How to Estimate the Impact of Changing Laboratory Methods

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Collaborators

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Outcomes Associated with a New Method

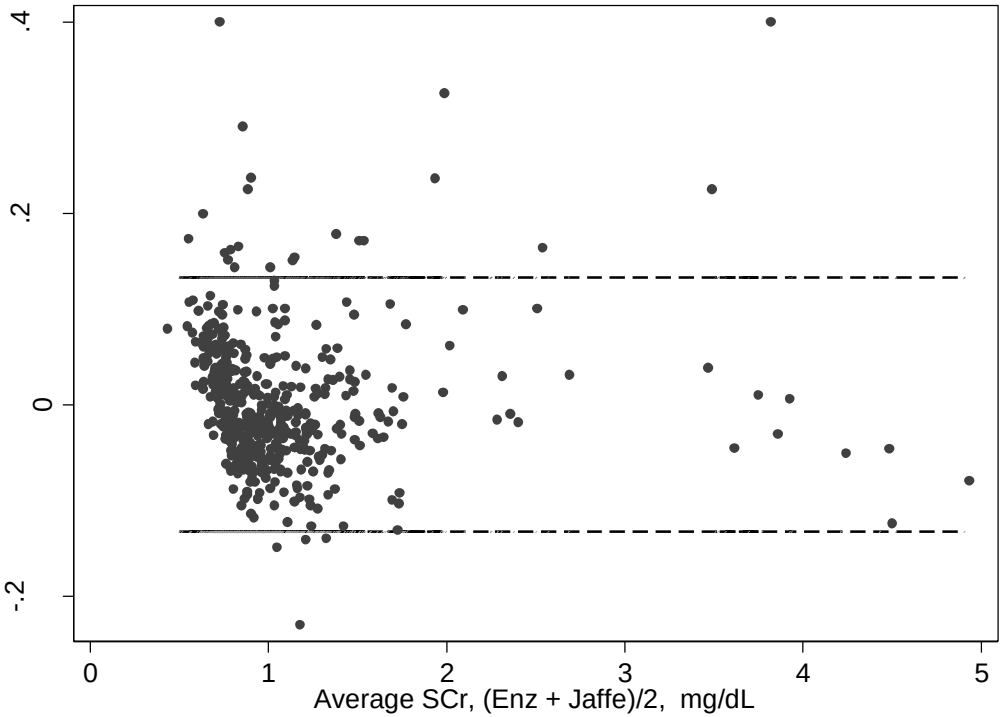
- Measurement Error
- Cost

Example: Creatinine Measurement

	Jaffe	Enzymatic
Cost per test	0.30	2.00
Coefficient of Variation	0.81	1.71
Interferences	Many	Few
Magnitude of Interference	Large	Small

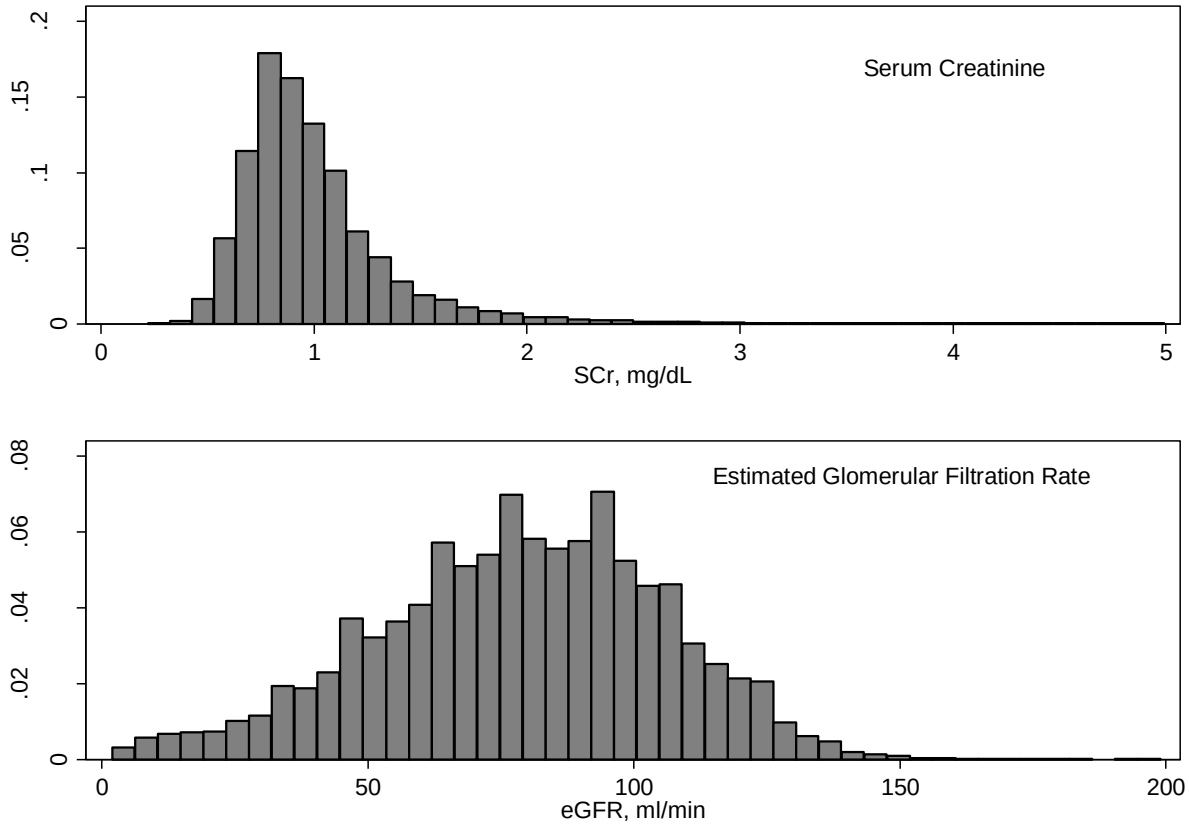
Bland-Altman Plot

Serum Creatinine



KDIGO Classification of Chronic Kidney Disease		
Glomerular Filtration Rate (GFR)		
Category	**GFR**	**Degree of Renal Function**
G1	≥90	Normal or High
G2	60-89	Mild Decrease
G3a	45-59	Mild to Moderate Decrease
G3b	30-44	Mild to Severe Decrease
G4	15-29	Severe Decrease
G5	<15	Kidney Failure

Creatinine and eGFR Distributions

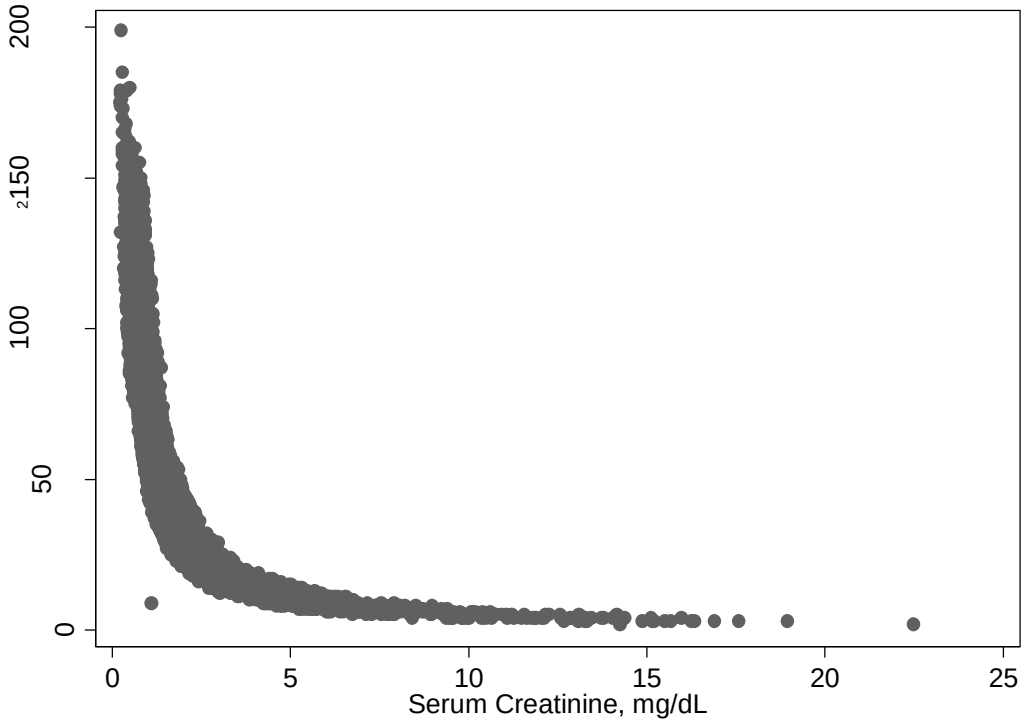


eGFR

$$eGFR_{CKD} = 141\left[\min\left(\frac{SCr}{\kappa},1\right)\right]^{\alpha}\left[\max\left(\frac{SCr}{\kappa},1\right)\right]^{-1.209}(0.993^{Age})K_3K_4$$

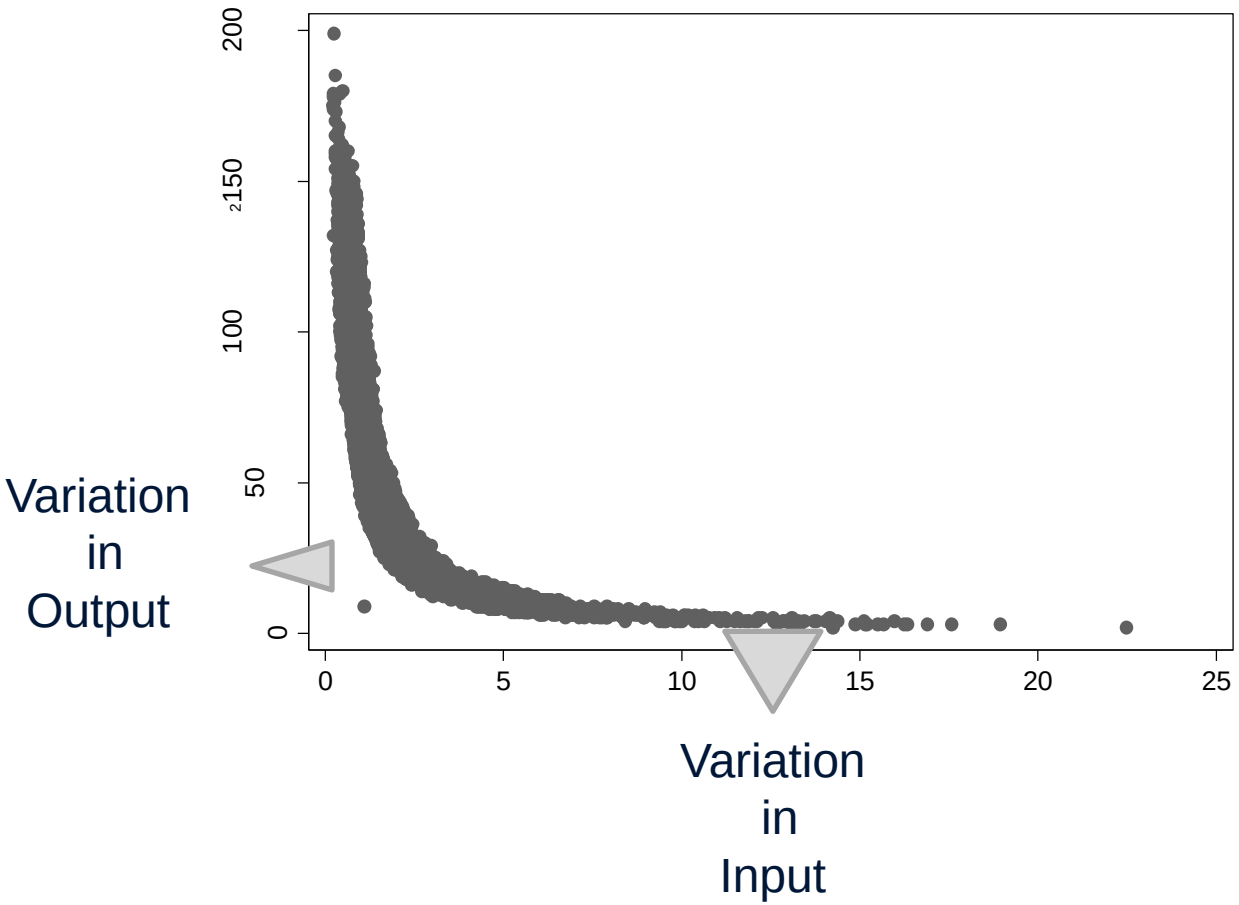
Where
α=-0.329 if female-0.411 otherwise,
κ= 0.7 if female0.9 otherwise,
K3= 1.018 if female1.0 otherwise,
K4= 1.159 if black1.0 otherwise

eGFR vs Serum Creatinine



Impact of Imprecision

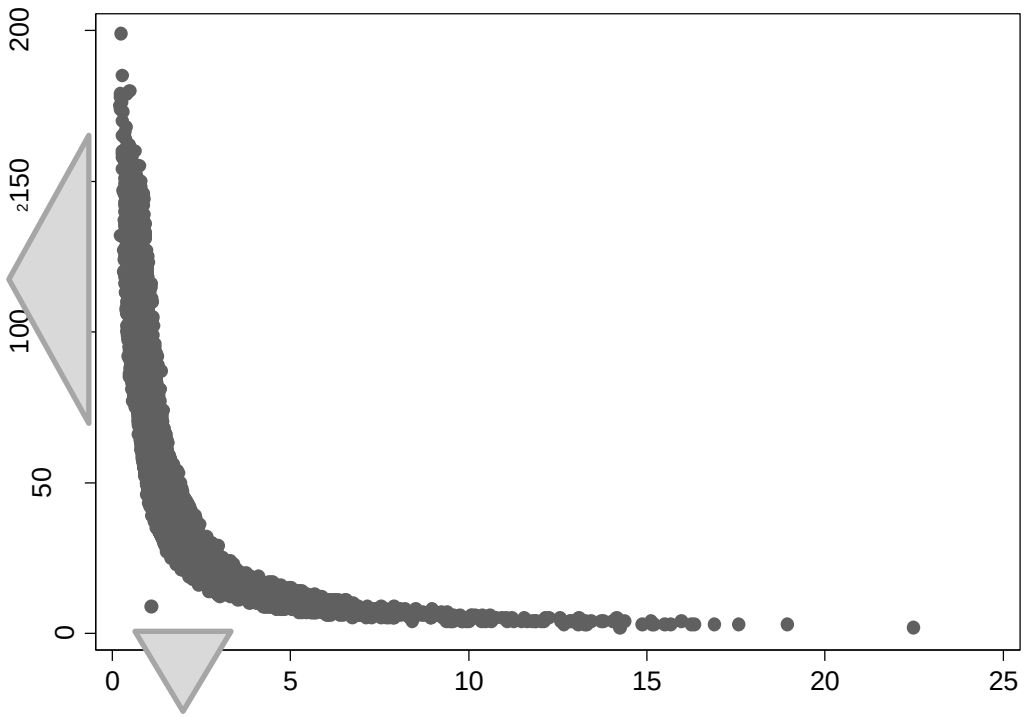
(high SCr)



Impact of Imprecision

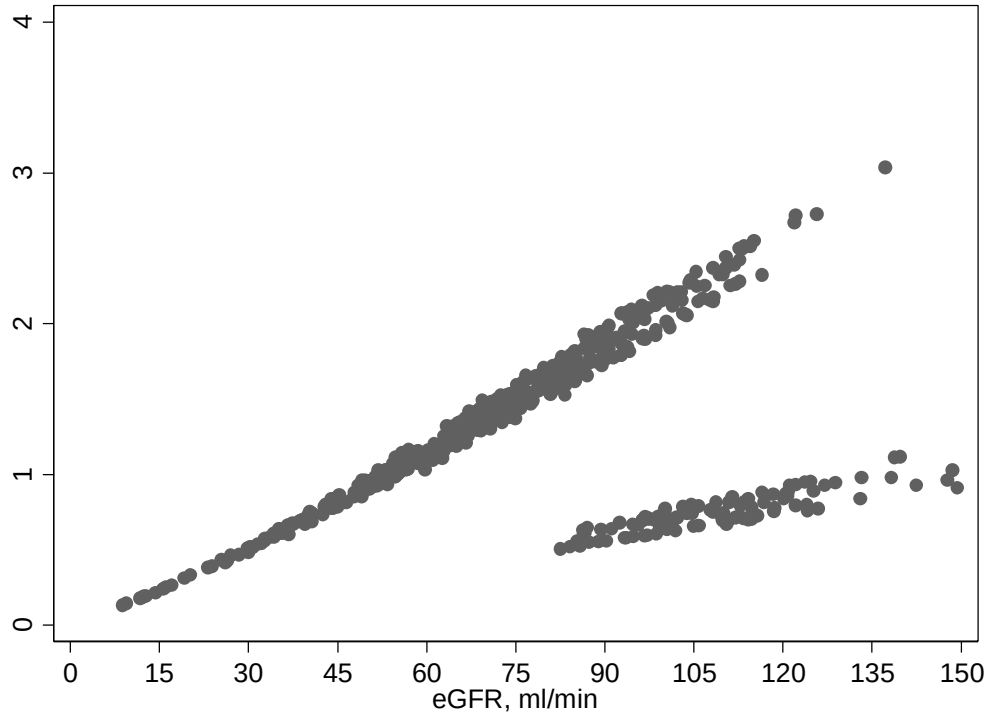
(Low SCr)

Variation in Output

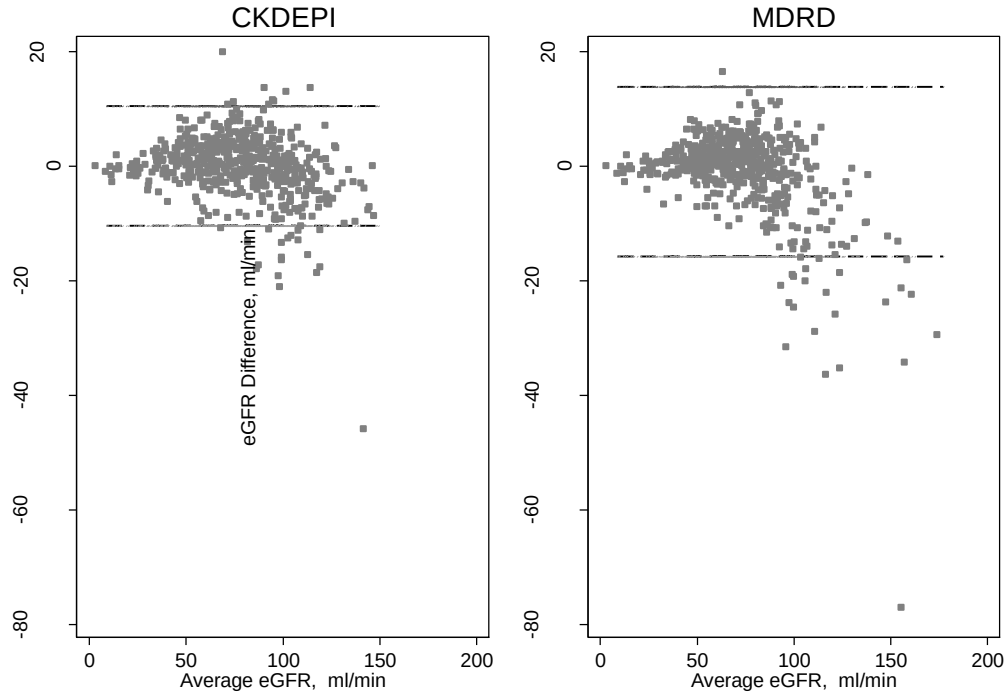


Variation in Input

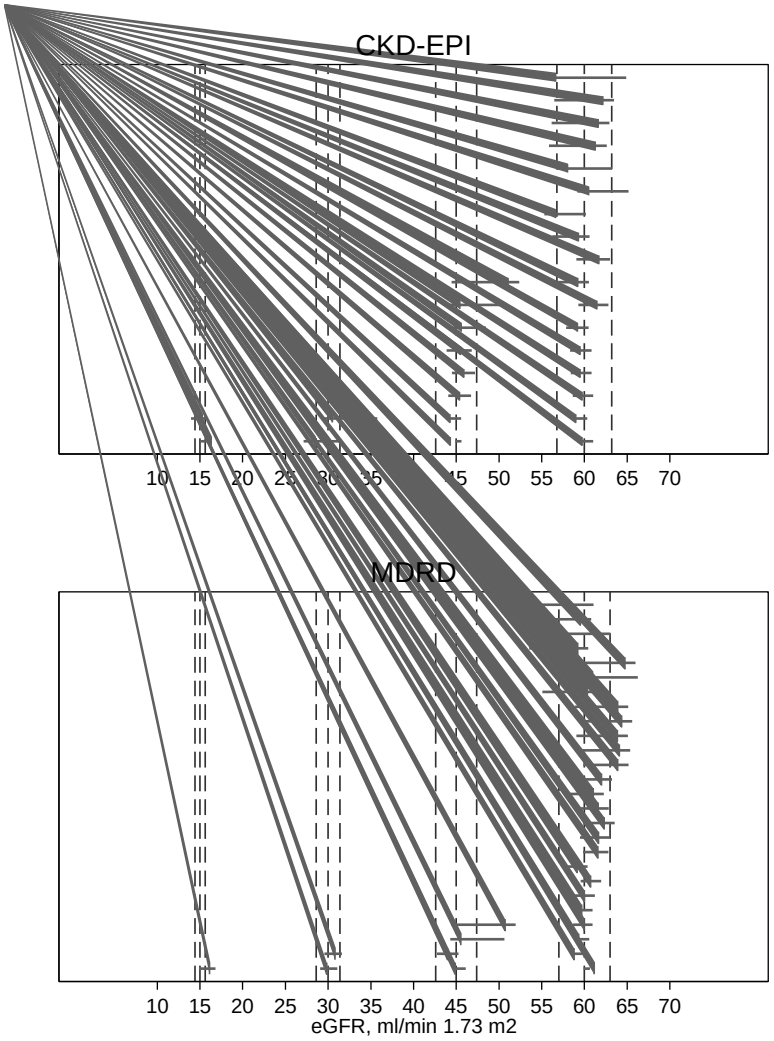
Precision Profile for eGFR



Bland Altman Plot for eGFR



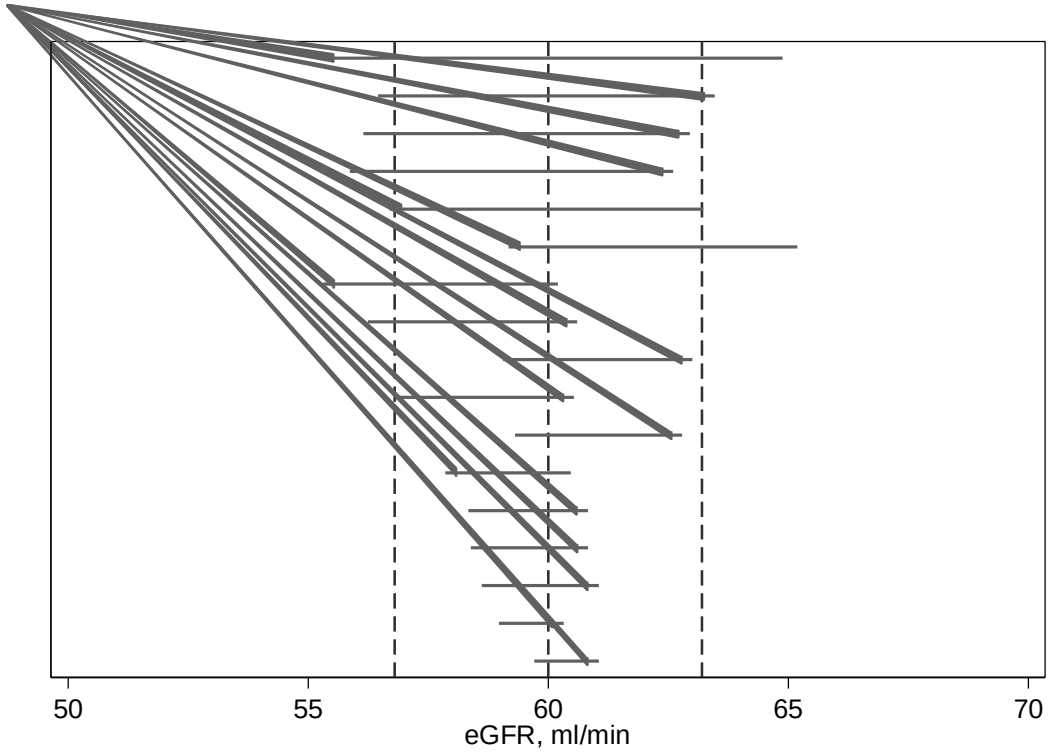
Discordances at Decision Limits



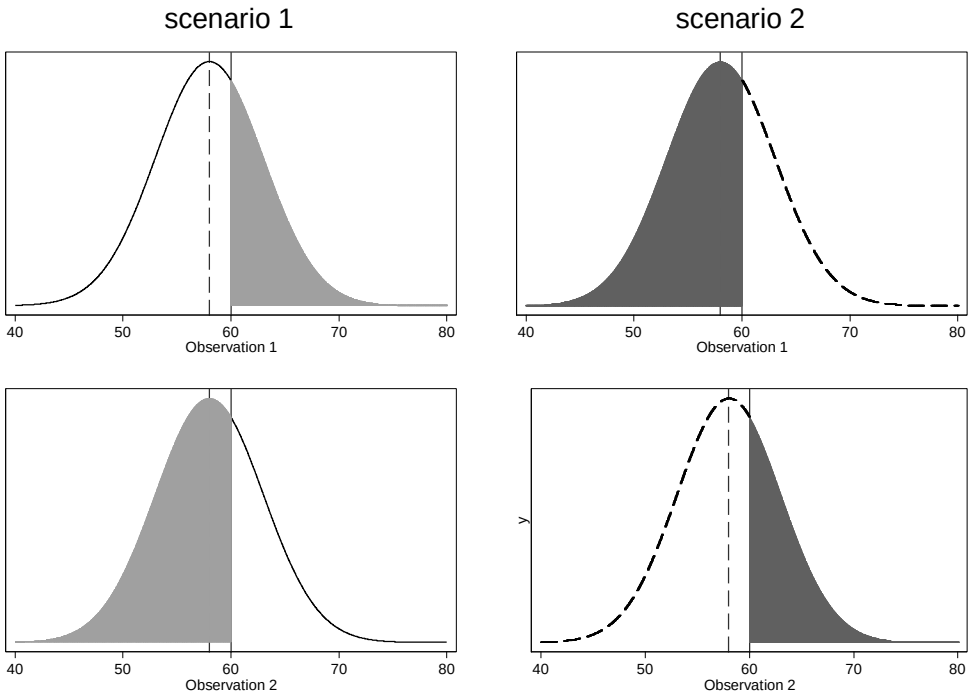
Discordance Rate at Decision Limits

eGFR Decision limit ml/min				Total
15	30	45	60	
0.37	0.37	1.49	3.13	5.36

Discordances at 60 mL

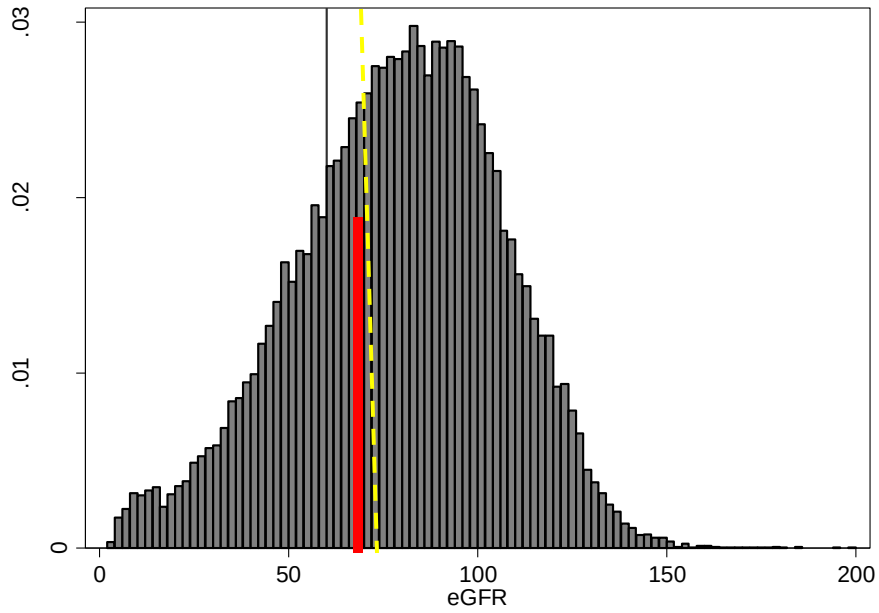


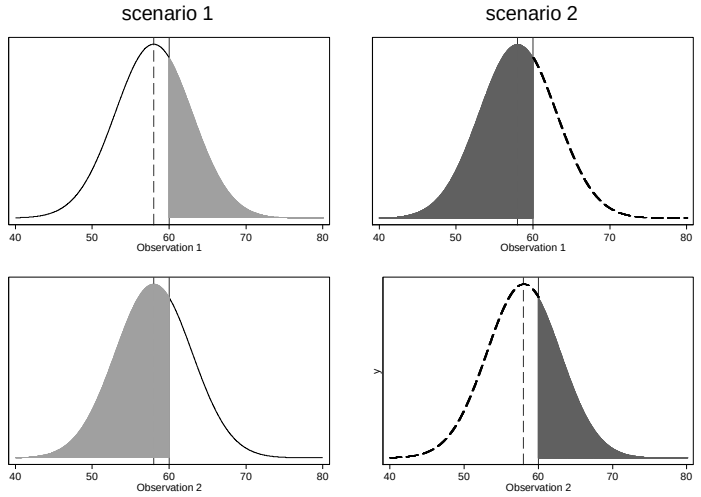
Discordance of Due to Imprecision



Discordance due to Imprecision

Given a true eGFR of 58 what is the probability of discordance at 60 ml/min?

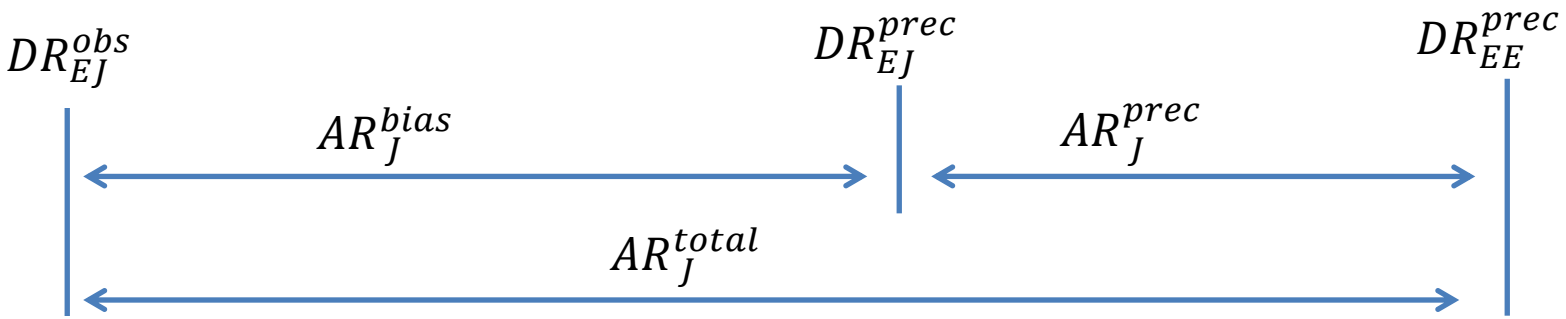




Prob(Discordance and eGFR=58) = Prob(Discordance|eGFR =58) Prob(eGFR=58)

$$\widehat{DR}_{EE}^{prec} = \frac{1}{N}\sum_{i=1}^{N}\left\{2\left[F_E(z_E(X_{E,i})\right]\left[1 - F_E(z_E(X_{E,i})\right]\right\}$$

Components of Discordance



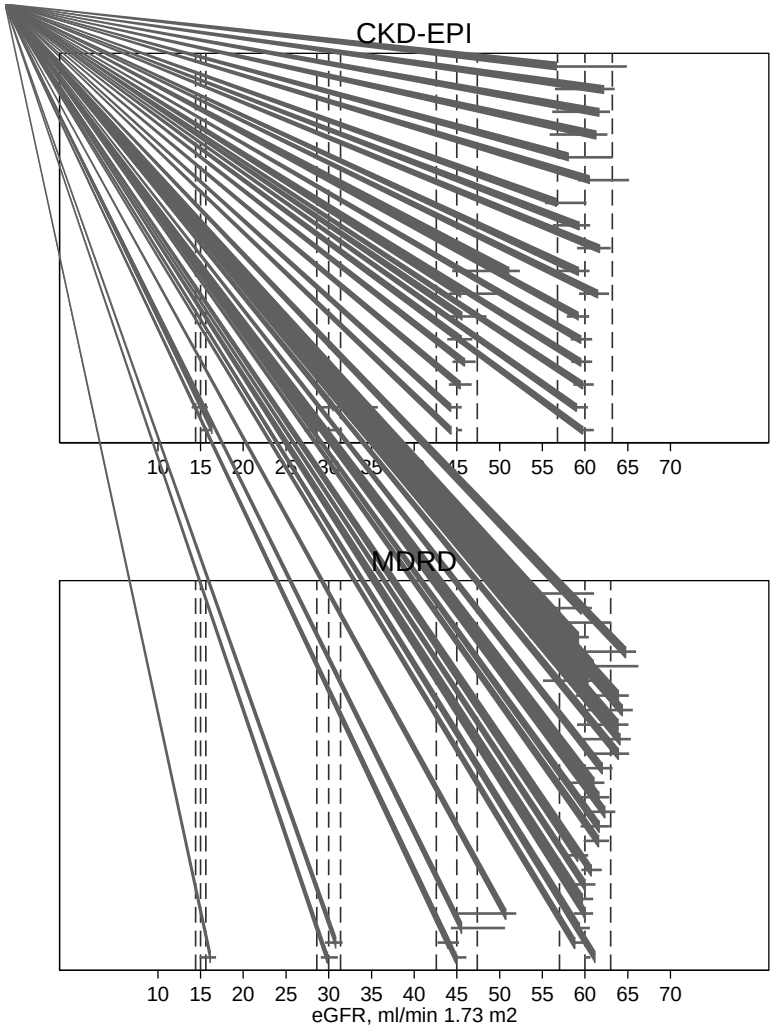
DR_{EJ}^{obs}= observed discordance rate between enzymatic and Jaffe

DR_{EE}^{prec}= discordance due only to precision for enzymatic method

DR_{EJ}^{prec}= discordance due only to precision for enzymatic and Jaffe method

DR_{EJ}^{bias}= discordance due only to precision for enzymatic method

Discordances at Decision Limits



Conditional Discordance Rates (percent)						
Method	CKD-EPI			MDRD		
Decision Limit	30	45	60	30	45	60
$DR_{J,E}^{obs}$	0.37	1.47	3.13	0.37	0.74	4.79
$\widehat{DR}_{E,E}^{prec}$	0.16	0.54	1.26	0.16	0.58	1.48
$\widehat{DR}_{J,E}^{prec}$	0.32	0.49	1.17	0.33	0.53	1.38
$\widehat{AD}_{J}^{total}$	0.21	0.94	1.88	0.21	0.16	3.33
$\widehat{AD}_{J}^{prec}$	0.16	-0.05	-0.09	0.18	-0.05	-0.10
$\widehat{AD}_{J}^{bias}$	0.16	-0.05	-0.09	0.04	0.21	3.44

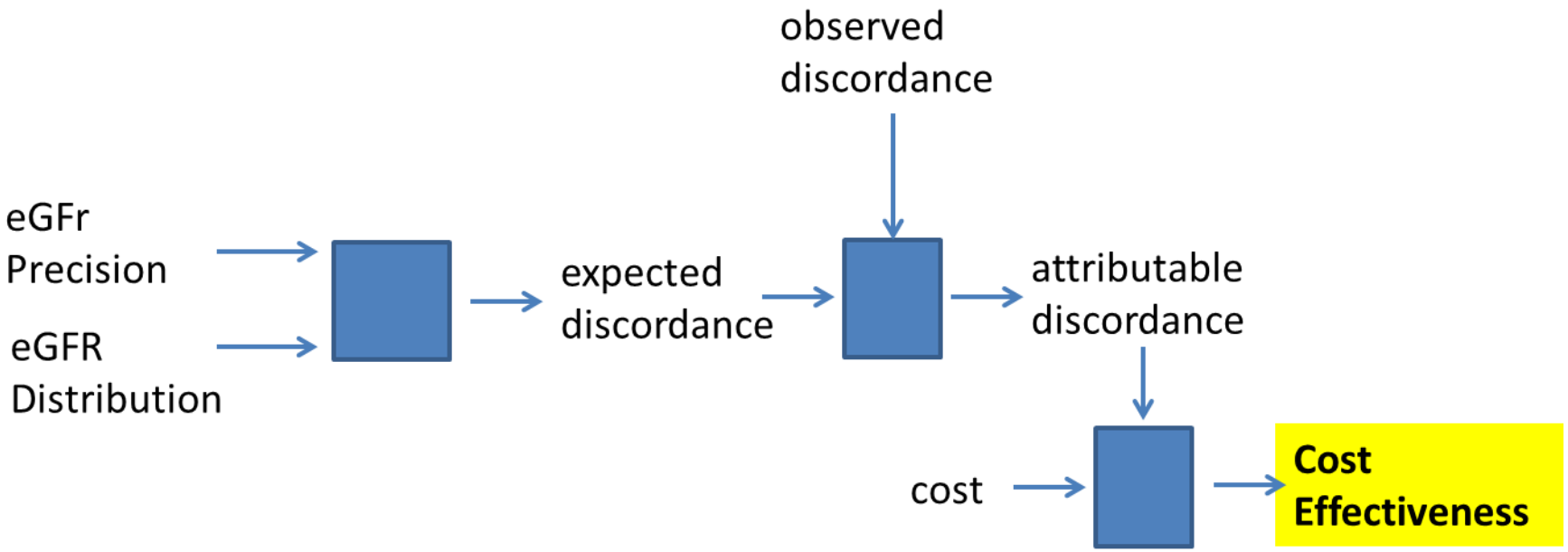
Cost Effectiveness

Jaffe vs Enzymatic

$$\text{ICER} = \frac{\Delta Cost}{\Delta\ Outcome} = \frac{\$1.70}{0.033\ misclassification}$$

$$= \$51 \text{ per misclassification prevented}$$

Summary


observed
discordance
eGFr
Precision
eGFR
Distribution
expected
discordance
attributable
discordance
cost
Cost
Effectiveness

Risk Assessment

- Risk = Probability x Consequence

Risk Assessment

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Our study

Consequences of Misclassification

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Evaluating a Change in Method

Jaffe vs Enzymatic