4

Misty Fjords National Monument, Alaska

CARDIOVASCULAR DISEASE IN PATIENTS WITH CKD

This chapter highlights the epidemiology of the relationship between CKD and cardiovascular disease, and documents the impressive graded risk of mortality associated with advanced CKD. Additionally, we present a temporal analysis of the changing approach to diagnostic evaluation in patients with CKD and CHF, include a new investigation on the distribution of fatal and nonfatal myocardial infarction by CKD stage, and look at medication use and associated outcomes by CKD stage.

We begin with a Venn diagram detailing the prevalence of cardiovascular disease with respect to CKD; this figure also provides a rough temporal analysis, as data are presented for 2005 and 2010. In both years there is an increased prevalence of associated cardiovascular disease in patients with CKD compared to those without. In 2005, for example, nearly half of elderly CKD patients had a concomitant diagnosis of CHF, and 15 percent had an AMI; among their non-CKD counterparts, these numbers fell to 22 and 7 percent. Similar clustering occurs in 2010, but data suggest there may have been a reduction in certain types of associated cardiovascular comorbidity (e.g., an absolute 6 percent reduction in CHF).

Later in the chapter, in Table 4.b, we provide data on medication use with respect to cardiovascular condition and CKD stage. In patients with CHF, for example, one notable finding is the increased use of beta blockers. In elderly non-CKD patients, 52 percent of those with CHF received a beta blocker in 2007; this rose to 60 percent in 2010; in the CKD population, use rose from 56 to 66 percent. There was a more modest increase in the use of ACEIS/ARBS, from 54 to 57 percent in the non-CKD population, and from 47 to 52 percent in those with CKD. One conclusion derived from these data is that, in 2010, there is really no discernible impact of "therapeutic nihilism" related to the use of beta blockers in patients with advanced CKD. The proportion of patients receiving a beta blocker was actually higher, at about 70 percent, than the 60 percent seen in patients without CKD. One can speculate that this may reflect both a change in practice patterns and the availability of Part D coverage, facilitating the administration of these evidence-based therapies. In patients with AMI, there was a high penetration in the use of beta blockers, similar across CKD stages, and reaching 77–78 percent in both CKD and non-CKD patients.

For ACEIS/ARBS, in contrast, there appears to be an inverse relationship between CKD stage and the use of these agents following AMI, with the medications prescribed to 66 percent of non-CKD patients, compared to 57 percent of those with CKD. Importantly, only 46 percent of patients with Stage 4–5 CKD receive an ACEI/ARB. There also appears to be an inverse relationship between CKD stage and warfarin use in patients with AFIB. In 2010, 56 percent of non-CKD patients, and 49 percent of those with CKD, were identified as receiving warfarin, numbers higher than the 48 and 40 percent seen in 2007, and suggesting the

Man's heart away from nature becomes hard.
LUTHER STANDING BEAR

progressive dissemination of this particular evidence-based therapy over time in the Medicare population (Shroff et al., Arch Internal Med, in press 2012, and Lakshminarayan et al.).

Finally, statins are widely used for secondary prevention in patients with known coronary artery disease, irrespective of CKD stage, a finding borne out in these data. In patients without identified cardiovascular events, the percentage receiving statins increased from 37 to 44 percent in the non-CKD population, and from 45 to 54 percent in those with CKD. » **Figure 4.1;** see page 143 for analytical methods. *December 31, 2005 & 2010 point prevalent Medicare enrollees, age 66 & older, with fee-for-service coverage for the entire calendar year.*

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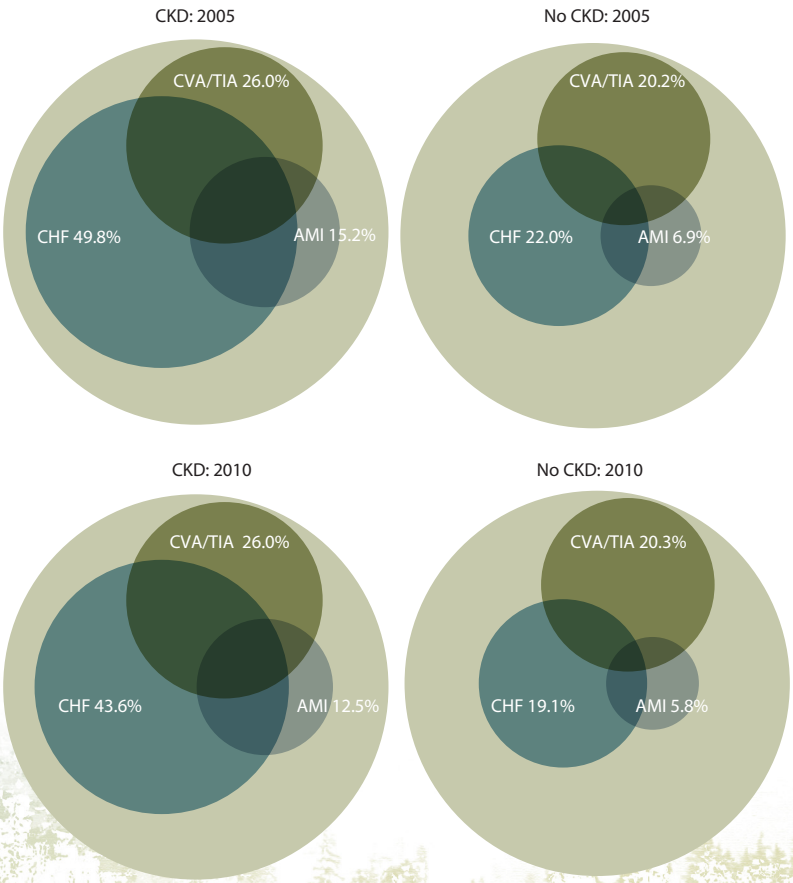
4.1 **Cardiovascular disease in patients with or without CKD**



This table provides a snapshot of cardiovascular disease prevalence related to demography and CKD stage. One uniform finding is the progressively increased representation for each cardiovascular condition with respect to advanced CKD stage and age. In the non-CKD population, for example, only 3.6 percent of patients age 66–69 have CHF, compared to 15 percent of those age 85 and older. Among patients with Stage 4–5 CKD, these numbers reach 34 and 48 percent. CHF is a common comorbid condition in elderly patients, particularly among those with advanced CKD.

After CHF, the next most common condition is atrial fibrillation. Four percent of patients age 66–69 and without identified CKD have atrial fibrillation, compared to 17 percent of those age 85 or older. Among patients with Stage 4–5 CKD, in contrast, these numbers rise to 16 and 32 percent. Surprisingly, percentages are lower for black/African American patients compared to whites. **» Table 4.a;** see page 143 for analytical methods. *December 31, 2010 point prevalent Medicare enrollees, age 66 & older.*

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4.a **Cardiovascular disease & intervention (percent), by CKD stage, age, & race, 2010**

	Overall	60–69	70–74	75–84	85+	White	Blk/Af Am	Other
CHF								
No CKD	7.3	3.6	4.8	8.1	15.0	7.2	8.8	6.0
All CKD	31.8	22.8	25.2	31.5	41.8	31.8	33.2	28.1
Stages 1–2	26.9	20.5	21.1	26.9	38.2	27.1	26.7	25.5
Stage 3	30.7	23.2	24.6	30.3	40.3	30.8	31.7	26.8
Stage 4–5	41.7	33.6	35.9	41.4	48.1	42.1	40.1	39.1
AMI								
No CKD	2.2	1.6	1.9	2.5	3.0	2.3	1.8	1.5
All CKD	9.1	7.9	8.8	9.2	9.9	9.4	8.1	7.7
Stages 1–2	7.8	6.8	7.3	8.2	8.4	8.1	6.1	6.6
Stage 3	8.7	7.7	8.1	8.7	9.9	9.0	7.6	7.1
Stage 4–5	10.4	8.3	11.7	10.4	10.6	10.7	9.6	8.9
PAD								
No CKD	9.3	4.7	6.5	10.6	17.9	9.3	10.4	7.8
All CKD	26.3	20.0	22.8	26.7	31.5	26.6	25.1	22.7
Stages 1–2	22.7	16.2	20.0	23.5	29.5	23.2	21.2	20.6
Stage 3	24.7	18.6	21.7	25.2	29.6	25.2	22.4	21.5
Stage 4–5	28.7	22.2	24.8	29.0	32.8	28.9	29.0	24.9
CVA/TIA								
No CKD	7.7	4.4	6.0	9.3	12.4	7.7	8.8	6.7
All CKD	19.0	14.5	16.2	20.0	21.7	18.8	21.1	17.6
Stages 1–2	17.5	12.5	14.5	18.6	22.8	17.3	19.2	17.7
Stage 3	17.9	14.0	15.0	19.0	20.4	17.9	19.2	16.2
Stage 4–5	19.2	17.1	16.5	19.9	20.5	18.8	22.6	17.3
Atrial fibrillation (AFIB)								
No CKD	9.3	4.1	6.5	11.5	16.9	10.0	4.5	5.1
All CKD	23.0	13.3	17.4	24.1	30.6	24.8	13.3	15.1
Stages 1–2	20.1	12.4	15.7	21.7	27.9	22.0	11.2	12.9
Stage 3	22.7	13.9	17.6	23.3	30.2	24.5	12.5	14.5
Stage 4–5	25.7	15.7	19.5	26.3	31.8	28.2	14.2	18.6
ICDs/CRT-D								
No CKD	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
All CKD	0.6	0.6	0.7	0.7	0.3	0.6	0.5	0.3
Stages 1–2	0.5	0.4	0.6	0.7	0.2	0.5	0.4	0.5
Stage 3	0.6	0.7	0.7	0.7	0.3	0.6	0.6	0.3
Stage 4–5	0.8	1.0	1.0	0.8	0.5	0.8	0.6	0.5
Revascularization (PCI)								
No CKD	0.9	0.9	1.0	0.9	0.5	0.9	0.6	0.6
All CKD	2.5	3.1	3.0	2.8	1.5	2.7	1.8	2.1
Stages 1–2	2.4	3.0	2.8	2.6	1.2	2.5	1.8	2.3
Stage 3	2.5	2.8	2.9	2.7	1.5	2.6	1.6	1.8
Stage 4–5	2.3	3.3	3.0	2.4	1.4	2.4	1.8	2.1
Revascularization CABG)								
No CKD	0.2	0.3	0.3	0.3	0.1	0.3	0.1	0.2
All CKD	0.9	1.3	1.3	1.0	0.4	1.0	0.5	0.8
Stages 1–2	0.9	1.0	1.5	0.9	0.3	1.0	0.7	0.9
Stage 3	1.0	1.3	1.3	1.0	0.4	1.0	0.6	0.8
Stage 4–5	0.6	0.6	1.0	0.7	0.3	0.7	0.2	0.4

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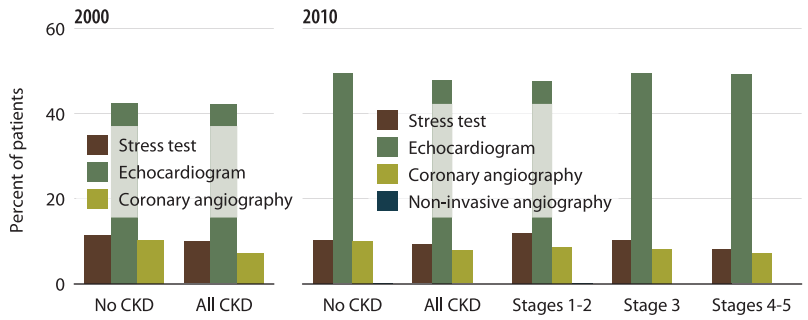
Patients with CHF who receive diagnostic testing within 90 days of diagnosis, by CKD status



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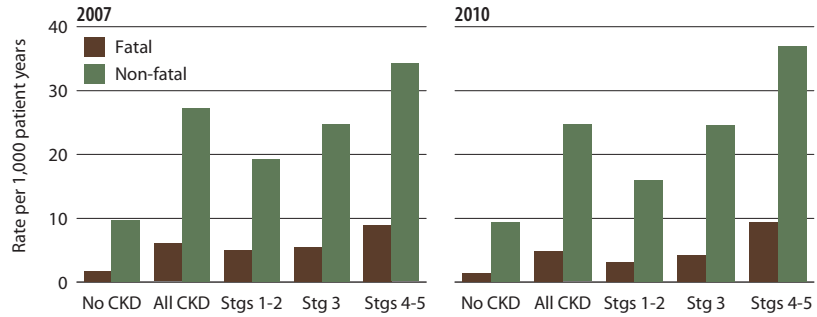
Rates of fatal & non-fatal AMI, by CKD status



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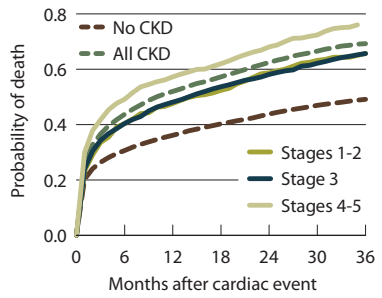
Probability of death following an AMI, by CKD status, 2007–2008



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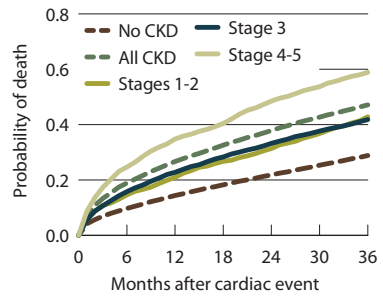
Probability of death following a CVA/TIA, by CKD status, 2007–2008



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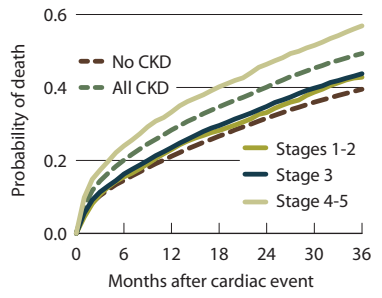
Probability of death following a CHF diagnosis, by CKD status, 2007–2008



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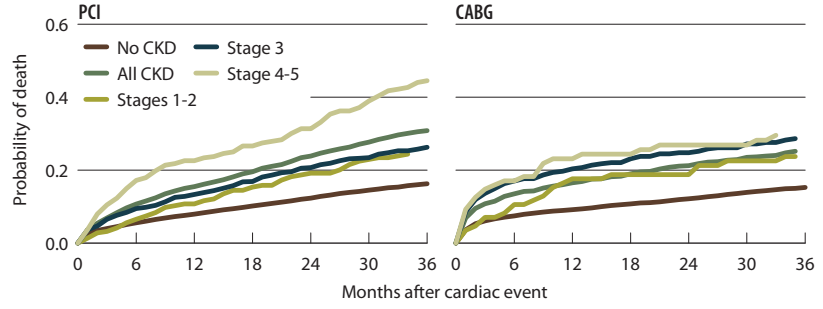
Probability of death following a cardiovascular procedure (PCI/CABG), by CKD status, 2007–2008



There has been little change by CKD status in the percentage of patients receiving stress tests, nor has the use of coronary angiography changed appreciably, despite the recognition of CKD as a risk factor for both coronary events and increased mortality. Data suggest that clinicians have not become materially more aggressive in using angiography to evaluate elderly CKD patients for coronary disease. The use of echocardiography in CKD patients with CHF, in contrast, has grown, from 42 percent in 2000 to 48 percent in 2010.

There is no clear temporal trend in the distribution of fatal and non-fatal myocardial infarctions (MIs), with the possible exception of a small increased rate of non-fatal MIs in patients with advanced CKD (this might reflect the dissemination of more sensitive cardiac biomarkers; most identified MIs are non-fatal). Mortality following MI in patients with advanced CKD, however, remains high, with long-term mortality approaching that reported in dialysis patients.

There is a graded increased risk of mortality with advancing CKD; the two-year mortality rate after MI, for example, at 44 percent in patients with no CKD, rises to 58 and 68 percent for those with Stage 3 and 4–5 CKD. Similar trends occur for death following CVA/TIA, CHF diagnosis, and coronary revascularization. Although the probability of death is lower in patients with advanced CKD who have CABG surgery compared to PCI, these are observational data and there may be confounding by indication. » **Figures 4.2–7;** see page 143 for analytical methods. *Jan. 1 pt. prev. Medicare pts. age 66 & older; first CHF diag. in 2000 or 2010 (4.2); first CVD diagnosis or procedure in 2007–2008 (4.4–7).*

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4.b Cardiovascular disease & pharmacological interventions (row percent), by diagnosis & CKD stage

	2007 N	ACEI/ARB	Beta blocker	Clopid-ogrel	Warfarin	Statin	Amio-darone	2010 N	ACEI/ARB	Beta blocker	Clopid-ogrel	Warfarin	Statin	Amio-darone
CHF														
No CKD	59,922	53.8	52.2	14.2	21.2	36.9	4.6	50,894	57.2	60.3	16.0	24.3	46.6	5.2
All CKD	12,611	47.4	56.4	18.3	19.0	38.9	5.7	16,348	52.2	66.4	20.3	23.2	50.8	7.7
Stages 1–2	650	50.5	54.2	19.2	18.9	39.5	3.8	666	57.1	64.3	21.3	19.2	50.6	7.5
Stage 3	2,274	52.6	60.6	19.6	19.7	45.8	5.9	4,505	55.0	68.2	21.4	24.8	55.0	8.0
Stages 4–5	2,129	42.4	62.0	19.7	16.8	41.2	6.1	3,316	44.4	69.9	21.4	21.3	52.8	8.8
AMI														
No CKD	4,078	64.7	74.5	49.4	13.7	59.5	6.5	3,491	65.5	77.4	50.5	14.4	66.8	6.7
All CKD	800	55.5	74.3	44.1	14.5	57.6	4.4	964	57.3	78.0	46.2	17.0	63.7	7.5
Stages 1–2	38	65.8	86.8	44.7	21.1	65.8	2.6	37	54.1	83.8	40.5	10.8	62.2	5.4
Stage 3	144	56.3	76.4	48.6	14.6	63.2	4.9	268	56.7	77.2	48.9	17.9	65.3	6.0
Stages 4–5	149	42.3	80.5	40.9	15.4	52.3	3.4	189	46.0	78.8	51.3	13.2	69.8	5.8
PAD														
No CKD	65,809	44.8	39.3	15.1	11.7	36.6	1.9	60,263	48.4	44.2	16.9	12.4	46.3	2.0
All CKD	9,938	47.3	52.2	20.9	15.1	40.8	4.3	12,988	51.1	57.8	22.8	16.8	51.9	4.7
Stages 1–2	538	52.0	51.9	22.1	14.7	41.3	4.1	625	55.4	56.6	24.6	14.9	55.0	4.3
Stage 3	1,855	53.1	54.3	22.8	15.0	49.7	4.6	3,646	54.9	60.6	25.0	17.6	56.6	4.8
Stages 4–5	1,555	44.8	59.0	21.0	13.0	45.2	5.0	2,289	45.0	64.1	23.9	16.0	56.5	6.2
CVA/TIA														
No CKD	48,437	46.9	40.8	21.4	14.0	41.8	1.9	40,372	51.2	45.4	23.1	14.8	53.5	2.1
All CKD	6,378	49.4	53.0	26.5	15.9	43.3	3.9	7,671	52.7	58.3	26.3	19.3	54.6	4.3
Stages 1–2	317	50.5	53.6	28.1	13.9	42.6	3.8	361	58.2	59.8	26.0	15.5	54.8	3.3
Stage 3	1,164	51.7	56.6	26.7	17.1	50.2	4.9	2,207	54.6	59.6	28.0	20.2	58.4	4.3
Stages 4–5	912	46.7	59.4	28.3	14.0	47.4	4.2	1,232	46.3	64.6	26.7	18.7	57.2	6.2
AFIB														
No CKD	53,590	44.7	50.4	9.0	47.5	33.1	7.8	54,002	50.2	60.4	9.6	56.2	46.1	8.5
All CKD	7,245	45.0	54.9	13.9	40.2	35.5	10.5	10,917	50.6	66.5	14.2	49.4	50.4	12.9
Stages 1–2	372	50.5	55.1	13.2	43.0	34.1	8.1	498	54.2	66.1	16.5	45.6	52.6	12.4
Stage 3	1,269	48.7	55.9	14.3	44.6	40.3	12.4	3,117	52.8	67.3	14.2	52.6	54.1	14.3
Stages 4–5	1,094	43.2	59.0	14.3	38.4	37.8	12.7	1,888	44.2	68.9	15.7	48.0	53.0	15.5
ICD/CRT-D														
No CKD	654	74.8	80.3	25.1	30.9	57.2	15.9	455	79.8	84.6	31.9	36.0	65.1	20.2
All CKD	241	65.1	82.2	28.2	32.8	53.5	18.7	179	64.8	88.3	31.3	43.6	60.9	21.2
Stages 1–2	7	42.9	71.4	42.9	57.1	42.9	14.3	5	100.0	100.0	40.0	20.0	40.0	0.0
Stage 3	54	66.7	83.3	29.6	38.9	51.9	18.5	61	59.0	93.4	31.1	39.3	59.0	16.4
Stages 4–5	41	53.7	73.2	31.7	29.3	58.5	17.1	36	47.2	86.1	33.3	44.4	63.9	19.4
Revascularization: PCI														
No CKD	4,695	64.7	73.5	89.3	10.3	72.2	4.0	4,319	66.1	75.3	87.0	10.7	76.1	3.7
All CKD	530	59.1	77.7	87.2	12.5	66.6	5.1	728	67.2	80.2	84.1	14.3	71.0	6.0
Stages 1–2	32	53.1	78.1	93.8	9.4	81.3	0.0	33	75.8	81.8	90.9	6.1	81.8	0.0
Stage 3	127	57.5	74.0	85.0	15.0	62.2	3.1	229	65.5	76.9	83.4	13.5	67.7	5.2
Stages 4–5	71	60.6	76.1	88.7	12.7	59.2	8.5	107	50.5	77.6	88.8	13.1	76.6	4.7
Revascularization: CABG														
No CKD	1,299	62.2	83.4	31.6	18.2	72.6	26.8	1,000	64.0	86.6	32.4	21.2	82.6	33.6
All CKD	129	63.6	82.9	32.6	27.9	67.4	29.5	139	56.8	85.6	36.7	17.3	77.7	23.7
Stages 1–2	12	75.0	91.7	41.7	33.3	66.7	33.3	8	37.5	62.5	25.0	0.0	87.5	37.5
Stage 3	29	79.3	82.8	44.8	24.1	69.0	27.6	51	56.9	88.2	41.2	17.6	80.4	25.5
Stages 4–5	15	53.3	80.0	20.0	33.3	86.7	33.3	18	33.3	88.9	38.9	11.1	83.3	16.7
No cardiac event														
No CKD	360,270	41.1	27.7	4.3	2.3	37.0	0.2	377,558	44.5	30.0	5.3	2.4	44.1	0.2
All CKD	13,360	59.5	43.8	7.5	4.5	45.4	0.5	22,513	62.5	47.3	8.8	5.0	53.9	0.6
Stage 1-2	791	65.5	45.3	8.1	3.3	52.1	0.3	1,254	65.9	45.1	8.1	4.6	58.0	0.2
Stage 3	3,133	69.3	48.1	8.1	3.8	53.6	0.5	7,572	69.2	49.9	9.2	4.3	60.1	0.6
Stage 4-5	2,253	60.1	53.5	8.4	3.8	48.3	1.0	3,555	60.6	57.8	10.1	5.1	55.6	1.0

» **Table 4.b;** see page 143 for analytical methods. *January 1 point prevalent Medicare patients with Medicare Parts A, B, & D enrollment.*

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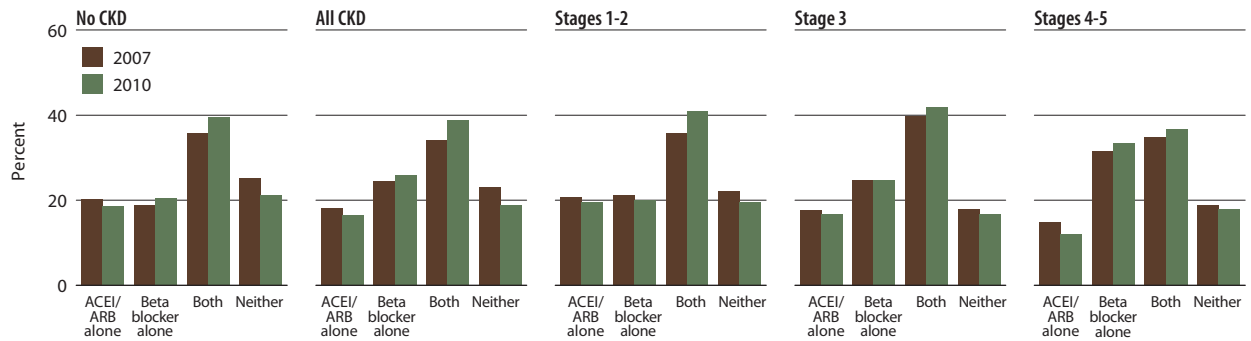
4.8 **Utilization of cardiac drugs, by drug class & CKD status, 2010**



Even in a short, three-year time period, the use of beta blockers has increased. Importantly, the number of patients receiving neither an ACEI/ARB nor a beta-blocker fell between 2007 and 2010.

Figures 4.9–10 demonstrate the apparent protective association, with respect to CKD, of combined ACEI/ARB therapy in patients with CHF and following MI. Although these are observational data (which should be interpreted with caution), it is interesting that results are concordant with clinical trial data on the use of ACEIs/ARBs and beta blockers in CHF and post-MI populations.

The cumulative incidence of death reported in these figures, and the relationship to the use of ACEIs/ARBs and beta blockers, are remarkably similar to what is shown in parallel figures in Chapter Four of Volume Two, with the main difference being the higher overall mortality in ESRD patients with these conditions and the smaller absolute difference in survival related to the individual therapies. The overall patterns, however, are similar, suggesting therapeutic benefit across all stages of CKD, including ESRD.

Although the figures in Volume Two pertain to ESRD rather than dialysis, their data are indicative of dialysis outcomes, as 92 and 94 percent of CHF and MI events, respectively, are among dialysis patients. The relative contribution of renal transplant recipients to these data is actually very small. » **Figures 4.8–10;** see page 143 for analytical methods. *January 1 point prevalent patients with Medicare Parts A, B, & D enrollment, with a first diagnosis of CHF or MI in the year; patients with baseline disease are excluded.*

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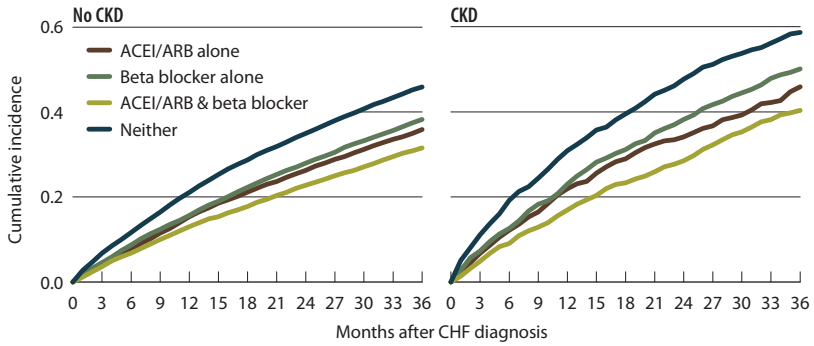
4.9 **Cumulative incidence of death following a diagnosis of CHF, by CKD stage & medication use, 2007**



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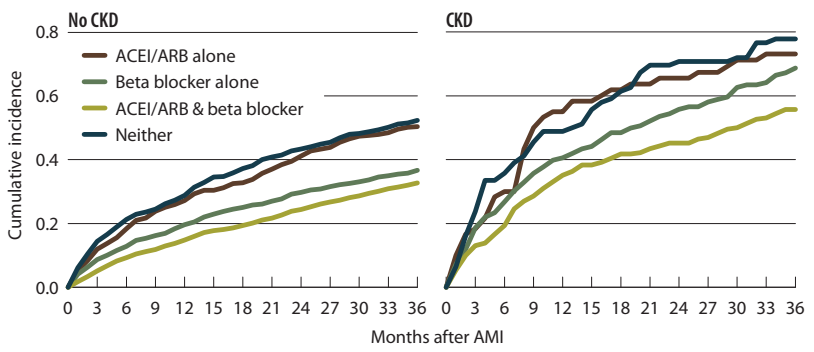
4.10 **Cumulative incidence of death following a diagnosis of AMI, by CKD stage & medication use, 2007**



PRESENCE OF CARDIOVASCULAR DISEASE

patients with cardiovascular disease (percent; Figure 4.1)

CKD: 2005	» CHF · 49.8	» CVA/TIA · 26.0	» AMI · 15.2
CKD: 2010	· 43.6	· 26.0	· 12.5
no CKD: 2005	» CHF · 22.0	» CVA/TIA · 20.2	» AMI · 6.9
no CKD: 2010	· 19.1	· 20.3	· 5.8

CARDIOVASCULAR MORTALITY

probability of death at two years following AMI, 2007–2008 (Figure 4.4)

» no CKD · 0.44 » all CKD · 0.63 » Stages 1–2 · 0.59 » Stage 3 · 0.58 » Stages 4–5 · 0.68

probability of death at two years following CVA/TIA, 2007–2008 (Figure 4.5)

» no CKD · 0.22 » all CKD · 0.38 » Stages 1–2 · 0.31 » Stage 3 · 0.33 » Stages 4–5 · 0.49

probability of death at two years following a CHF diagnosis, 2007–2008 (Figure 4.6)

» no CKD · 0.32 » all CKD · 0.40 » Stages 1–2 · 0.33 » Stage 3 · 0.35 » Stages 4–5 · 0.46

probability of death at two years following PCI, 2007–2008 (Figure 4.7)

» no CKD · 0.12 » all CKD · 0.24 » Stages 1–2 · 0.19 » Stage 3 · 0.21 » Stages 4–5 · 0.31

probability of death at two years following CABG, 2007–2008 (Figure 4.7)

» no CKD · 0.12 » all CKD · 0.21 » Stages 1–2 · 0.19 » Stage 3 · 0.25 » Stages 4–5 · 0.27

MEDICATION USE & SURVIVAL IN PATIENTS WITH CVD

cumulative incidence of death at two years following a diagnosis of CHF (Figure 4.9)

no CKD	» ACE/ARB · 0.26	» beta blocker · 0.28	» both · 0.23	» neither · 0.35
CKD	· 0.34	· 0.38	· 0.29	· 0.48

cumulative incidence of death at two years following a diagnosis of AMI (Figure 4.10)

no CKD	» ACE/ARB · 0.41	» beta blocker · 0.30	» both · 0.24	» neither · 0.43
CKD	· 0.66	· 0.56	· 0.45	· 0.71