



Hepatitis C Virus Infection and the Risk of Coronary Disease

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Background

- **Several infectious etiologies for CAD have been proposed based on epidemiological associations, but there is no consensus regarding a causative role (1-3)**
 - *C. pneumoniae*, Cytomegalovirus, *H. pylori*, *M. pneumoniae*
- **HIV infected persons have been reported to have a higher risk of CAD, which is at least partly attributed to antiretroviral therapy, lipid abnormalities and higher levels of inflammation in these persons (4)**
- **Studies on the association between HCV and CAD have shown conflicting results (5-7)**

(1) Danesh *Lancet*. 1997;350:430-436.

(2) Sheehan *Heart*. 2005;91:19-22.

(3) Fong *CMAJ*. 2000;163:49-56.

(4) Friis-Moller *N Engl J Med*. 2003;349:1993-2003.

(5) Arcari *Clin Infect Dis*. 2006;43:e53-e56.

(6) Volzke *Atherosclerosis*. 2004;174:99-103.

(7) Momiyama *Atherosclerosis*. 2005;181:211-213.



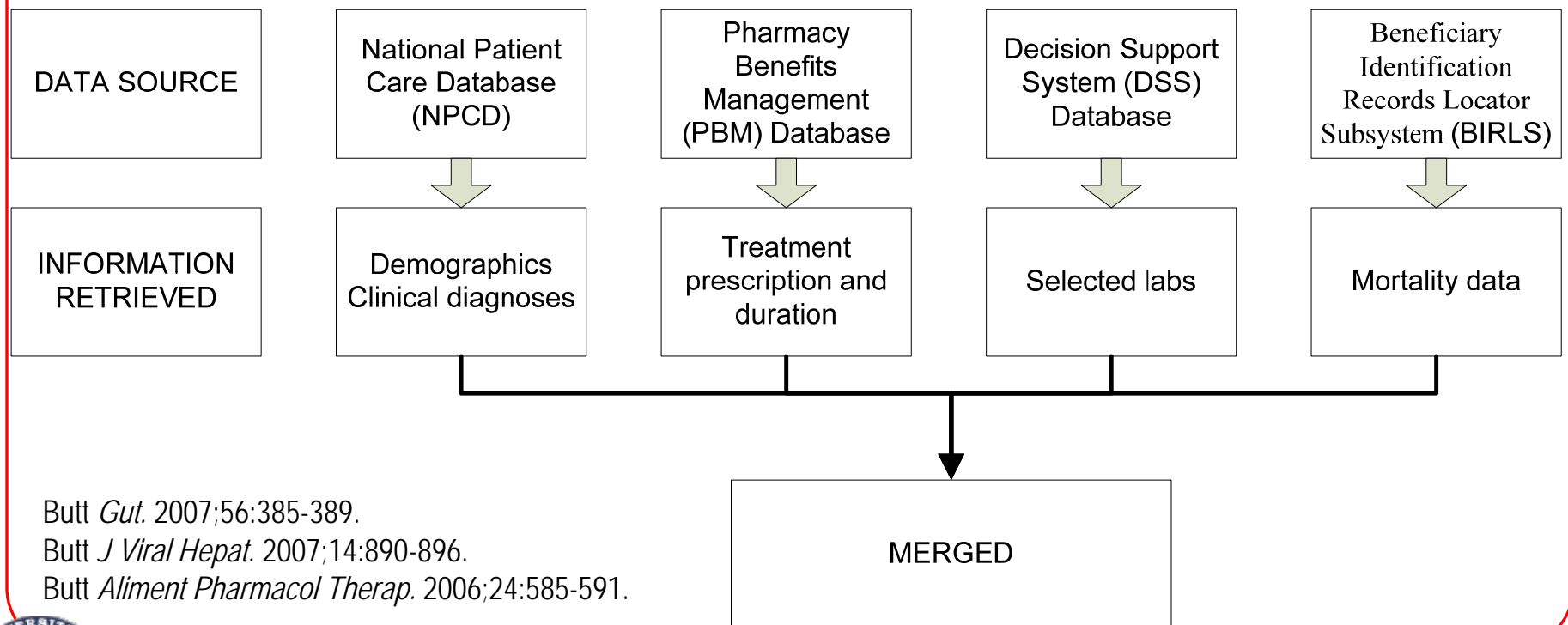
Aims

- **To determine whether HCV infection is associated with an increased incidence of coronary artery disease**
- **Compare risk factors and predictors for CAD in HCV infected and uninfected persons**



Methods: Creation of ERCHIVES

- Study was conducted in the ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans)



Methods: Definitions

HCV	Any positive HCV antibody, OR positive HCV RNA
Coronary artery disease (CAD)	2 or more of the following in any combination, any time: <ul style="list-style-type: none"> •ICD-9 code for CABG (coronary artery bypass grafting) •Procedure code for CABG •ICD-9 code for PTCA (percutaneous transluminal coronary angioplasty) •Procedure code for PTCA •ICD-9 code for myocardial infarction (MI)
Comorbidities	≥ 1 inpatient or ≥ 2 outpatient ICD-9 codes anytime
Anemia	Hemoglobin <13 g/dl for men, < 12g/dl for women
Dyslipidemia	Any of the following <ol style="list-style-type: none"> 1. total cholesterol > 200 mg/dl on 2 separate occasions 2. total cholesterol > 200 mg/dl once PLUS LDL-C > 130 mg/dl once anytime 3. prescription of cholesterol lowering medication > 30 days
Renal Failure	Estimated glomerular filtration rate (GFR) < 30 mL/min/1.73 m²
Diabetes	Any of the following <ol style="list-style-type: none"> 1. Glucose ≥ 200 mg/dl on two separate occasions; 2. ICD-9 codes (two outpatient OR one inpatient) PLUS treatment with an oral hypoglycemic or insulin for ≥ 30 days 3. ICD-9 codes (two outpatient OR one inpatient) PLUS glucose ≥ 126 mg/dl on two separate occasions 4. Glucose ≥ 200 mg/dl on one occasion PLUS treatment with a hypoglycemic for > 30 days.

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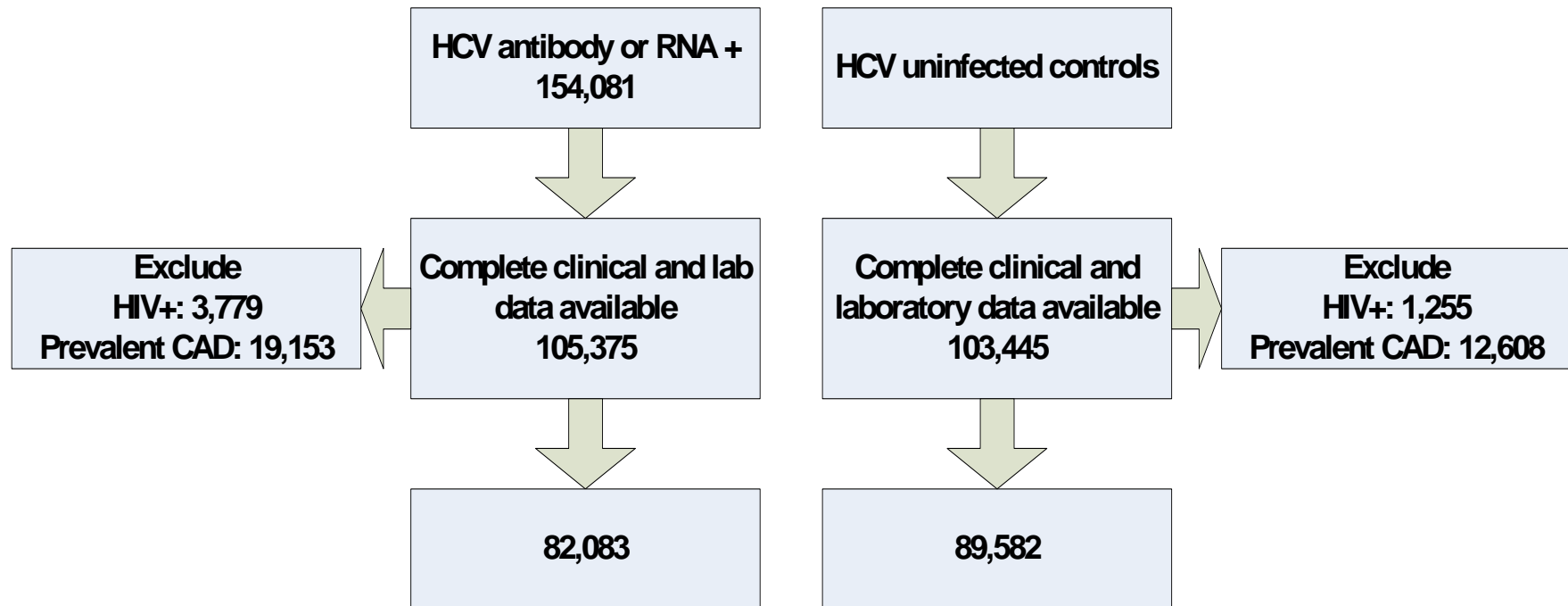
Methods

- **Cases and controls retrieved from 2001-2006**
- ***Baseline/ t_0 was the date of first HCV diagnosis***
- **Exclude HIV+**
- **Exclude prevalent cases of CAD**



Results

A flow chart depicting the number of subjects included in the study.



Results:

Baseline Characteristics

	HCV+ (n=82,083)	HCV- (n=89,582)	<i>P-value</i>
Mean age, years (SD)	51.2 (7.3)	51.8 (7.8)	
Race			
White	55.4	55.8	
Black	29.5	29.5	
Hispanic	1.9	2.2	
Other/unknown	13.2	12.5	
Gender, % male	97.1	97.0	
Hypertension	41.6	50.4	<0.001
Diabetes	20.8	21.8	<0.001
Dyslipidemia	39.4	72.2	<0.001
Total cholesterol: Mean, (SD)	175 (40.8)	198 (41.9)	<0.001
LDL-C: Mean, (SD)	102 (36.8)	119 (38.2)	<0.001
TG (mg/dl): Mean, (SD)	144 (119)	179 (151)	<0.001
HDL (mg/dl): Mean, (SD)	46 (16.8)	46 (15.2)	<0.001
Renal failure	2.6	1.4	<0.001
Alcohol abuse/dependence	38.6	19.1	<0.001
Drug abuse or dependence	31.4	11.6	<0.001



Results:

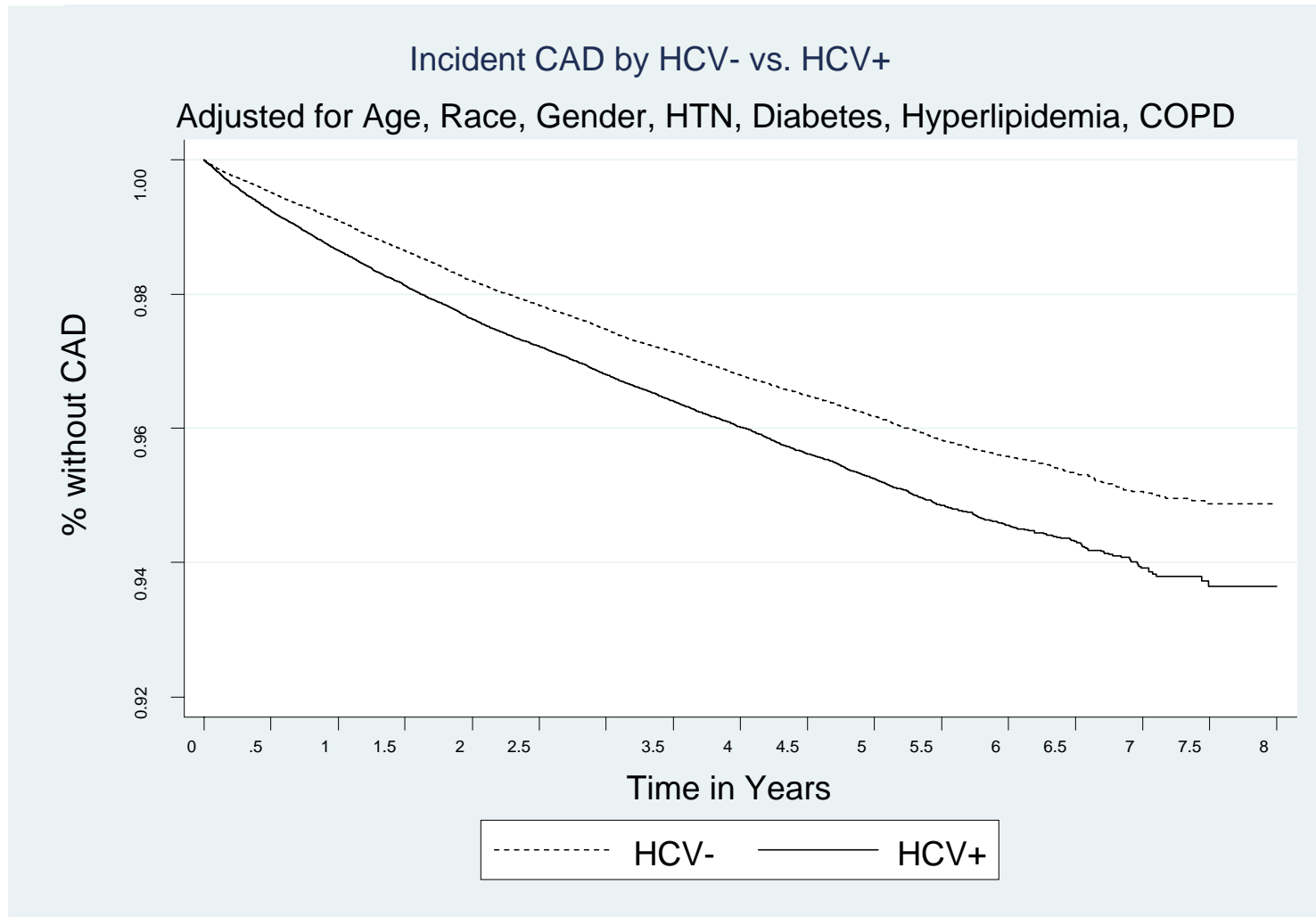
Factors associated with CAD (multivariable Cox)

	Overall	HCV+	HCV-
HCV	1.27 (1.22-1.31)	-----	-----
Age (5 year increment)	1.14 (1.13-1.16)	1.14 (1.12-1.15)	1.15 (1.13-1.17)
Race (comparator: white)			
Black	0.89 (0.86-0.93)	0.90 (0.85-0.95)	0.89 (0.84-0.94)
Hispanic	0.71 (0.62-0.81)	0.58 (0.47-0.73)	0.81 (0.68-0.96)
Other/unknown	0.75 (0.70-0.80)	0.64 (0.58-0.70)	0.87 (0.80-0.95)
Female gender	0.70 (0.62-0.81)	0.72 (0.60-0.86)	0.69 (0.56-0.84)
Hypertension	1.37 (1.32-1.43)	1.50 (1.42-1.58)	1.25 (1.18-1.32)
COPD	1.46 (1.39-1.54)	1.44 (1.34-1.54)	1.48 (1.38-1.59)
Diabetes	1.82 (1.75-1.90)	1.79 (1.69-1.89)	1.87 (1.76-1.98)
Hyperlipidemia	2.08 (2.00-2.18)	2.06 (1.95-2.17)	2.14 (1.97-2.31)
Renal failure	2.78 (2.57-3.00)	2.82 (2.56-3.11)	2.57 (2.25-2.94)
Anemia	1.37 (1.30-1.44)	1.42 (1.32-1.53)	1.32 (1.22-1.43)
Alcohol abuse or dependence	1.04 (0.99-1.09)	1.06 (0.99-1.13)	1.01 (0.93-1.10)
Drug abuse or dependence	1.10 (1.04-1.16)	1.10 (1.03-1.17)	1.07 (0.96-1.19)



Results:

Risk of CAD in HCV infected and uninfected subjects. ($P < 0.0001$)



Conclusions

- **Despite a favorable risk profile, HCV is associated with an increased risk of incident CAD**



Implications/Future Directions

- **HCV infected persons should be specifically targeted for early evaluation and intervention for CAD**
- **In HCV infected persons, such evaluation and intervention might need to be triggered even when the classic risk factors are absent**
- **Further studies to understand the mechanism of CAD in HCV infected persons are warranted**



Strengths and Limitations

- Largest known study to our knowledge
- National population
- Centralized data recording
- Longitudinal follow up
- Strengths of the VHA system
- Analysis of administrative database
- Exact time of HCV infection unknown
- CAD diagnosis based on ICD-9 codes
- Lack of BMI/anthropometric measures
- ?Point-of-care bias for CAD care



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Treatment Disparities and Clinical Outcomes in HCV and HCV-HIV Coinfected Veterans



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