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Earlier Depression Treatment Reduces the Risk of Incident Cardiovascular Disease: A Follow-Up Study of the IMPACT Trial

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Presented at the 33rd Annual Meeting and Scientific Sessions
of the Society of Behavioral Medicine
April 14, 2012

This research was supported by National Institute on Aging Grants
R01 AG031222 and K24 AG024078.

Previous Clinical Trials

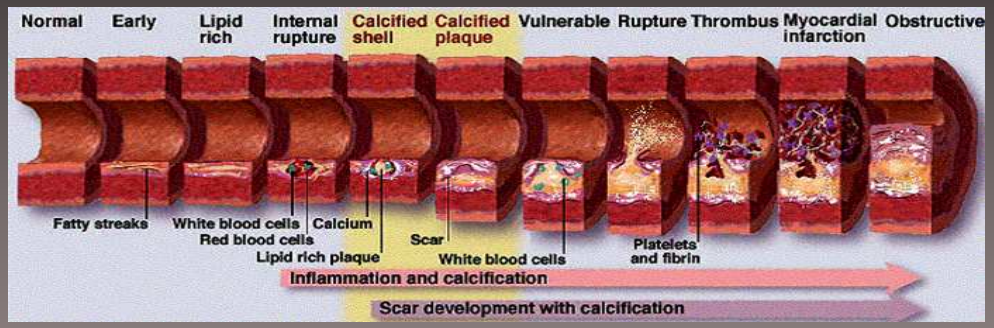
- Evidence suggests that depression is an independent risk and prognostic factor for cardiovascular disease (CVD), including coronary artery disease (CAD) and cerebrovascular disease (CBV).
  (Van der Kooy et al., 2007; Meijer et al., 2011)

- In general, past trials of depression treatments in cardiac patients have not observed the anticipated reduction in CVD events.
  - ENRICHD: psychotherapy (Berkman et al., 2003)
  - MIND-IT: pharmcotherapy (van Melle et al., 2007)

- Although other reasons have been offered, an unexplored explanation is that the depression interventions were delivered *too late in the natural history of CVD*.

Earlier Depression Treatment?

- We hypothesize that treating depression before, versus after, the onset of clinical CVD could reduce the risk of CVD events because:
  1) Atherosclerosis appears to be more reversible before the onset of advanced lesions.
  2) Depression exerts a cardiotoxic influence early in the pathogenesis of CVD.
  3) The prevalence of vascular depression is likely to be lower in depressed patients free of CVD.
  4) Conventional prognostic factors may override the effect of depression during the later stages of CVD.



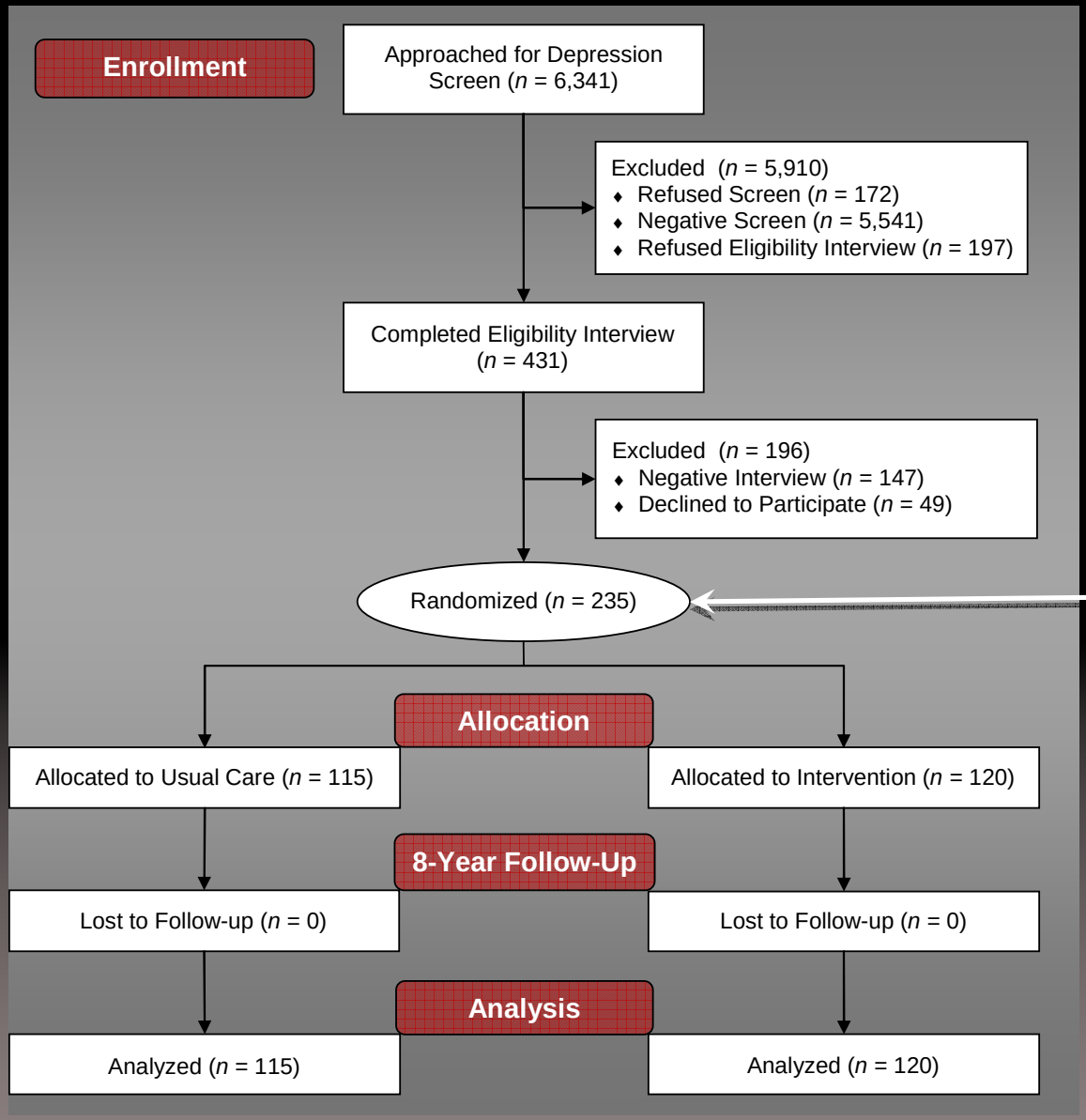
The Present Study

- Objective: To test our hypothesis that depression treatment delivered before the onset of clinical CVD reduces the risk of CVD events

- Design: 8-year follow-up study of patients from the Indiana sites of the Improving Mood-Promoting Access to Collaborative Treatment (IMPACT) trial
  - A multisite RCT of collaborative care for late-life depression with recruitment from 1999-2001
  - Positive for the depression outcomes

- Setting: Primary care clinics of an academic group practice

Flowchart for Participants from the Indiana Sites of the IMPACT Trial



Participants

PC patients

MDD or Dysthymia

≥ 60 years

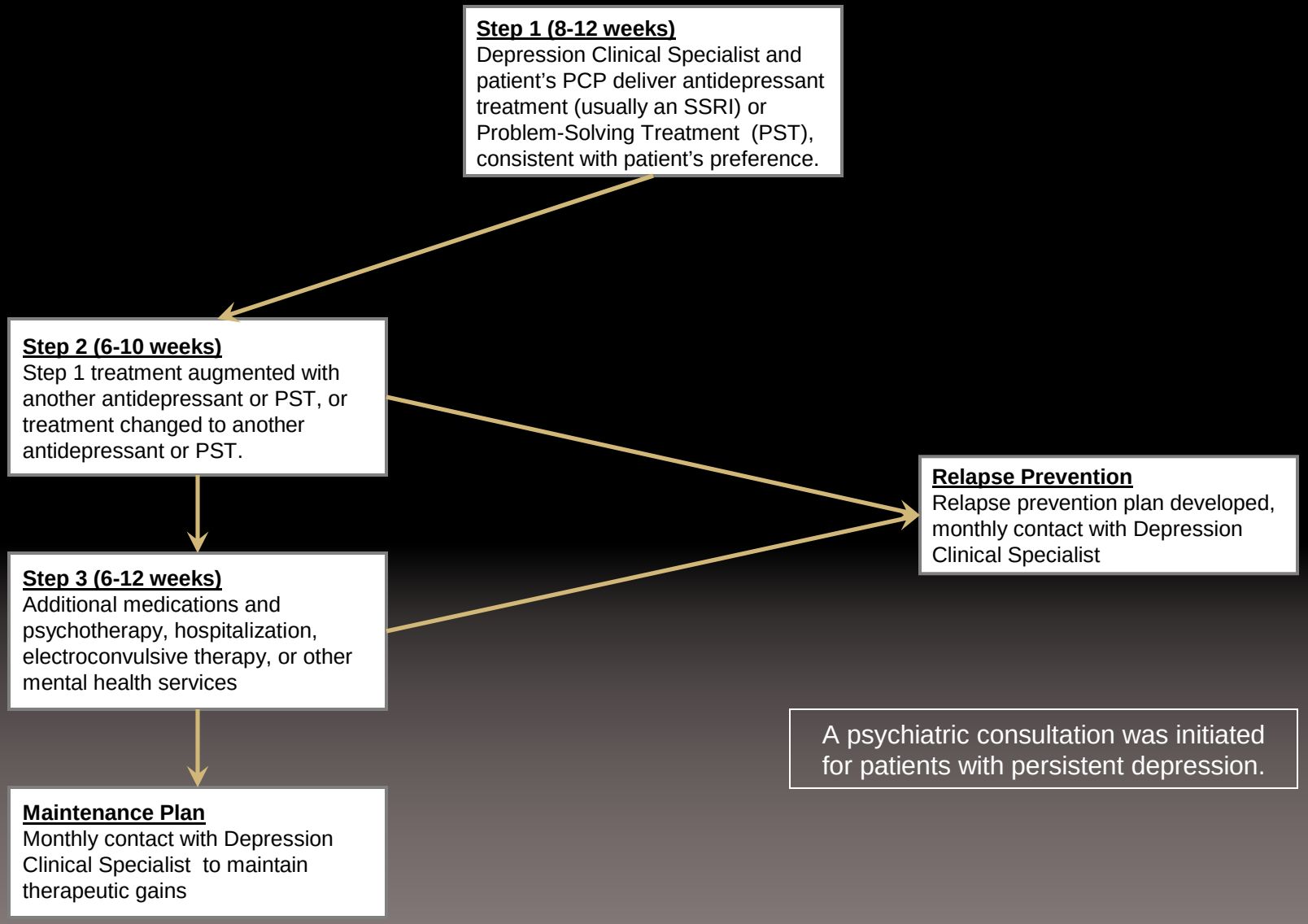
76% female

48% African Amer.

52% with CVD

The IMPACT Intervention (12 months)

Collaborative Stepped Care Program Involving Antidepressants and/or Brief Psychotherapy



Outcome Measure: 8-Year Incidence of CVD

- The presence of any of the following in the electronic medical record or Medicare/Medicaid data between the IMPACT enrollment date and December 31, 2008:

  a) Coronary artery disease (CAD) or cerebrovascular disease (CBV) death (death certificates)

  b) New CAD or CBV diagnosis (ICD-9 codes)

  c) Laboratory evidence of acute myocardial infarction (CK-MB > 3.0 ng/ml or troponin > 0.3 µg/L)

  d) CVD procedure (percutaneous coronary intervention, coronary artery bypass graft, thrombolytic therapy) (ICD-9 & CPT codes)

Results

Participant Characteristics: No Baseline CVD (*n* = 112)

Characteristic	No Baseline CVD		
	IMPACT (*n* = 62)	Usual Care (*n* = 50)	*p* value
Demographic Factors			
Age, mean (SD)	67.1 (6.4)	67.0 (6.2)	.91
Male, %	17.7	20.0	.76
African-American†, %	45.2	56.0	.25
Baseline Cardiovascular Risk Factors			
Hypertension, %	69.4	66.0	.71
Diabetes, %	29.0	38.0	.32
Smoker, %	29.0	44.0	.10
Body-Mass Index (kg/m^2), mean (SD)	33.0 (10.3)	31.2 (10.7)	.38
Baseline Depression Variables			
MDD only, %	9.7	10.0	.96
Dysthymia only, %	35.5	36.0	.96
MDD and Dysthymia, %	54.8	54.0	.93
SCL-20 score, mean (SD) (range: 0-4)	1.3 (0.5)	1.5 (0.6)	.06
Antidepressant Use in Past 3 Months, %	53.2	46.0	.45
Depression Care and Outcomes			
SCL-20 Change, mean (SD)	-0.3 (0.6)	0.0 (0.6)	.01
Antidepressants during the trial, %	72.6	58.0	.11
Psychotherapy during the trial, %	61.3	16.0	<.001

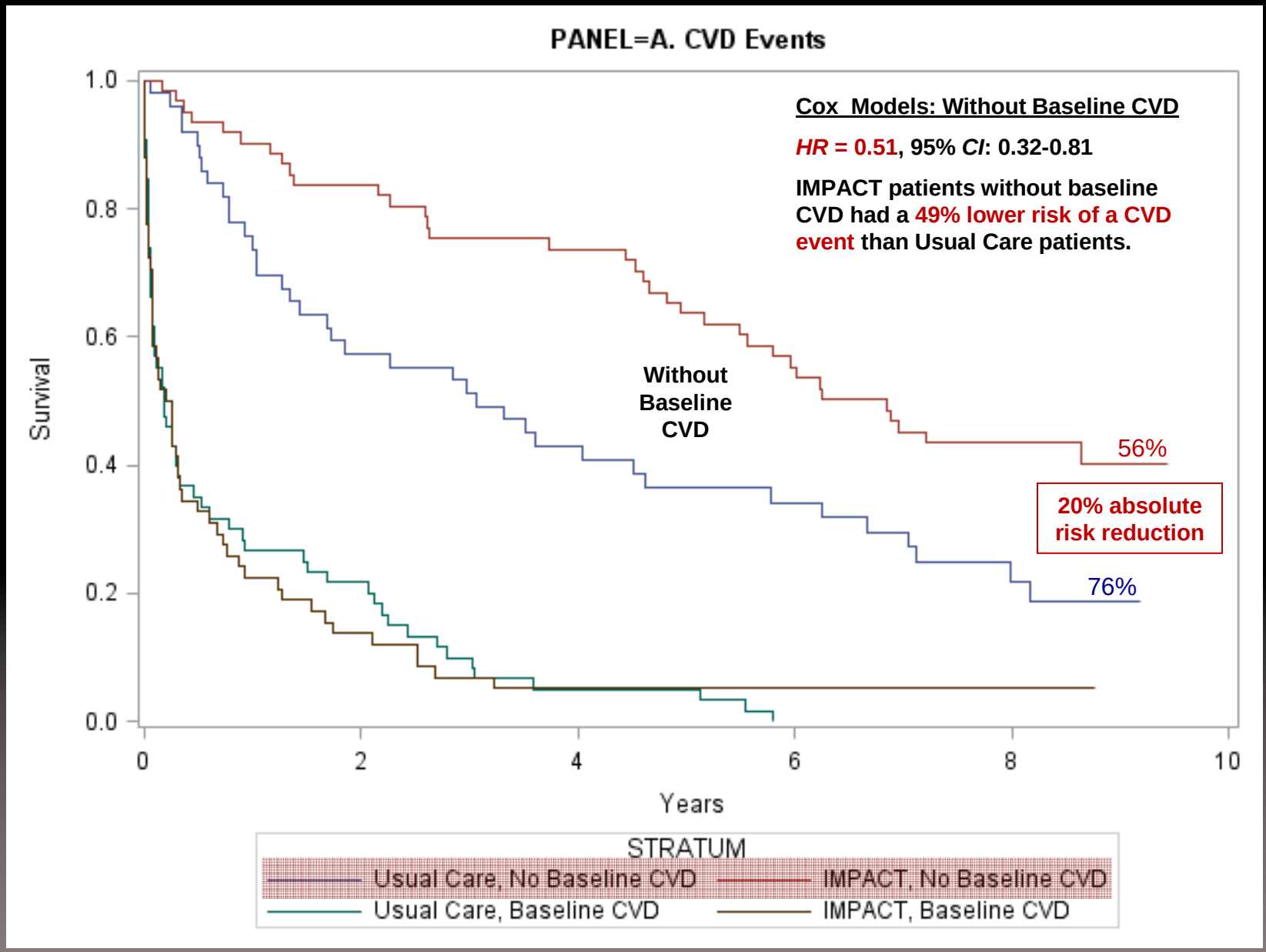
d = 0.50

Participant Characteristics : Baseline CVD (*n* = 123)

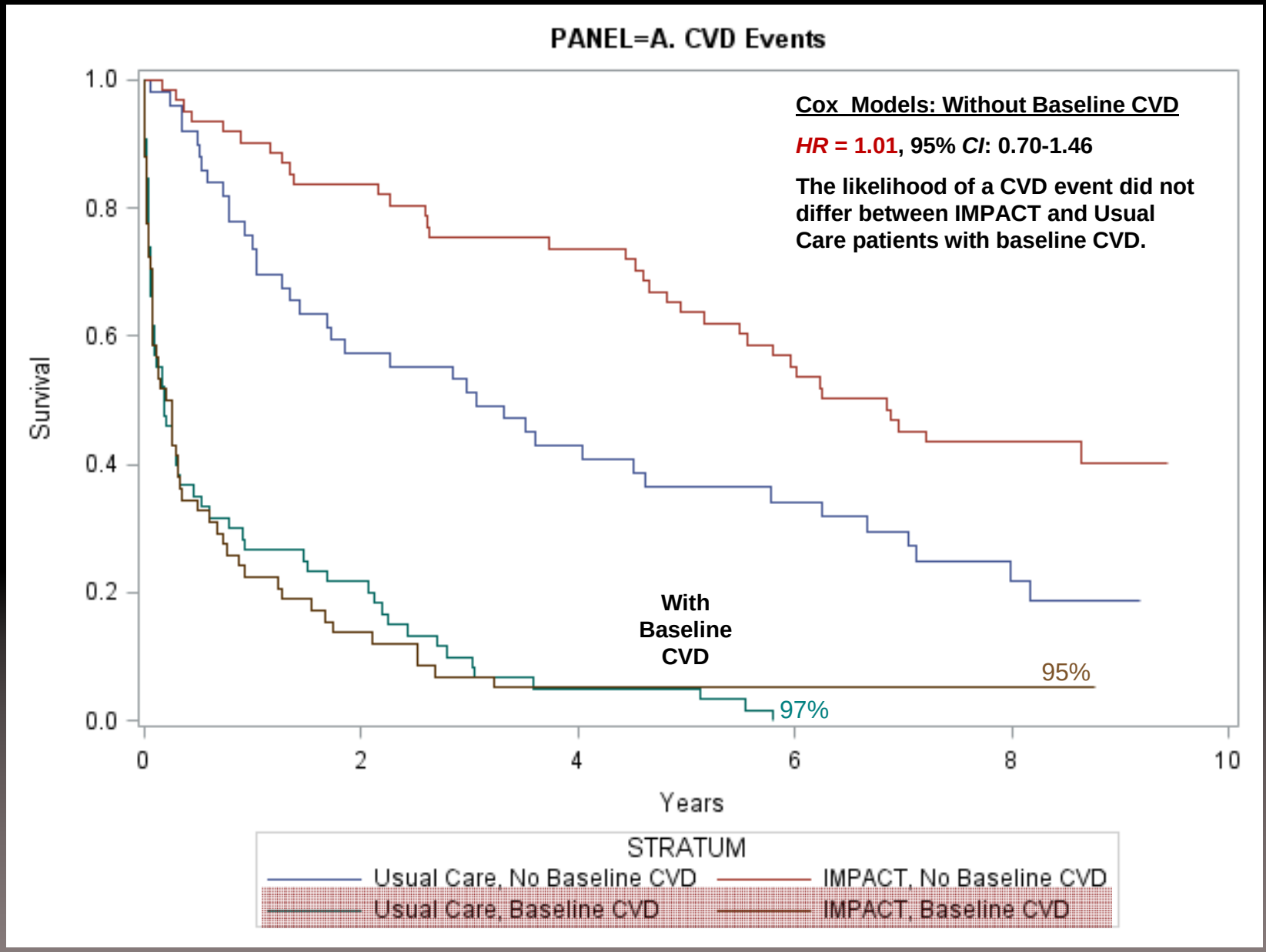
Characteristic	Baseline CVD		
	IMPACT (*n* = 58)	Usual Care (*n* = 65)	*p* value
Demographic Factors			
Age, mean (SD)	67.1 (6.6)	68.4 (7.4)	.32
Male, %	27.6	29.2	.84
African-American†, %	41.4	47.7	.48
Baseline Cardiovascular Risk Factors			
Hypertension, %	81.0	84.6	.60
Diabetes, %	43.1	36.9	.49
Smoker, %	29.3	33.8	.59
Body-Mass Index (kg/m^2), mean (SD)	32.3 (9.1)	29.8 (7.6)	.10
Baseline Depression Variables			
MDD only, %	19.0	9.2	.12
Dysthymia only, %	37.9	40.0	.81
MDD and Dysthymia, %	43.1	50.8	.40
SCL-20 score, mean (SD) (range: 0-4)	1.6 (0.5)	1.6 (0.5)	.51
Antidepressant Use in Past 3 Months, %	48.3	55.4	.73
Depression Care and Outcomes			
SCL-20 Change, mean (SD)	-0.4 (0.7)	0.0 (0.7)	.01
Antidepressants during the trial, %	80.7	73.4	.34
Psychotherapy during the trial, %	61.4	18.8	<.001

d = 0.53

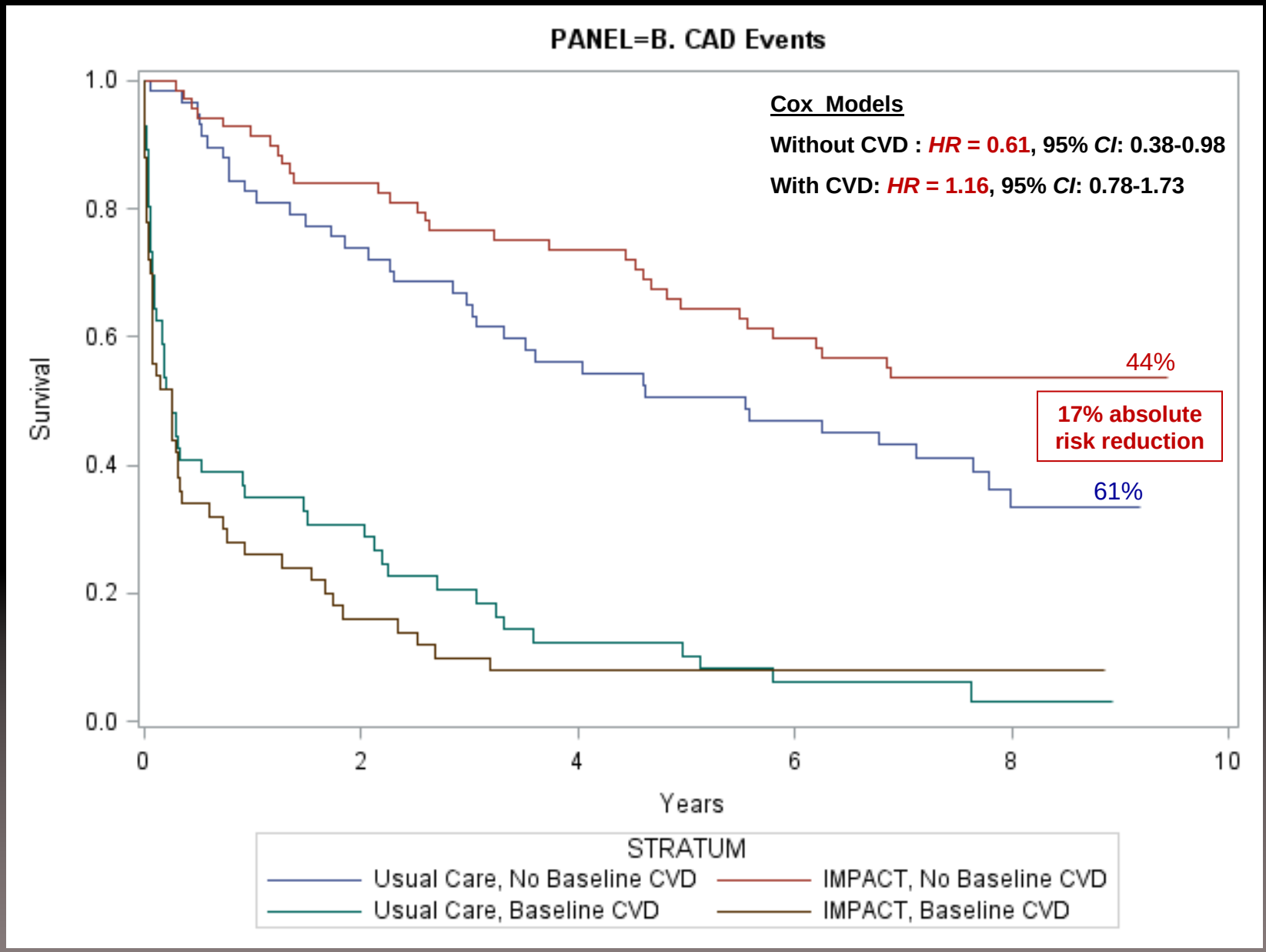
Survival Curves for Time to *CVD Events* (*n* = 191)



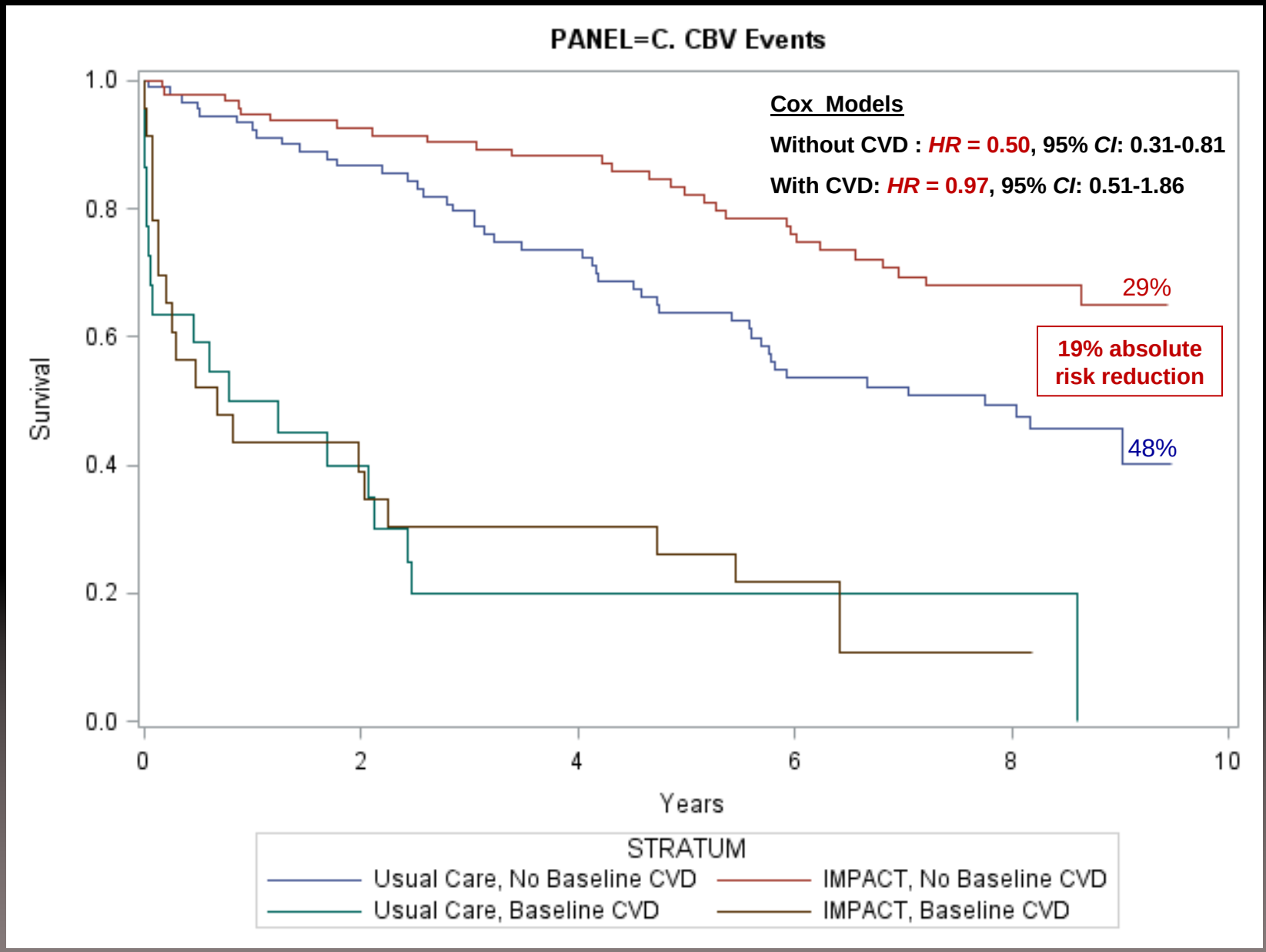
Survival Curves for Time to *CVD Events* (*n* = 191)



Survival Curves for Time to *CAD Events* (*n* = 164)



Survival Curves for Time to *CBV Events* (*n* = 111)



Sensitivity Analyses

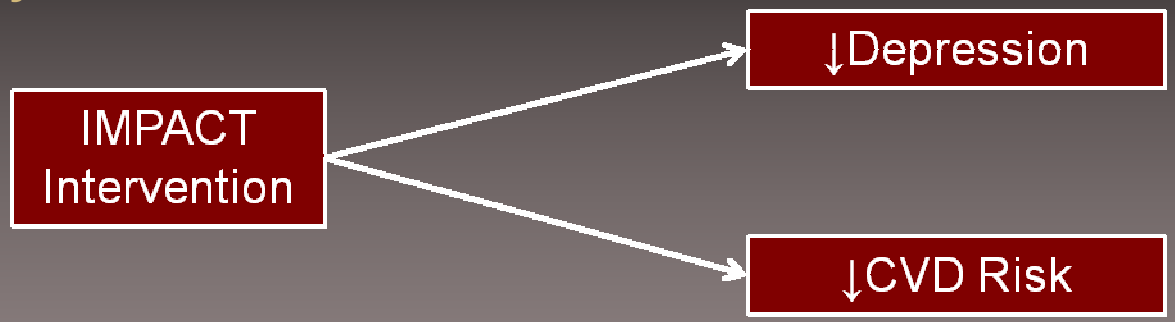
		Treatment		Treatment x Baseline CVD	Treatment: No Baseline CVD		Treatment: Baseline CVD	
Outcome	**Events (%)**	***HR***	**95% *CI***	***p* value**	***HR***	**95% *CI***	***HR***	**95% *CI***
CVD Events†	191 (81%)	0.66**	0.49-0.88	.07	0.51**	0.32-0.81	1.01	0.70-1.46
Women Only	140 (78%)	0.65*	0.47-0.91	.16	0.52*	0.31-0.87	1.05	0.68-1.61
Men Only	51 (91%)	0.67	0.39-1.17	.24	0.45	0.17-1.23	0.94	0.47-1.86
Covariate-Adjusted‡	191 (81%)	0.73*	0.54-0.98	.05	0.55*	0.34-0.89	1.00	0.69-1.47
CAD Events§	164 (70%)	0.75	0.55-1.03	.06	0.61*	0.38-0.98	1.16	0.78-1.73
CBV Events‖	111 (47%)	0.63*	0.43-0.92	.24	0.50**	0.31-0.81	0.97	0.51-1.86
Non-CVD Mortality†	84 (36%)	0.89	0.58-1.37	.16	0.64	0.33-1.25	1.20	0.69-2.09

‡Adjusted for age, sex, race, hypertension, diabetes, smoking status, body mass index, baseline Symptom Checklist-20, and baseline antidepressant use.

*$p < .05$ **$p < .01$

Conclusions

- The present findings support our hypothesis that depression treatment delivered before the onset of clinical CVD is cardioprotective.
- Our results indicate that depression may be a causal risk factor for CAD and CBV.
- These findings raise the possibility that, among older adults, providers could utilize the IMPACT intervention as both a depression treatment and CVD prevention strategy.



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THANK YOU

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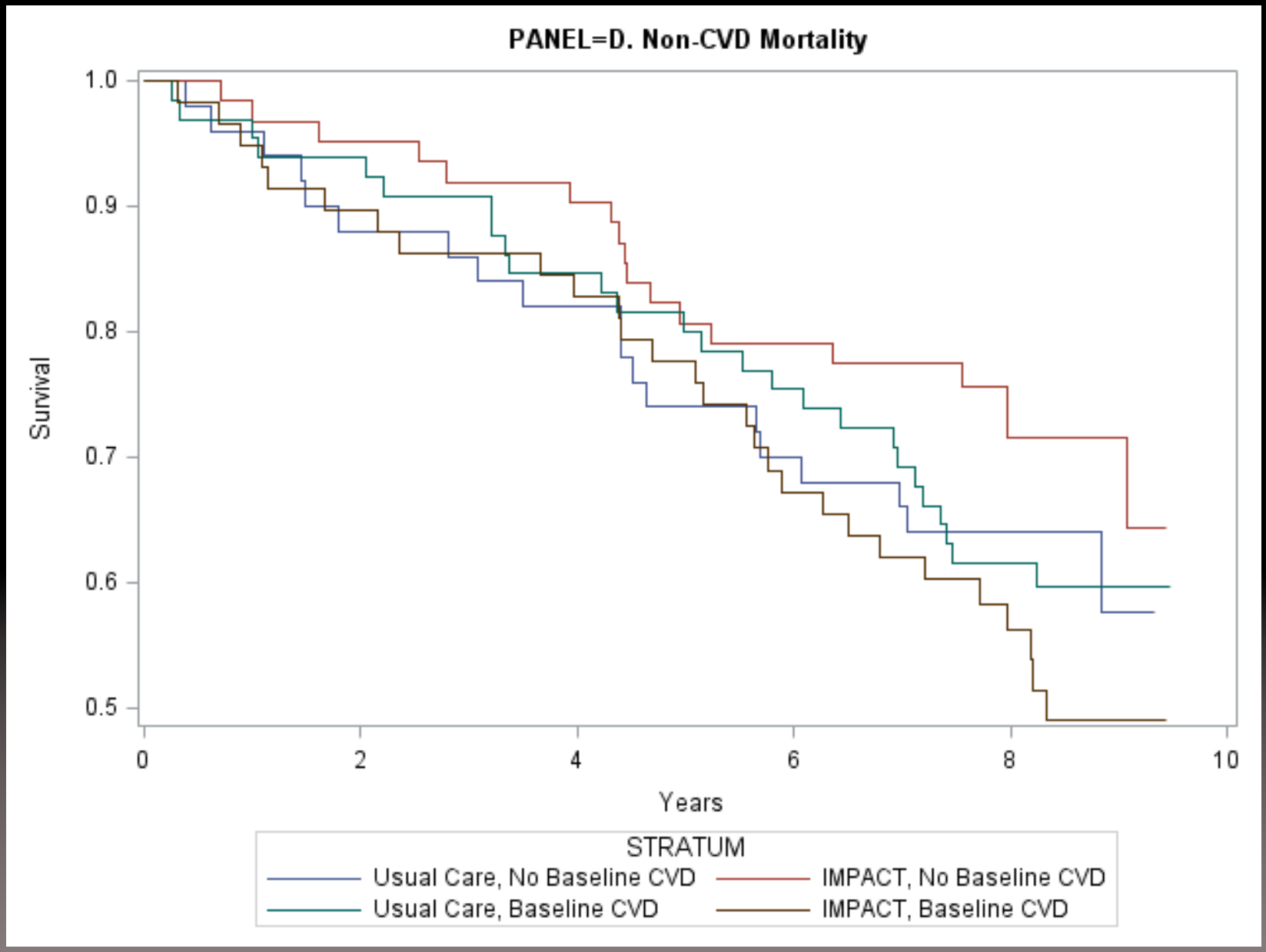
Treatment received during the IMPACT trial

	UC	Intervention
% Neither	28.1	11.8
% Antidepressants only	54.4	26.9
% Psychotherapy only	5.3	11.8
% Both	12.3	49.6

Survival Curves for Time to *Non-CVD Mortality*



Do the Depression Care and Outcomes Variables Explain the Treatment Effect?

- Adjusting for:
  - 12-month depressive symptoms change: +9% (*HR* = 0.48, *p* = .003)
  - Trial antidepressants (yes, no): -11% (*HR* = 0.55, *p* = .01)
  - Trial psychotherapy (yes, no): -15% (*HR* = 0.56, *p* = .03)
  - Trial antidepressants + trial psychotherapy: -26% (*HR* = 0.61, *p* = .53)

- Treatment effect may still be depression mediated (long-term depression data are not available).

- Receiving SSRIs may have reduced CVD risk due to their direct inhibitory effect on platelet reactivity.

- Receiving Problem-Solving Therapy may have reduced CVD risk by decreasing the likelihood of depression relapse.