Intellia THERAPEUTICS

ESC Cardiovascular Round Table

Ricardo Rocha, MD
VP and Head of Medical Affairs

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Disclaimer

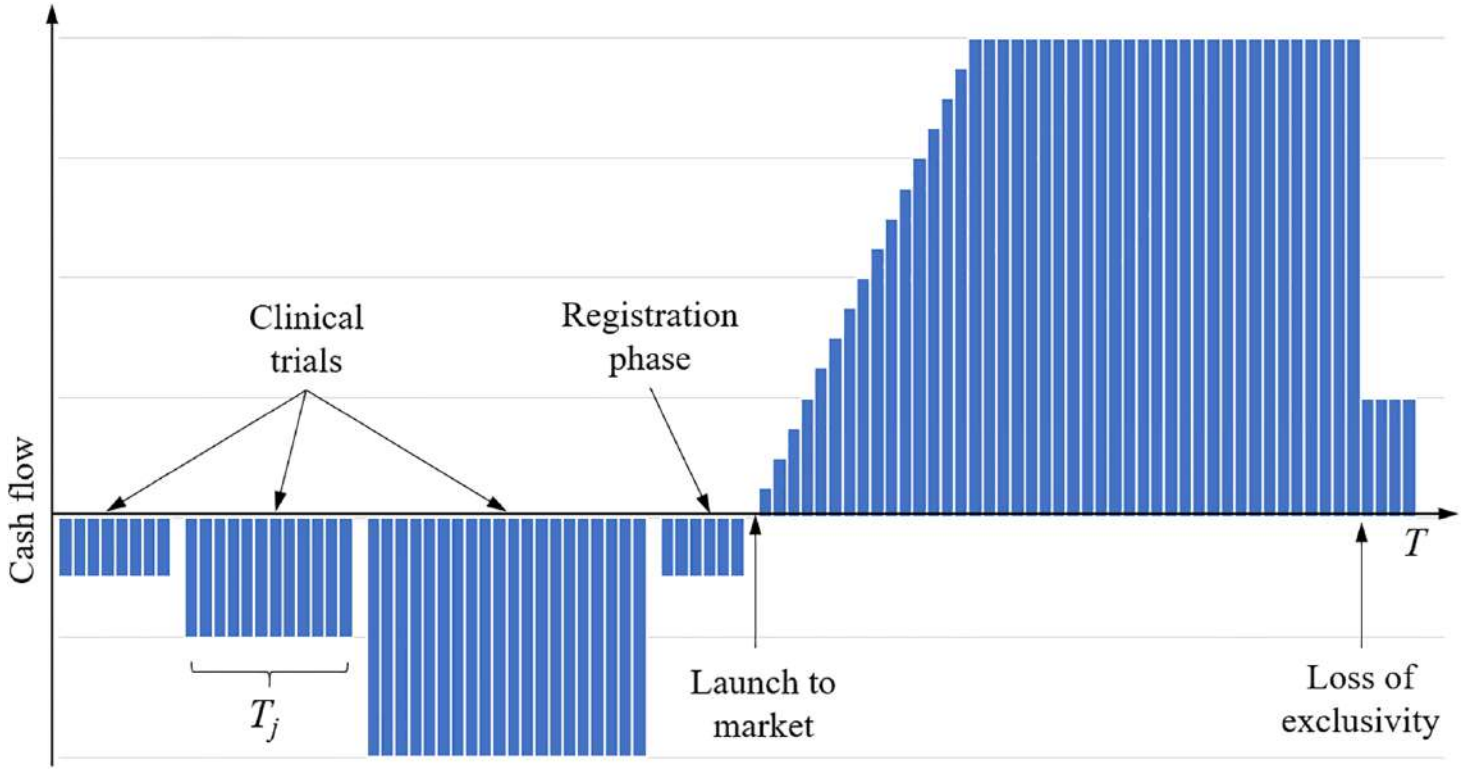
- I am currently an employee of Intellia Therapeutics. The views expressed in this presentation are my own and may not reflect those of my employer

Pharmaceutical Innovation in CV Disease: a Risky Business…

- The pharmaceutical industry has been instrumental to advance medical innovation, delivering life-saving cures and improving health in patients with CV disease
- Investment in medical innovation tackling important cardiometabolic diseases including hypertension, hyperlipidemia and diabetes has decreased substantially
- New product approvals in the past decade have been concentrated in “specialty” drugs intended to treat patients with complex, rare, or ‘orphan’ diseases
- The recent introduction of advanced therapies for CVD has faced multiple challenges, limiting access and broad clinical adoption, even when recommended by current guidelines

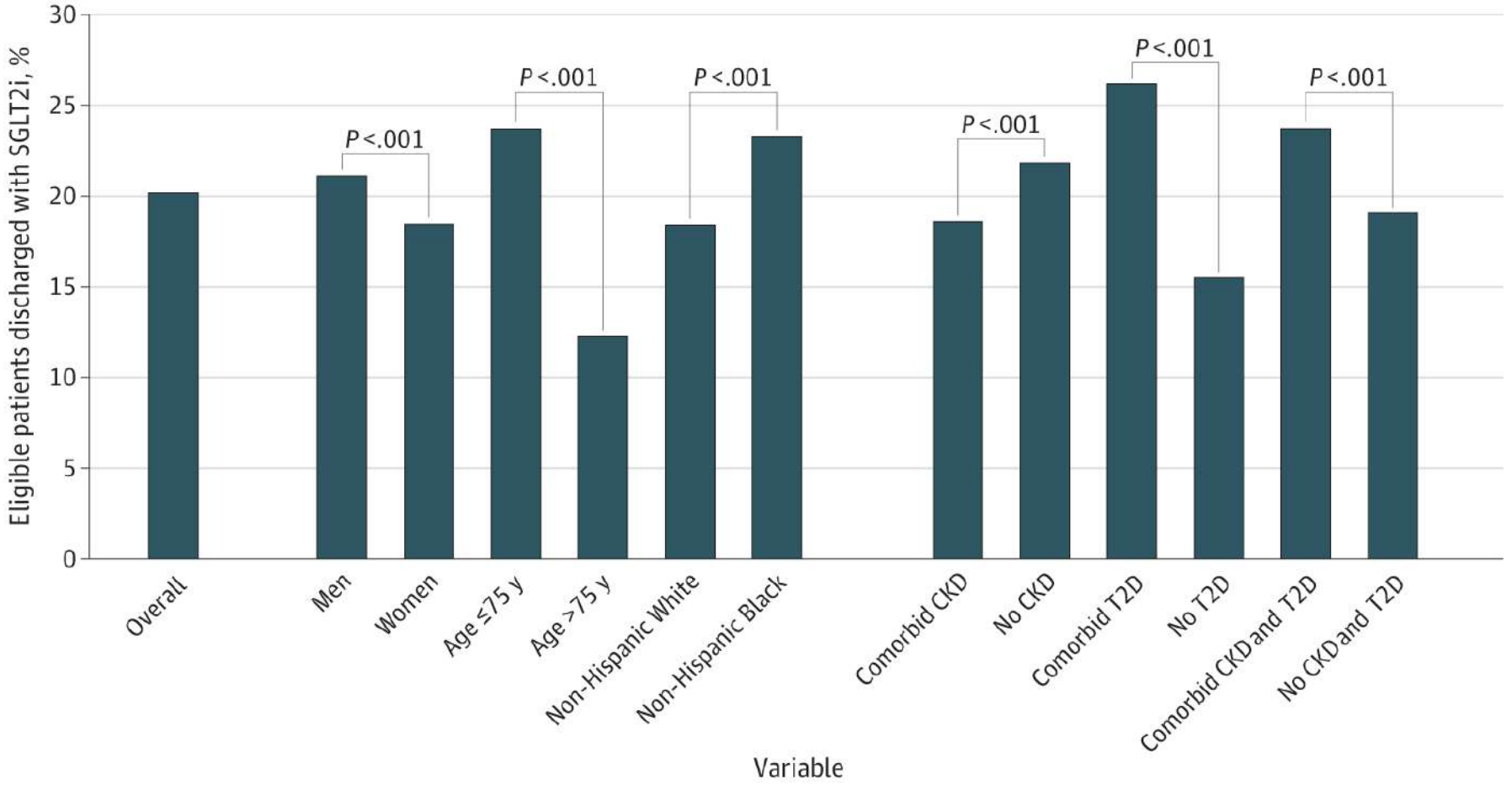
The development of a new drug is an extremely high-risk enterprise

- Typical cash flow profile from a development program



Wiklund SJ et al. https://doi.org/10.1371/journal.pone.0220812

Significant gaps remain in use of SGLT2i among eligible patients with HFrEF

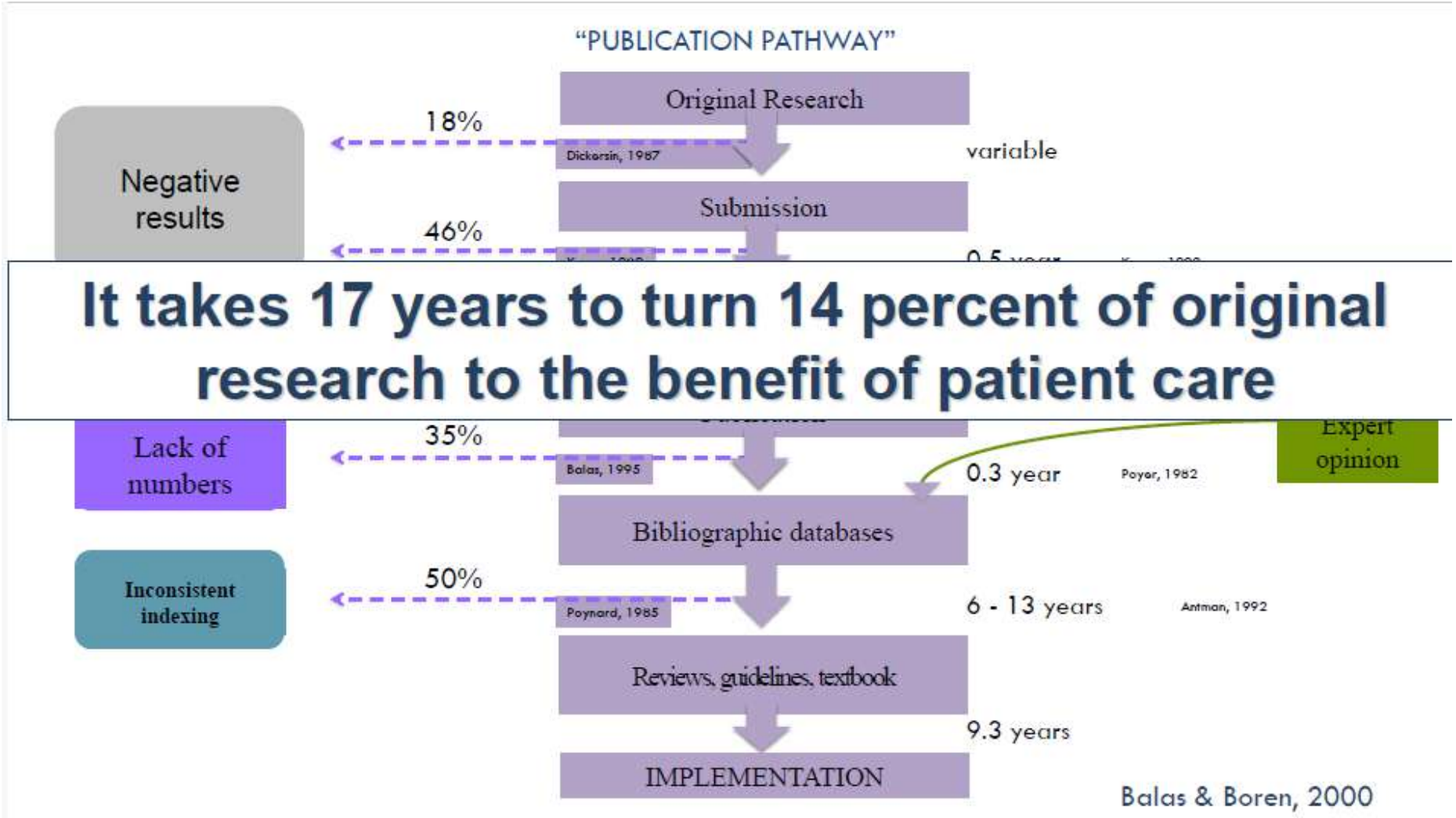


Pierce JB et al. JAMA Cardiol. 2023 Jul 1;8(7):652-661

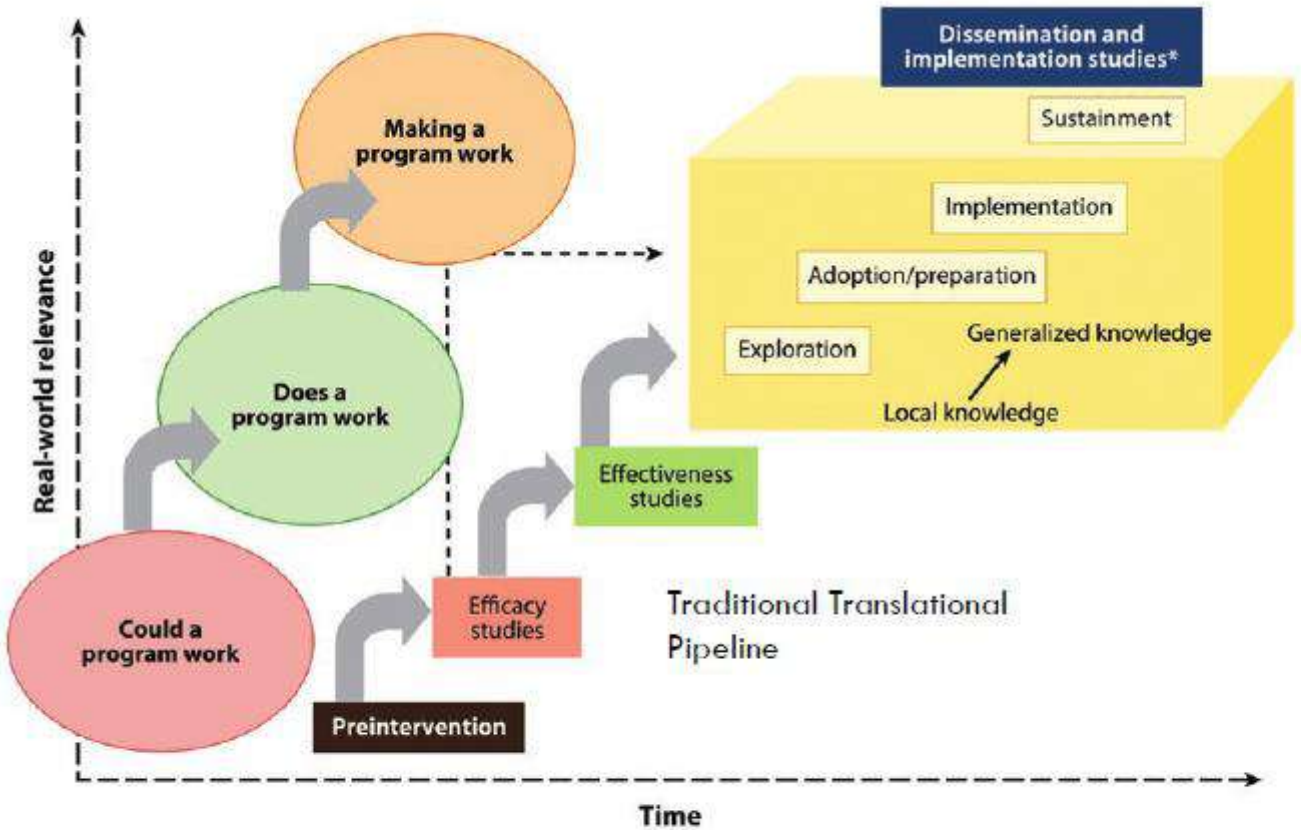
Significant challenges and barriers potentially impacting pharmaceutical development of CV medicines

- CV outcomes trials, requiring significant investment and time are needed for most new medicines
- Major gaps exist for generation of scientific, practical, timely and relevant evidence to demonstrate the value of new therapies and inform patient care
- Significant access barriers due to pricing and payer restrictions at launch
- CV HCP community and public reluctant to adopt new therapies, especially advanced medicines
- Current healthcare system not incentivized to **implement** medical innovation

Implementing Medical Innovation into Clinical Practice is a Well-Recognized Challenge



Guideline Implementation: A Multi-Step Process to Translate Clinical Evidence into Routine Patient Care

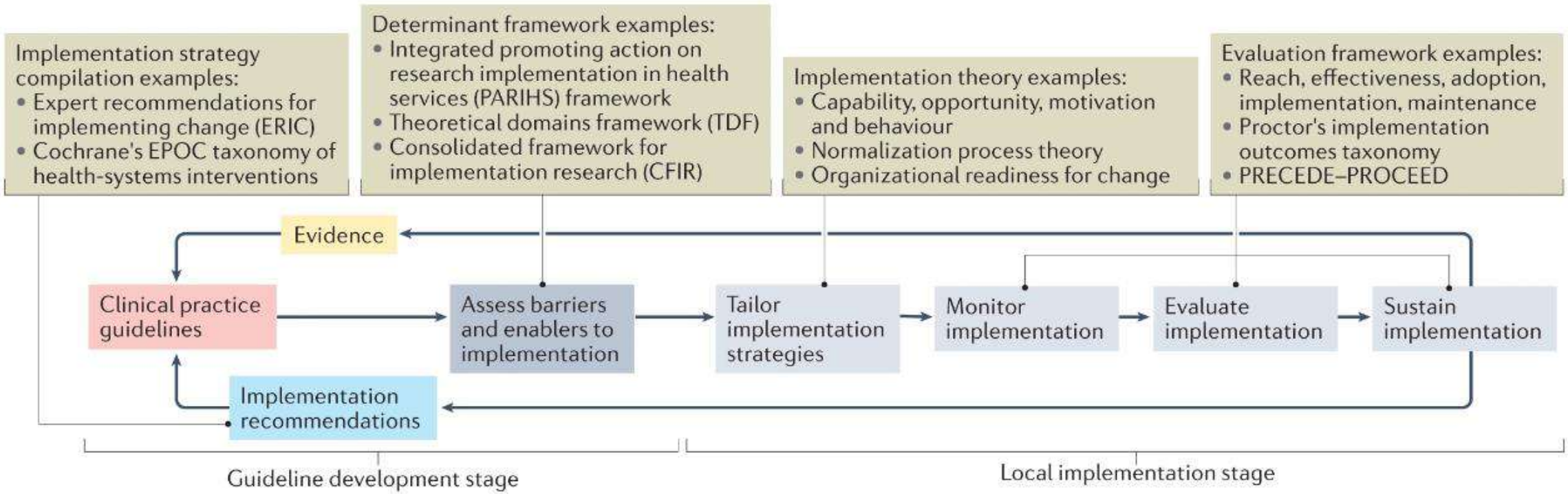


*These dissemination and implementation stages include systematic monitoring, evaluation, and adaptation as required.

Landsverk et al: Dissemination & Implementation Research in Health. Oxford, 2012

Brown CH, Curran G, Palinkas LA, et al. An overview of research and evaluation designs for dissemination and implementation. Annu Rev Public Health. 2017;38:1–22.

Guideline Implementation Requires Clinical Care Recommendations AND Implementation Recommendations



Sarkies MN et al. Nat Rev Cardiol 19, 3–4 (2022)

Implementation Science can Help Accelerate Guideline Implementation into Routine Clinical Practice – The AHA GWTG IMPLEMENT-HF Study

IMPLEMENT-HF Initiative

3-Year Initiative (2021-2023) across 7 regions: Chicago, Eastern Rural North Carolina, Kansas City, Milwaukee, New Jersey, Philadelphia, St. Louis

Goal

Increase the healthy time at home for all patients with HF, with an overarching aspirational national goal of decreasing all-cause mortality by 5%.

Vision

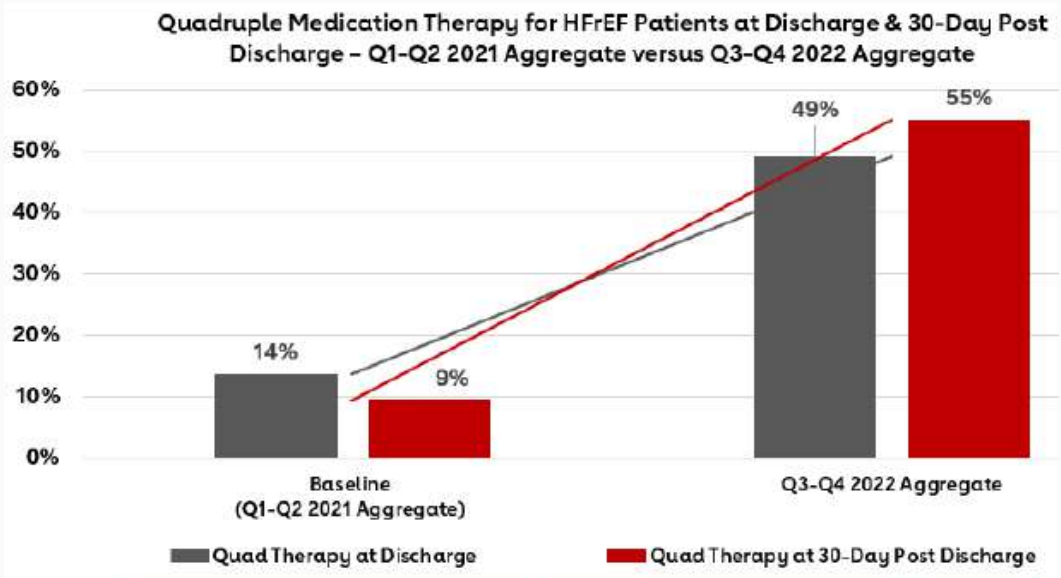
Building a multi-stakeholder community where implementation science is embraced by learning health care systems to achieve precise HF management and improve outcomes for all patients.

The American Heart Association's National Heart Failure Initiative, IMPLEMENT-HF, is made possible with funding by founding sponsor, Novartis and national sponsor, Boehringer Ingelheim and Eli Lilly and Company.

Implementation Science can Help Accelerate Guideline Implementation into Routine Clinical Practice – The AHA GWTG IMPLEMENT-HF Study

Results

- Data from 78 initiative sites of 9,102 HFrEF patient hospitalization episodes (median age 68, 33% females, median LVEF 26%) demonstrated that prescribing Q-GDMT at discharge increased from 14% at baseline to 49% for Q3-Q4 2022 **(+35%, p value <0.001)**
- 30-day post discharge data from 55 initiative sites of 2,894 HFrEF patient hospitalization episodes (median age 68, 30% females, median LVEF 27%) demonstrated an increase from 9% at baseline to 55% for Q3-Q4 2022 **(+46%, p value <0.001)**



	Baseline (Q1 & Q2 2021 Aggregate)		Q3 & Q4 2022 Aggregate		P Value
	Numerator	Denominator	Numerator	Denominator	
Discharge Q-GDMT for HFrEF Patients	549	4030	2018	4112	<0.001
30-Day Q-GDMT for HFrEF Patients	100	1064	879	1593	<0.001

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FOUNDING SPONSOR NOVARTIS
NATIONAL SPONSOR Boehringer Ingelheim Lilly

Healthcare Systems-Industry Partnerships May Also Help Foster Implementation of New Evidence for Better Care

CardioHealth Alliance

Partnering to provide **proactive evidence-based** health care

By turning evidence into practice in real time, the CardioHealth Alliance aims to enable our health care systems to move away from a model of reactively treating disease and instead deliver transformative care that prevents disease and accounts for the overall wellbeing of an individual.

The Alliance's four pillars include:

Use real-world data to inform real-world care

Scale and optimize best practices

Develop and test new pathways and practices

Continuously address value of care through effective policy

"The CardioHealth Alliance is focused on taking new approaches to the clinical study and implementation of heart health care. Together, we are focused on disrupting how we prevent and care for this pervasive disease which costs substantial loss of life, as well as billions of dollars each year in health care."

Ken Mahaffey, MD, Stanford University School of Medicine

https://cardiohealthalliance.org/

Healthcare Systems are Uniquely Positioned to Generate the Key Evidence that Patients and Providers (and Payers…) Really Need

ACT@POC™
Coalition for Advancing Clinical Trials at the Point of Care

Closing Evidence Gaps By Integrating Research and Care Delivery

- Ascension
- CURE Drug Repurposing Collaboratory (C-Path + NCATS + FDA)
- CVS Health
- Duke Margolis Center for Health Policy
- Duke University Health System
- Emory-Morningside Center for Innovative and Affordable Medicine
- Intermountain Healthcare
- Medable
- Mayo Clinic
- MITRE
- Quantum Leap Healthcare Collaborative
- The Broad Institute
- UMass Med
- University of California Irvine
- University of California San Francisco
- Vanderbilt University Medical Center

- Generating quality clinical research evidence in real time to better evaluate treatments and therapeutics
- Engaging a broader, more diverse group of patients and providers and develop digital health tools that make clinical trials simpler to run and more accessible to patients
- Driving implementation of large-scale clinical trials at the community level
- Complementing current academic trial networks by addressing timely “real-world” research questions in diverse populations and health care settings

Coalition for Advancing Clinical Trials (actpoc.org)

In Summary…

- How can we adjust/create incentives to accelerate broad adoption of new clinical evidence and treatment guidelines?
  - Academic society-industry partnerships to evaluate and demonstrate optimal implementation models that accelerate adoption of evidence into practice
  - Healthcare System-industry partnerships in which systems actively support clinical trials to generate timely evidence that patients and providers really need
  - Multi-stakeholder partnerships, where phase III protocols and RWE studies are co-developed and conducted at the point of care to evaluate clinical and economic endpoints, ideally ahead of approvals
  - Patient involvement in all the above!