Modulator Treatments for Cystic Fibrosis: Effectiveness and Value

Public Meeting — August 27, 2020

Meeting materials available at: https://icer-review.org/topic/cystic-fibrosis/

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Why are we here today?

- What happens the day these treatments are approved by the FDA?
- Patients can have difficulty accessing drugs
  - Coverage eligibility
  - Costs (out of pocket and insurance premiums)
- What happens to patients and others in the health care “system”

The personal trade-offs when a dollar spent on health insurance can't be spent on something else

"I live in a constant state of fear"
Whitney Whitman, Alaska

"We don't have enough money to go out to eat, or take my grandchildren to the movies, much less pay for health insurance"
Tara Sullivan, West Virginia

"We're not poor people but we can't afford health insurance,"
Mimi Owens, Louisiana

"My wife is a little more antsy than I am about not having insurance, it worries her"
Gustavo Bendeck, Texas

"If we can control our health-care costs for a couple of years, the difference that makes on our household income is phenomenal"
Keith Buchanan, North Carolina

"Every single decision that you make has to be very carefully calculated so that your finances don't fall apart"
Corinne Bobbie, Arizona

"This isn't just philosophical or moral support, it is a financial issue for my business. Turnover costs are so high, and we need to be able to retain employees. We do whatever we can to create a stress-free and healthy work environment, but we often lose people to larger companies that have the scale to provide health care"
Luke Breen, Minnesota

"I'm almost 60 years old and I can't go see a doctor"
Tara Sullivan, West Virginia

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https://www.bloomberg.com/news/features/2018-03-26/why-some-americans-are-risking-it-and-skipping-health-insurance 3/20
https://www.minnpost.com/community-voices/2019/12/employer-centered-health-insurance-is-hurting-small-businesses/

The personal trade-offs when a dollar spent on health insurance can't be spent on something else

Gustavo Bendeck, Lubbock, Texas

Gustavo is a 62-year-old physician assistant from Lubbock, Texas. He and his wife, Shirley, received a letter from their health insurance provider telling them that their $1,000-a-month premium was more than doubling to $2,200. Shirley asked Bendeck what would happen next.

"I'm not going to pay this amount of money," he told her. He looked for other comparable plans, but most wanted about the same. He makes about $117,000 a year after taxes, he said. He and his wife are healthy, so they decided to chance it.

Life hasn't changed too much since, though they have a little more free cash even though the prescriptions they both take cost more without insurance. Shirley takes a cholesterol drug and a blood-pressure treatment that together cost about $350 a month, more than double when they had insurance coverage. Gustavo takes a blood-pressure drug that costs $70 to $80 for a 90-day supply, compared to $20 when he was insured.

"My wife is a little more antsy than I am about not having insurance, it worries her," Bendeck said. "What keeps me calmer is that there's a lot of us out there that do not have insurance."

The Whitmans, Bird City, Alaska

The Whitman family last had health insurance in 2016. When they last looked, the cheapest plan Whitman could find was $1,734 per month, with a deductible of $10,500 for the family of four. She splits her time between mental health counseling and mediating legal disputes, such as divorces. She made about $110,000 before taxes in 2016.

This lack of coverage means they delay medical care, such as waiting until the 7-year-old daughter had been sick for almost two weeks before taking her to the pediatrician or taping up husband Jason's finger when he had broken it. Jason's knee injury and concussion also went untreated..

It's a tradeoff they are not entirely comfortable:

"I live in a constant state of fear," Whitney Whitman said.

Luke Breen, Minneapolis, Minnesota

Luke has been a small business owner for 25 years and has seven year-round employees with an additional nine summer seasonal employees. One of his biggest challenges, and one of the biggest challenges for small business owners across America, is the inability of his business to afford health care for my employees.

For small businesses, the ability to complete in their own markets is dictated by outside industries: health insurance markets. Luke's best employee recently left to take another job, because she turned 27 and was no longer eligible to be on her parents' health insurance. She didn't want to leave, but she needed employer-funded health care, so she truly had no choice.

https://www.bloomberg.com/news/features/2018-03-26/why-some-americans-are-risking-it-and-skipping-health-insurance 3/20
https://www.minnpost.com/community-voices/2019/12/employer-centered-health-insurance-is-hurting-small-businesses/

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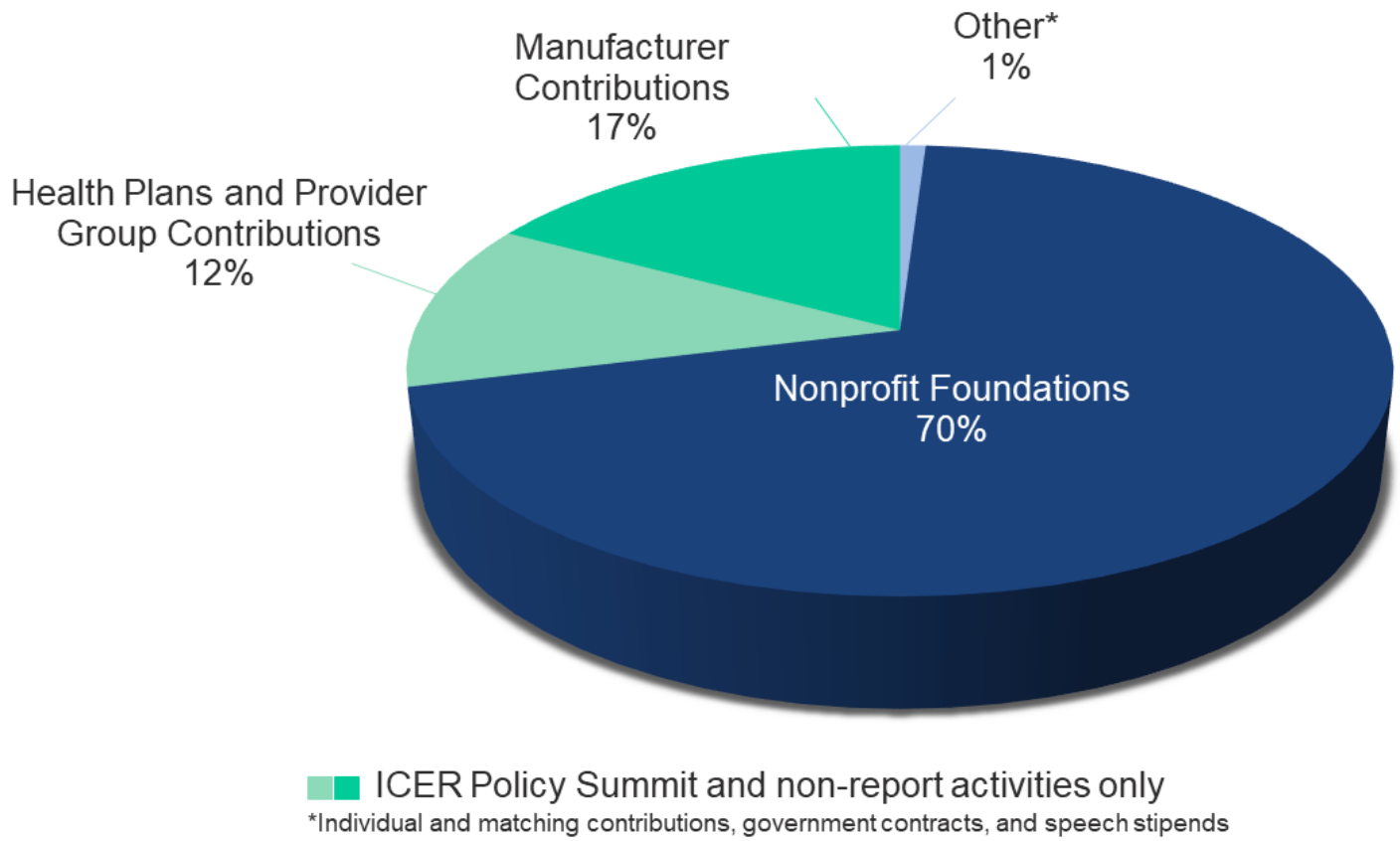
Organizational Overview

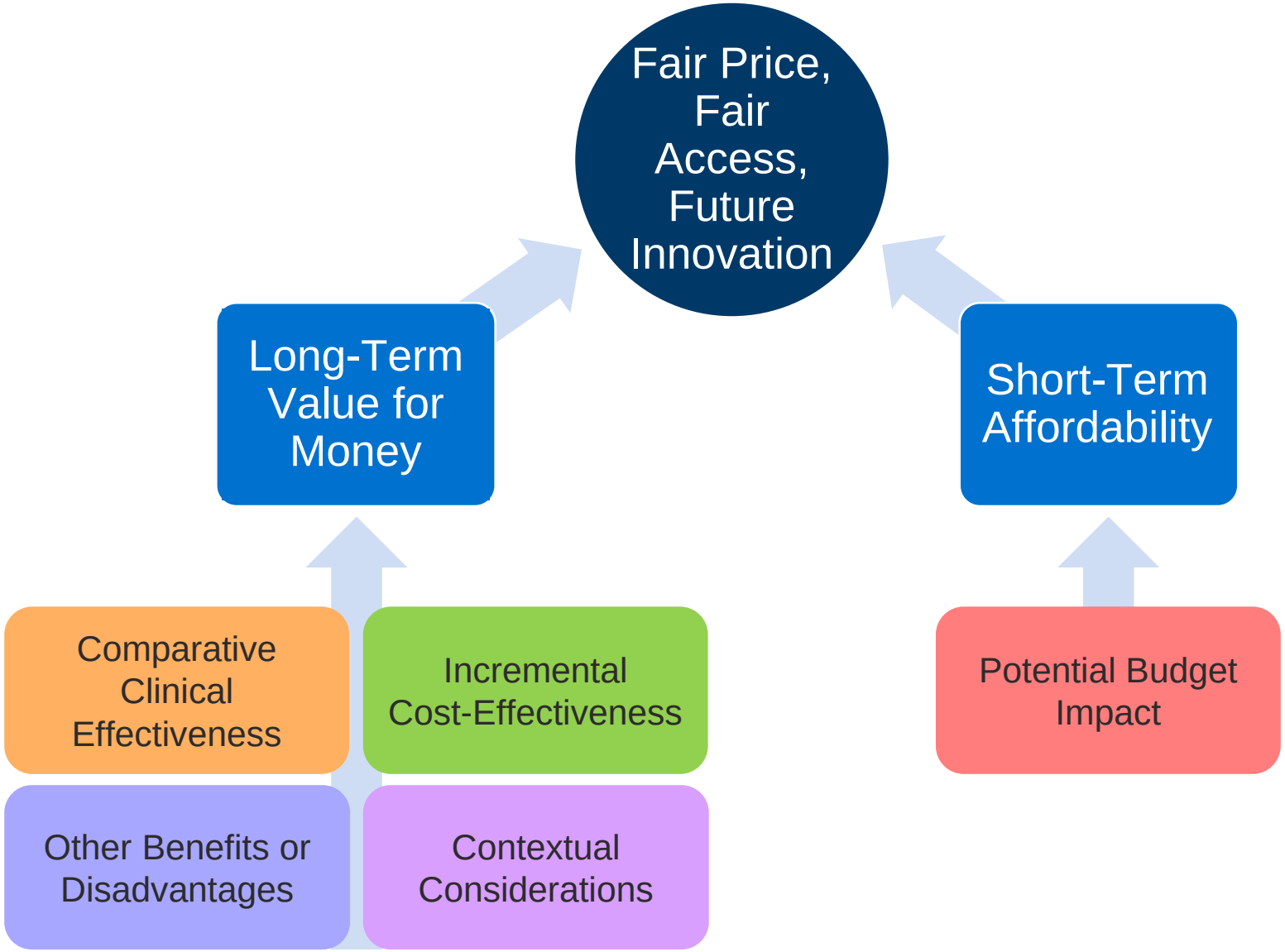
- The California Technology Assessment Forum (CTAF)
- The Institute for Clinical and Economic Review (ICER)

Sources of Funding, 2020
https://icer-review.org/about/support/



How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- UCSF and internal ICER staff: evidence analysis
- University of Minnesota: cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - Manu Jain, MD, MSc Professor, Department of Medicine (Pulmonary and Critical Care); Department of Pediatrics, Northwestern University
  - Carlos Milla, MD, Professor of Pediatrics, Pulmonology, Stanford University School of Medicine
  - Brian P. O'Sullivan, MD, Professor of Pediatric Pulmonology, Geisel School of Medicine, Dartmouth College
  - Cystic Fibrosis Foundation
- How is the evidence report structured to support CTAF voting and policy discussion?



Agenda

Time	Activity
9:00 am—9:10 am PT	**Meeting Convened and Opening Remarks** Steven D. Pearson, MD, MSc
9:10 am—10:00 am PT	**Presentation of the Evidence** Jeffrey A. Tice, MD, University of California, San Francisco Karen Kuntz, ScD, University of Minnesota
10:05 am – 10:45 am PT	**Public Comments and Discussion**
10:45 am—11:00 am PT	**Break**
11:00 am—11:45 am PT	**CTAF Deliberation and Vote**
11:45 am—12:30 pm PT	**Lunch**
12:30 pm—1:30 pm PT	**Policy Roundtable**
1:30 pm—2:00 pm PT	**Reflections from CTAF and Closing Remarks**
2:00 pm PT	**Meeting Adjourned**

Clinical Experts

Manu Jain, MD, MSc Professor, Department of Medicine (Pulmonary and Critical Care); Department of Pediatrics, Northwestern University

- *Dr. Jain has received in excess of $5,000 in advisory fees and research funding from Vertex Pharmaceuticals. He is also on the Speaker's Bureau of Vertex Pharmaceuticals and Gilead Sciences*

Carlos Milla, MD Professor of Pediatrics, Pulmonology, Stanford University School of Medicine

- *Dr. Milla has received in excess of $5,000 in advisory fees and research funding from Vertex Pharmaceuticals, Proteostasis Inc., and Eloxx Pharma. He also receives advisory board honorarium from Vertex Pharmaceuticals*

Patient Experts

Mary Dwight, Senior Vice President of Policy and Advocacy, Cystic Fibrosis Foundation

- *CFF has received charitable contributions and/or fees for service in excess of $5,000 from health care companies including Vertex Pharmaceuticals.*
- *CFF has the option to acquire equity interests >$10,000 from a pharmaceutical company unrelated to this report.*
- *CFF has entered into therapeutic development award agreements that may result in intellectual property and royalty rights from various pharmaceutical companies.*

Mariah Hanley, JD, Individual with CF

- *No financial conflicts of interest to disclose*

Don Maurice Kreis, JD, MS, Parent of Individual with CF

- *No financial conflicts of interest to disclose*

Presentation of the Clinical Evidence

Jeffrey A. Tice, MD

Division of General Internal Medicine

University of California San Francisco

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Key Review Team Members

Patty Synnott, MALD, MS, ICER (former)

Noemi Fluetsch, MPH, ICER

Avery McKenna, **BS,** ICER

Special thanks to **Judith Walsh, MD, MPH**, UCSF

Disclosures:

We have no conflicts of interest relevant to this report.

CF Pathogenesis

- Mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (*CFTR*) gene
- CFTR protein is important for chloride and other anion transportation across cell membranes
- >1,800 *CFTR* mutations associated with CF
- Mutations in each of the 2 copies of the *CFTR* gene to have disease

Clinical Presentation: Multi-system

- Lungs
  - Chronic cough
  - Infections throughout life
  - Progressive decline in lung function
  - End stage disease: lung transplant or death
- Pancreas
  - Pancreatic insufficiency / poor growth
  - CF-related Diabetes
- Skin, liver, intestines, fertility
- Quality of life, anxiety, depression

Disease Management

- Early diagnosis and treatment has greatly improved quality and length of life
- Best supportive care
  - Chest PT, inhaled therapies
  - Pancreatic enzymes and nutritional support
  - Insulin
  - Antibiotics
- CFTR modulators

CFTR Modulators

- Interventions (all with best supportive care)
  - **Trikafta® (elexacaftor/tezacaftor/ivacaftor, Vertex Pharmaceuticals, Inc.) – focus of this update**
  - Symdeko® (tezacaftor/ivacaftor, Vertex)
  - Orkambi® (lumacaftor/ivacaftor, Vertex)
  - Kalydeco® (ivacaftor, Vertex)
- Comparators
  - Best supportive care
  - The CFTR modulators when indicated for the same population

Population

- 4 populations
  - Population 1: Individuals with CF mutations with FDA indications for Kalydeco
  - Population 2: Individuals with CF homozygous for the *F508del* mutation
  - Population 3: Individuals with CF heterozygous for the *F508del* mutation and a residual function mutation
  - Population 4: Individuals with CF heterozygous for the *F508del* mutation and a minimal function mutation
- 90% of individuals with CF have mutations eligible for Trikafta

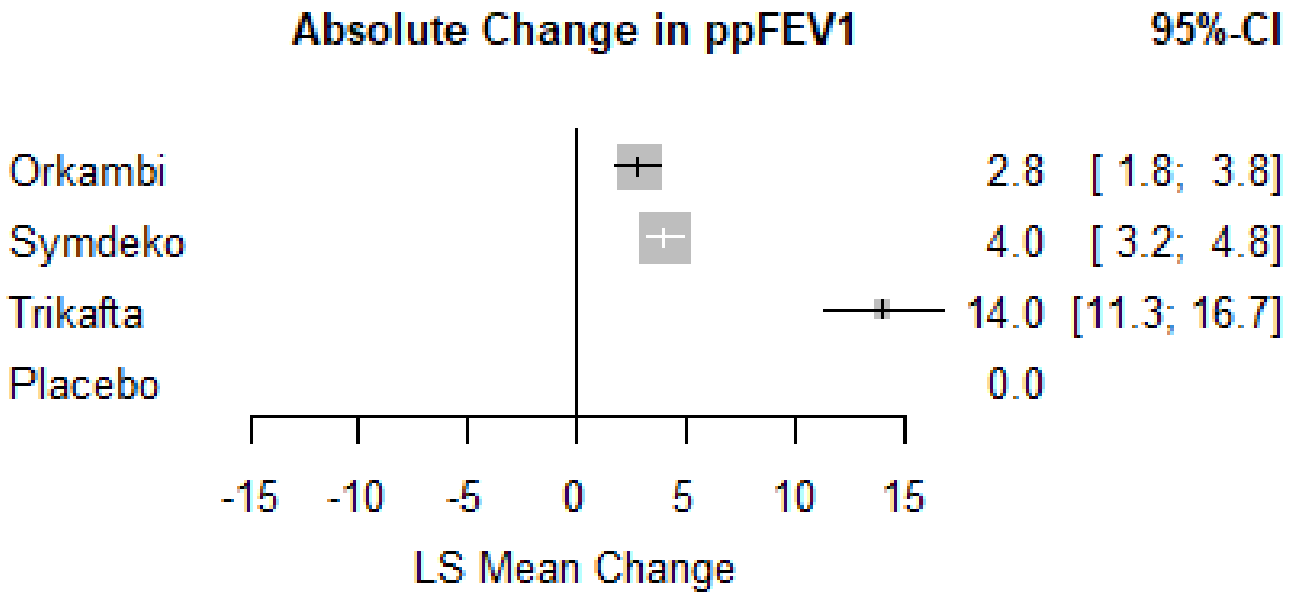
Outcomes

- Pulmonary
  - Percent predicted forced expiratory volume 1 sec (ppFEV$_1$)
  - Pulmonary exacerbations
- Quality of life
  - CF Questionnaire, Revised (CFQ-R) Respiratory Domain
- Other
  - Weight and growth
  - Death, hospitalizations, lung transplantation
  - Adverse events
  - Additional outcomes: Fertility, pancreatitis, functional status, mental health, work/school attendance, social function, finances, caregiver/family burden

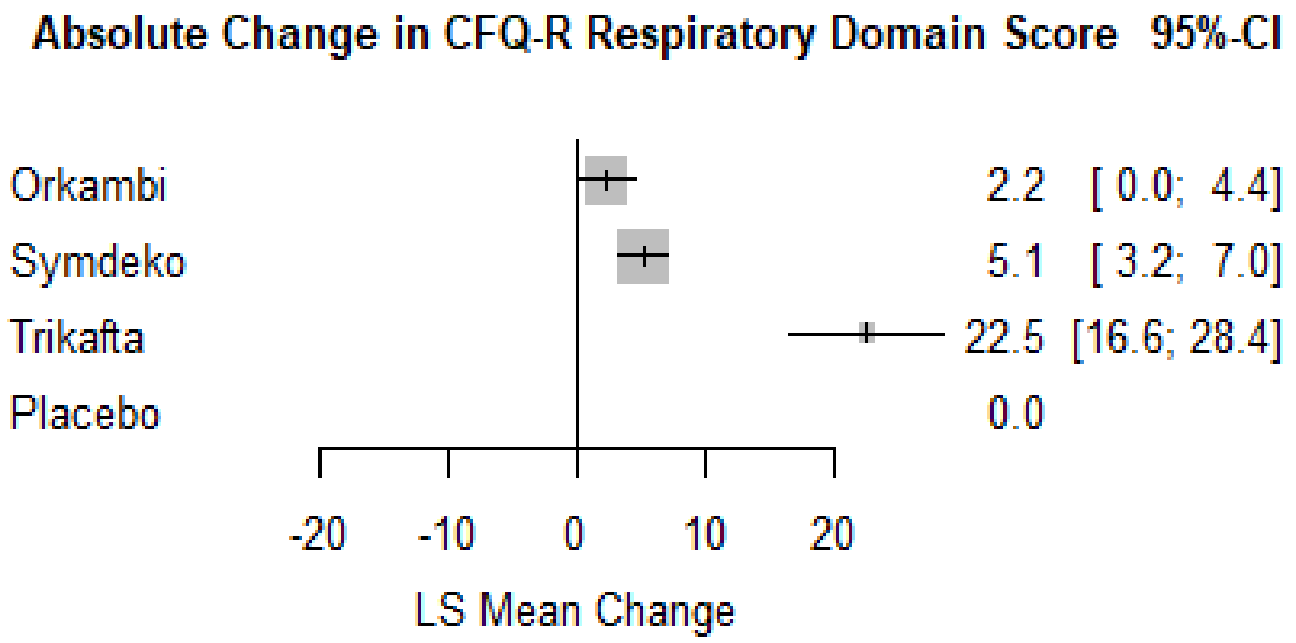
Population 2: Homozygous *F508del* Trikafta

- Pivotal Trial: Head to Head with Symdeko
  - 107 participants, age ≥ 12 years
  - 4-week run-in with Symdeko, 4-week trial
  - Good quality
  - Primary outcome: absolute change in $ppFEV_1$
    - + 10.0% (95% CI 7.4-12.6) versus Symdeko
  - Respiratory domain CFQ-R (MCID 4 points)
    - + 17.4 points (11.8-23) versus Symdeko

Population 2: Homozygous *F508del* Network Meta-Analysis ppFEV$_1$



Population 2: Homozygous *F508del*
Network Meta-Analysis Respiratory QOL



Population 3: Heterozygous *F508del* / Residual Function

- No data for Trikafta except recent press release without details of the results in this population
- Trikafta = Symdeko + elexacaftor
- No additional AEs seen with Trikafta
- Expect benefits to be at least as good as those of Symdeko and likely greater

Population 4: Heterozygous *F508del* / Minimal Function

- Pivotal Trial: Trikafta versus placebo for 24 weeks
  - N = 403, ages ≥ 12 years
  - Good Quality
  - Primary outcome: absolute change in $ppFEV_1$
    - + 14.3% (95% CI 12.7-15.8)
  - Respiratory domain CFQ-R
    - +20.2 points (95% CI 17.5-23.0)
  - Pulmonary exacerbations
    - RR 0.37 (95% CI 0.25-0.55)

Harms with CFTR Modulators

- Adverse events generally mild or self-limited
  - No reported deaths ascribed to drugs
- Trikafta
  - SAE: rash – did not discontinue therapy
  - Drug discontinuation due to adverse event: 1%

Uncertainties and Controversies

- CF: lifelong illness, Trikafta trials 4 and 24 weeks
  - Uncertain long-term benefits and harms
- $ppFEV_1$ is a surrogate measure of CF severity and change in $ppFEV_1$ does not fully capture the benefits of therapy
- Heterogeneity of disease by gene mutation combination and age at initiation of therapy likely impact the magnitude of benefit
- Reduction in disease management therapies may be possible
- Patients ≤12 years of age

Potential Other Benefits and Contextual Considerations

- Trikafta **may reduce the burden** of therapy, caregiver/family burden, school/work, social stressors
- Trikafta is the **first effective modulator therapy** for patients with *F508del* / minimal function
- CF is **severe** with large impacts on both length and QOL
- CF has a **high lifetime burden of illness**
- **Uncertainty** remains about the lifetime impact of Trikafta

Public Comments Received

- Evidence ratings for Trikafta were downgraded for limited evidence
  - Most ratings were “A”
  - No penalties were given for limited evidence in a rare disease where large trials are difficult

Summary

- Among those ≥12 years old, Trikafta
  - Substantially increases ppFEV$_1$
  - Markedly improves respiratory-related QOL
  - Markedly reduces the rate of pulmonary exacerbations
- Harms appear to be non-serious and self-limited
- Uncertainties
  - Long term benefits and harms
  - Safety and efficacy in patients younger than 12 years of age

Evidence Ratings

- Trikafta for homozygous *F508del*
  - **“A”** (**superior**, high certainty of substantial benefit)
- Trikafta for heterozygous *F508del* / residual function
  - **”C++”** (**comparable, small, or substantial net heath benefit** compared with Symdeko)
  - "**B+**" (**incremental or better**, moderate certainty of small or substantial benefit, high certainty of at least a small benefit compared with BSC). No data yet, but Symdeko B+
- Symdeko for heterozygous *F508del* / minimal function
  - **“A”** (**superior**, high certainty of substantial benefit)

Questions?

Presentation of the Evidence and Economic Modeling

Karen M. Kuntz, ScD

Division of Health Policy and Management

University of Minnesota, School of Public Health

Key Review Team Members

- **Kael Wherry, PhD**, University of Minnesota, School of Public Health
- **Rick Chapman, PhD**, ICER

Disclosures:

We have no conflicts of interest relevant to this report.

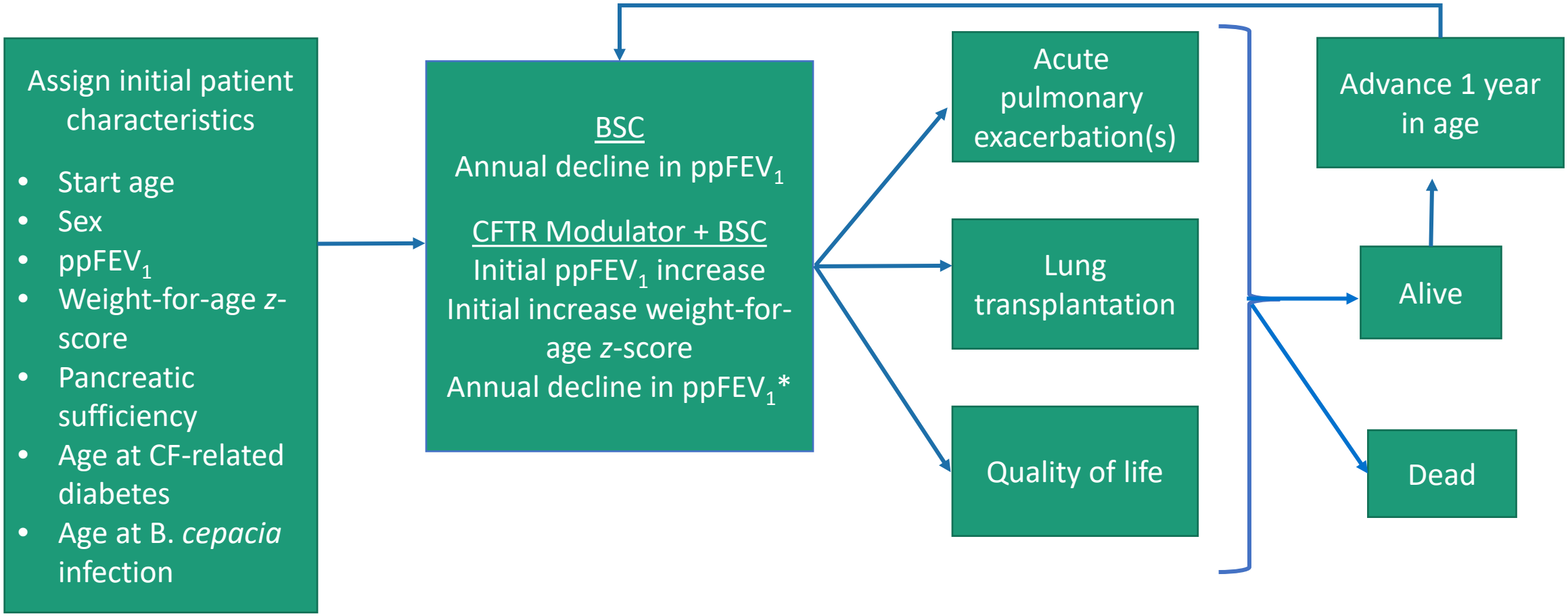
Objective

To compare lifetime health effects, costs, and cost-effectiveness of CFTR modulator treatment plus best supportive care versus best supportive care alone for CF patients

Methods Overview

- **Model**: Updated previously developed *de novo* discrete-time microsimulation models
- **Setting**: United States
- **Perspective**: Health Care Sector
- **Time Horizon**: Lifetime
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: Annual
- **Outcomes**: Cost per quality-adjusted life year (QALY) gained; cost per life year gained (LYG); cost per equal value LYG (evLYG); cost per acute pulmonary exacerbation averted

Model Schematic

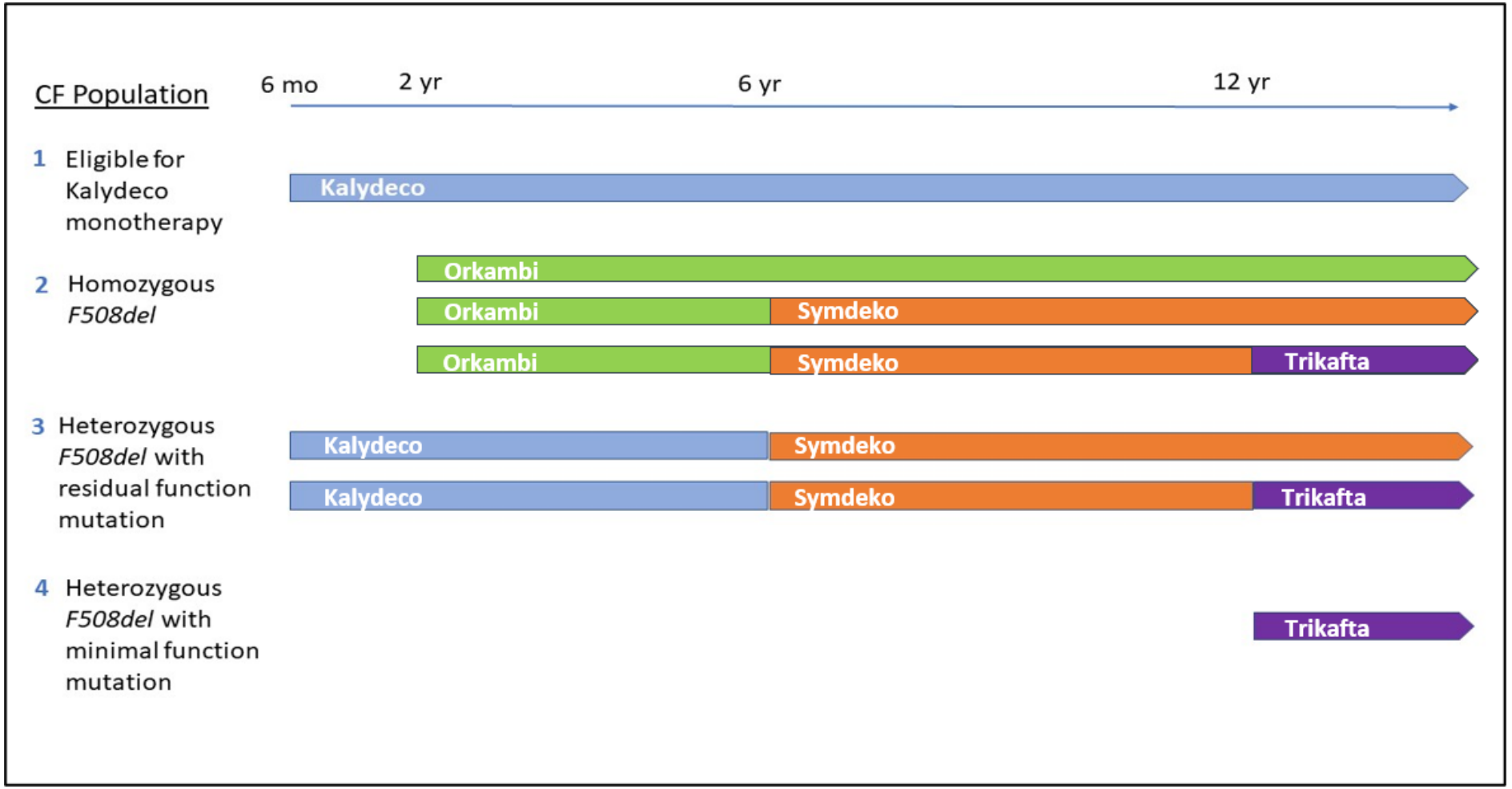


*Annual decline in $ppFEV_1$ begins two years after treatment and is half that of BSC

Key Model Assumptions

- The intensity of best supportive care varies by lung function category (ppFEV$_1$ ≥70%, 40%-69%, <40%).
- CFTR modulator drugs decrease the annual number of acute pulmonary exacerbations both through the increase in ppFEV$_1$ as well as an independent effect.

Populations and CFTR Modulators



All treatments are in addition to best supportive care

Key Model Inputs: Direct Costs by Disease Severity

Costs (2019 US$)	$ppFEV_1$ ≥70%	$ppFEV_1$ 40%-69%	$ppFEV_1$ <40%
Disease Management	$30,258	$39,914	$68,240
PEx (age <18)	$63,204	$100,143	$148,368
PEx (age 18+)	$57,273	$91,037	$130,460
Lung Transplant	---------- $948,437 ----------		
Post-Transplant (Year 1)	---------- $365,773 ----------		
Post-Transplant (Year 2+)	---------- $131,738 ----------		

Key Model Inputs: Annual CFTR Modulator Costs

CFTR Modulator Drug	Annual Drug Cost
Kalydeco	$311,704
Orkambi	$272,623
Symdeko	$292,200
Trikafta	$311,741

Key Model Inputs: Utilities

$ppFEV_1$	EQ-5D Utility
>90	0.920
80-89	0.873
70-79	0.801
60-69	0.765
50-59	0.765
40-49	0.729
30-39	0.692
20-29	0.653
<20	0.625

Base-Case Results: Lifetime Health Outcomes (undiscounted)

Treatment	Average Number of PEx	% With Lung Transplant
Population 2 – Homozygous for the *F508del* Mutation		
BSC	21.13	32.9%
Trikafta plus BSC	10.51	3.2%
Population 3 – Heterozygous *F508del* with Residual Function Mutation		
BSC	23.99	36.8%
Trikafta plus BSC	11.20	3.1%
Population 4 – Heterozygous *F508del* with Minimal Function Mutation		
BSC	18.31	32.5%
Trikafta plus BSC	8.90	5.9%

PEx: acute pulmonary exacerbation

Base-Case Results: Incremental Effectiveness Measures (discounted)

Treatment	QALYs Gained	evLYG
Population 2 – Homozygous for the *F508del* Mutation		
Trikafta plus BSC vs. BSC	5.49	6.15
Population 3 – Heterozygous *F508del* with Residual Function Mutation		
Trikafta plus BSC vs. BSC	6.08	7.03
Population 4 – Heterozygous *F508del* with Minimal Function Mutation		
Trikafta plus BSC vs. BSC	5.04	6.06

QALYs: quality-adjusted life years; evLYG: equal value life years gained; BSC: best supportive care

Base-Case Results: Incremental Costs (2019 US$)

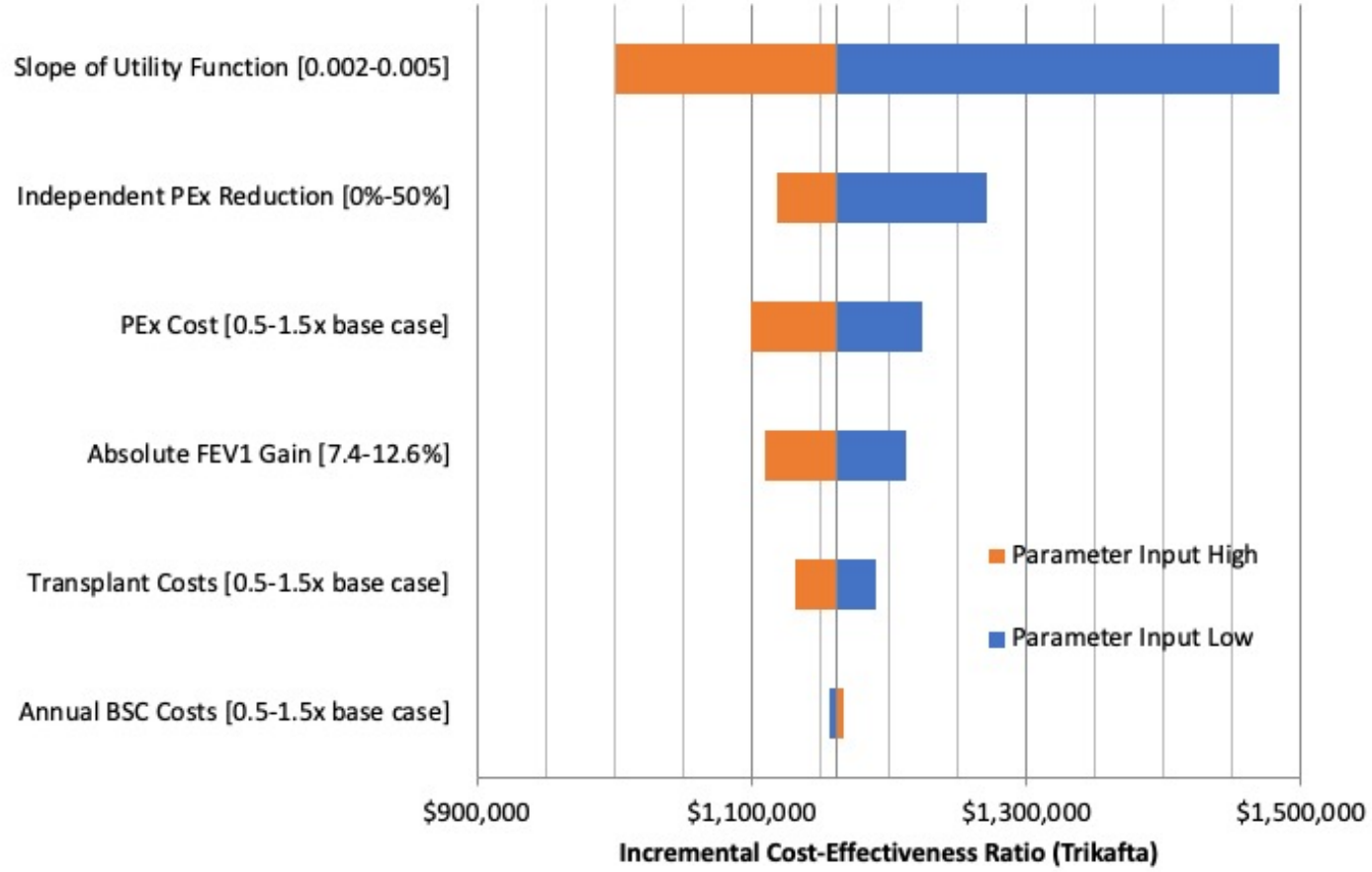
Treatment	Trikafta	Total
Population 2 – Homozygous for the *F508del* Mutation		
Trikafta plus BSC	$7,339,000	$6,385,000
Population 3 – Heterozygous *F508del* with Residual Function Mutation		
Trikafta plus BSC	$7,743,000	$6,687,000
Population 4 – Heterozygous *F508del* with Minimal Function Mutation		
Trikafta plus BSC	$6,310,000	$5,317,000

Base-Case Incremental Cost-Effectiveness Results

Drug vs BSC (Population)	Cost Per QALY Gained	Cost Per evLYG
Kalydeco (Eligible for Kalydeco only)	$1,370,000	$1,180,000
Orkambi (Homozygous for *F508del* mutation)	$1,480,000	$1,360,000
Symdeko (Homozygous for *F508del* mutation)	$1,380,000	$1,200,000
Trikafta (Homozygous for *F508del* mutation)	$1,160,000	$1,040,000
Symdeko (Heterozygous *F508del* / residual function)	$1,340,000	$1,100,000
Trikafta (Heterozygous *F508del* / residual function)	$1,100,000	$951,000
Trikafta (Heterozygous *F508del* / minimal function)	$1,050,000	$877,000

QALY: quality-adjusted life year; evLYG: equal value life year gained

One Way Sensitivity Analyses (Trikafta, Population 2)



Scenario Analyses: Modified Societal Perspective

- Incorporated lost productivity for patients unable to work full time as well as lost productivity for patients and caregivers due to acute pulmonary exacerbations.
  - Population 2: $1.15 million per QALY
  - Population 3: $1.09 million per QALY
  - Population 4: $1.04 million per QALY

Scenario Analyses: Curative Scenario

- Provided an extreme favorable cost-effectiveness ratio for Trikafta
- Assumed patients live a life span and experience quality of life similar to US population
- Assumed 100% adherence with medication starting at 6 months of age and the only CF costs were Trikafta costs
- Incremental cost-effectiveness ratio was $612,000 per QALY at current prices

Limitations

- Modeled lifetime outcomes derived from short-term trial outcomes
- As with any surrogate marker of disease, ppFEV$_1$ is not a perfect marker
- We did not have trial-based measures of CFTR modulator benefit on utilities

Comments Received

- Lack of long-term real-world data on these therapies, seriously limiting the utility and reliability of the report.
  - Models are most useful in this situation where assumptions can be explored with sensitivity analysis.
- The disease-management costs derived are not valid estimates for current standard of care.
  - We did need to incorporate several assumptions in our cost derivations but received confidential confirmation from two private payers that our annual costs are in line with their observed costs.

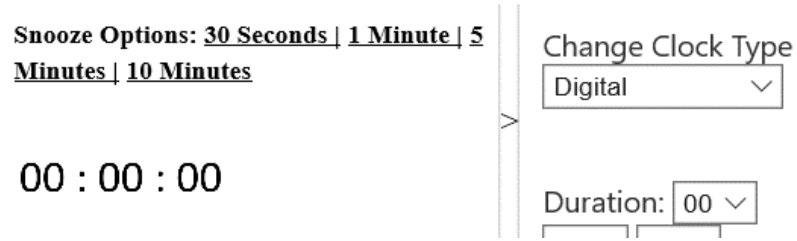
Conclusions

- Trikafta plus best supportive care substantially improves health outcomes compared with best supportive care alone
- However, in proportion to the clinical benefits, the added cost of Trikafta well exceeds commonly used thresholds for cost-effectiveness.
- If we assumed a scenario where Trikafta was curative we found that the cost-effectiveness ratio would reduce to $612,000 per QALY at current prices, which is still far from commonly cited thresholds.

Questions?

Public Comment and Discussion

JP Clancy, MD, Vice President of Clinical Research Cystic Fibrosis Foundation

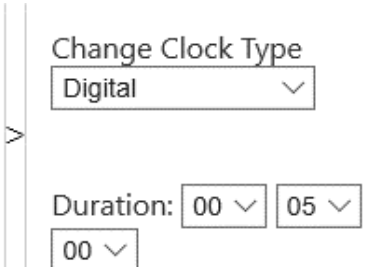


Conflicts of Interest:

- *Contributions: CFF has received charitable contributions and/or fees for service >$5,000 from health care companies, including Vertex Pharmaceuticals.*
- *Equity Interests and Intellectual Property: CFF has entered into therapeutic development award agreements that have and may continue to provide CFF with intellectual property, equity interests, and royalty and milestone payment rights from various pharmaceutical companies.*
- *Research Support: CFF provides financial support to the Therapeutics Development Network (TDN) which delivers high-quality clinical trials to CF patients in the search for better therapies and a cure. CFF provides financial support to the Data Safety Monitoring Board whose primary responsibility is to protect the safety and welfare of people with CF who participate in TDN approved studies.*
- *Other Relationships: CFF facilitated, but did not participate in, the development of the CFF Pulmonary Guidelines: Use of CFTR Modulator Therapy in Patients with CF.*

Siri Vaeth, MSW, Executive Director
Cystic Fibrosis Research, Inc.

00 : 05 : 00



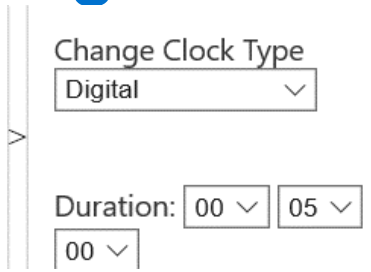
Conflicts of Interest:

- *CFRI receives educational grants to support our services to the CF community from Vertex Pharmaceuticals, Genentech, Gilead Sciences, AbbVie, Chiesi USA, and Ionis Pharmaceuticals. These grants represent > 25% CFRI's total budget.*

Juliana Keeping, Parent of Individual with CF
Communications Director, Patients for Affordable Drugs

Conflicts of Interest:

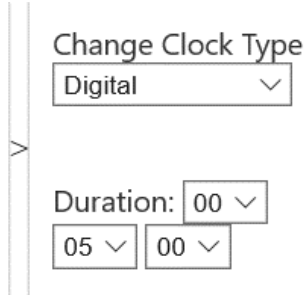
00 : 05 : 00



- *No conflicts of interest to disclose.*

Laura Rogers
Parent of an Individual with CF

00 : 05 : 00

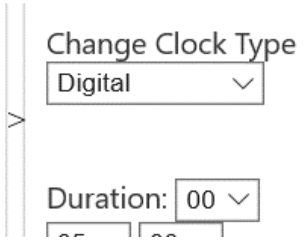


Conflicts of Interest:

- *Laura's daughter has been enrolled with the Vertex Trikafta trial(s) since July of 2018. There has been appointment, travel and meal reimbursement throughout the trial, and she is currently still enrolled.*

Chad Riedy, National Advocacy Chair
Cystic Fibrosis Foundation

00 : 05 : 00



Conflicts of Interest:

- *Chad is the National Advocacy Co-Chair for the Cystic Fibrosis Foundation.*

Break

Meeting will resume at 11:00 am PT

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Voting Questions

0. Test Question: In what year did Labor Day become a federal holiday?

A. 1890

B. 1894

C. 1905

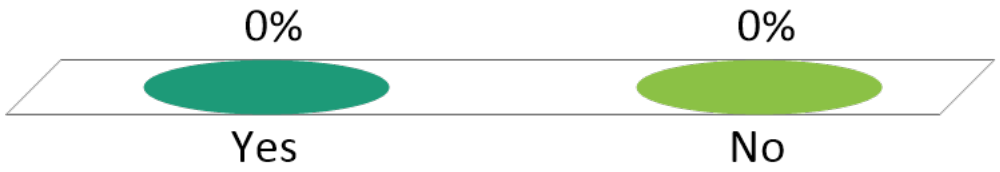
D. 1913

Patient Population 2 (Questions 1-2):
Individuals with CF who are homozygous for the F508del *mutation*

1. Is the evidence adequate to demonstrate that the net health benefit of treatment with Trikafta with best supportive care is greater than that of best supportive care alone?

A. Yes

B. No



Patient Population 2 (Questions 1-2):
Individuals with CF who are homozygous for the F508del *mutation*

2. If the answer to Q1 is Yes: Is the evidence adequate to demonstrate that the net health benefit of treatment with Trikafta and best supportive care is greater than that of treatment with Symdeko and best supportive care?

A. Yes

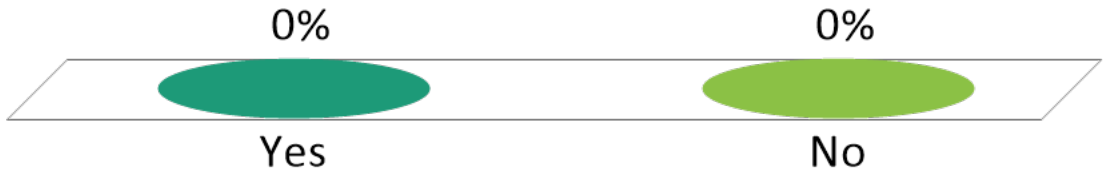
B. No

Patient Population 3 (Questions 3-4):
Individuals with CF who are heterozygous for the F508del *mutation with a residual function mutation.*

3. Is the evidence adequate to demonstrate that the net health benefit of treatment with Trikafta with best supportive care is greater than that of best supportive care alone?

A. Yes

B. No

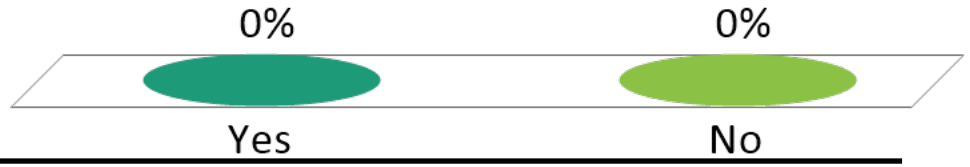


Patient Population 3 (Questions 3-4):
Individuals with CF who are heterozygous for the F508del *mutation with a residual function mutation.*

4. If the answer to Q3 is Yes: Is the evidence adequate to demonstrate that the net health benefit of treatment with Trikafta and best supportive care is greater than that of treatment with Symdeko and best supportive care?

A. Yes

B. No

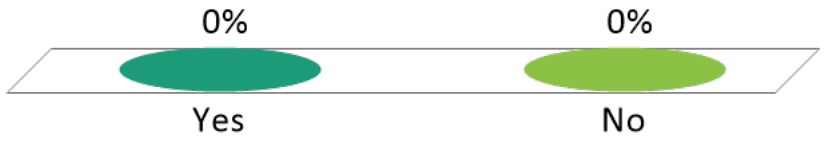


Patient Population 4:
Individuals with CF who are heterozygous for the F508del *mutation with a minimal function mutation.*

5. Is the evidence adequate to demonstrate that the net health benefit of treatment with Trikafta with best supportive care is greater than that of best supportive care alone?

A. Yes

B. No



6. When compared to best supportive care, does treating patients with Trikafta offer one or more of the following potential “other benefits?” (select all that apply)

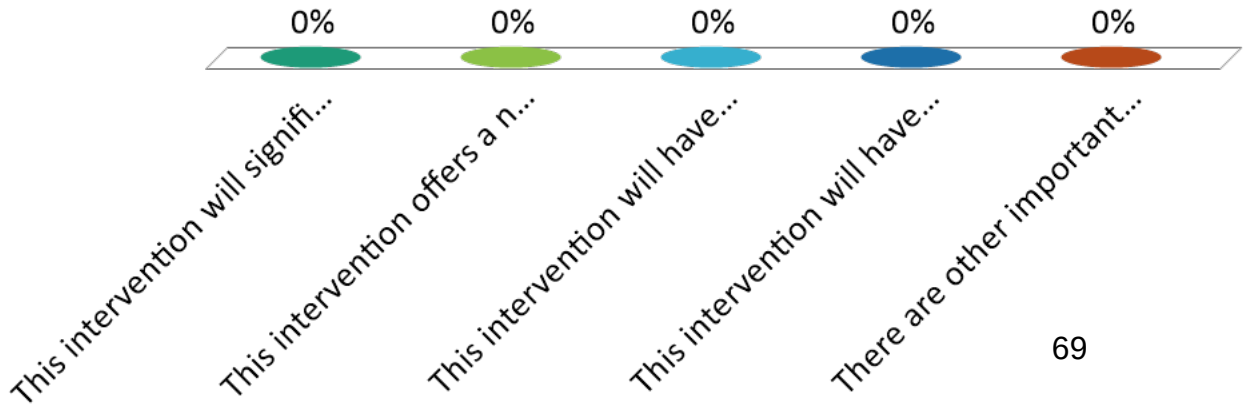
A. This intervention will significantly reduce caregiver or broader family burden.

B. This intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients for whom other available treatments have failed.

C. This intervention will have a significant impact on improving patients’ ability to return to work and/or their overall productivity.

D. This intervention will have a significant positive impact outside the family, including on schools and/or communities.

E. There are other important benefits or disadvantages that should have an important role in judgments of the value of this intervention: _____



7. Are any of the following contextual considerations important in assessing Trikafta's long-term value for money? (select all that apply)

A. This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.

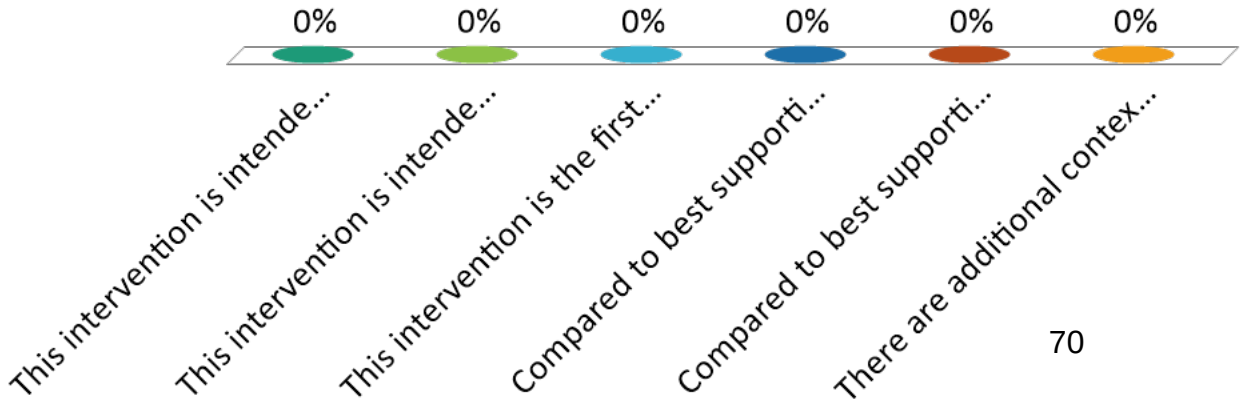
B. This intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.

C. This intervention is the first to offer any improvement for patients with this condition.

D. Compared to best supportive care, there is significant uncertainty about the long-term risk of serious side effects of this intervention.

E. Compared to best supportive care, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.

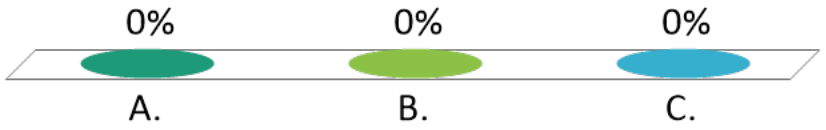
F. There are additional contextual considerations that should have an important role in judgments of the value of this intervention: _____.



***Patient Population 2**:*
Individuals with CF who are homozygous for the F508del *mutation*

8. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of Trikafta with best supportive care compared with best supportive care alone?

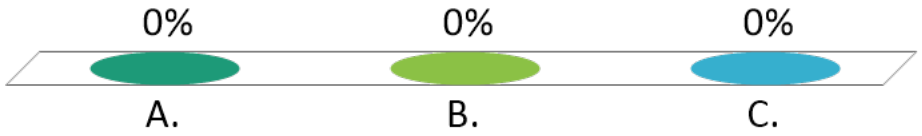
A. Low long-term value for money at current pricing
B. Intermediate long-term value for money at current pricing
C. High long-term value for money at current pricing



Patient Population 3:
Individuals with CF who are heterozygous for the F508del *mutation with a residual function mutation.*

9. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of Trikafta with best supportive care compared with best supportive care alone?

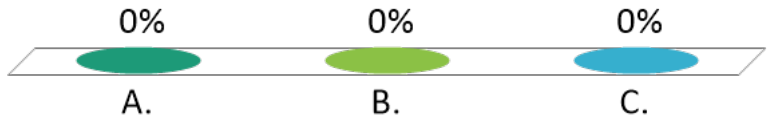
A. Low long-term value for money at current pricing
B. Intermediate long-term value for money at current pricing
C. High long-term value for money at current pricing



Patient Population 4:
Individuals with CF who are heterozygous for the F508del *mutation with a minimal function mutation.*

10. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of Trikafta with best supportive care compared with best supportive care alone?

A. Low long-term value for money at current pricing
B. Intermediate long-term value for money at current pricing
C. High long-term value for money at current pricing



Lunch

Meeting will resume at 12:30 pm PT

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Carlos Milla, MD, Professor of Pediatrics, Pulmonology, Stanford University School of Medicine	Dr. Milla has received in excess of $5,000 in advisory fees and research funding from Vertex Pharmaceuticals, Proteostasis Inc., and Eloxx Pharma. He also receives advisory board honorarium from Vertex Pharmaceuticals.
Don Maurice Kreis, JD, MS, Parent of Individual with CF	No financial conflicts of interest to disclose.
Janet Zachary-Elkind, Deputy Director, NY State Department of Health, Office of Health Insurance Programs	Janet Zachary-Elkind is an employee of the NY State Department of Health (Medicaid).
Jeff White, PharmD, MS, Staff Vice President, Clinical Pharmacy Services, IngenioRX (Anthem)	Dr. White is an employee of IngenioRx (Anthem) and owns stock in Anthem.
Manu Jain, MD, MSc, Professor, Department of Medicine (Pulmonary and Critical Care); Department of Pediatrics, Northwestern University	Dr. Jain has received in excess of $5,000 in advisory fees and research funding from Vertex Pharmaceuticals. He is also on the Speaker's Bureau of Vertex Pharmaceuticals and Gilead Sciences
Mariah Hanley, JD Patient Expert, Cystic Fibrosis Foundation	No financial conflicts of interest to disclose.
Mary Dwight, Senior Vice President of Policy and Advocacy, Cystic Fibrosis Foundation	CFF has received charitable contributions and/or fees for service in excess of $5,000 from health care companies including Vertex Pharmaceuticals. CFF has the option to acquire equity interests >$10,000 from a pharmaceutical company unrelated to this report. CFF has entered into therapeutic development award agreements that may result in intellectual property and royalty rights from various pharmaceutical companies

CTAF Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around September 23, 2020
    - Includes description of CTAF votes, deliberation, policy roundtable discussion
- Materials available at: https://icer-review.org/topic/cystic-fibrosis/

Adjourn

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