



Finerenone Across CKM Stages: A Secondary Analysis of FIDELITY

Kevin Bryan Lo MD, MS

Brigham and Women's Hospital

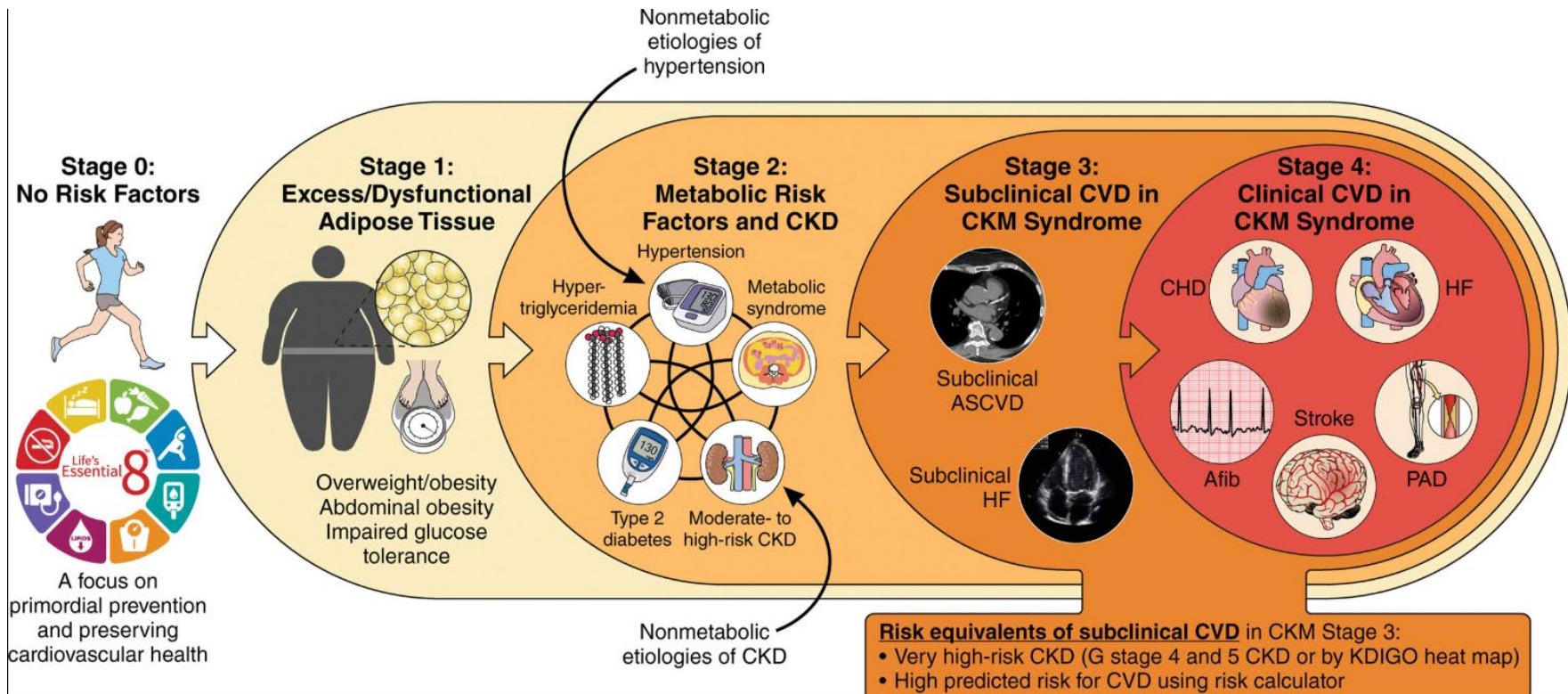
Harvard Medical School



Disclosures

- FIDELITY (FIDELIO-DKD and FIGARO-DKD) was sponsored by Bayer AG

Cardiovascular Kidney Metabolic (CKM) syndrome



Finerenone

Results



Endpoint CV composite

HR (95% CI)
0.86 (0.78 – 0.95)

p-value
0.0018

Risk ↓
14%

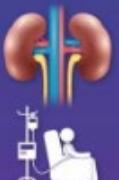


HF

HR (95% CI)
0.78 (0.66 – 0.92)

p-value
0.0030

Risk ↓
22%



Kidney composite

HR (95% CI)
0.77 (0.67 – 0.88)

p-value
0.0002

Risk ↓
23%



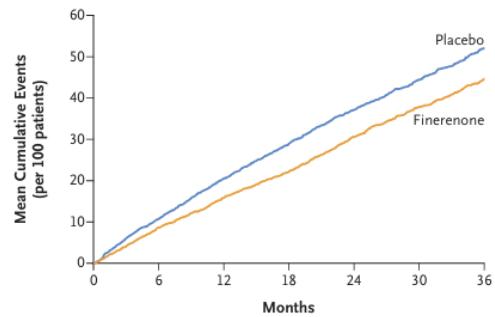
Dialysis

HR (95% CI)
0.80 (0.64 – 0.99)

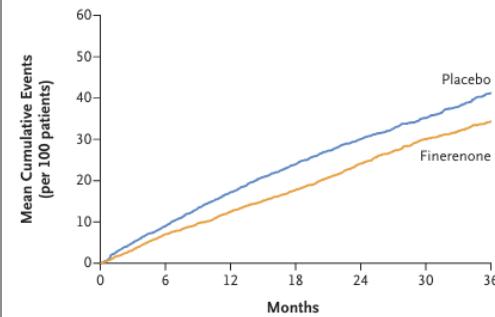
p-value
0.040

Risk ↓
20%

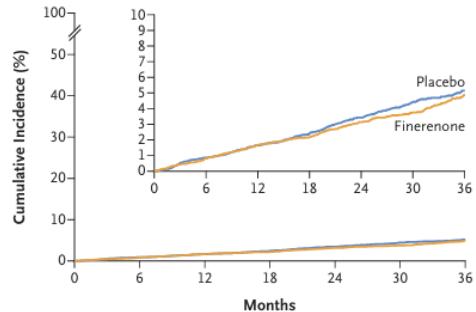
A Total Worsening Heart Failure Events and Death from Cardiovascular Causes



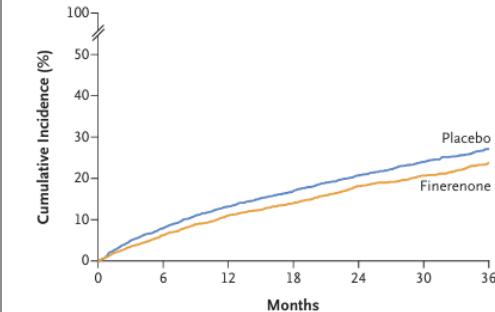
B Total Worsening Heart Failure Events



C Death from Cardiovascular Causes



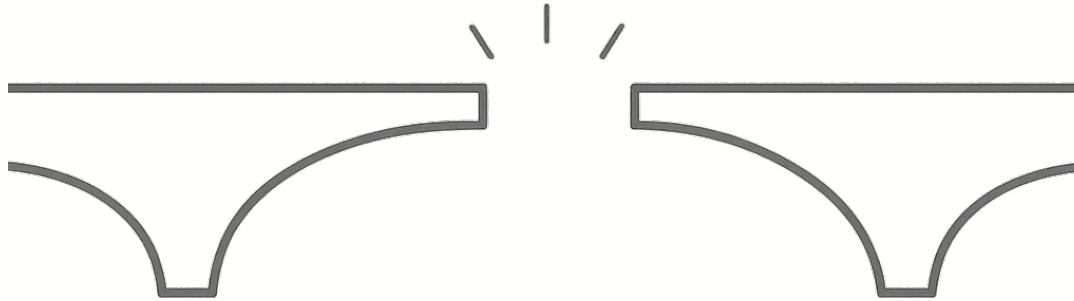
D First Worsening Heart Failure Event or Death from Cardiovascular Causes



Agarwal et al., Eur Heart J. 2021
Solomon et al., NEJM. 2024

CVCT

Gaps



- Limited data on **prognostic** value of CKM staging
- Unclear **feasibility** and **progression** of CKM stages in trials
- Limited evidence on finerenone's effects **across CKM stages**

Methods

Study population:

FIDELITY full analysis pooled cohort n=12,990



- T2D+CKD
- eGFR \geq 25ml/ min/ 1.73m²
- Serum K \leq 4.8mmol/ L
- Maximally tolerated RASi
- Excluding: symptomatic HFrEF

Primary Outcomes:

cardiovascular composite:

- CV death,
- non-fatal MI,
- non-fatal stroke
- HFH



kidney composite:

- kidney failure
- $\geq 7\%$ decrease in eGFR over ≥ 4 weeks
- renal death



CKM stages

Stage 2: metabolic risk factors (e.g., type 2 diabetes) or moderate- to high-risk CKD by KDIGO

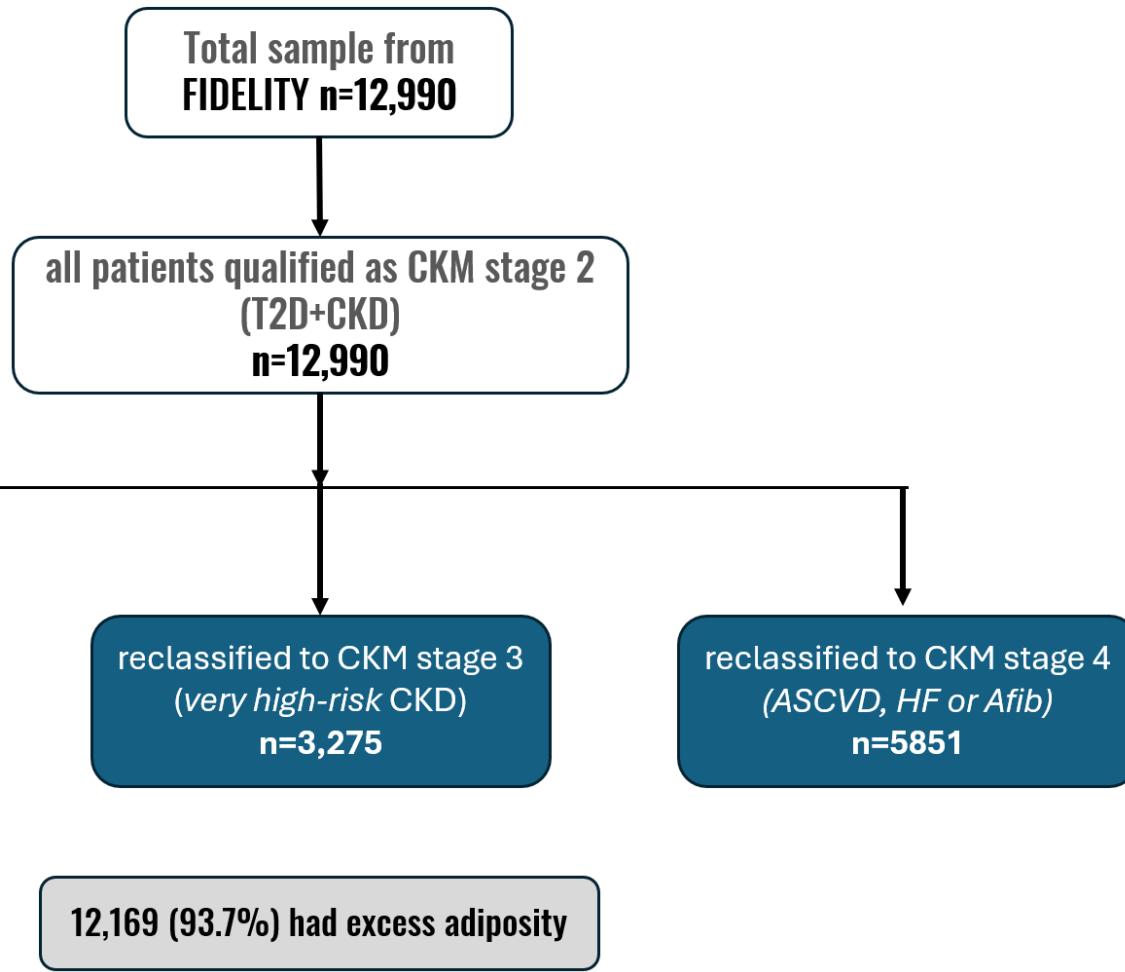
Stage 3: very high-risk CKD

Stage 4: clinical CVD

			Albuminuria categories		
			A1	A2	A3
CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73 m ²)	Description and range				
G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

 Low risk (if no other markers of kidney disease, no CKD)
 High risk
 Moderately increased risk
 Very high risk

Results



Results

Clinical Outcomes by CKMstage

Adjusted: age, sex, smoking, treatment group

Stratified: study, region, eGFR, UACR, CVD history

Outcomes by CKMstage		aHR ^a (95% CI)	P value
Cardiac composite outcome/MACE ^a			
CKM stage2		Referent	
CKM stage3		1.05 (0.84, 1.29)	0.68
CKM stage4		1.87 (1.56, 2.24)	<0.001
Kidney composite outcome ^b			
CKM stage2		Referent	
CKM stage3		1.68 (1.22, 2.30)	0.001
CKM stage4		1.96 (1.43, 2.69)	<0.001
Cardiovascular death + heart failure hospitalizations			
CKM stage2		Referent	
CKM stage3		1.03 (0.79, 1.34)	0.84
CKM stage4		2.19 (1.75, 2.75)	<0.001
Cardiovascular death			
CKM stage2		Referent	
CKM stage3		1.16 (0.82, 1.63)	0.41
CKM stage4		2.05 (1.54, 2.72)	<0.001
Heart failure hospitalizations			
CKM stage2		Referent	
CKM stage3		1.08 (0.72, 1.61)	0.71
CKM stage4		2.99 (2.12, 4.24)	<0.001
All-cause mortality			
CKM stage2		Referent	
CKM stage3		1.07 (0.82, 1.38)	0.63
CKM stage4		1.79 (1.44, 2.22)	<0.001

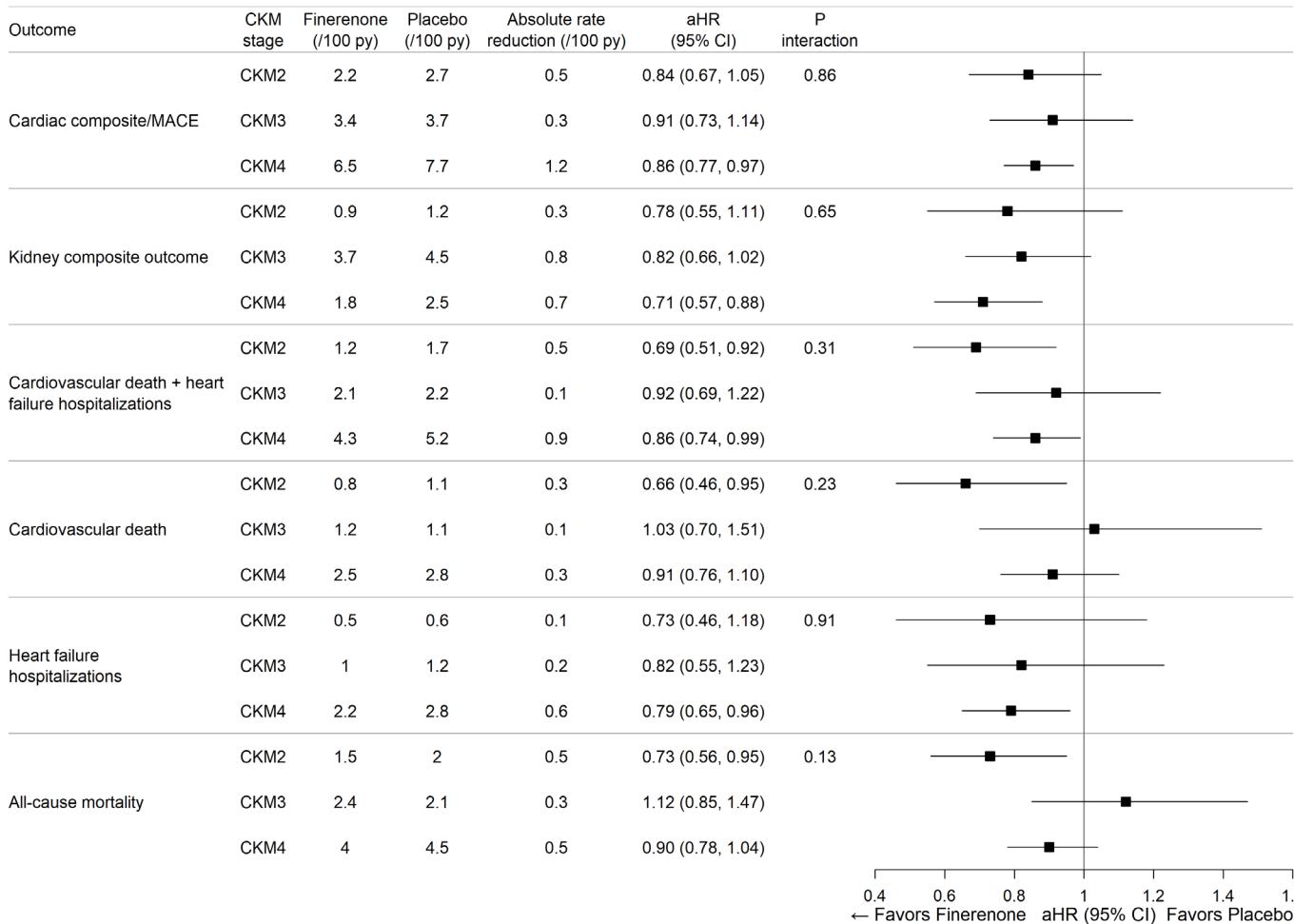
Results

Sensitivity analysis in subset with NT-proBNP (n=1559)
reclassified 137 individuals from Stage 2 to 3

Outcomes by CKM stage	CKM stage baseline (per 100 py)	CKM stage with NTpro BNP (per 100 py)	Absolute diff	aHR ^a (95% CI) baseline CKM stage	aHR (95% CI) CKM stage with NT-proBNP
Cardiovascular composite/MACE					
CKM stage2	2.4 (1.7, 3.4)	1.1 (0.6, 2.0)	1.3	Referent	Referent
CKM stage3	3.9 (2.9, 5.2)	4.1 (3.3, 5.3)	0.2	0.80 (0.42, 1.52)	2.61 (1.19, 5.72)
CKM stage4	8.5 (7.3, 9.7)	8.5 (7.3, 9.7)	0	2.00 (1.13, 3.55)	5.10 (2.30, 11.30)
Kidney composite outcome^b					
CKM stage2	1.3 (0.8, 2.1)	1.1 (0.6, 2.1)	0.2	Referent	Referent
CKM stage3	2.2 (1.5, 3.3)	2.0 (1.4, 2.9)	0.2	0.82 (0.28, 2.38)	1.75 (0.67, 4.58)
CKM stage4	2.3 (1.8, 3.0)	2.3 (1.8, 3.0)	0	1.17 (0.42, 3.25)	2.09 (0.72, 6.08)

Results

Treatment Effects of Finerenone by Baseline CKM Stage



Results

Safety events

Category	Safety events/treatment group:			
	Finerenone	Placebo	OR (95% CI)	P _{interaction}
Any serious adverse event	0.50			
CKM stage 2	556 (29.1%)	580 (29.8%)	0.96 (0.84, 1.11)	
CKM stage 3	494 (30.1%)	543 (33.5%)	0.85 (0.74, 0.99)	
CKM stage 4	1024 (34.9%)	1081 (37.2%)	0.91 (0.82, 1.01)	
Any adverse event leading to drug discontinuation	0.41			
CKM stage 2	83 (4.3%)	79 (4.1%)	1.07 (0.78, 1.47)	
CKM stage 3	121 (7.4%)	110 (6.8%)	1.09 (0.84, 1.43)	
CKM stage 4	211 (7.2%)	161 (5.5%)	1.32 (1.07, 1.64)	
Acute kidney injury	0.20			
CKM stage 2	29 (1.5%)	46 (2.4%)	0.64 (0.40, 1.02)	
CKM stage 3	65 (4.0%)	61 (3.8%)	1.05 (0.74, 1.50)	
CKM stage 4	126 (4.3%)	127 (4.4%)	0.98 (0.76, 1.27)	
Acute kidney injury leading to treatment discontinuation	0.50			
CKM stage 2	2 (0.1%)	2 (0.1%)	1.02 (0.14, 7.22)	
CKM stage 3	3 (0.2%)	4 (0.3%)	0.74 (0.16, 3.30)	
CKM stage 4	9 (0.4%)	4 (0.2%)	2.23 (0.69, 7.25)	

Results

Safety events

Category	Safety events/treatment group:			
	Finerenone	Placebo	OR (95% CI)	P _{interaction}
Hyperkalemia leading to treatment discontinuation				0.66
CKM stage 2	18 (0.9%)	4 (0.2%)	4.61 (1.56, 13.64)	
CKM stage 3	37 (2.3%)	13 (0.8%)	2.85 (1.51, 5.38)	
CKM stage 4	55 (1.9%)	21 (0.7%)	2.63 (1.59, 4.36)	
Hyperkalemia leading to hospitalization				0.28
CKM stage 2	5 (0.3%)	1 (0.1%)	5.09 (0.59, 43.62)	
CKM stage 3	21 (1.3%)	6 (0.4%)	3.49 (1.40, 8.66)	
CKM stage 4	35 (1.2%)	3 (0.1%)	11.71 (3.60, 38.11)	
Any serum potassium >5.5 mmol/L ^a				0.29
CKM stage 2	216 (11.4%)	106 (5.5%)	2.22 (1.74, 2.83)	
CKM stage 3	364 (22.4%)	151 (9.4%)	2.78 (2.27, 3.41)	
CKM stage 4	542 (18.7%)	258 (9.0%)	2.33 (1.99, 2.73)	
Any serum potassium >6.0 mmol/L ^a				0.25
CKM stage 2	46 (2.4%)	18 (0.9%)	2.65 (1.53, 4.58)	
CKM stage 3	80 (4.9%)	25 (1.6%)	3.27 (2.08, 5.16)	
CKM stage 4	99 (3.4%)	49 (1.7%)	2.04 (1.44, 2.88)	

Results

CKM Stage Progression



*overall OR refers to participants with either stage 2 or 3 at baseline,

**logistic regression adjusted for diabetes duration, smoking status, trial and region

Limitations

relatively smaller number of patients in CKMstage 2 and 3

no CVrisk calculation performed to support CKMstaging (e.g., PREVENT)

potential under-classification of CKMstage 3

does not include CKMstage 1 by indication

Insights

- CKMstaging criteria broadly captured the patient population in this analysis
- Trials may have challenges in optimally classifying subclinical CVD(stage 3 CKM) given variable biomarker availability
- Improving kidney function may be a major avenue for CKMstage regression
- CVevents remain the dominant driver of morbidity and mortality in CKM

End

Thank you!