World Evidence (RWE)[42,43,44]

The Efficacy Evidence Gap

Pros: real-world treatment patterns, safety, and comparative effectiveness

Cons: internal validity, reporting bias, data quality, observational, transparency

Life Cycle Management

- Coverage with evidence development: studies can be expensive, costly, and lengthy
- NICE – temporary reimbursement for therapies (cancer) for 2 years

RWE allows us to understand how a medication works for the larger population and to evaluate its efficacy and safety over the long-term

Case Study: Hereditary Angioedema[42]

- 24-month RWE update for hereditary angioedema prophylactic therapies (post-launch)
- **Pre-launch**: attack rate 3.39, $/QALY
- **24 months post-launch**: attack rate 1.88, $/QALY

45

Table 3.3. Comparison of 2018 and Observational RWE Update Base-Case Results for HAE Prophylaxis versus no Prophylaxis

Treatment	2018 Report Cost per QALY gained	Observational RWE Update Cost per QALY gained
Cinryze	$5,950,000	$30,070,000
Haegarda	$328,000	$13,430,000
Takhzyro	$1,110,000	$12,370,000

QALY: quality-adjusted life year

Real-world evidence can be used to validate assumptions in cost-effectiveness models to improve their accuracy

How do we elevate value in the US health care system?

Payers and use of VFA:
What's the core problem?[2,28,35]

Policy

- CMS does not allow for cost-per-QALY thresholds in decision-making
- QALYs are controversial

US Customer Expectations

- Tension between innovation, access, and cost

Implementation

- Outcomes-based pricing is resource intensive and lacks proven savings

Significant conflicts of interest and incentive misalignment lead to difficulties implementing value framework assessments in the US

What is the future of payers and VFA?[46]

Government policy

- Intermediary solutions (IRA, Biden new budget proposal)
- Segmented strategic approach

Increased use of real-world evidence

- FDA focus on evaluating RWE

Incorporation of patient-reported/patient-centered outcomes (PROs)

- FDA requiring PROs in trials to understand impact on the patient

A government/policy approach will likely encourage use of HTAs for pricing discussions

Will VFAs help us get more for our money?

Post-test Question 1

U.S. spend drivers include all of the following except:

a. More chronic conditions

b. New therapies and technologies

c. An aging population

d. Health inequities

e. A higher number of uninsured

Post-test Question 2

All of the following are true, except:

a. ICER uses QALYs as part of its framework

b. The AHA/ACA conducts their own trials for cost-effectiveness

c. NCCN is designed to be used in shared decision making between the patient and provider

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Post-test Question 3

Which of the following are ways that the U.S. is moving towards a more value focused assessment

a. The Inflation Reduction Act

b. FDA requirement for Patient Reported Outcomes in trials

c. FDA focus on real world evidence generation

d. Both A and C

e. A, B and C

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Value Framework Assessments

How Health Care Systems and Payers Can Use Data to Inform Decision-Making

Break Networking Exhibits

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Federal Legislative Update: Inflation Reduction Act

Moderated by

Jennifer L. Mathieu, MA

Senior Vice President, Professional & Government Affairs, AMCP

Learning Objectives

1. Explain the basic timeline for Medicare drug price provisions
2. Describe how the IRA will impact drug affordability
3. Identify potential unintended consequences of IRA requirements

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Panelists

AMCP Florida

Shawn Barger, PharmD

Director, Medicare Formulary Strategy
Aetna

Javier Gonzalez, PharmD

Chief Growth & Commercial Officer
Abarca Health

Cynthia Griffin, PharmD

Vice President, Medicare
Pharmacy Programs
Florida Blue

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Panelists

AMCP Florida

Jonathan Hickman, PharmD

Medical Executive Director
Genentech

Ashley Peterson, MHA

Medicaid Pharmacy Director,
Contracting & Analytics
Artia

Inflation Reduction Act Overview

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Political Outlook

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Narrow majorities in both House and Senate

No looming “must pass” health care-related legislation

Debt ceiling, inflation, military aid to Ukraine crowding out other issues

Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.

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Inflation Reduction Act (H.R. 5376)

- Originally introduced as the Build Back Better Act by Congressman John Yarmuth (D-KY-03)
- Signed into law by President Biden on August 16, 2022
- Drug pricing provisions include:
  - Drug price negotiation program
  - Inflationary rebates
  - Part D redesign
- Enhances payments for biosimilars, extends expanded Affordable Care Act (ACA) tax credits, and delays the Trump-era Rebate Rule

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Inflation Reduction Act – Drug Pricing Provisions

- Drug Price Negotiation Program
  - Requires government negotiation of the prices of certain prescription drugs under Medicare beginning in 2026
- Inflationary Rebates
  - Requires manufacturers to pay rebates for certain drugs paid under Medicare Parts B or D if their average price increases faster than the rate of inflation
- Part D Redesign

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Inflation Reduction Act – Other Healthcare Provisions

- Enhanced Payments for Biosimilars
  - Temporarily increases the Part B add-on payment for qualifying biosimilars from 6% to 8% of the reference product's Average Sales Price for a 5-year period
- Extension of Expanded ACA Premium Tax Credit
  - Extends the temporary ACA premium tax credit expansions that were included in the American Rescue Plan Act through 2025
- Rebate Rule Delay
  - Prevents implementation or enforcement of the Trump-era Rebate Rule until January 1, 2032

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Key Concerns

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Cost-shifting to commercial sector

Additional instability for generic and biosimilar market

Higher launch prices resulting from inflation penalty rebates

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Inflation Reduction Act – Regulatory Implementation

- January 11 - HHS issued a timeline for implementation of IRA:
  - CMS will seek feedback on implementation through a series of 3 information collection requests (ICRs) and will issue draft guidance to solicit comments on key elements of the Medicare Drug Price Negotiation Program.
  - Among the key dates:
    - By Sept. 1, 2023, CMS will publish the first 10 Medicare Part D drugs selected for the Medicare Drug Price Negotiation Program.
    - The negotiated maximum fair prices for these drugs will be announced by Sept. 1, 2024 and prices will be effective starting Jan. 1, 2026.
    - CMS will select 15 additional Part D drugs for 2027, 15 more Part B or Part D drugs for 2028, and 20 more Part B or Part D drugs for each subsequent year.

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Inflation Reduction Act – Regulatory Implementation

- Center for Medicare and Medicaid Innovation (CMMI) announced the selection of three new healthcare payment and delivery models that will test relating to the prescription drug provisions of the Inflation Reduction Act (IRA), with the intent of lowering drug costs and promoting access to innovative drug therapies.
- Medicare Part D manufacturer discount program (MDP) beginning Jan. 1, 2025
- Participating manufacturers must enter into agreements with CMS by Mar. 1, 2024 to participate in the MDP in 2025.

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Inflation Reduction Act – Regulatory Implementation

- On Feb. 7, 2023, CMS issued an information collection request under the Paperwork Reduction Act of 1995 (PRA). Information in this collection is needed to set up agreements between manufacturers and CMS. Note that this is a notice about CMS' intention to collect this information and comments can be submitted until April 10, 2023.
- Information will be collected from respondents electronically, through HPMS.

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Key Dates

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Jan. 2025: Full Part D redesign takes effect

Sept. 2023: Initial 10 Part D drugs selected for negotiation identified

Sept. 2024: Negotiated price for initial Part D drugs published

Sept. 2025: Selection of 15 Part D drugs for negotiation for CY 2027

Jan. 2027: Second 15 negotiated prices effective

Oct. 2022: Inflation penalty rebates for Part D drugs begin

Late 2025: CMS begins sending inflation penalty rebate invoices to manufacturers

Jan. 2026: First 10 negotiated prices effective

How does a potential change in Presidential administration impact implementation?

Source: Congress.gov. H.R. 5376, Inflation Reduction Act of 2022. Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.

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Commercial Takeaways

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Understand relationship between and commercial market exposure of drugs selected for negotiation

Consider how increased uncertainty in generic/biosimilar market could have ripple effects

Consider Medicare market exposure for new drugs and how inflation penalty rebates may influence launch prices

Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.

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Manufacturer Takeaways

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Are IRA reforms “enough”?

Consider how government price negotiation could change standard approach for end of drug’s lifecycle or generic/biosimilar industry

Impact of delayed rebate invoices

Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.

Panel Discussion

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NOVA SOUTHEASTERN UNIVERSITY

Panelists

AMCP Florida

Shawn Barger, PharmD

Javier Gonzalez, PharmD

Cynthia Griffin, PharmD

Jonathan Hickman, PharmD

Ashley Peterson, MHA

Lunch
Networking
Exhibits

Kahoot Game

https://create.kahoot.it/share/amcp-day-education-2023-kahoot-2/e325b175-b2a0-4335-9e4a-62b457e8f002

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The Evolving Biosimilars Landscape: Panel Discussion

Moderated by

Wendy Bailey, RPh, BS Pharm, MS Pharm, MBA

Vice President, Health Plan Pharmacy Strategy,
Centene Corporation

Learning Objectives

1. Discuss the current level of understanding of biosimilars in the marketplace
2. Describe the scientific evidence that supports the use of biosimilars, interchangeability, and the adoption of biosimilars in the healthcare community
3. Identify nuances between medical and pharmacy billing/dispensing for biosimilars

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Panelists

AMCP Florida

Jorge Garcia, PharmD, MS, MHA, MBA, FACHE
Assistant Vice President – System Oncology Pharmacy Service Line

Baptist Health South Florida

Jennifer Miles, PharmD, BCACP, BCMTMS
Assistant Director of Ambulatory Clinical Pharmacy Services

Jackson Health Ambulatory Care

Richard Gourash, RPh, MBA
Vice President of Oncology

BioPlus Specialty Pharmacy

David Fox, PharmD
Administrator of Clinical Pharmacy Services

Florida Healthcare Plan

Biosimilar Overview

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Biosimilar History

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EU

- The European Medicines Agency (EMA) developed guidelines for the approval of biosimilars in 2005.
- Omnitrope (somatropin) was the first biosimilar approved in the EU in 2006.

USA

- The Biologics Price Competition and Innovation Act was signed into law in 2010, paving the way for biosimilars in the US.
- Filgrastim-sndz (Zarxio) was the first biosimilar approved in the US on March 6, 2015.

USA

- Adoption of biosimilars was slow due to negative messaging from innovator/originator companies.
- Both the Ensuring Innovation Act and the Advancing Education on Biosimilars Act were signed into law on April 23, 2021.

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Current State

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Biosimilars launched to date account for 24% of competitive molecule volume

Exhibit 4: Percentage of biologics sales accessible to approved and launched biosimilars and biosimilar efficiency, Q1 2015–Q3 2022

Source: IQVIA MIDAS, Sep 2022; IQVIA Institute, Dec 2022.

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Current State

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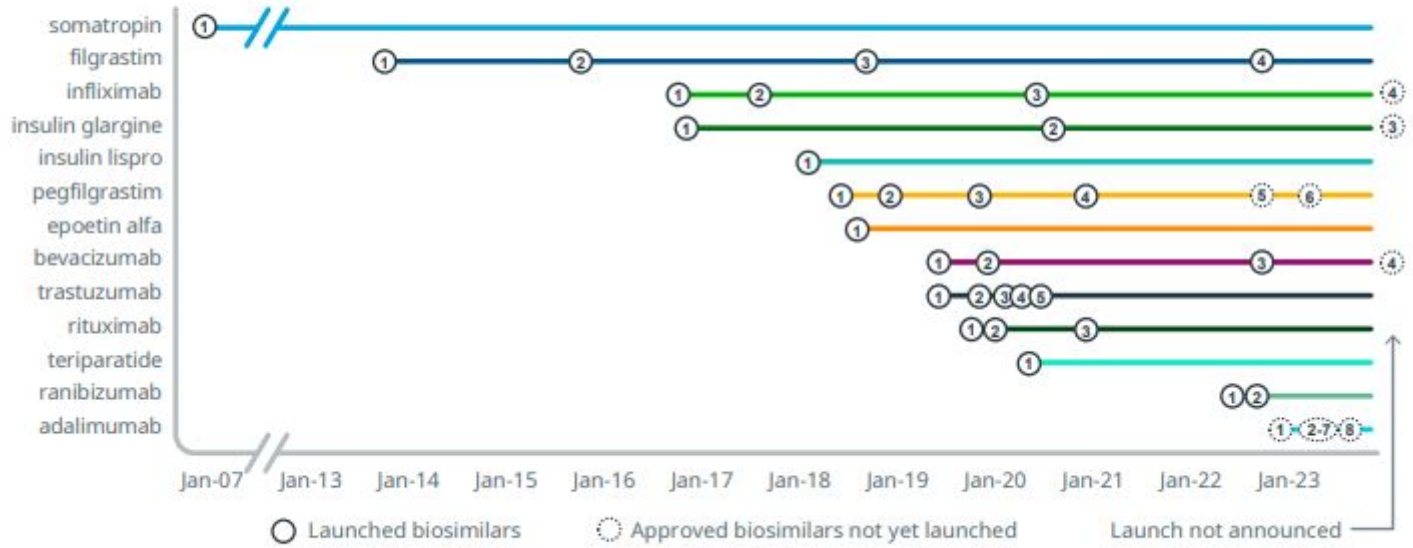
Since 2007, 30 biosimilars have launched in the U.S. with 10 more approved and set to launch by the end of 2023

Exhibit 5: Biosimilars approved and launched in the U.S.



Source: IQVIA Institute, Dec 2022.

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Future State

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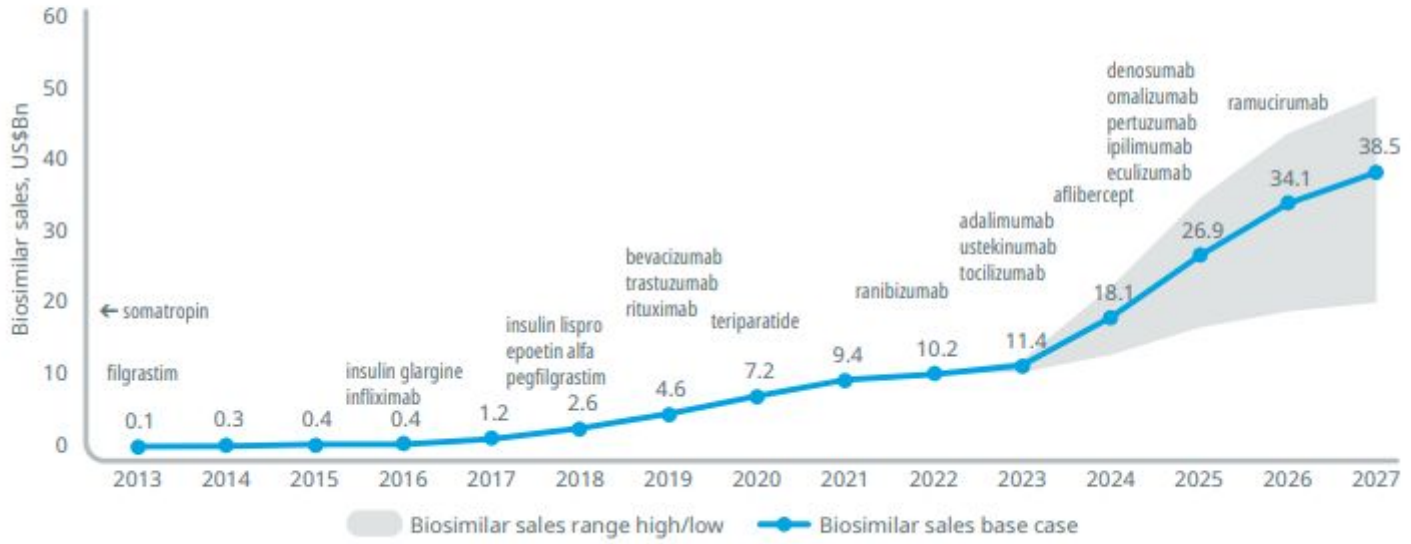
Expected launches and uptake are likely to increase overall spending on biosimilars significantly to $20–49Bn in 2027

Exhibit 21: Biosimilar historical sales 2013–2022 and outlook scenarios 2023–2027, US$Bn



Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Nov 2022.

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Future State

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Savings over the next five years as a result of biosimilars are projected to exceed $180Bn, though uncertainties remain

Exhibit 22: Biologic estimated savings from biosimilars at invoice prices

Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Nov 2022.

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Future State

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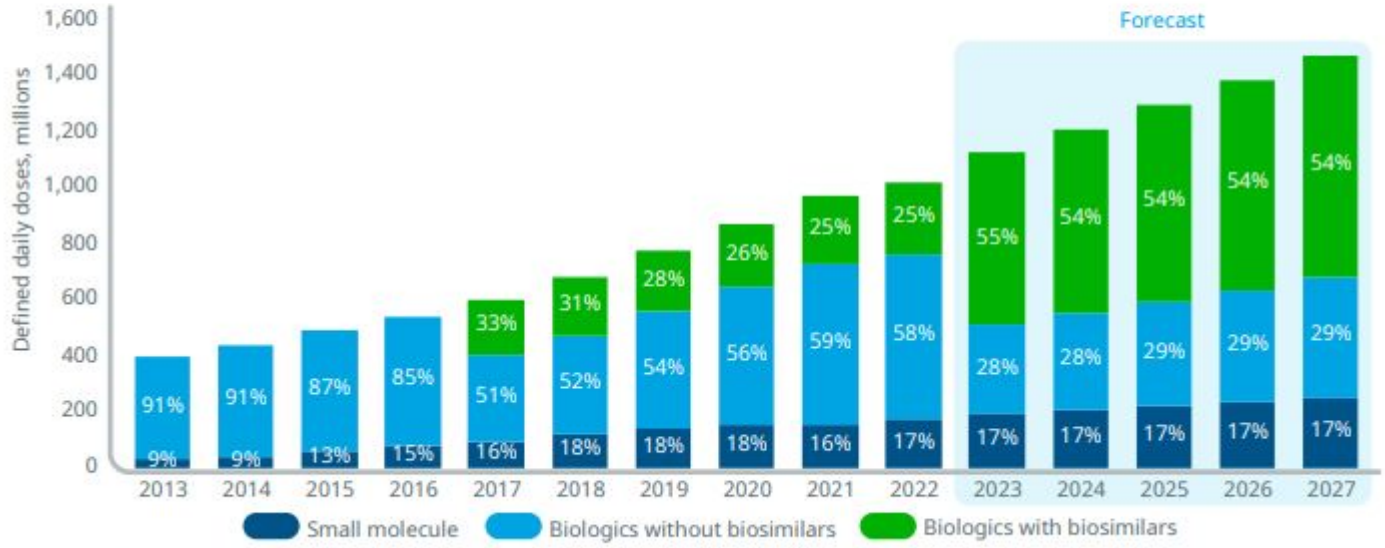
Entry of new immunology biosimilars in 2023 will increase competition in a rapidly growing market

Exhibit 23: Historic and future immunology volume in defined daily doses (DDDs) by biosimilar competition, 2013–2027



Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Dec 2022.

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Adoption Rates

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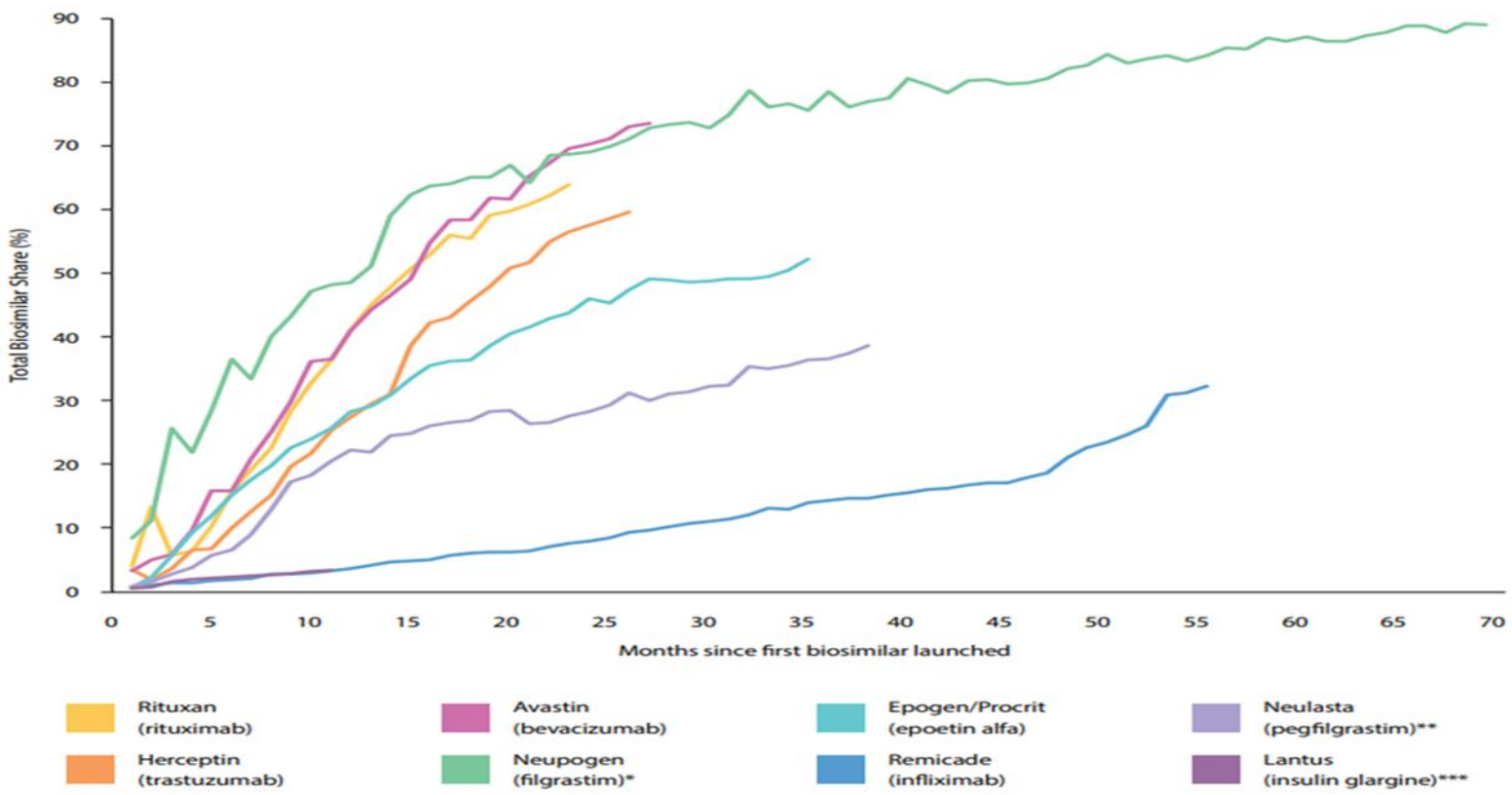
Figure 4. **Adoption of biosimilars typically accelerates quickly after market introduction.**



Source: IQVIA: Accessed via IQVIA National Sales Perspective (NSP) SMART Data. (October 2021).

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Payer/PBM Formulary Considerations

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- Will Biosimilar Partners Commit Long Term and Deliver Value
- Patient Support- Copay/Device Replacement
- Rebate Strategy can be a Defensive Maneuver to Preserve Brand Market Share
  Payer/PBM Execution Risk in Removing/Disadvantaging Brand
- Brand Company Lowers Price/Offers Non-Branded Products
  Will This Discourage Pharma-Companies to Invest in Biosimilars
- Can Biosimilars Bring Value Outside of the Initial Innovator Product?
  Biosimilar Humira Vs Other TNFs or Interleukins (ie. IL 17, IL 23, IL 12-23)

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ASP Trends

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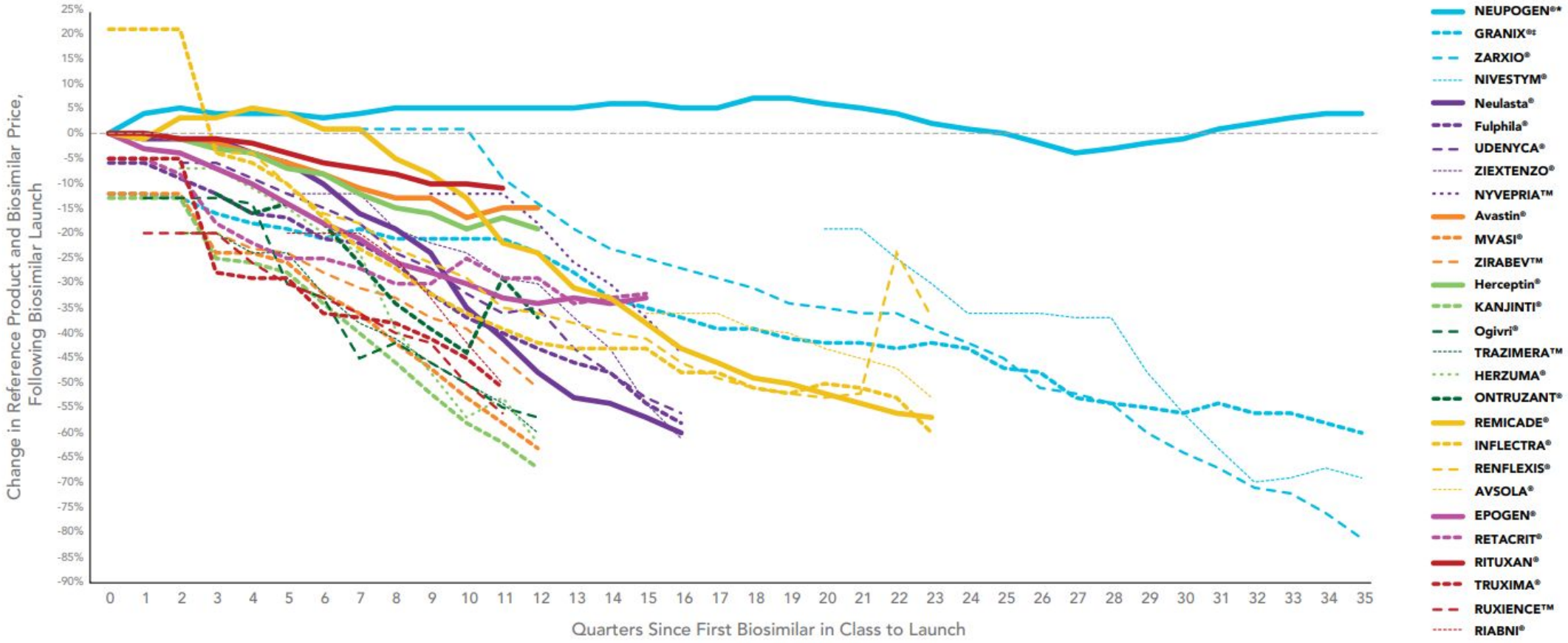
Figure 5. *Downward Trend in ASP for Biosimilars and Reference Products Over Time*[8,†]



Source: Amgen 2022 Biosimilar Trend Report

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The Evolving Biosimilars Landscape: Panel Discussion

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Wendy Bailey, RPh, BS Pharm, MS Pharm, MBA

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Health Equity in Health Car

Shanada Monestime, PharmD, BCOP
Director, Community Engaged Research
GO2 for Lung Cancer

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Disclosures

- Research is supported by
  - Bristol Myers Squibb
  - Merck Corporation
  - Sanofi
  - Mirati Therapeutics

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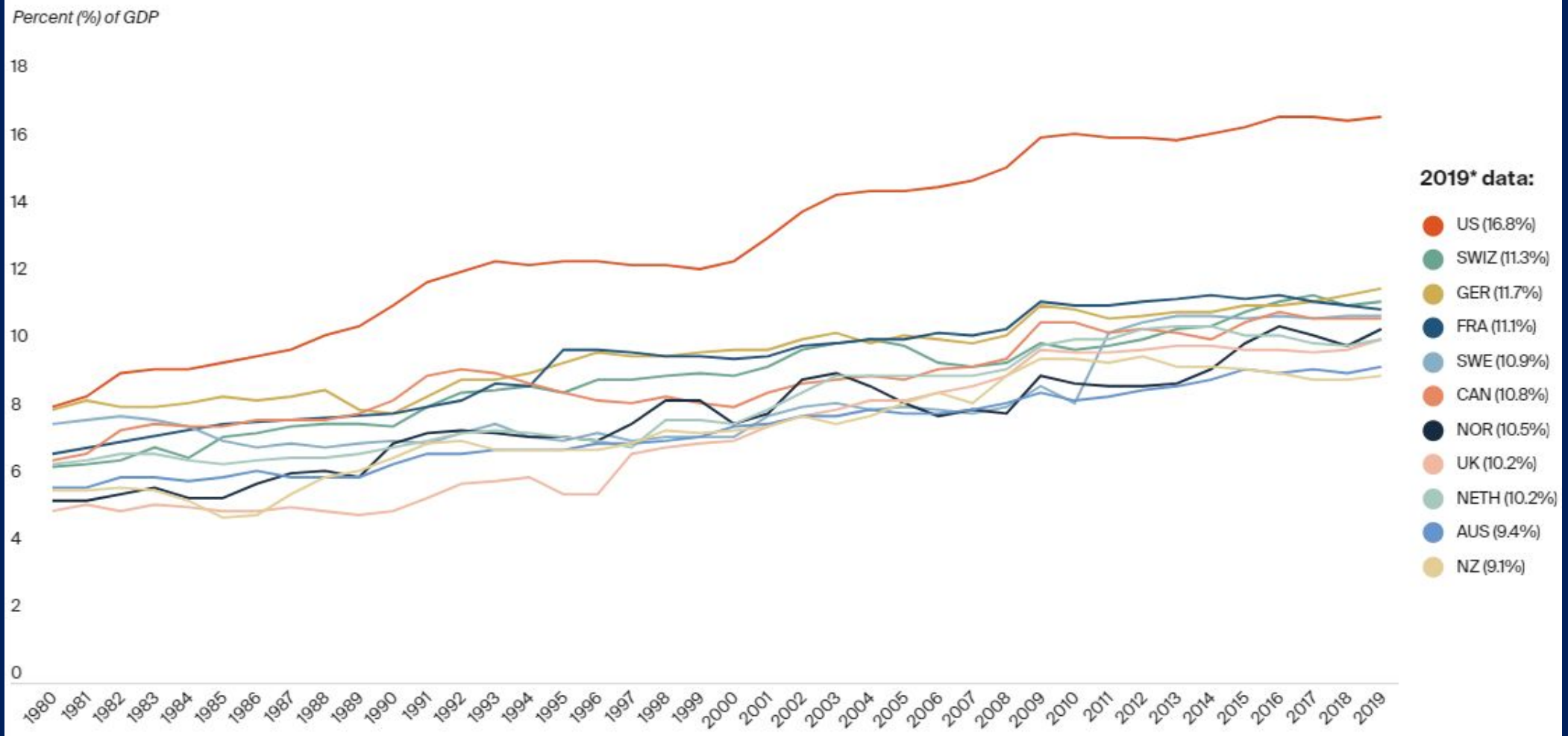
Learning Objectives

- Discuss local/national health care performance and historical factors that result in health inequities
- Describe the social and structural factors that contribute to different health outcomes in marginalized populations
- Understand the interconnections and relationships between individual outcomes, socioeconomic context, and systemic barriers contributing to health inequalities
- Summarize how various stakeholders can advance health equity in their practice or organization

Health Care Spending as a Percentage of GDP, 1980–2019

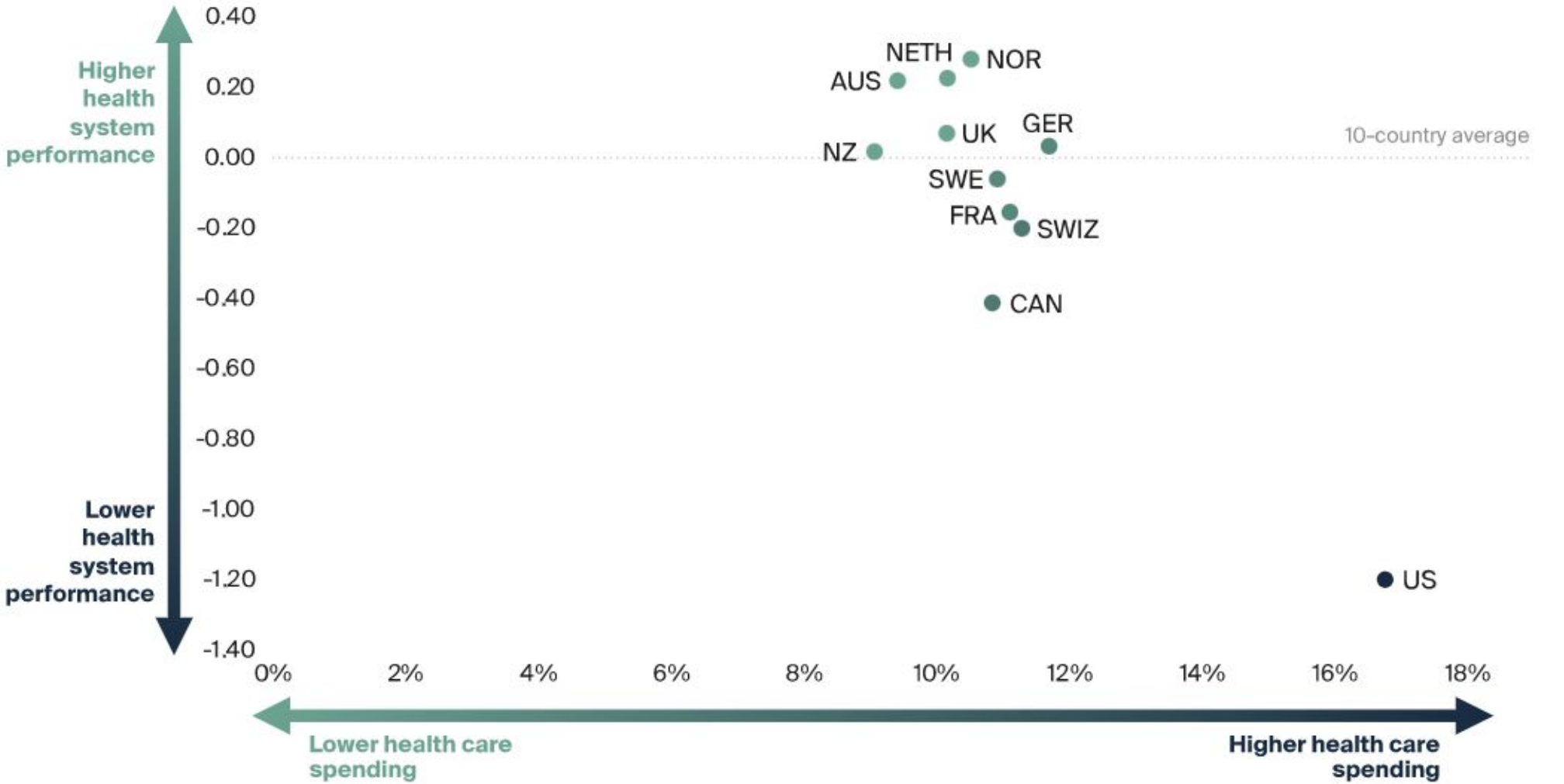


Notes: Current expenditures on health. Based on System of Health Accounts methodology, with some differences between country methodologies. GDP refers to gross domestic product.
* 2019 data are provisional or estimated for Australia, Canada, and New Zealand.

Data: OECD Health Data, July 2021.

Source: Eric C. Schneider et al., *Mirror, Mirror 2021 — Reflecting Poorly: Health Care in the U.S. Compared to Other High-Income Countries* (Commonwealth Fund, Aug. 2021).
https://doi.org/10.26099/01DV-H208

Health Care System Performance Compared to Spending



Note: Health care spending as a percent of GDP. Performance scores are based on standard deviation calculated from the 10-country average that excludes the US. See How We Conducted This Study for more detail.

Data: Spending data are from OECD for the year 2019 (updated in July 2021).

Source: Eric C. Schneider et al., *Mirror, Mirror 2021 – Reflecting Poorly: Health Care in the U.S. Compared to Other High-Income Countries* (Commonwealth Fund, Aug. 2021). https://doi.org/10.26099/0IDV-H208

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EXHIBIT 1

Health Care System Performance Rankings

	AUS	CAN	FRA	GER	NETH	NZ	NOR	SWE	SWIZ	UK	US
OVERALL RANKING	**3**	**10**	**8**	**5**	**2**	**6**	**1**	**7**	**9**	**4**	**11**
Access to Care	8	9	7	3	1	5	2	6	10	4	11
Care Process	6	4	10	9	3	1	8	11	7	5	2
Administrative Efficiency	2	7	6	9	8	3	1	5	10	4	11
Equity	1	10	7	2	5	9	8	6	3	4	11
Health Care Outcomes	1	10	6	7	4	8	2	5	3	9	11

Data: Commonwealth Fund analysis.

Source: Eric C. Schneider et al., *Mirror, Mirror 2021 — Reflecting Poorly: Health Care in the U.S. Compared to Other High-Income Countries* (Commonwealth Fund, Aug. 2021). https://doi.org/10.26099/01DV-H208

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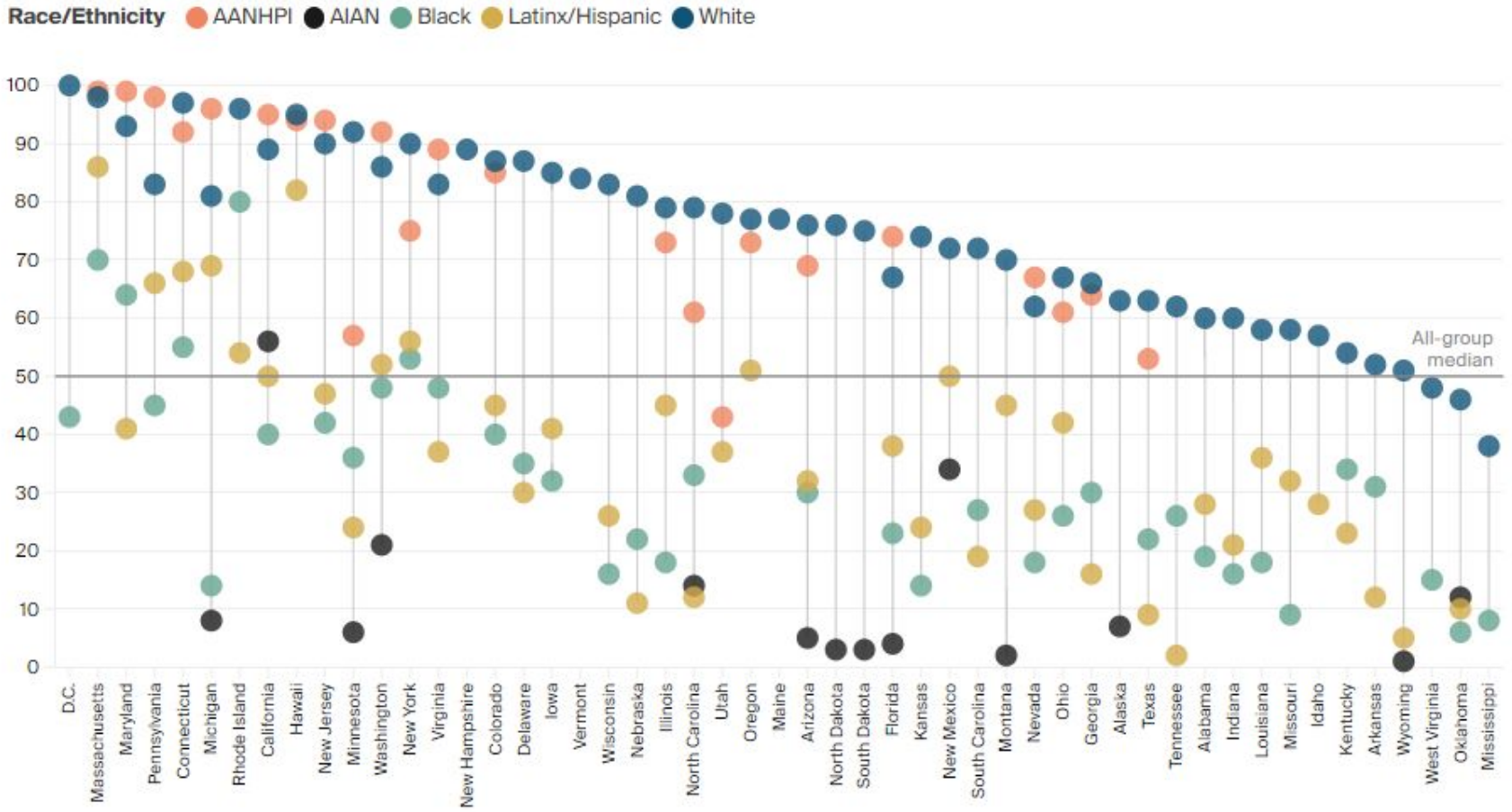
What is Health Equity?

- Health equity provides everyone with a fair and just opportunity to be as healthy as possible
- Avoidable differences in health outcomes
- Removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to good jobs with fair pay, quality education and housing, safe environments, and health care

Profound racial and ethnic inequities in health and health care exist across and within states.

Health system performance scores, by state and race/ethnicity



Notes: Scores are based on the percentile distribution of each group's final composite z-score across all indicators/dimensions; rank-ordered by score of state's highest group. The 50th percentile represents the median health performance score among all the groups measured. Summary performance scores not available for all racial and ethnic groups in all states; missing dots for a particular group indicate that there are insufficient data for that state. AANHPI = Asian American, Native Hawaiian, and Pacific Islander; AIAN = American Indian/Alaska Native.

Data: Commonwealth Fund 2021 Health System Performance Scores.

Source: David C. Radley et al., *Achieving Racial and Ethnic Equity in U.S. Health Care: A Scorecard of State Performance* (Commonwealth Fund, Nov. 2021).

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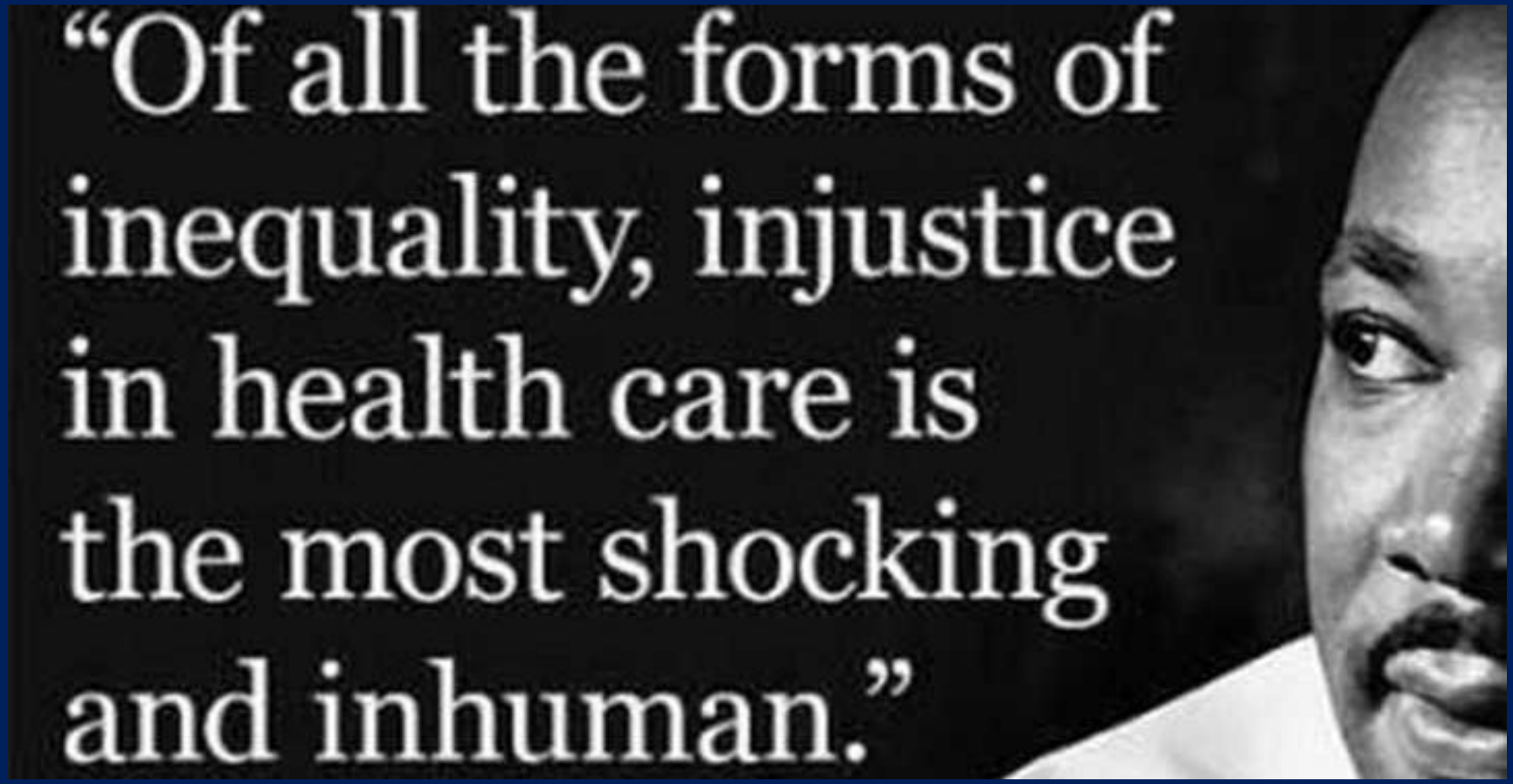

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Why Health Equity Matters?

$93b

Estimated total annual cost of racial and ethnic health disparities in the US in excess medical care costs.[1]

$230b

Direct medical care expenses from health disparities from 2003-2006, in which 1 trillion dollars could have been reduced in indirect cost by eliminating health disparities. [2]

- Delayed care and inadequate health care coverage may increase the cost of care exponentially
- Longer-term reliance on the health care system for preventable chronic diseases
- Lost productivity from illness-related employee absenteeism (costs employers $530 billion per year)[3]

1. Turner, A., THE BUSINESS CASE FOR RACIAL EQUITY in *A STRATEGY FOR GROWTH*. 2018, W.K Kellog Foundation, 2. National Academies of Sciences, E., et al., in *Communities in Action: Pathways to Health Equity*, A. Baciu, et al., Editors. 2017, National Academies Press (US) 3. Poor Health Costs US Employers $530 Billion and 1.4 Billion Work Days of Absence and Impaired Performance According to Integrated Benefits Institute. 2018: Integrated Benefits Institute

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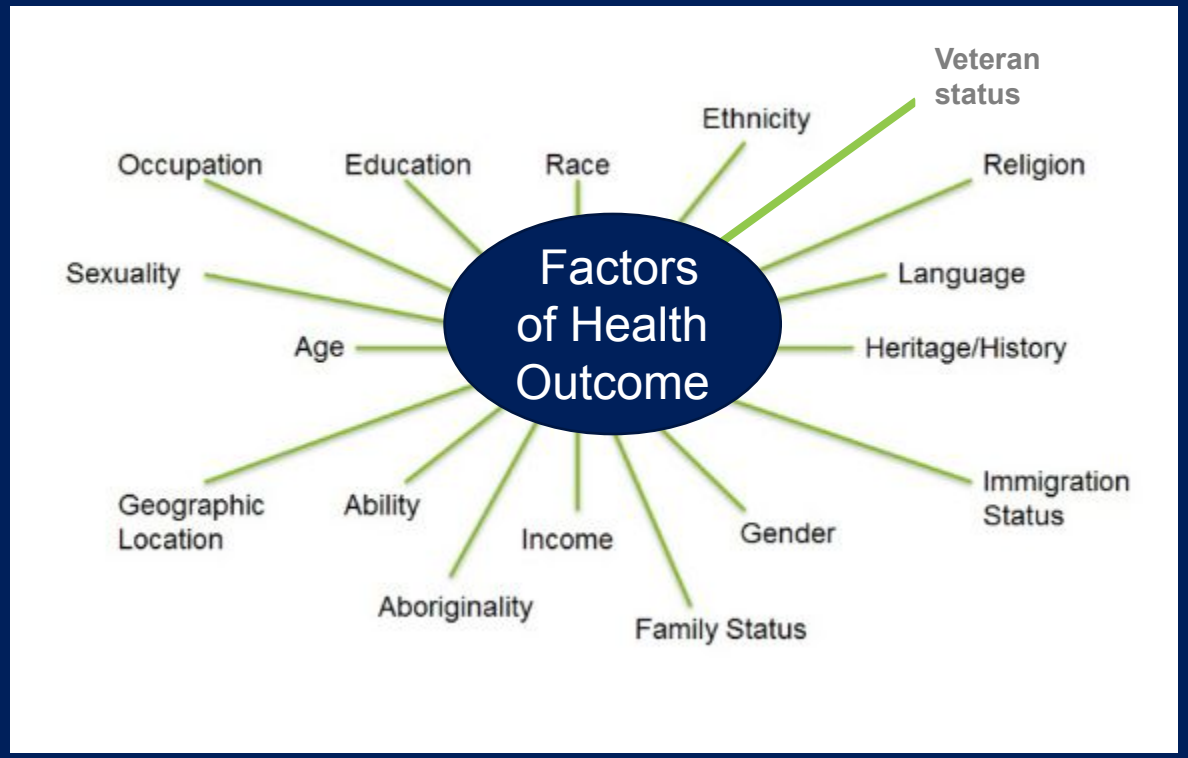
2 People, Same Zip Code, Different Outcomes



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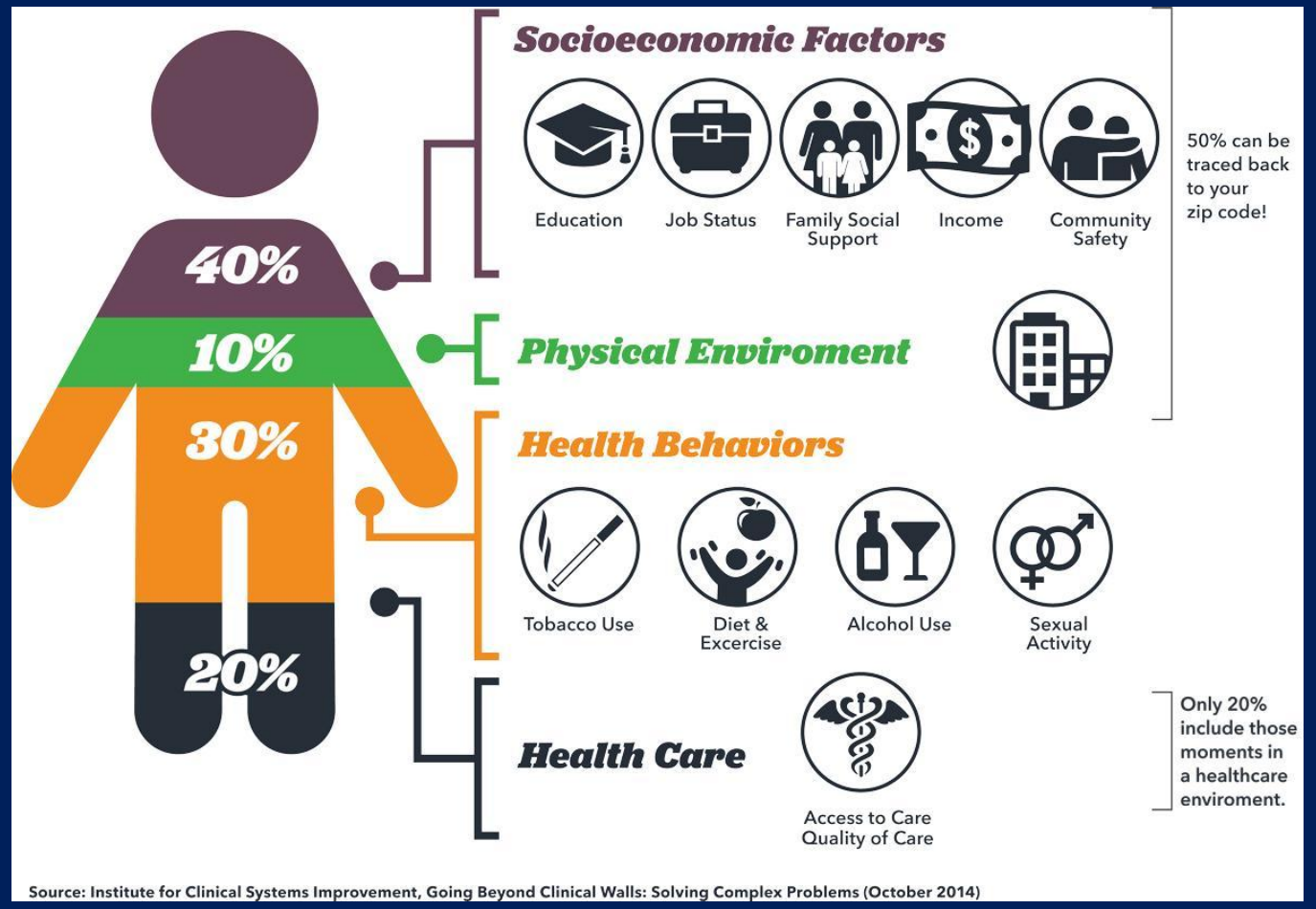
Social Determinants of Health

- Conditions in which people are born, grow, live, work and age
- These circumstances are shaped by the distribution of money, power and resources at global, national and local levels



Source: Institute for Clinical Systems Improvement, Going Beyond Clinical Walls: Solving Complex Problems (October 2014)

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Structural Racism

- Laws and policies that allocate resources in ways that disempower and devalue members of racial and ethnic minority groups, resulting in inequitable access to high-quality care[1]
- Residential segregation
  - Redlining
  - Jim crow era

1. *Structural Racism In Historical And Modern US Health Care Policy.* Health Affairs, 2022. **41**(2): p. 187-194.

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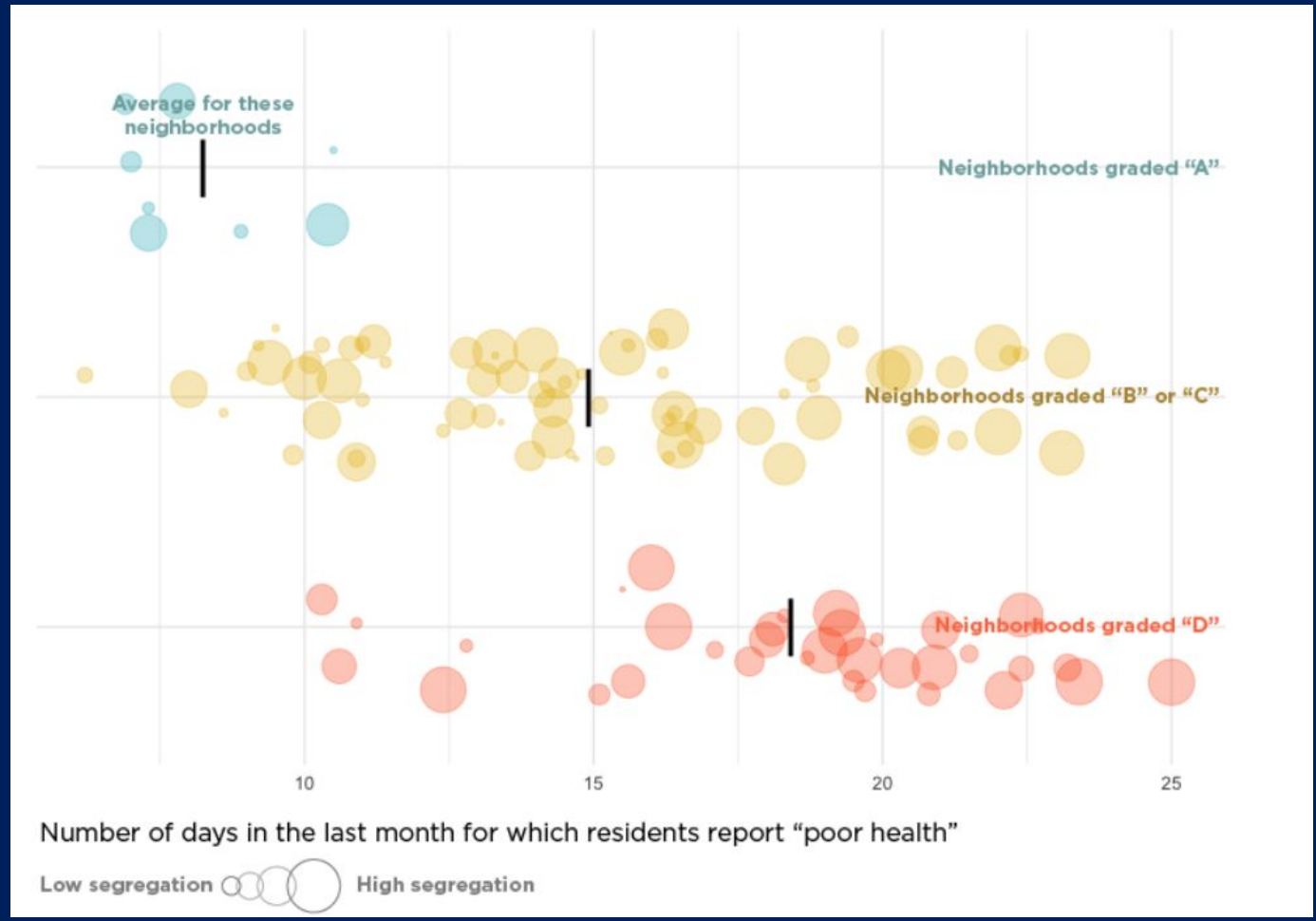
Residential Segregation[1]

- Home Owner Loan Corporation (HOLC) was established in 1933 for the purpose of stabilizing the mortgage lending system in the nation

- HOLC residential security maps neighborhoods classification:
- A – “Best” areas, colored green
- B – “Desirable” areas, colored blue
- C – “Declining” areas, colored yellow
- D – “Hazardous” areas, colored red



1. Jeramy Townsley, U.A., Matt Nowlin, *The Lasting Impacts of Segregation and Redlining*. 2021: SAVI

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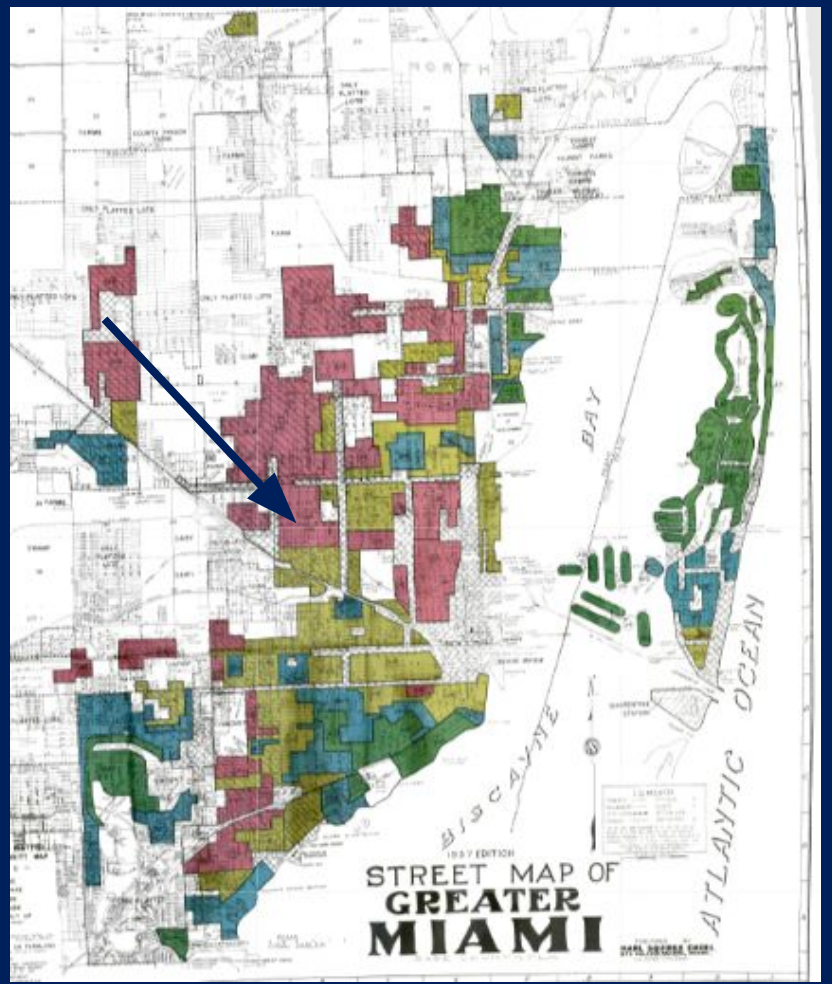
Impact of Residential Segregation[1,2]

- Substandard housing
- Underfunded public schools
- Employment disadvantages
- Exposure to crime
- Environmental hazards
- Physician shortages
- Food deserts
- Health inequities/hospital closures
- Economic stress may induce "maladaptive" coping behaviors, such as smoking and alcohol use



1. Fiscella, K. and D.R. Williams, *Health disparities based on socioeconomic inequities: implications for urban health care.* Acad Med, 2004. **79**(12): p. 1139-47. 2. Gee, G.C. and D.C. Payne-Sturges, *Environmental health disparities: a framework integrating psychosocial and environmental concepts.* Environ Health Perspect, 2004. **112**(17): p. 1645-53

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Physical Environment[1]

- Communities of color are often disproportionately exposed to fine particles in the air called $PM_{2.5}$
- In counties where Black people were highly segregated from White people, total $PM_{2.5}$ levels were twice as high as in well-integrated counties
- Populations living in racially segregated communities breathe a form of pollution that is much more concentrated in toxic, cancer-causing compounds

1. Kodros, J.K., et al., *Unequal airborne exposure to toxic metals associated with race, ethnicity, and segregation in the USA.* Nature Communications, 2022. **13**(1): p. 6329.

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Health Care Access: Safety Net Providers[1]

- Safety-net providers play a valuable role in reducing health inequities because of their commitment to and experiences with underserved communities
- Tend to score lower on patient satisfaction surveys, underperform on evidence-based metrics, and report higher rates of adverse safety events and complications

1. *Structural Racism In Historical And Modern US Health Care Policy.* Health Affairs, 2022. **41**(2): p. 187-194.

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Safety Net Challenges[1]

- Influx of patients with complex biopsychosocial challenges
- Patients with low levels of health literacy require more time to explain treatment
- Posttraumatic stress management among refugees requires working across differences in language and cultural beliefs
- Specialty services are often not easily available for the uninsured
- Preventive care services may be neglected in the face of multiple and competing providers' demands

Fiscella, K. and D.R. Williams, *Health disparities based on socioeconomic inequities: implications for urban health care.* Acad Med, 2004. **79**(12): p. 1139-47.

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Health Care Access: Reimbursement

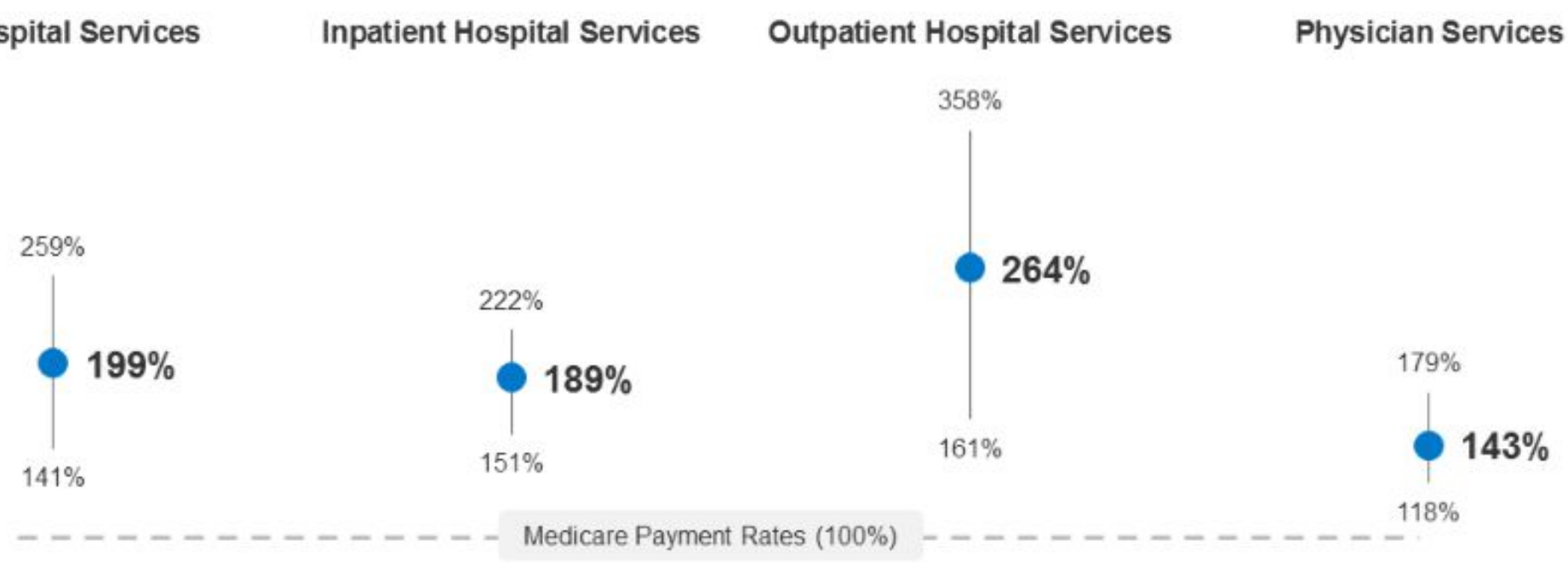
- Federal laws require reimbursement to be sufficient to ensure equitable access to high-quality health care for Medicaid beneficiaries
- Medicaid payments are notoriously low and have been cited as a reason for low provider participation[1]
- Numerous lawsuits have challenged low rates as violations of federal Medicaid requirements
  - In 2017, Medicaid beneficiaries and providers in California challenged rates on antidiscrimination grounds, alleging that the low Medicaid rates were discriminatory against the growing Latino population, creating “a separate and unequal system of health care”[2]

1. Clark BR. Medicaid access, rate setting, and payment suits: how the Obama Administration is undermining its own health reform goals. Howard L J 2012;55(3):771–853. Google Scholar 2. Mexican American Legal Defense and Education Fund [Internet]. Los Angeles (CA): MALDEF. Press release, Advocates file lawsuit alleging California’s separate and unequal Medi-Cal system violates the rights of millions; 2017 Jul 12 [cited 2021 Dec 10]. Available from: https://www.maldef.org/2017/07/advocates-file-lawsuit-alleging-californias-separate-and-unequal-medi-cal-system-violates-the-right-of-millions/ Google Scholar

ES Figure 1

Private Payment Rates Are Higher Than Medicare Rates for Hospital and Physician Services

Average Private Insurance Rates as a Percentage of Medicare Rates, Across Studies Using 2010-2017 Data



SOURCE: KFF analysis of 19 published studies comparing private insurance and Medicare payments to providers. Because some studies analyze payments to providers in multiple service categories, the number of studies across all categories is greater than 19.

KFF
HENRY J KAISER FAMILY FOUNDATION

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Health Care Access: Reimbursement

- Value-based payment reform is a Medicare pay-for-performance program to improve health care quality and reduce costs
- Programs do not account for social determinants of health when determining provider performance, ranking, and payment
- Safety-net providers serving low-income minorities are more likely to be penalized and receive lower Medicare reimbursement[1]

1. Gilman, M., et al., *Safety-Net Hospitals More Likely Than Other Hospitals To Fare Poorly Under Medicare's Value-Based Purchasing.* Health Affairs, 2015. **34**(3): p. 398-405.

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Health Care Access: Insurance Coverage

- Inadequate health insurance coverage is one of the largest barriers to health care access
- The unequal distribution of coverage contributes to disparities in health
- Many low-income employees to fall into the Medicaid coverage gap—unable to afford private insurance, not eligible for Medicaid or subsidies through the Affordable Care Act

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Health Care Access: Insurance Coverage

- Medicaid expansion allows for more low-income individuals to qualify for Medicaid, without additional stipulations of pregnancy, children, elderly or having a disability
- Many states have not expanded Medicaid, which leaves high-risk patients who are in the low SES to go without insurance coverage, leaving significant coverage gaps

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Coverage: Medicaid Expansion

- Reinforces racial hierarchy and results in inequities in coverage
- Evident in southern states with large numbers of Black and Latino residents

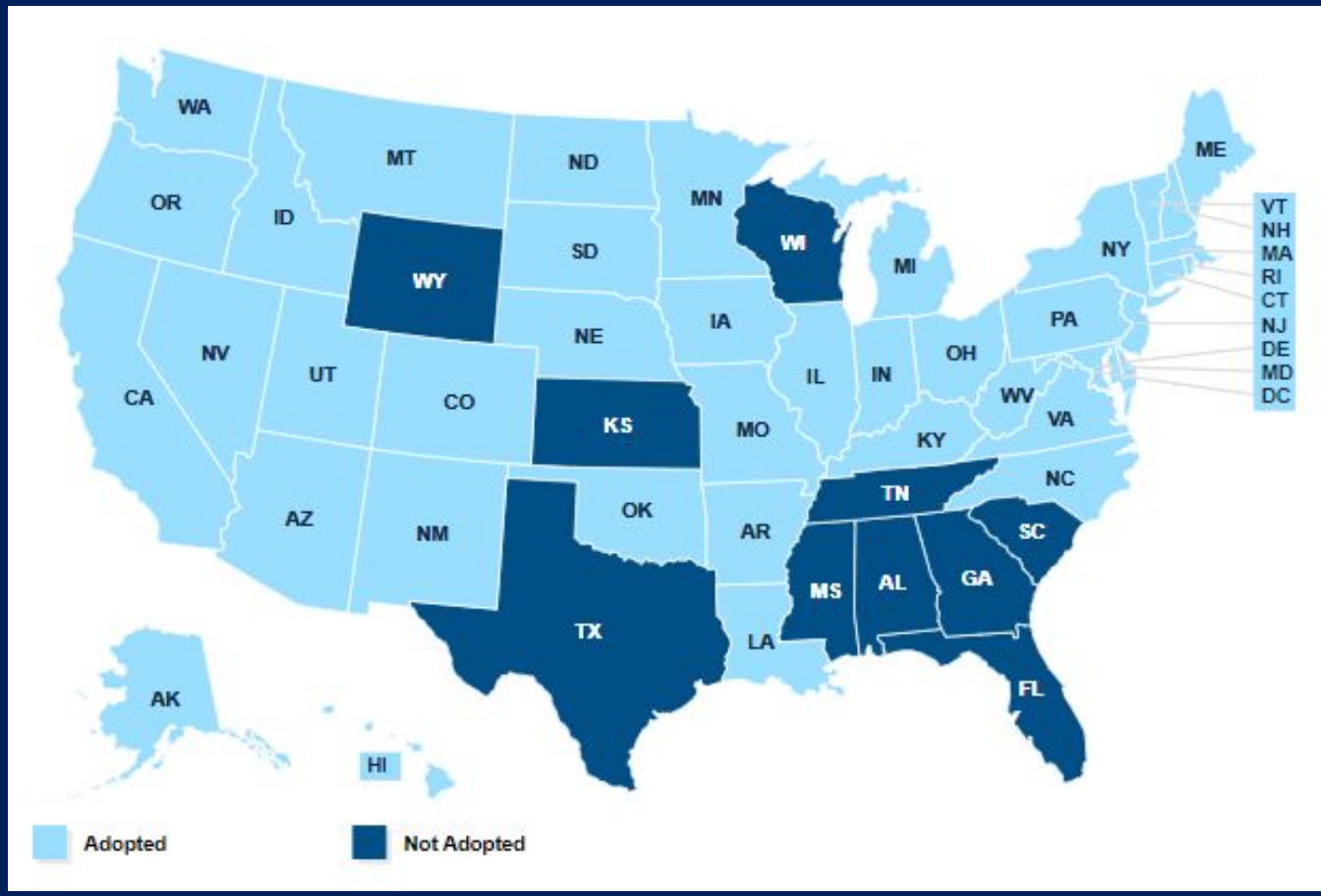

Figure: Status of State Action on the Medicaid Expansion Decision. 2023; Available from: https://www.kff.org/health-reform/state-indicator/state-activity-around-expanding-medicaid-under-the-affordable-care-act/?activeTab=map&currentTimeframe=0&selectedDistributions=status-of-medicaid-expansion-decision&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D

Health Care Access: Individual Barriers

- Unfortunately, Americans too often do not receive the care they need, or they receive care that causes harm[1]
  - Provider Bias/Stigma[2,3]
  - Poor provider-patient communication[4]
  - Lack of cultural awareness[5]
- Care can be delivered too late or without full consideration of a patient's preferences and values[1]

1. *HEALTHCARE QUALITY REPORT*, in *Highlights From the 2011 National Healthcare Quality and Disparities Reports.* 2011: Agency for Healthcare Research and Quality 2. Sabin, J.A., *Tackling Implicit Bias in Health Care.* New England Journal of Medicine, 2022. 387(2): p. 105-107. 3. Nyblade, L., et al., *Stigma in health facilities: why it matters and how we can change it.* BMC Medicine, 2019. 17(1): p. 25. 4. Schut, R.A., *Racial disparities in provider-patient communication of incidental medical findings.* Soc Sci Med, 2021. 277: p. 113901. 5. Butler M, McCreedy E, Schwer N, et al. Improving Cultural Competence to Reduce Health Disparities [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Mar. (Comparative Effectiveness Reviews, No. 170.) 1, Introduction. Available from: https://www.ncbi.nlm.nih.gov/books/NBK361130/

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Outcomes of Health Inequities[1,2]

- Ample evidence suggests that Black and Latino people receive lower-quality care compared with White people, even after insurance coverage and income are adjusted for
- Racial and ethnic minority patients are less likely to receive:
  - Evidence-based cardiovascular care
  - Kidney transplants when indicated
  - Age-appropriate diagnostic screening for breast and colon cancer
  - Timely treatment related to cancer and stroke
  - Appropriate mental health treatment
  - Adequate treatment when presenting suffering from pain

1. *Structural Racism In Historical And Modern US Health Care Policy.* Health Affairs, 2022. **41**(2): p. 187-194.2. Agency for Healthcare Research and Quality. 2019 national healthcare quality and disparities report [Internet]. Rockville (MD): AHRQ; 2020 Dec [last updated 2021 Jun; cited 2021 Dec 10]. Available from: https://www.ahrq.gov/research/findings/nhqrdr/nhqdr19/index.html Google Scholar

Comparative Health Care System Performance Scores

Note: To normalize performance scores across countries, each score is the calculated standard deviation from a 10-country average that excludes the US. See How We Conducted This Study for more detail.

Data: Commonwealth Fund analysis.

Source: Eric C. Schneider et al., *Mirror, Mirror 2021 — Reflecting Poorly: Health Care in the U.S. Compared to Other High-Income Countries* (Commonwealth Fund, Aug. 2021). https://doi.org/10.26099/01DV-H208

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High Performing Countries Solutions[1]

1. Provide for universal coverage and remove cost barriers so people can get care when they need it and in a manner that works for them
2. Invest in primary care systems to ensure that high-value services are equitably available locally in all communities to all people, reducing the risk of discrimination and unequal treatment
3. Reduce the administrative burdens on patients and clinicians that cost them time and effort and can discourage access to care, especially for marginalized groups
4. Invest in social services that increase equitable access to nutrition, education, child care, community safety, housing, transportation, and worker benefits that lead to a healthier population and fewer avoidable demands on health care

1. Eric Schneider, A.S., Michelle Doty, Roosa Tikkanen, Katharine Fields, Reginald Williams, *Health Care in the U.S. Compared to Other High-Income Countries*, in *Mirror, Mirror 2021: Reflecting Poorly*. 2021: The Commonwealth Fund.

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Clinicians

- Offer treatment and screening to eligible patients
- Follow the “no”
- Inclusive support groups to support several marginalized patient needs

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Health Care Systems

- Representation in healthcare
- Establishing coordinated care models (i.e., navigators/telehealth services/social workers) through more systematic engagement
- Disaggregating data
- Recognize that biases may be unintentionally built into current algorithms and artificial intelligence platforms
- Reviewing formulary restrictions and exclusion policies

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Researchers/Academicians

- Develop and test culturally appropriate educational materials for patients within your catchment area to improve health and health insurance literacy
- Implementation of community partnered/based participatory research

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Insurance Companies[1]

- Acknowledge and consider that racial disparities may exist in initial benefit design process
- Consider variable cost-sharing and premiums, such as on a sliding scale based on income
- Offer a preventive medication benefit with a low or $0 copay
- Use automated tools such as real-time benefit checks and electronic prior authorization to assist those with less time or fewer resources to navigate benefits and utilization management
- Identify opportunities for new or revised programs around payment incentives or disincentives for health care providers who participate in equity efforts

AMCP Partnership Forum: Racial health disparities—a closer look at benefit design. Journal of Managed Care & Specialty Pharmacy, 2021. **28**(1): p. 125-131.

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It Takes a Village

AWARENESS

GRANT FUNDING/RESEARCH

REVISING/DESIGNING FRAMEWORKS

BUILDING DEI STRATEGY/ORGANIZATIONAL REBRANDING

PROGRAM DEPARTMENT EXPANSION

COLLABORATION

Thank you

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Oncology Accelerated Drug Approvals that Lack Confirmatory Trials

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Learning Objectives

1. Explain the FDA Accelerated Approval Program process and how it applies to medications used for oncology treatment.
2. Discuss indication withdrawals and failed confirmatory trials for oncology agents.
3. Review key clinical and financial implications when reviewing oncology medications approved via the Accelerated Approval Program pathway.

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What is the Accelerate Approval Pathway?

Expedites authorization of new therapies that:

- Treat serious conditions, like cancer
- Fill an unmet medical need
- Based on surrogate endpoints, likely to predict clinical benefit (e.g., ORR, DOR)

Subject to post-marketing research, confirmatory trial(s), to confirm clinical benefit outweighs risks

Did the confirmatory trial use another surrogate endpoint?

Was the confirmatory trial done timely?

Has a confirmatory trial been done at all?

ORR = Overall Response Rate; DOR = Duration of Response; FDA. https://www.fda.gov/drugs/information-health-care-professionals-drugs/accelerated-approval-program

Background

- Accelerated Approval Pathway developed by the FDA in 1992 in response to the HIV/AIDs crisis
- Codified into law under the Food and Drug Safety and Innovation Act (FDASIA) in 2012
- Majority Accelerated Approvals granted for oncology
  - Due to the serious & life-threatening nature of cancer
  - Can improve access to life-saving or life-prolonging therapy a median of 3.1 years before available otherwise
  - Availability of surrogate clinical endpoints in oncology

FDA. Project Confirm. https://www.fda.gov/drugs/information-health-care-professionals-drugs/accelerated-approval-program. Accessed April 1, 2023.

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Oncology Surrogate Endpoints

Measure thought to predict clinical benefit but is not itself a measure of clinical benefit

OBJECTIVE RESPONSE RATE

% with partial response (PR) or complete response (CR); ≥ 30% decrease in size

DURATION OF RESPONSE

Time to disease progression or death in patients with a PR or CR

PATHOLOGICAL COMPLETE RESPONSE

Absence of cancer in tissue removed during surgery after treatment

PROGRESSION FREE SURVIVAL

Time to disease progression or death

DISEASE FREE SURVIVAL

Time to disease recurrence or death

Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics Guidance for Industry. https://www.fda.gov/media/71195/download. Accessed April 1, 2023. NCI Dictionary of Cancer Terms, https://www.cancer.gov/publications/dictionaries/cancer-terms. Accessed April 1, 2023.

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Expedited FDA Approval Programs

Approval based on surrogate endpoint (e.g. ORR) in an unmet need

Facilitates expedited review in an unmet need

6 Month application decision goal

Substantial improvement over available therapies in preliminary data

Cellular therapy addresses unmet need (e.g. CAR-T)

Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review. https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review. Accessed April 2, 2023.
Regenerative Medicine Advanced Therapy Designation.

How Do You Know it's an Accelerated Approval?

FDA states therapy is "granted accelerated approval" in indication announcement on FDA's website

On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx (Elahere, ImmunoGen, Inc.) for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha directed antibody and microtubule inhibitor conjugate. Patients are selected for therapy based on an FDA-approved test.

Accelerated approval status listed in the "Indications and Usage" Section (section1) of prescribing information

----------INDICATIONS AND USAGE----------

ELAHERE is a folate receptor alpha (FRα)-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Select patients for therapy based on an FDA-approved test. (1, 2.1)

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. (1, 14)

FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant. Accessed April 1, 2023. Elahere. Prescribing information. Immunogen; 2023.

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FDA Draft Guidance on Oncology Accelerated Approvals

- FDA recommendations (not legally enforceable) to sponsors for designing, conducting, and analyzing data for oncology accelerated approval trials
- FDA considers a randomized controlled trial (RCT) the preferred approach over single-arm studies
- Single-arm trials have been commonly used to support accelerated approval
  - Lack direct comparisons to available therapy
  - Add uncertainty to the assessment of a drug's safety/efficacy
- RCT can address limitations of single-arm trials
- Guidance goal: increase RCTs

Clinical Trial Considerations To Support Accelerated Approval of Oncology Therapeutics; Draft Guidance for Industry; Availability. https://www.fda.gov/media/166431/download. Access
April 1, 2023.

FDA Draft Guidance on Oncology Accelerated Approvals

FDA suggests 2 clinical trial approaches:

- Single randomized controlled trial
  - Supports accelerated approval & verifies clinical benefit (the “one-trial” approach)
  - Sample size should be adequately powered to detect clinically meaningful & significant improvement in endpoints for accelerated approval (e.g., ORR), plus verify clinical benefit (e.g., PFS or OS) for full approval
- 2 separate trials
  - One for accelerated approval & another confirmatory trial
  - FDA **strongly recommends** the confirmatory trial be well underway, if not fully enrolled, by the time of the accelerated approval

Clinical Trial Considerations To Support Accelerated Approval of Oncology Therapeutics; Draft Guidance for Industry; Availability. https://www.fda.gov/media/166431/download. Accessed April 1, 2023.

FDA Draft Guidance on Oncology Accelerated Approvals

- Confirmatory trial may be acceptable to evaluate the drug in the same cancer type but in another line of therapy
- Timely completion of the trial(s) intended to verify clinical benefit is critical
- Evidence *should* be provided to support the individual contribution of components to the claimed effect(s)
- Control arm *should* represent the current appropriate available therapy

Clinical Trial Considerations To Support Accelerated Approval of Oncology Therapeutics; Draft Guidance for Industry; Availability. https://www.fda.gov/media/166431/download. Accessed April 1, 2023.

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Confirmatory Trials

- Postmarketing requirements agreed to by the company & FDA, including projected date by which confirmatory trial will be completed & projected date by which the final report of these studies will be submitted to FDA
- Full approval is granted based on results of confirmatory trial
- Often conducted in earlier lines of therapy and in different combinations of drugs than original trial
    - Patients may not want to enroll in a trial with a control arm if an effective therapy is already available on the market

Hard to identify what is the confirmatory trial for an accelerated approval indication

Clinical Trial Considerations To Support Accelerated Approval of Oncology Therapeutics; Draft Guidance for Industry; Availability. https://www.fda.gov/media/166431/download. Accessed April 1, 2023.

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Top of Mind Questions

- Is the confirmatory trial underway?
- Are patients fully enrolled?
- When are the results of the confirmatory trial expected?
- What is the primary endpoint of the confirmatory trial?
  - Same surrogate endpoint as the primary study? Is it overall survival?
- What is the design of the confirmatory trial?
  - Inclusion/exclusion criteria may adjust your coverage criteria

Example: Mirvetuximab soravtansine

- Accelerated approval (AA) November 14, 2022
- Indication: Folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer patients after 1-3 prior systemic treatments

SORAYA: single-arm trial supported AA

- Sample size: 104 patients
- Prior bevacizumab required
- ORR 31.7%, median DOR 6.9 months
- Trial fully published January 30, 2023
- Median OS 15 months available March 25, 2023

MIRASOL: confirmatory trial

- RCT MIRV vs. chemo in similar patient population but no bevacizumab required
- Enrollment: ~ 453 patients
- Underway, results expected H2 2023
- Primary endpoint: PFS

FDA.
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant.

Example: Mirvetuximab soravtansine

- Accelerated approval (AA) November 14, 2022
- Indication: Folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or pri… …rior systemic treatments

Cost ~ $24,880 - $39,808/month

SORAYA: single-arm trial supported AA

- Sample size: 104 patients
- Prior bevacizumab required
- ORR 31.7%, median DOR 6.9 months
- Trial f… …l H2 2023
- Media…

MIRASOL: confirmatory trial

- RCT MIRV vs. chemo in similar patient population but no bevacizumab required
- Enrollment: ~ 453 patients

If step therapy was added requiring prior bevacizumab, that may need to be revisited if MIRASOL results are positive

FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant.

Need More Info?

- Find the NCT# and look up the study on clinicaltrials.gov
- Helpful estimated study completion dates
- More detailed inclusion/exclusion criteria

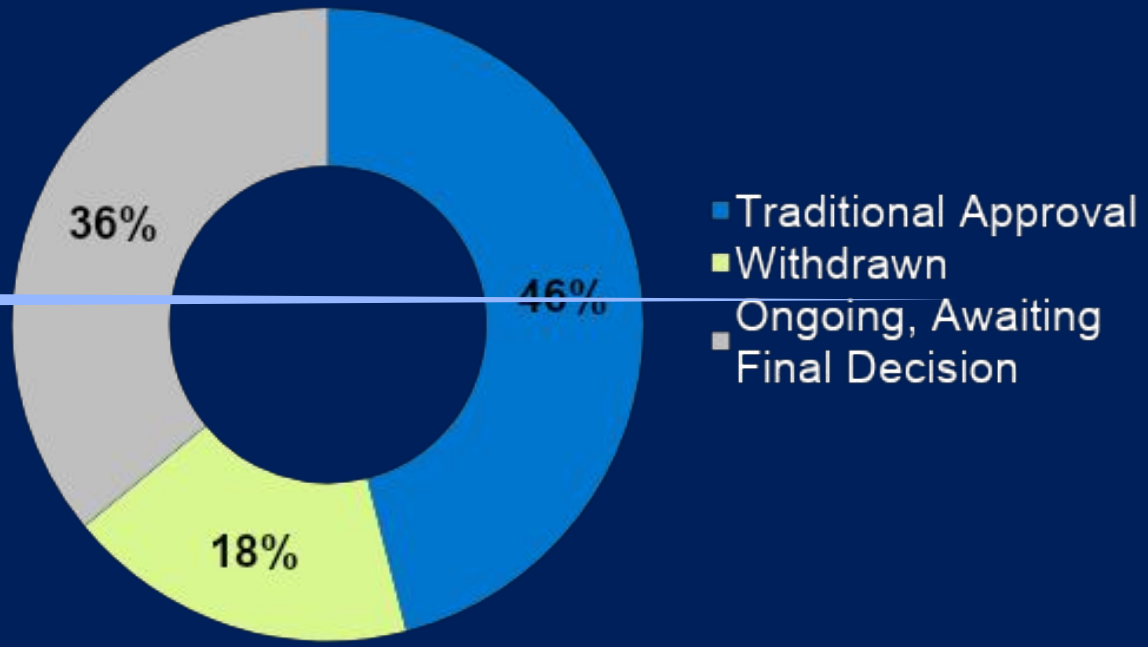
Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT04209855. Accessed April 2, 2023

Status of Accelerated Approvals

190

Total Accelerated Approvals in Oncology Since 1995

Accelerated Approval Status*



* As of April 18 2023. Oncology (Cancer) / Hematologic Malignancies Approval Notifications. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed April 1, 2023

Lack of Confirmatory Trials

- Over **1/3rd** of oncology accelerated approvals are **"ongoing"** – without confirmatory results supporting full approval
- From 2009-2022, average **2.8 years (range: 0.05 - 13.56 years)** on market without obtaining full approval
- Creates uncertainty around long-term safety & effectiveness of these drugs

Sept 2009
Pralatrexate in peripheral T-cell lymphoma

"Ongoing" oncology accelerated approvals

April 2023
Pembrolizumab + enfortumab vedotin in urothelial cancer

Oncology (Cancer) / Hematologic Malignancies Approval Notifications.
https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications.Accessed April 1, 2023

Oncology Accelerated Approvals Past 5 Years

- Only **23%** of accelerated approvals from 2018-2022 are now fully approved
- FDA approved the **most accelerated approvals in 2020** during the pandemic
- **42%** of 2018-2019 accelerated approvals are ongoing, lacking confirmatory trials supporting full approval
- Concerns confirmatory trials are not always conducted & some drugs later prove to be ineffective

*Based on approval date; Oncology (Cancer) / Hematologic Malignancies Approval Notifications. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed April 1, 2023

Ongoing Therapies Lacking Confirmatory Trials

FDA "Project Confirm"

- FDA Oncology Center of Excellence initiative to promote the transparency of outcomes related to accelerated approval in oncology
- Goal: Enhance the balance of access and verification of oncology drug benefit
- FDA provides a searchable database with information on the status of all oncology accelerated approvals, although data is as current as the humans that maintain it!

FDA. https://www.fda.gov/about-fda/oncology-center-excellence/project-confirm. Accessed April 1, 2023.

Ongoing Therapy Example: Lurbinectedin

- Accelerated approval June 15, 2020
- Indication: metastatic small cell lung cancer (SCLC) with disease progression on/after platinum-based chemo
- Efficacy (Study B-005; NCT02454972)
  - Among the 105 patients, the ORR was 35%, median DOR 5.3 months

Drug Name	Accelerated Approval (AA) Indication	AA Date	AA Post-Marketing Requirement	Original Projected Completion [1]
Zepzelca (lurbinectedin)	Treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after prior platinum-based chemotherapy.	6/15/2020	3831-1: Submit the final report and datasets for the OS and PFS analysis as determined by an Independent Review Committee from a clinical trial to confirm the clinical benefit of lurbinectedin in SCLC that may inform product labeling. This could be from the Study titled, "Phase III Randomized Clinical Trial of Lurbinectedin (PM01183)/Doxorubicin Versus Cyclophosphamide, Doxorubicin and Vincristine (CAV) or Topotecan as Treatment in Patients With SCLC Who Failed One Prior Platinumcontaining Line (ATLANTIS)".	2/28/2021

Confirmatory trial, ATLANTIS due 2/28/21 per FDA

FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/ongoing-cancer-accelerated-approvals. Accessed April 1, 2023.

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Cost ~ $20,085/month

Confirmatory trial, ATLANTIS due 2/28/21 per FDA

FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/ongoing-cancer-accelerated-approvals. Accessed April 1, 2023.

Lurbinectedin Lacks Confirmation of Benefit

ATLANTIS Confirmatory trial:

- Phase III RCT in relapsed SCLC, randomized to lurbinectedin + doxorubicin (n=307) vs chemo (topotecan (n=127) or CAV (n=179))
- Lurbinectedin + doxorubicin did not improve overall survival vs control
- mOS 8.6 months L+D vs 7.6 months control (HR, 0.97, p=0.70)

Lurbinectedin was given at a lower dose in combo therapy, remains on market due to perceived unmet need

Dec 2, 2020
ATLANTIS failure press release

Sept 13, 2021
ATLANTIS OS numbers presented

Dec 2021
Company initiated LAGOON, another confirmatory trial

Oct 14, 2022
ATLANTIS Published

Oct 24, 2022
Citizens petition to withdraw lurbinectedin denied by FDA

June 2025
LAGOON results anticipated

Endpoints News. https://endpts.com/fda-explains-why-it-wont-pull-jazzs-accelerated-approval-despite-a-failed-confirmatory-trial/. Accessed April 1, 2023

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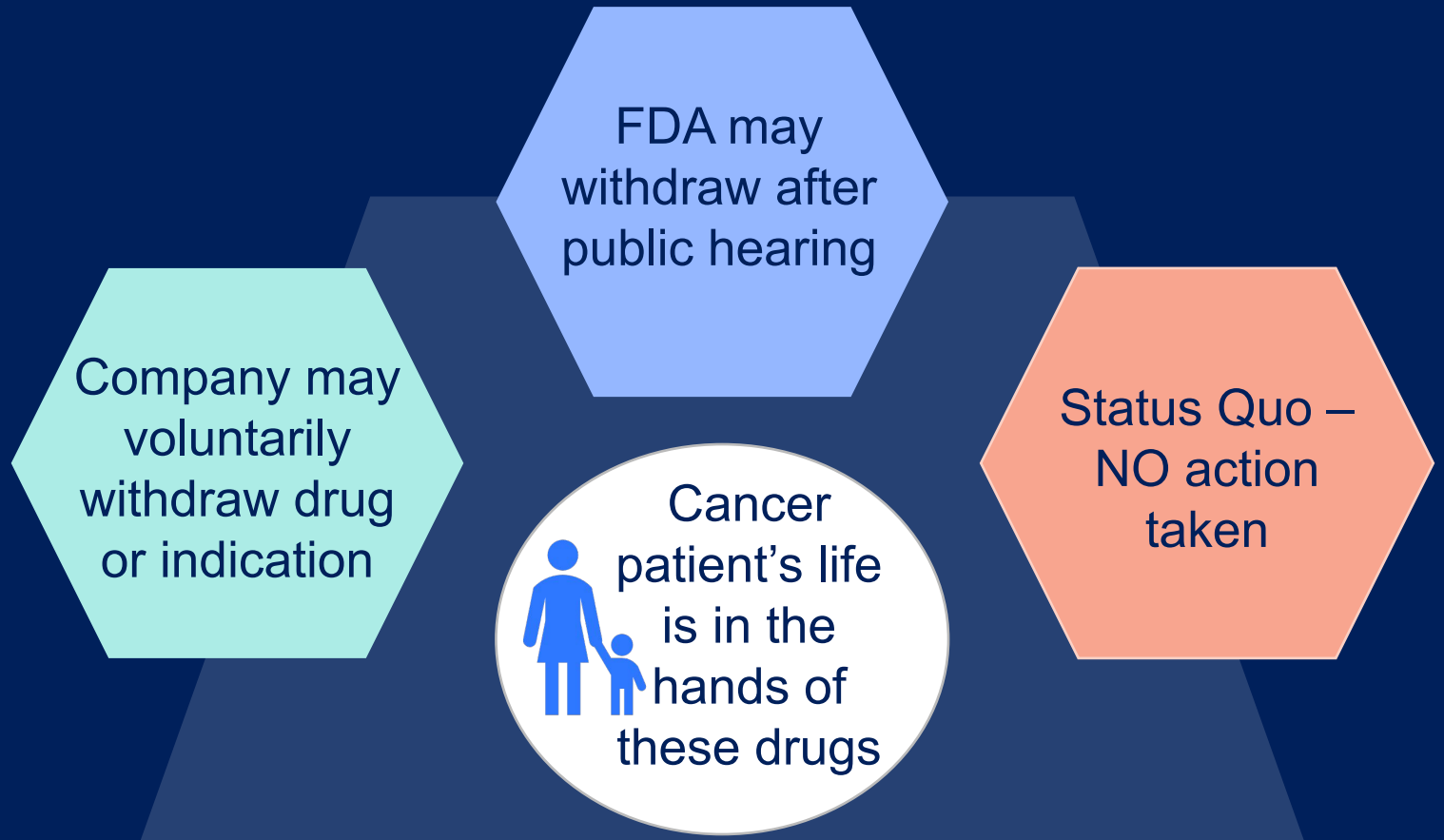
When Confirmatory Trials Fail



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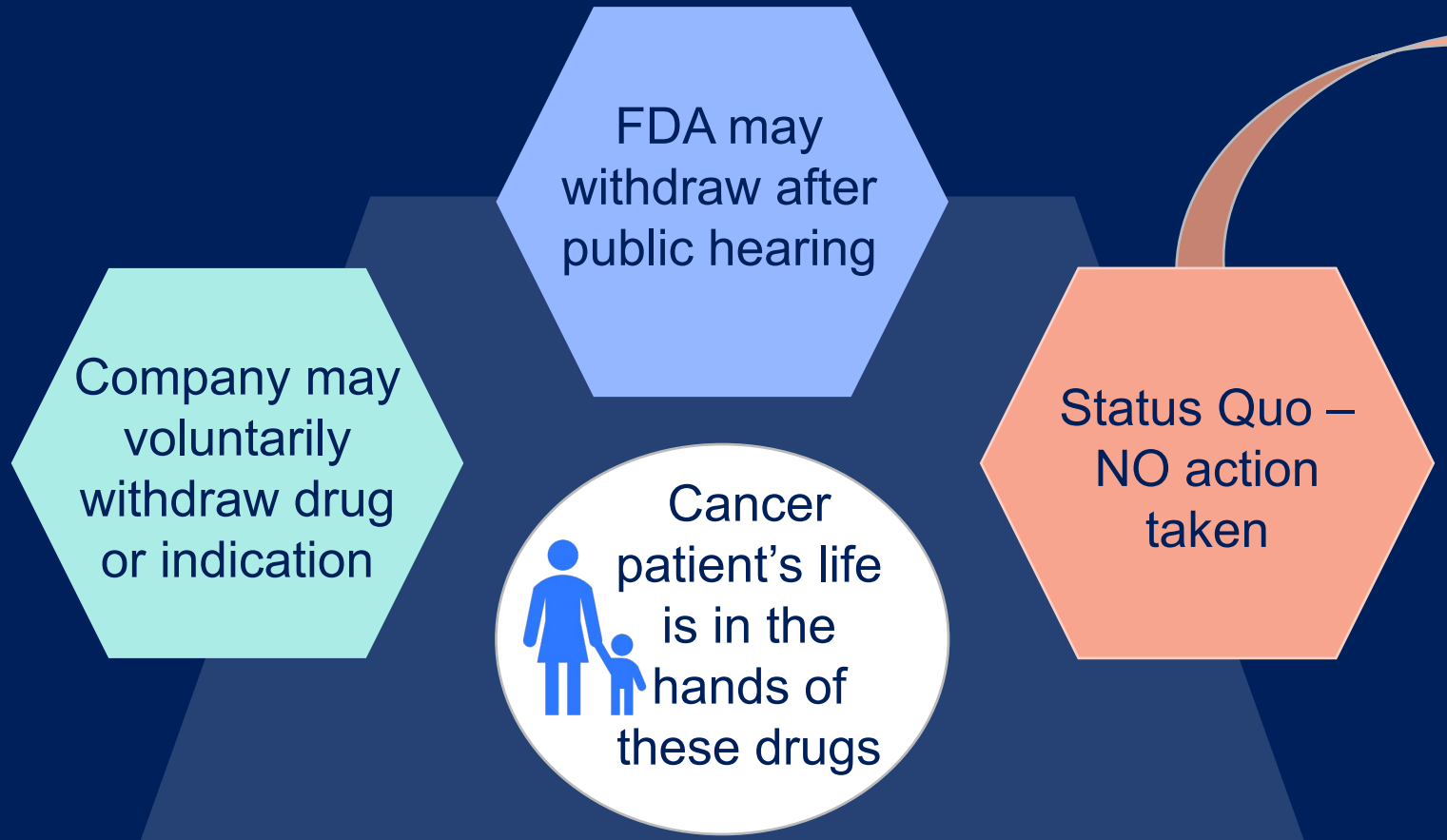
When Confirmatory Trials Fail



""Dangling" Accelerated Approval

- Negative confirmatory trial that did not verify clinical benefit yet the therapy is still on the market
- FDA may wait for another confirmatory trial to result

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Therapy Failure or Withdrawal: What's Next?

Evaluate each subsequent authorization request carefully

- Reauthorizations
  - May consider continuing auth if no disease progression
- New starts
  - Evaluate if other coverage sources continue to support the therapy, which may require coverage

Review NCCN Compendium Language

- Coverage may still be required
  - Lag in NCCN removal
  - Lag in NCCN Category 3 (deems therapy not medically necessary)
  - NCCN may continue to support therapy as Category 1or 2A

What can WE do? Learn about negative clinical trials or withdrawals
 Educate providers and offer more efficacious alternatives

Withdrawn but Still in NCCN: Pembrolizumab in SCLC

- Accelerated approval June 17, 2019
  - Indication: Metastatic small cell lung cancer (SCLC) with disease progression on/after platinum-based chemo & ≥ 1 other prior line of therapy
- Company voluntarily withdrew use March 30, 2021
  - Confirmatory KEYNOTE-604 trial met one of its dual primary endpoints of PFS but did not reach statistical significance for OS (announced Jan 2020)
- Today: Remains supported NCCN Category 2A for SCLC
  - As subsequent single agent therapy for either relapse following response or stable disease w/ primary treatment (*discouraged* if progression on maintenance atezolizumab or durvalumab), or primary progressive disease

Merck. https://www.merck.com/news/merck-provides-update-on-keytruda-pembrolizumab-indication-in-metastatic-small-cell-lung-cancer-in-the-us/. Accessed April 1, 2023. NCCN Drugs & Biologics Compendium. https://www.nccn.org/professionals/drug_compendium/content/. Accessed April 1, 2023. FDA https://www.fda.gov/drugs/resources-information-approved-drugs/withdrawn-cancer-accelerated-approvals. Accessed April 1, 2023.

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PARP Inhibitors Withdrawn: Ovarian Cancer Treatment

3 PARP inhibitors were withdrawn in 2022 for later line **treatment** of advanced ovarian cancer after data found a 31 - 33% increased risk of death vs chemo

	FDA Approval	Withdrawal	
Olaparib	12/19/2014*	2022	= 7.7 yrs
Rucaparib	12/19/2016*	2022	= 5.5 yrs
Niraparib	10/23/2019	2022	= 2.9 yrs

Cost ~ $19,064 - $31,121/month

- Today these agents are used as **maintenance** therapy in earlier lines, limiting the impact of these withdrawals
- What about the thousands of patients that received these agents for treatment?
- How many millions in healthcare dollars were spent on suboptimal care?

*Accelerated Approval. Medscape. https://www.medscape.com/viewarticle/981369. Accessed April 1, 2023

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Practical Tips: Learning About Failures/ Withdrawals

- Browse biotech websites (e.g., FiercePharma.com)
- Browse oncology-specific websites (e.g., OncLive.com)
- Sign up for email alerts (FDA, ASCO Post)
- Read press releases
- Talk with the colleagues you work with, educate each other
- Communicate openly with pharmaceutical colleagues

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Accelerated Approvals: Take the Good with the Bad

Advantages

- Faster time to market for lifesaving or life prolonging therapies
- Shorter clinical trials
- Accelerated scientific advances
- Nearly half of accelerated approvals have gone on to full approval

Limitations

- Questionable value
- Small sample sizes
- Response rates may not predict long-term outcomes
- Multiple agents may obtain similar accelerated approval indication
- Risk of withdrawal
- Risk of financial toxicity for potentially suboptimal therapy

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Managed Care Strategies for Accelerated Approvals

KEEP UP WITH LATEST DATA

Monitor data as it constantly evolves in oncology with positive and negative results

EDUCATE

Communicate latest data with internal clinical teams and educate providers of negative data/withdrawals

DRAFT DETAILED CRITERIA

Consider drafting more detailed coverage criteria as the value of the therapy may not be fully understood

MAINTAIN CRITERIA

May need to remove indication or adjust criteria based on withdrawal or full approval

INTERVENE IF BETTER OPTION

Engage providers to discuss patient-tailored alternatives in lieu of therapy with low value

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Managed Care Strategies for Accelerated Approvals

- Consider drafting prior authorization criteria closer to clinical trial inclusion/exclusion criteria

Consider adding ECOG performance status

Evaluate WHAT data can be readily collected during PA

Add drugs to criteria if included or excluded in trial

- Accelerated approval indications may not be added to clinical oncology pathways or value-based care provider incentives
- ?Outcomes-based contracting?

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Conclusion

- The FDA's accelerated approval process in oncology can help bring drugs to market faster that meet an unmet clinical need
- The accelerated approval pathway is widely used in oncology, many times with limited data available at the time of approval and unknown long-term outcomes
- Managed care pharmacists must diligently access the value of an oncology therapy that has obtained accelerated approval and monitor data releases for confirmatory trial results

Oncology Accelerated Drug Approvals that Lack Confirmatory Trials

Laura R. Bobolts, PharmD, BCOP
SVP, Clinical Strategy and Growth
OncoHealth

Thank you for attending the AMCP Florida 2nd Annual Day of Education!