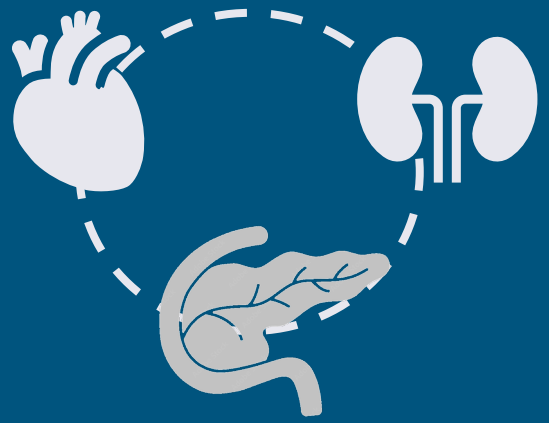
Practical Implementation of Guideline-Directed Medical Therapies in Diabetic Kidney Disease



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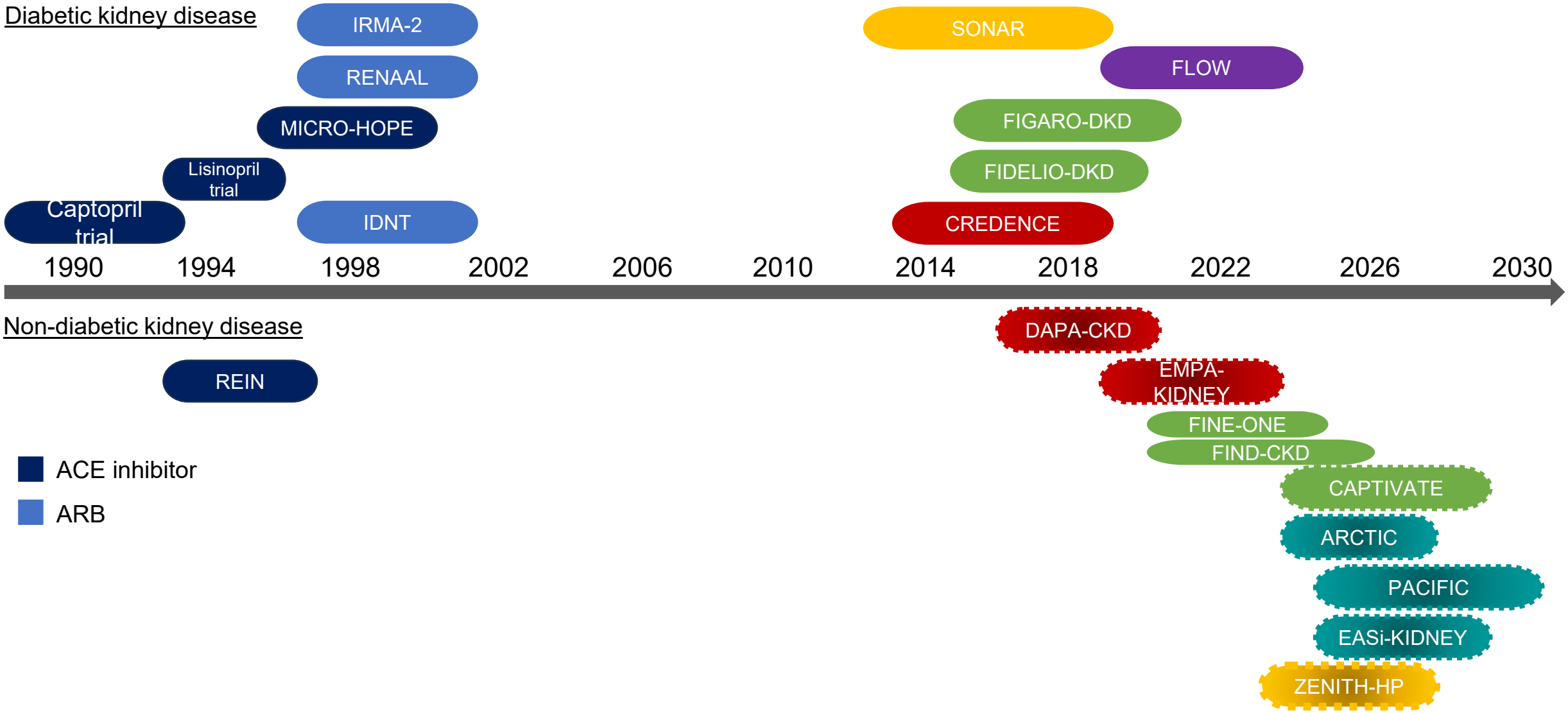
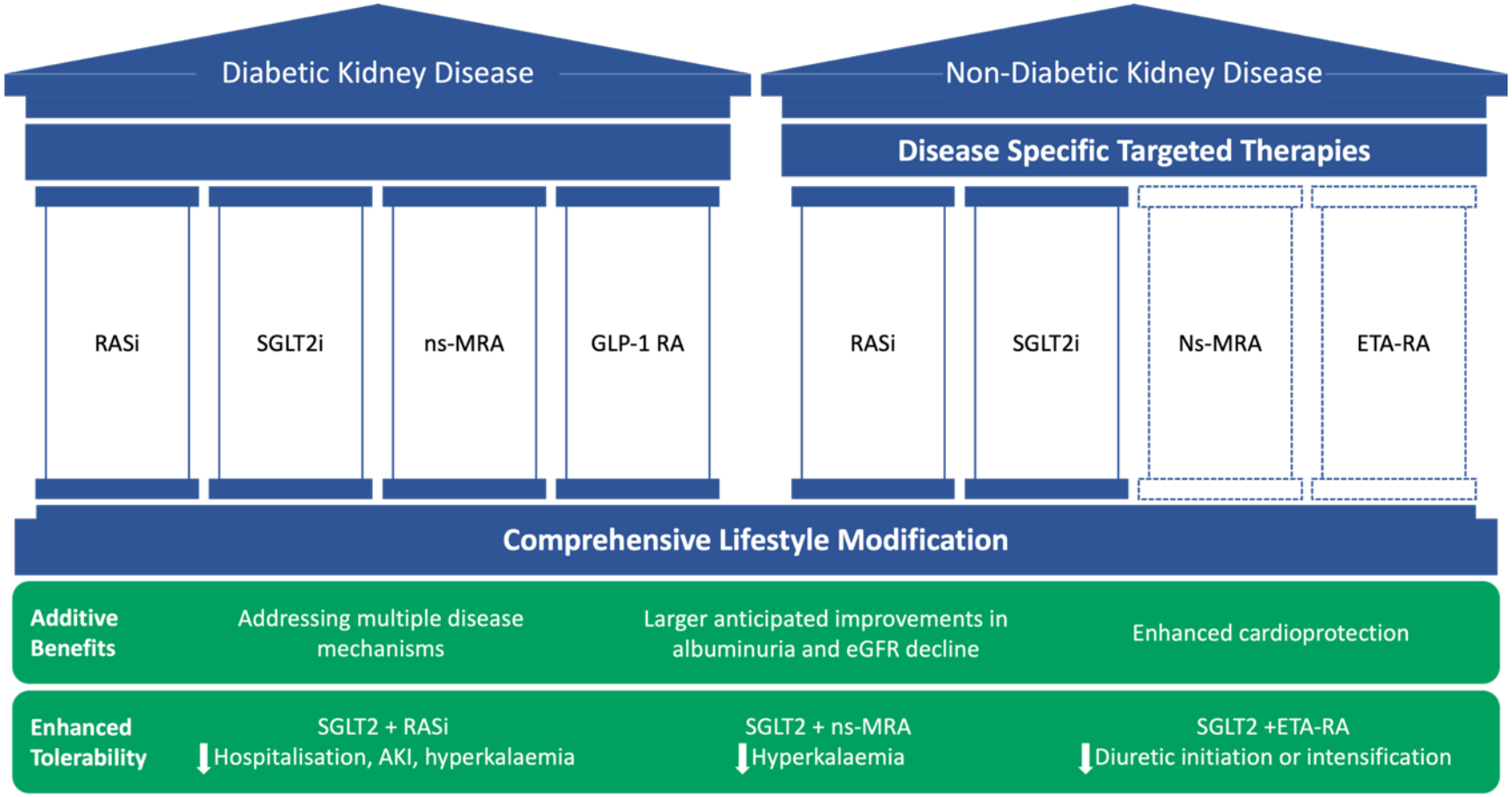
Disclosures: Dr. Vaduganathan has received research grant support, served on advisory boards, or had speaker engagements with Alnylam Pharmaceuticals, American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, BMS, Boehringer Ingelheim, Chiesi, Cytokinetics, Esperion, Fresenius Medical Care, Idorsia Pharmaceuticals, Lexicon Pharmaceuticals, Merck, Milestone Pharmaceuticals, Novartis, Novo Nordisk, Pharmacosmos, Recordati, Relypsa, Roche Diagnostics, Sanofi, and Tricog Health, and participates on clinical trial committees for studies sponsored by Amgen, AstraZeneca, Bayer AG, Boehringer Ingelheim, Galmed, Impulse Dynamics, Novartis, Occlutech, and Pharmacosmos.

Therapeutic landscape for CKD in 2025

(not including disease specific therapies)

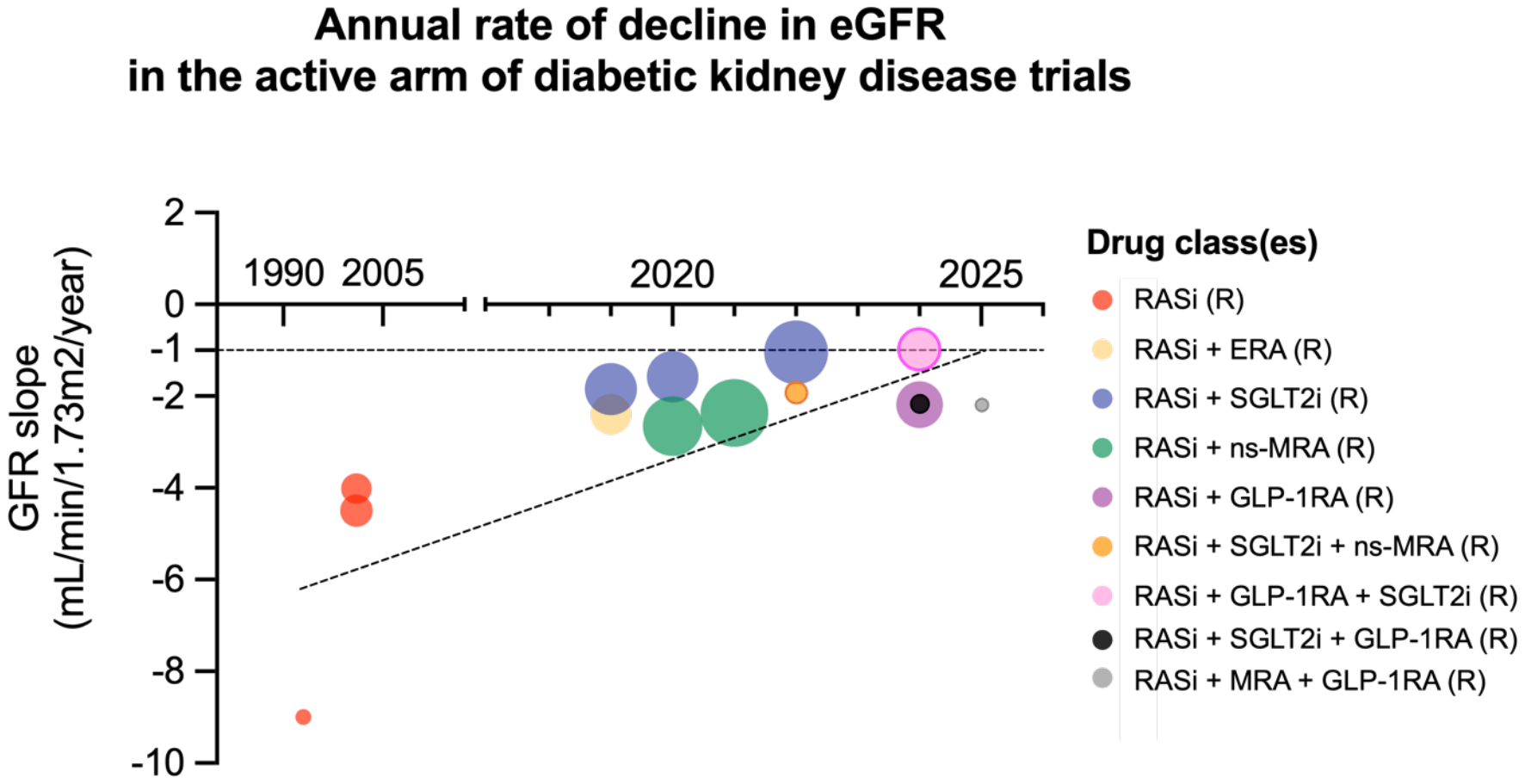


Combination Therapy as the New Standard of Care



Neuen BL…Vaduganathan M. NDT 2025

~~"SLOW CKD PROGRESSION"~~ ACHIEVE CKD REMISSION



Tangri N et al. Kidney Int 2025

Theoretical Framework for Implementation of Kidney GDMT

TRADITIONAL APPROACH

RAS blockade, add SGLT2i, re-assess in 3-6 months, add ns-MRA, consider GLP-1 RA

Limitations: Ignores excess early cardiovascular risk, very high risk of therapeutic inertia

RAPID SEQUENCE APPROACH

Rapid sequence implementation of “kidney GDMT”

Considerations: Assumes all patients with CKD are at equally high-risk, cost-effectiveness and early safety uncertain

ACCELERATED RISK-BASED APPROACH

Identify patients at highest risk using validated risk score, prioritise accelerated implementation of guideline recommended combination therapy

Appeal: Match intensity of treatment to risk, prioritise patients likely to obtain greatest absolute benefits

Neuen BL Tuttle KR & Vaduganathan M. Circulation 2024

Timing and Sequencing of Kidney GDMT

Traditional/conservative approach

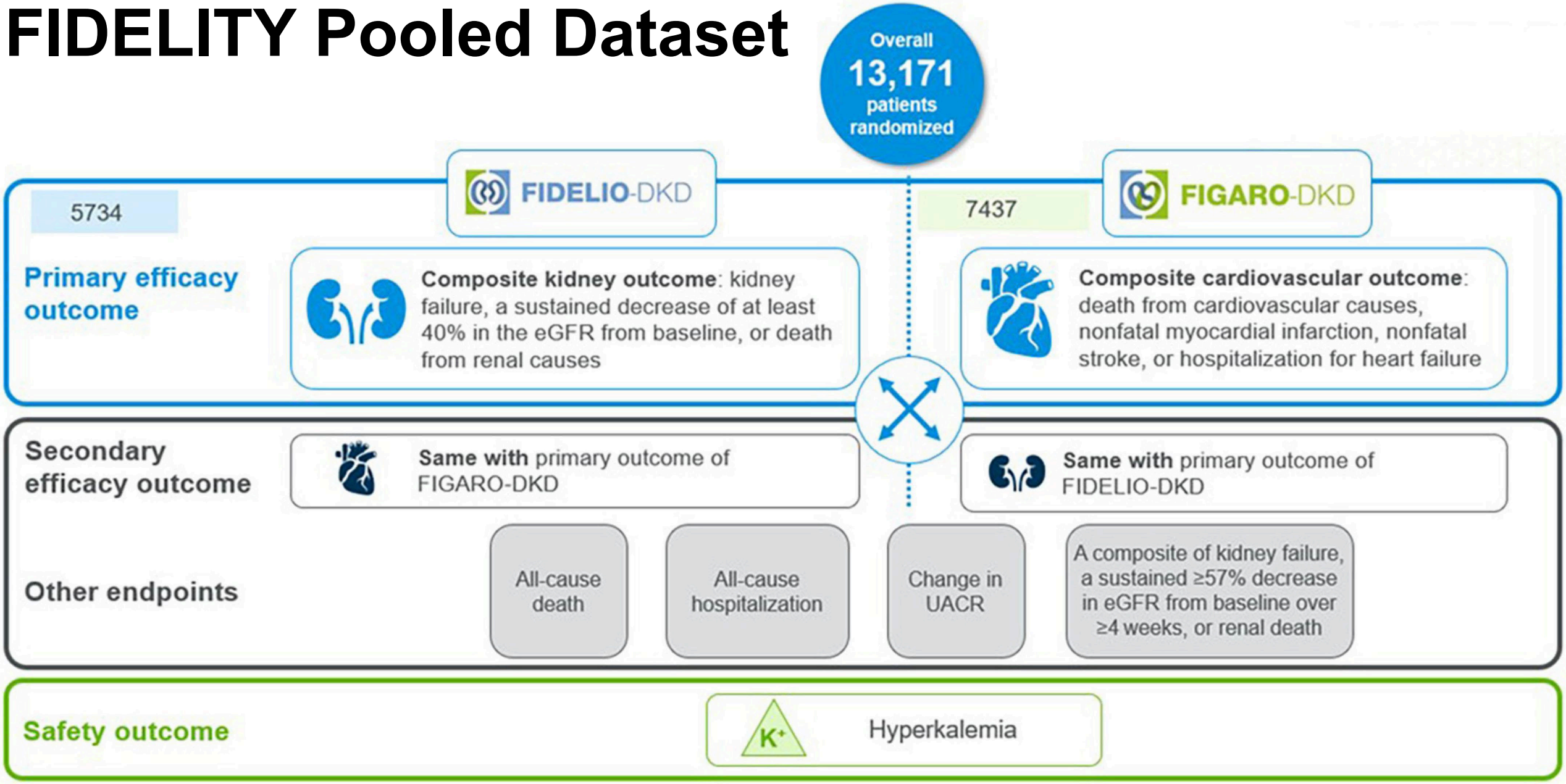
Accelerated approach

Rapid sequence approach

It can take up to 12-18 months until guideline-directed medical therapy for type 2 diabetes and CKD is fully implemented

Neuen BL, Tuttle KR, Bakris G & Vaduganathan M. Clin J Am Soc Nephrol 2024

FIDELITY Pooled Dataset



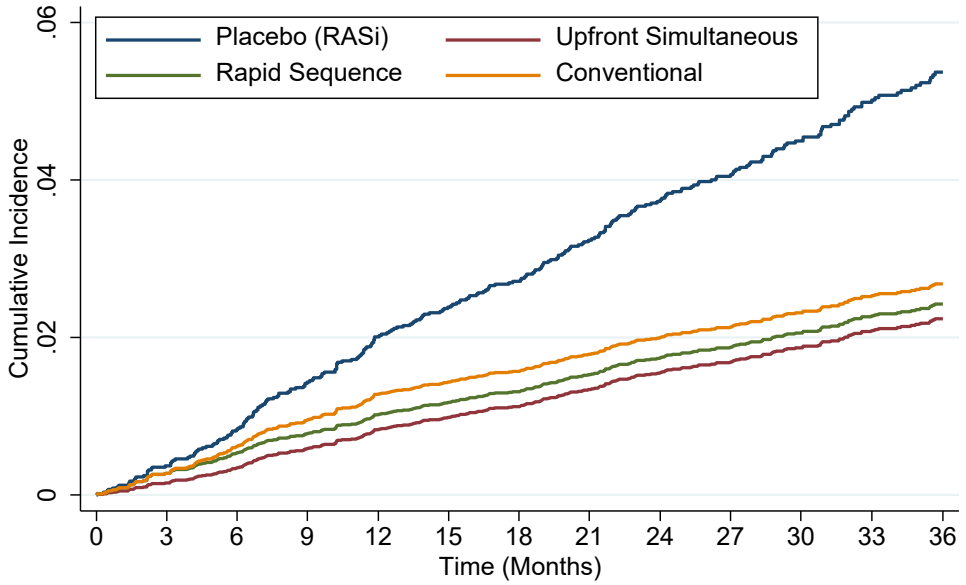
Agarwal R et al. EHJ 2022

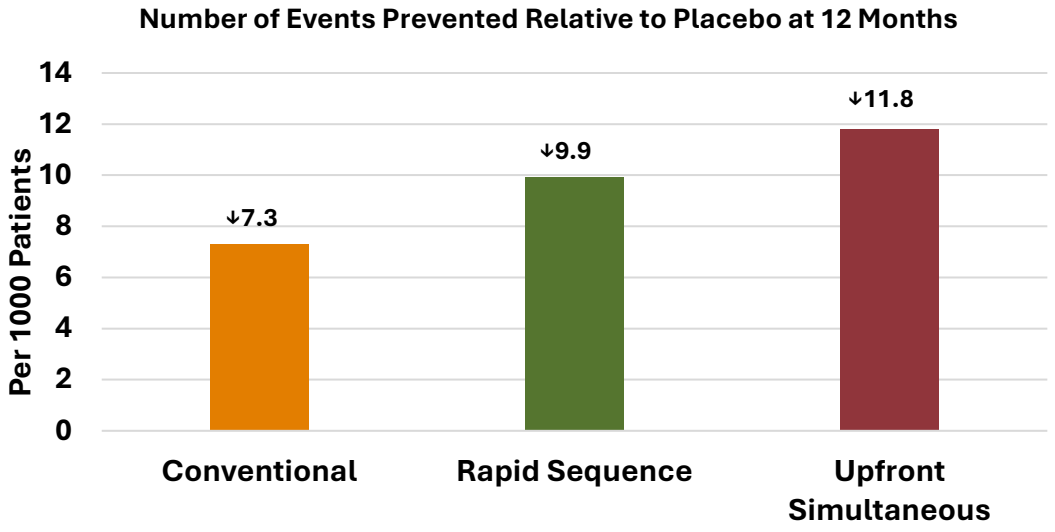
Strategies of Implementation of Kidney GDMT

Among patients in the placebo arm of FIDELITY receiving RASi alone (n=5,690)

- **RASi alone**
- **Simultaneous Initiation:** Starting SGLT2i nsMRA GLP1RA (all at time 0)
- **Rapid Sequence:** SGLT2i at time 0, nsMRA at 3mo, GLP1RA at 6mo
- **Conventional:** SGLT2i at time 0, nsMRA at 6mo, GLP1RA at 12mo

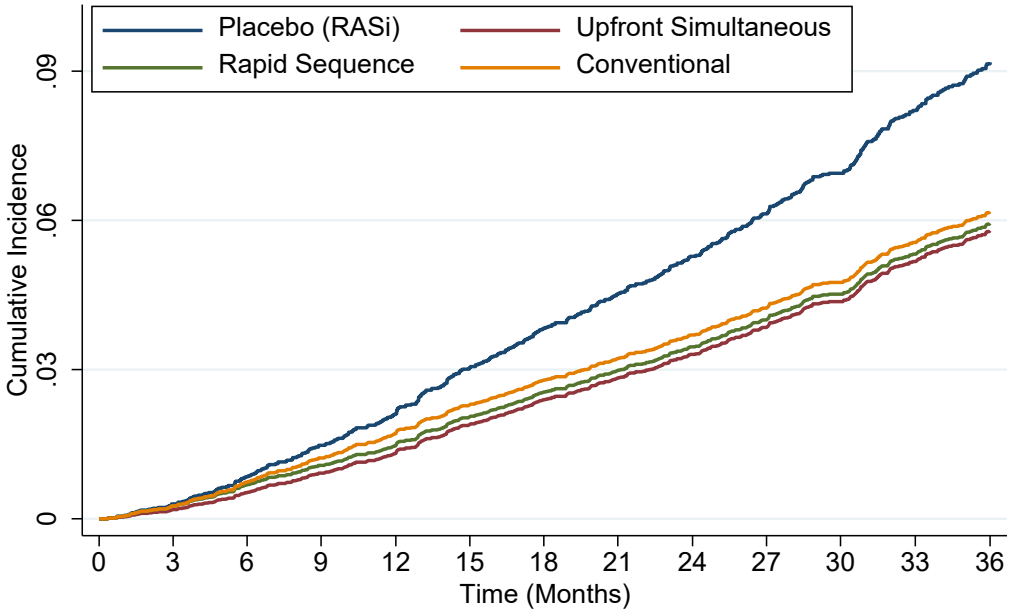
CV Death or HF Hospitalization by Sequencing Strategy

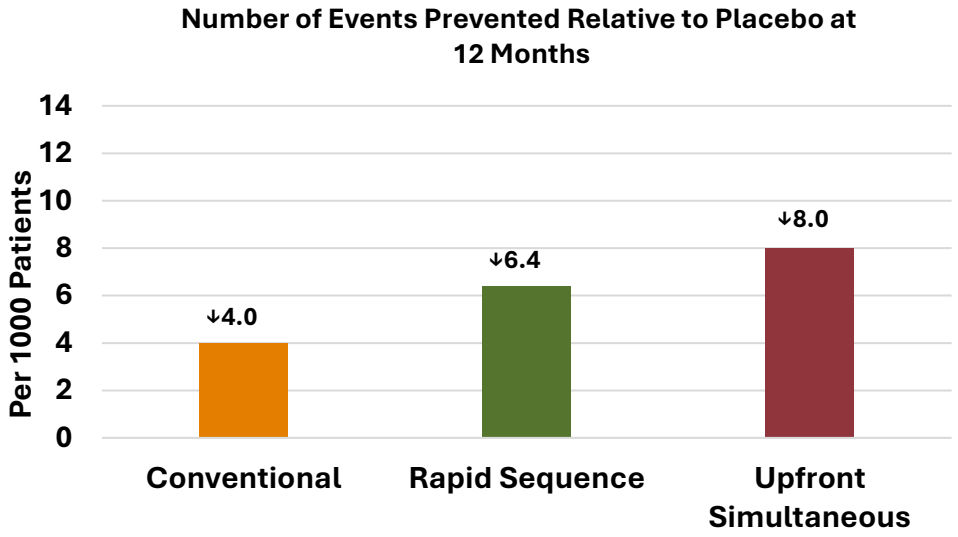




Over 12 months, combination therapy was projected to prevent 7, 10, and 12 CV death or HF hospitalization events per 1,000 patients treated with the conventional, rapid-sequence, and upfront simultaneous strategies, respectively

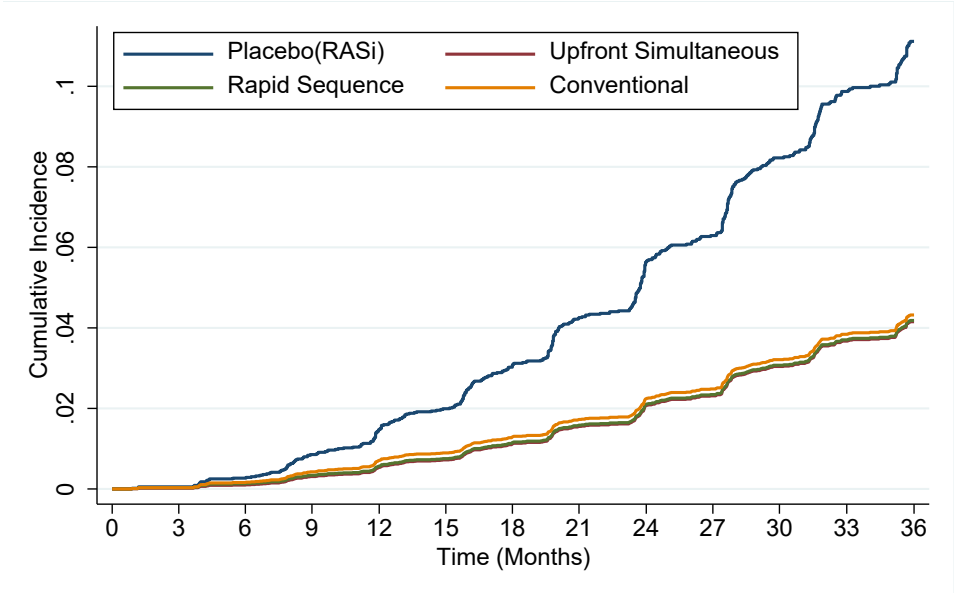
All Cause Death by Sequencing Strategy

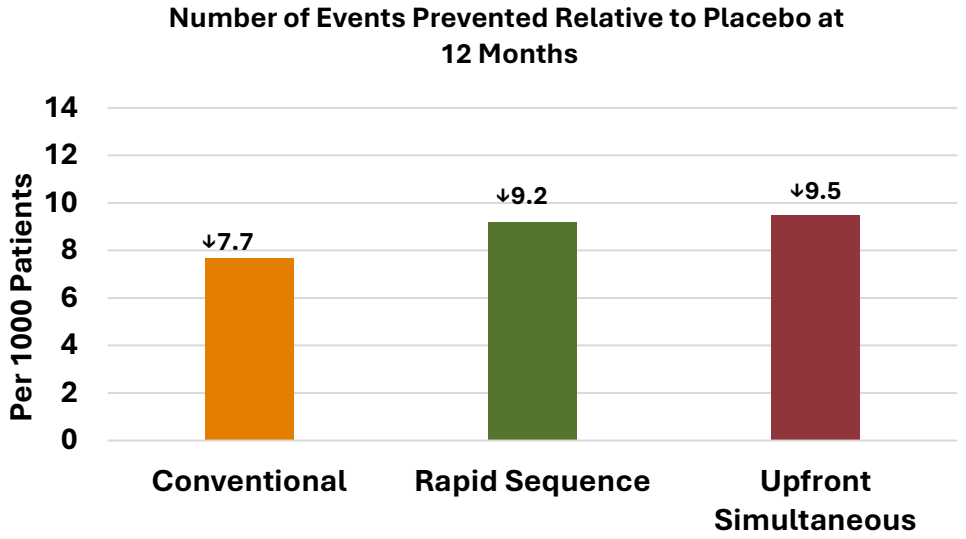




Over 12 months, combination therapy was projected to prevent 4, 6, and 8 deaths per 1,000 patients treated with the conventional, rapid-sequence, and upfront simultaneous strategies, respectively

Kidney Composite by Sequencing Strategy





Over 12 months, combination therapy was projected to prevent 8, 9, and 10 kidney events per 1,000 patients treated with the conventional, rapid-sequence, and upfront simultaneous strategies, respectively

Conclusions

- **Among patients with type 2 diabetes and CKD, earlier and more comprehensive initiation of combination therapy was projected to yield progressively greater reductions in cardiovascular and kidney events.**

- **These data support the potential of accelerated implementation strategies to maximize cardio-kidney protection and highlight the need for randomized evidence to inform the optimal sequencing of therapy initiation.**