

# DISCLOSURES

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# DISCLOSURES

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Upon successful completion of this activity 1 contact hour will be awarded

Successful completion of this continuing education activity includes the following:

- Attending the entire CE activity;
- Completing the online evaluation;
- Submitting an online CE request.

Your certificate will be sent via email

If you have any questions about this CE activity, contact Michelle Daugherty at [mdaugherty@cardeaservices.org](mailto:mdaugherty@cardeaservices.org) or (206) 447-9538



# CONFLICT OF INTEREST

Lisa Townshend-Bulson is a principal co-investigator on a grant that is partially funded by Gilead.

None of the other planners or presenters of this CE activity have any relevant financial relationships with any commercial entities pertaining to this activity.

# Acknowledgement

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The Indian Health Service HIV Program  
and

The Secretary's Minority AIDS Initiative Fund



# The Impact of SVR on Cirrhosis and Non-Liver Complications

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# Agenda

- Acknowledge impact of SVR in interferon/pre-DAA era
- Recognize impact of SVR by cirrhosis status in the DAA era
- Identify impact of SVR on extrahepatic manifestations of liver disease in DAA era

# Liver Disease Progression



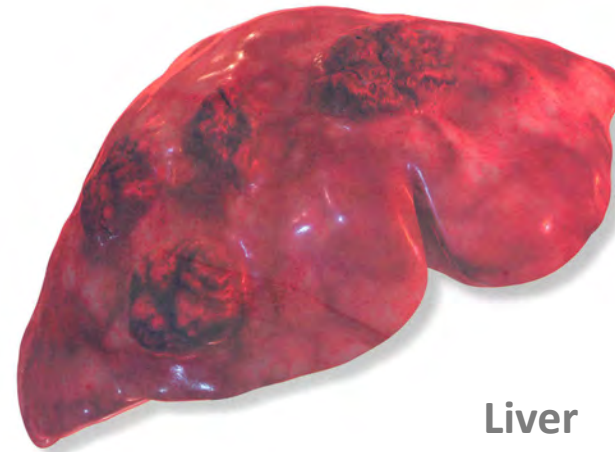
Healthy Liver



Fibrotic Liver

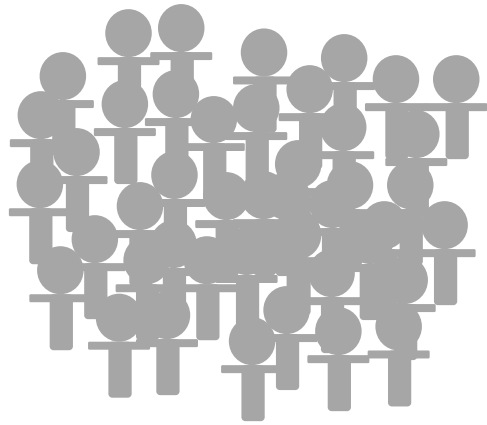


Cirrhotic Liver



Liver  
Cancer

# Natural History of hepatitis C



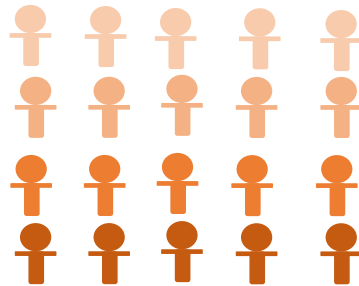
Of **100** people  
infected with the  
hepatitis C virus...



... **75-85** will develop  
chronic hepatitis C  
infection...



... of those persons with  
chronic hepatitis C  
infection, **5-20** will develop  
cirrhosis of the liver over  
20-30 years....



... and **1-5** will die from  
cirrhosis or liver cancer.





# HISTORICAL BENEFIT OF TREATMENT

- Sustained virologic response (SVR)\* results in a 90% reduction in cirrhosis and 70% reduction in liver cancer<sup>1,2,3</sup>

<sup>1</sup>Morgan, RL, et al. Ann Intern Med. 2013;158 (5 Pt 1):329-337.

<sup>2</sup>van der Meer, et al. JAMA. 2012;308(24):2584-2593.

<sup>3</sup>Veldt, BJ et al. Ann Intern Med. 2007;147(10):677-684.

SVR= no detected hepatitis C virus 12 weeks after the end of treatment



BC Centre for Disease Control  
An agency of the Provincial Health Services Authority

# The impact of HCV SVR from direct acting antiviral and interferon-based treatments on mortality in a large population based cohort study

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Cook D<sup>1</sup>, Alvarez M<sup>1</sup>, Tyndall M<sup>1,2</sup>, Kraiden M<sup>1,3</sup>, The BC Hepatitis Testers Cohort Team

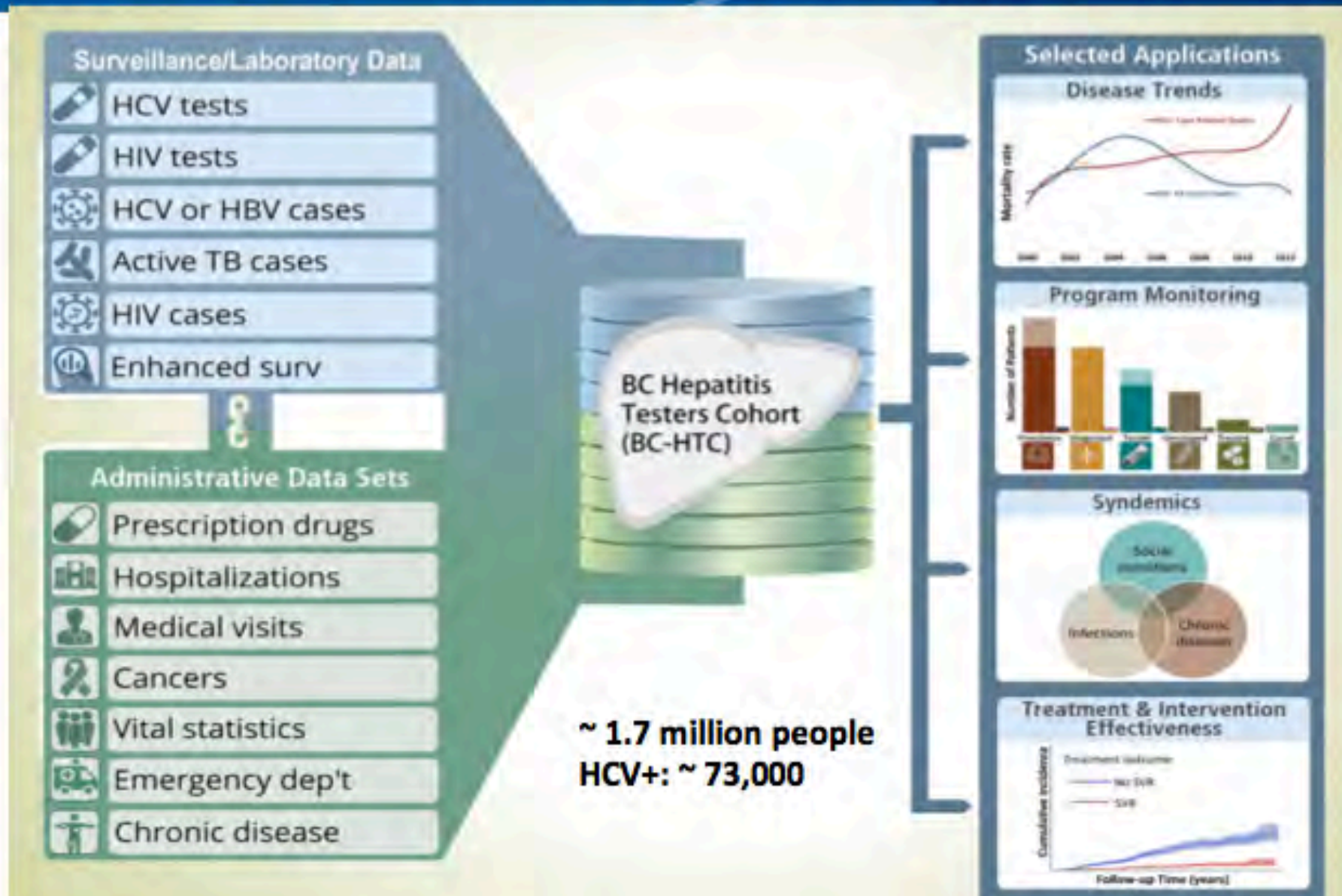
1. British Columbia Centre for Disease Control; 2. School of Population and Public Health; 3. Department of Pathology and Laboratory Medicine; 4. Simon Fraser University, Vancouver, Canada.



Web: <http://bchtc.med.ubc.ca>



# The BC Hepatitis Testers Cohort (BC-HTC)



# Methods

- **Study population:** Patients who filled at least one prescription of HCV treatment and underwent HCV RNA monitoring
- **Exposure: SVR** → defined SVR as undetectable HCV RNA at  $\geq 12$  weeks post treatment
- **Outcome: Mortality** → death records in British Columbia Vital Statistics Agency until June 30, 2018
- **Follow-up time:** Persons followed from treatment initiation to end of follow-up (June 30, 2018) or death, whichever occurred earlier

# Analysis

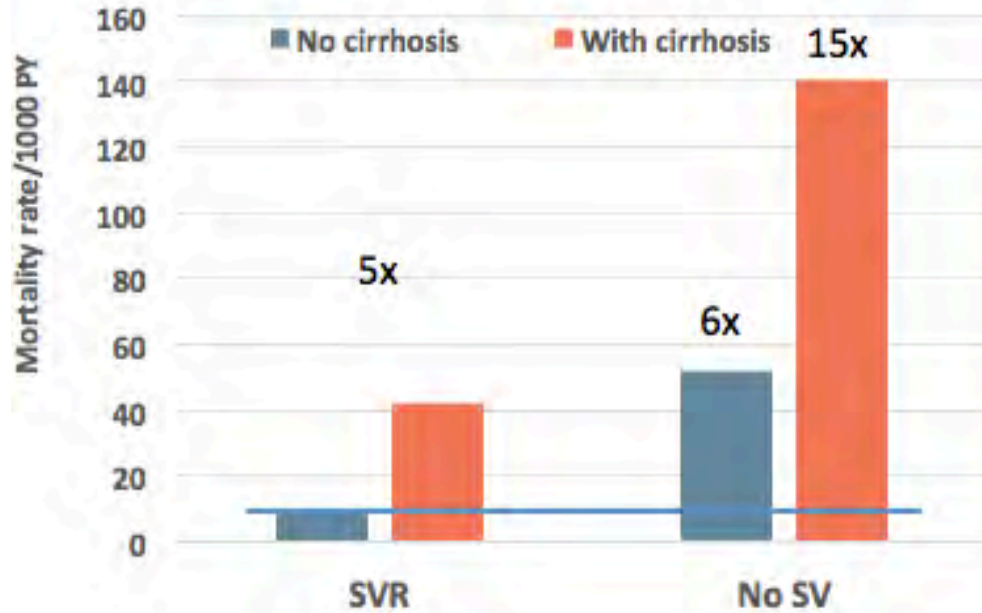
- Mortality rate among those who achieved SVR and those who did not, by dividing deaths by person years (PY) at risk
  - By interferon based and DAA treatments
- Survival curves comparing mortality rates among those with and with out SVR
  - Stratification by treatment type and cirrhosis at the time of treatment
- Cox proportional hazards regression overall, by cirrhosis status and treatment

# Participant profile

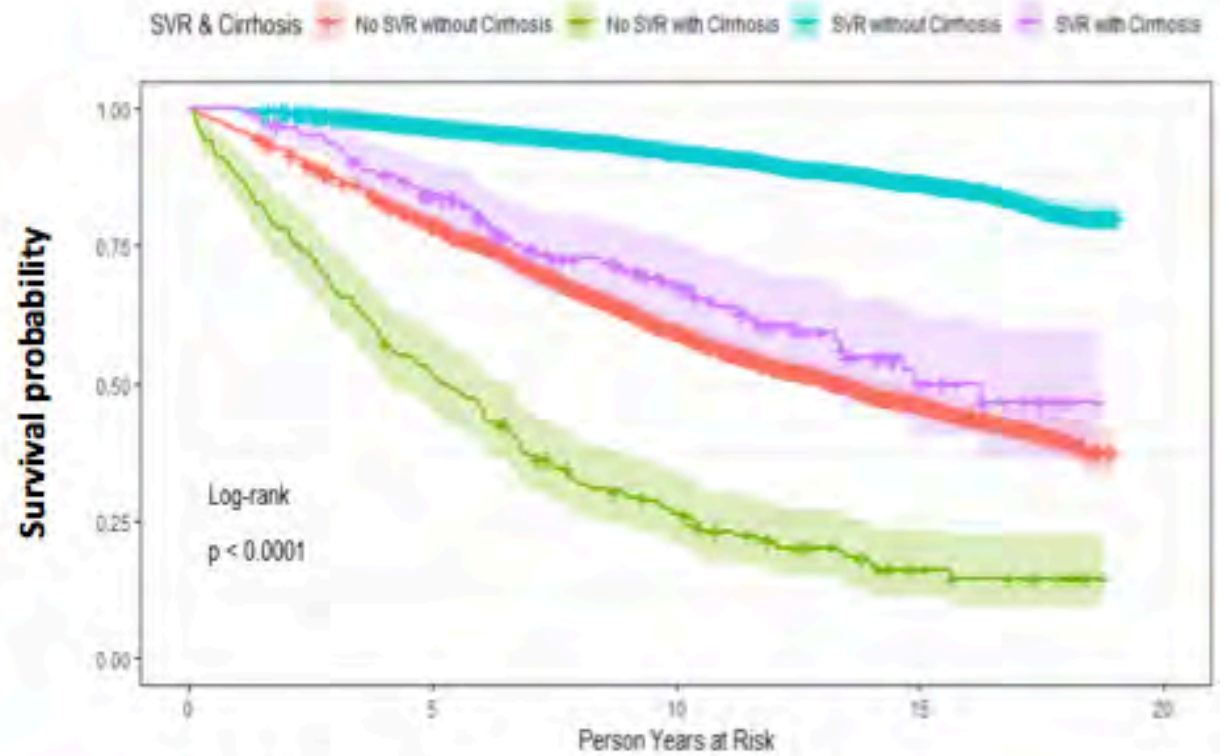
	SVR	No SVR		All treated	Treated DAA
Covariates	n(%)	n(%)	Row %	n(%)	n(%)
N	<b>13127(83)</b>	<b>2768(17)</b>		<b>15895</b>	<b>7126</b>
Treatment, interferon	6551(49.9)	2218(80.1)	74.7	8769(55.2)	
Treatment, DAA	6576(50.1)	550(19.9)	92.2	7126(44.9)	7126
<b>Previous treatment</b>	2016(15.4)	397(14.3)	83.5	2413(15.2)	<b>1511(21.2)</b>
Birth cohort, 1945-64	9420(71.8)	2008(72.5)	82.4	11428(71.9)	5264(73.9)
Age, median[IQR]	54[46 - 60]	52[45 - 58]		<b>53[46 - 60]</b>	<b>59[52 - 63]</b>
Sex, Male	8663(66)	1952(70.5)	81.6	10615(66.8)	4721(66.3)
<b>Genotype 1</b>	7288(55.5)	1481(53.5)	83.1	<b>8769(55.2)</b>	<b>4957(69.6)</b>
<b>Cirrhosis</b>	752(5.7)	269(9.7)	73.7	<b>1021(6.4)</b>	<b>660(9.3)</b>
HBV co-infection	726(5.5)	115(4.2)	86.3	841(5.3)	479(6.7)
HIV co-infection	882(6.7)	158(5.7)	84.8	1040(6.5)	654(9.2)
Injection drug use	3215(24.5)	700(25.3)	82.1	3915(24.6)	2157(30.4)
Problematic alcohol use	2896(22.1)	683(24.7)	80.9	3579(22.5)	1871(26.2)
Mental illness	3562(27.1)	730(26.4)	83.0	4292(27)	2257(31.7)
Diabetes	1723(13.1)	441(15.9)	79.6	2164(13.6)	1259(17.7)
<b>Elixhauser comorbidity index</b>	6895(52.5)	1587(57.3)	81.3	<b>8482(53.4)</b>	<b>4381(61.5)</b>

# Survival by SVR and cirrhosis

Mortality rate



Survival by SVR and Cirrhosis

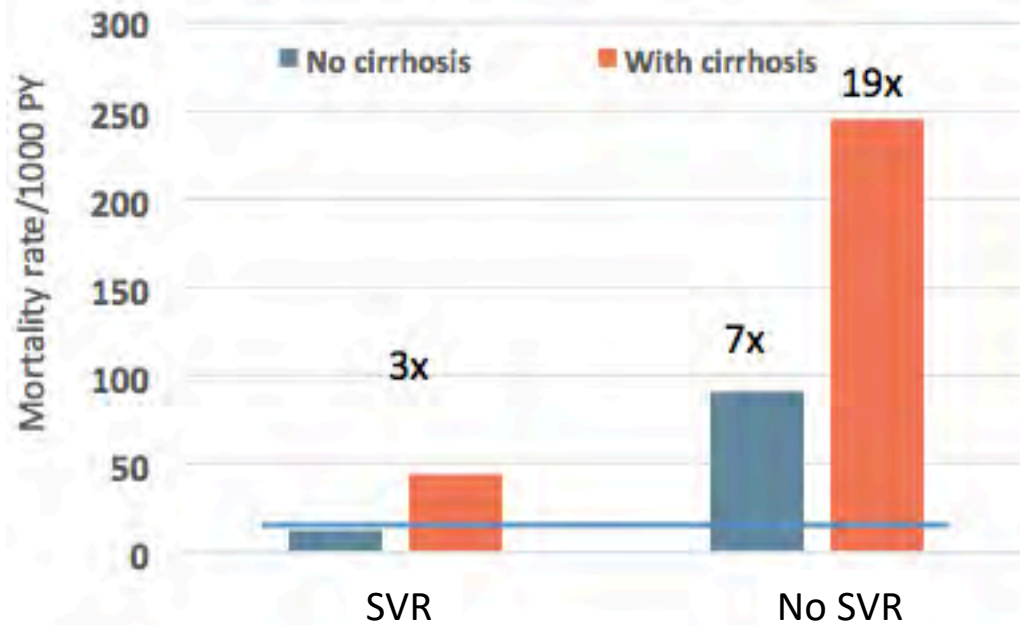


Number at risk

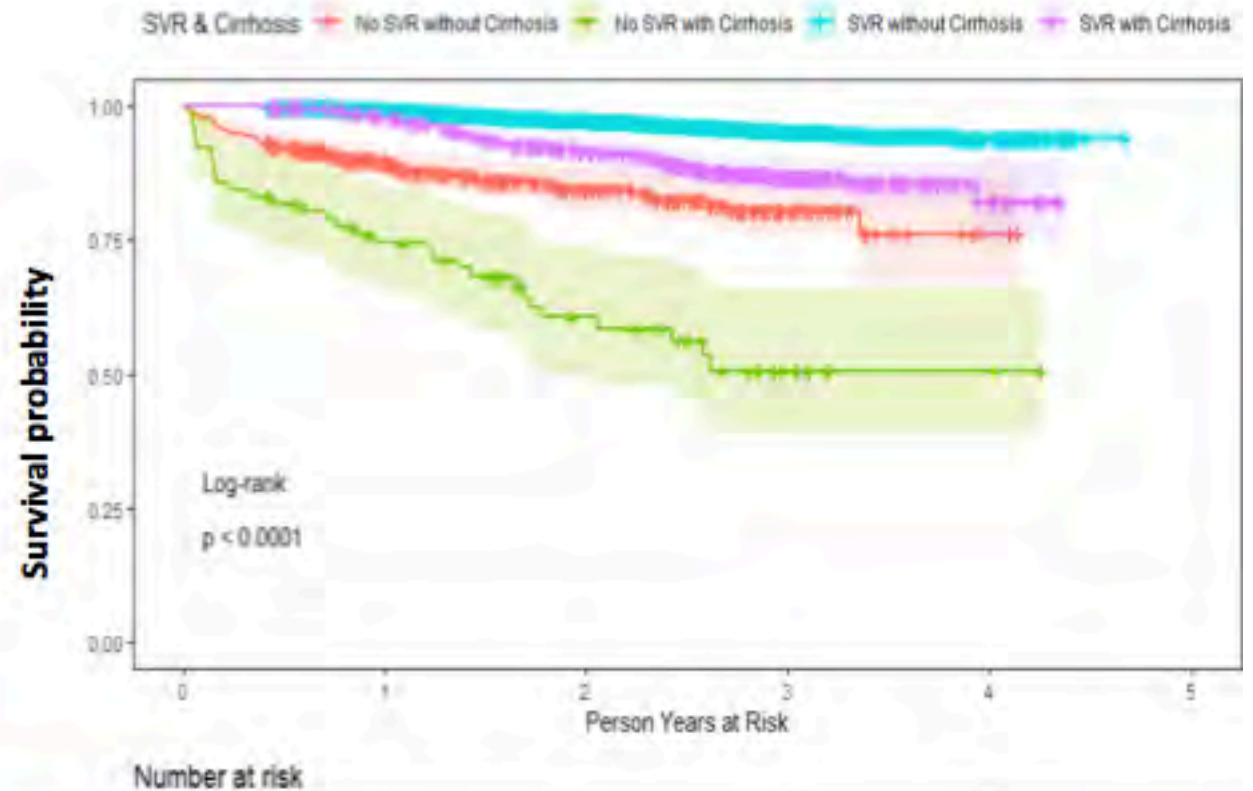
	0	5	10	15	20
No SVR without Cirrhosis	2026	1549	867	273	0
No SVR with Cirrhosis	192	97	43	11	0
SVR without Cirrhosis	6382	5704	3337	900	0
SVR with Cirrhosis	169	130	69	21	0

# Survival by SVR and cirrhosis in those treated with DAAs

## Mortality rate



## Survival by SVR and Cirrhosis



SVR & Cirrhosis	0	1	2	3	4	5
No SVR without Cirrhosis	473	270	148	40	4	0
No SVR with Cirrhosis	77	49	30	10	3	0
SVR without Cirrhosis	5993	4823	3102	958	93	0
SVR with Cirrhosis	583	533	417	174	22	0



# Survival by SVR and treatment type

## Median age [IQR]

Interferon: 50 [42 - 55] yrs

DAA: 59 [52 - 63] yrs

Survival probability

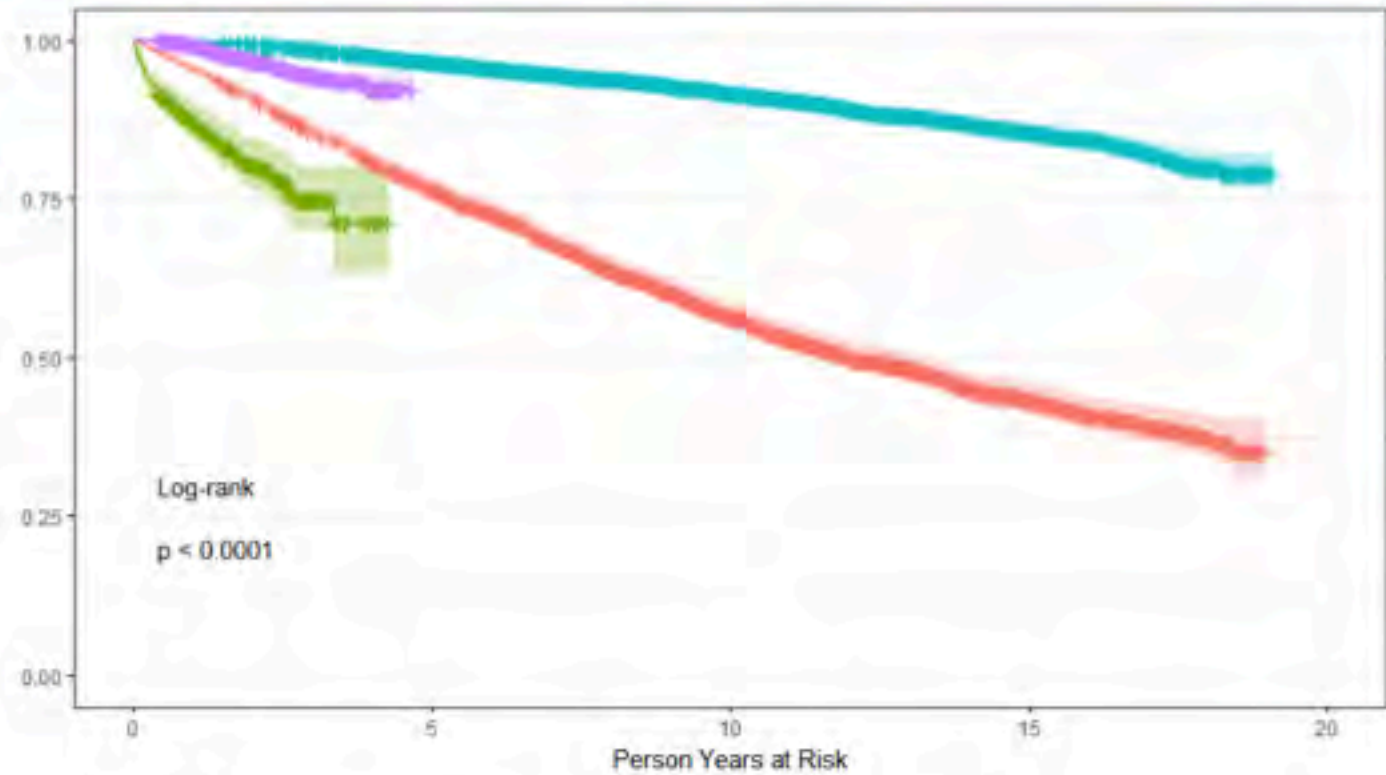
## Median follow-up time:

Interferon: 9.9 [0.04 - 19.0]

DAA: 2.06 [ $< 1$  - 4.7]

SVR & Treatment Type

- + No SVR with interferon
- + No SVR with DAA
- + SVR with interferon
- + SVR with DAA



Number at risk

	0	5	10	15	20
No SVR with interferon	2218	1646	910	284	0
No SVR with DAA	550	0	0	0	0
SVR with interferon	6551	5834	3406	921	0
SVR with DAA	6576	0	0	0	0

# Summary

- DAA and interferon-based SVR substantially reduces all-cause mortality
- Slightly lower effect with DAA, related to aging population
- As expected, lower reductions in those with cirrhosis
- Early treatment could further improve survival
- Thus, a substantial reduction in mortality could be achieved by DAA scale-up to meet WHO HCV mortality goals

# Extrahepatic Manifestations of HCV(EHM)



Diabetes

Kidney Disease

Depression



Stroke

Heart Disease

Anxiety

Arthralgias

Fatigue

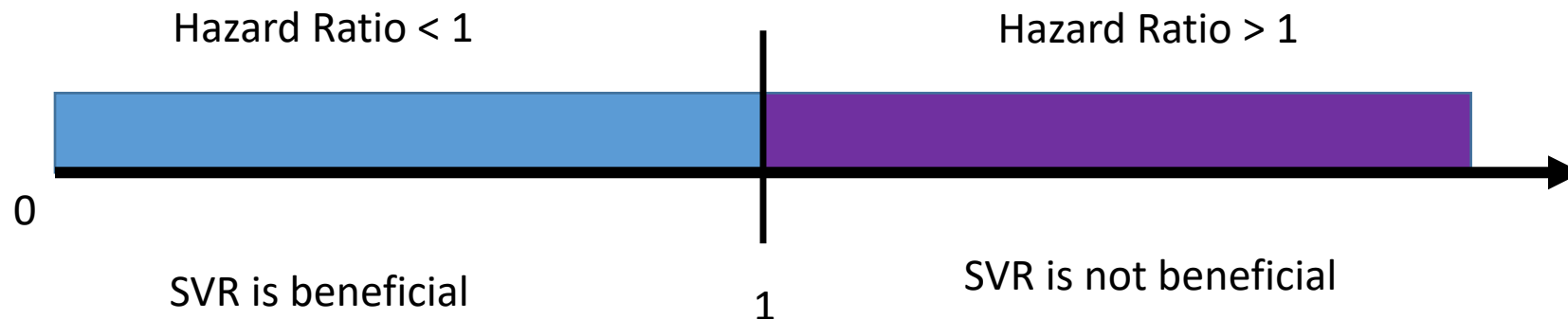
Mood

Rheumatoid  
Arthritis

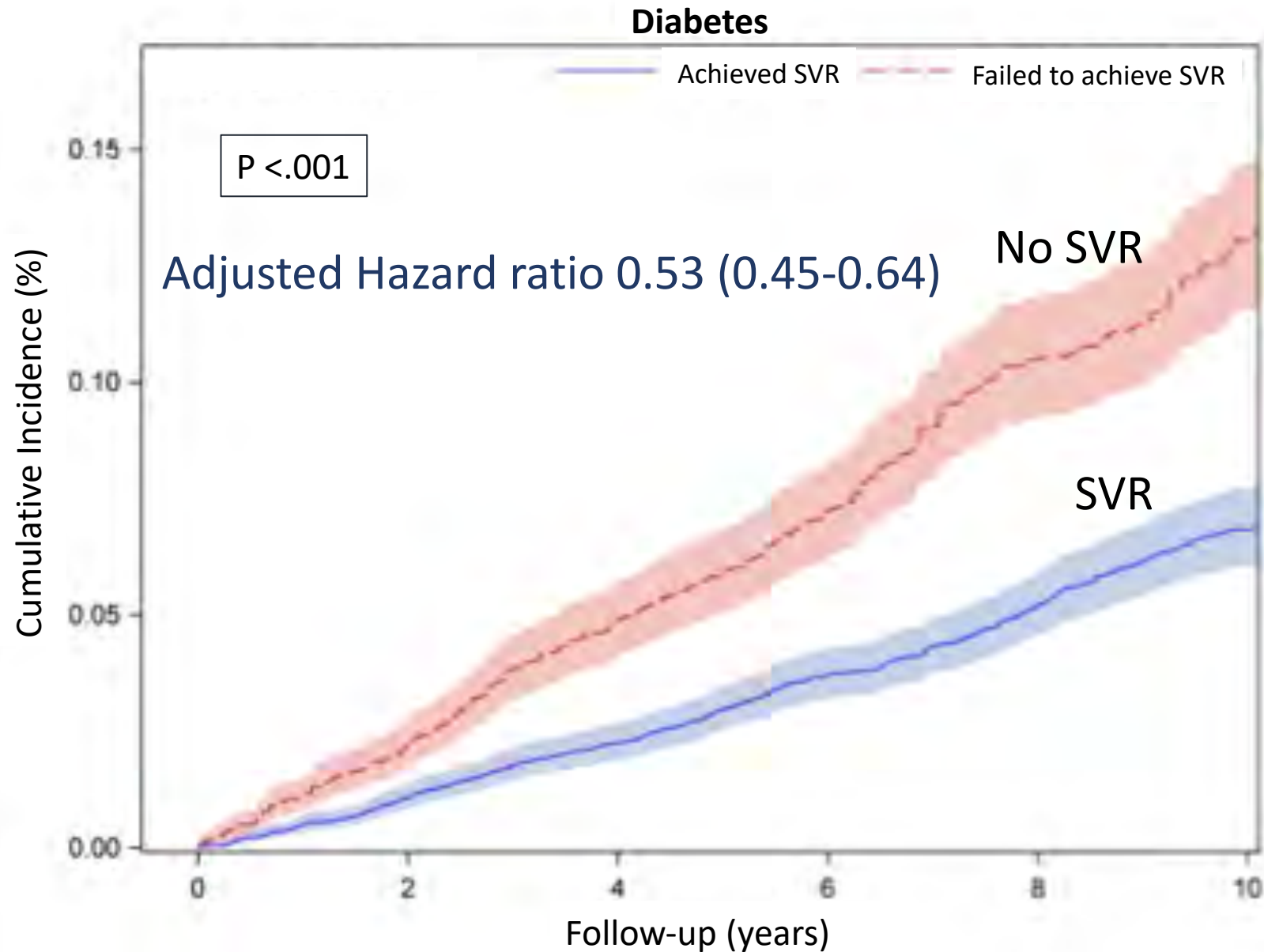


# What is the Hazard Ratio (HR)

- Comparison between 2 groups
- HR of  $<1$ : decreased incidence of EHM
- HR of 1: no difference in incidence of EHM
- HR of  $>1$ : increased incidence of EHM

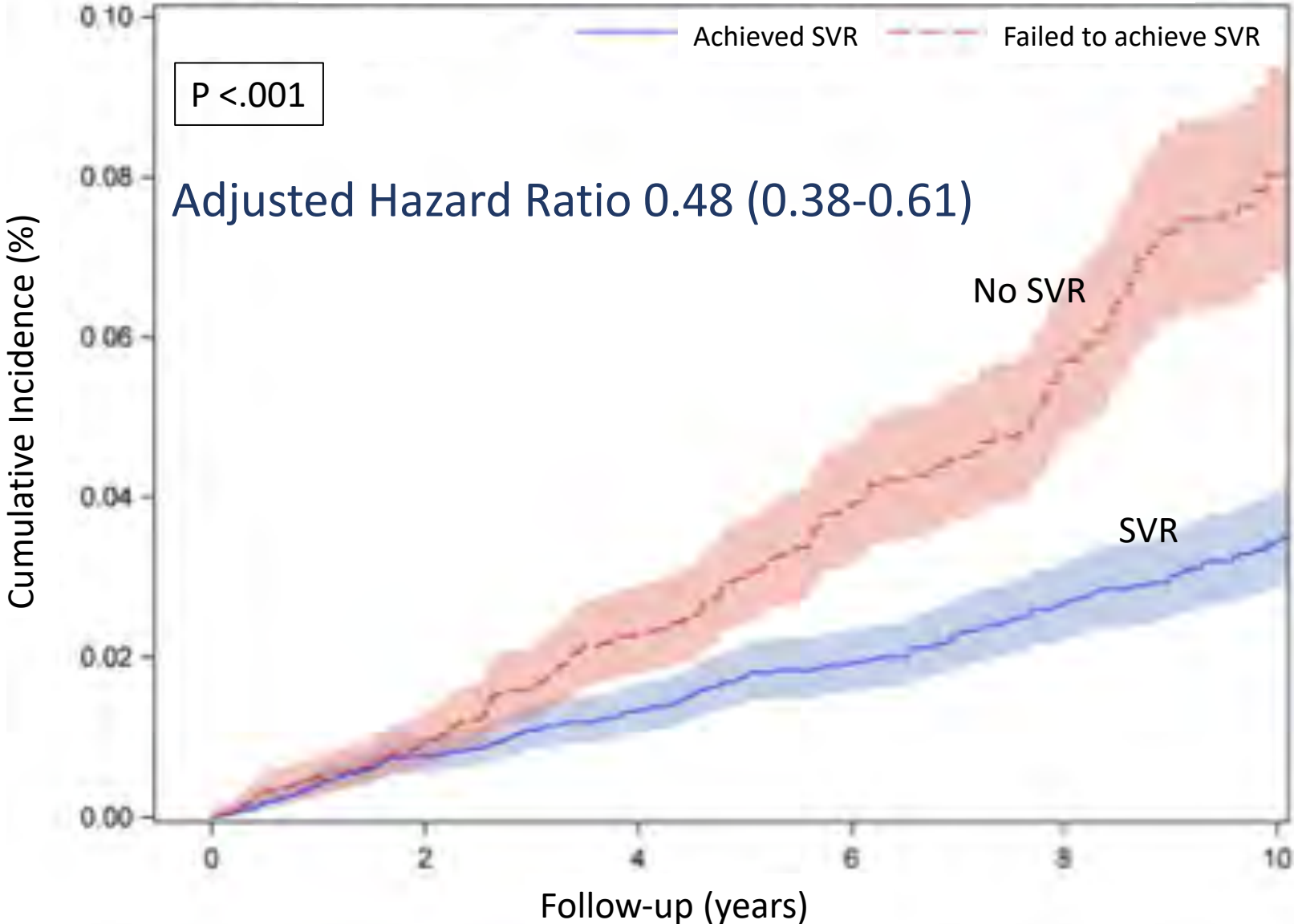


# Benefit of SVR on Incidence of Diabetes

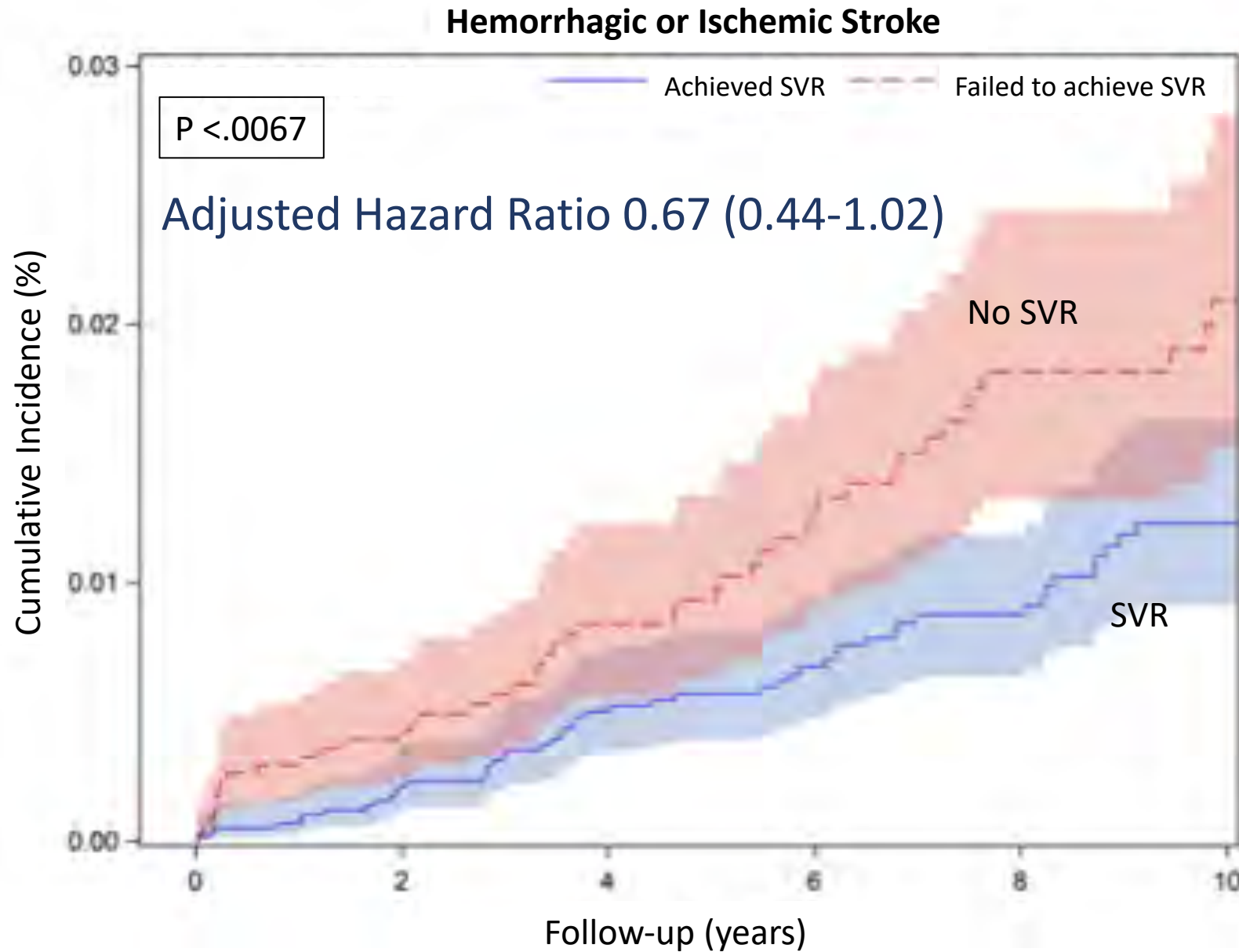


# Benefit of SVR to the Kidney

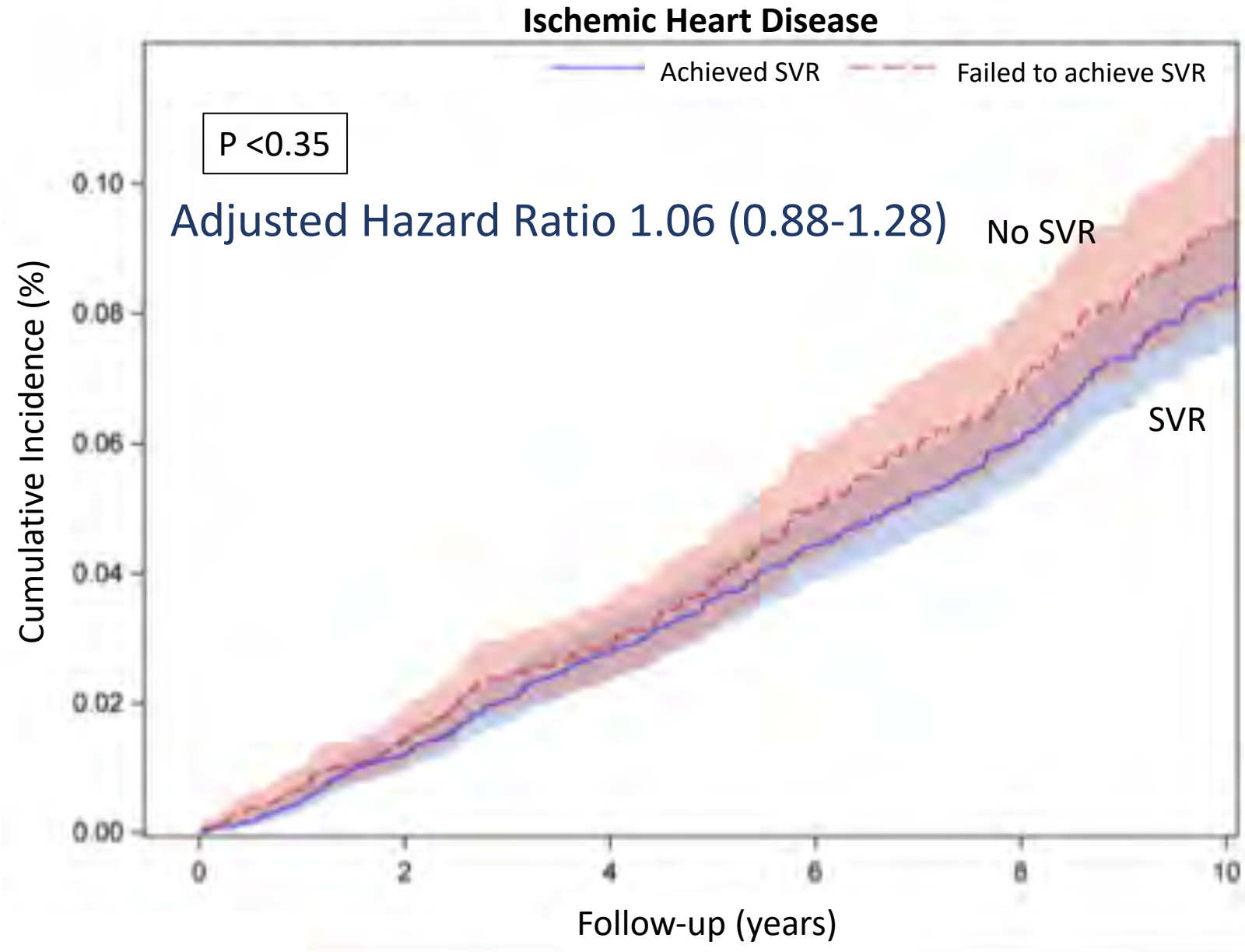
Chronic Kidney Disease or End-Stage Renal Disease



# Benefit of SVR on Stroke

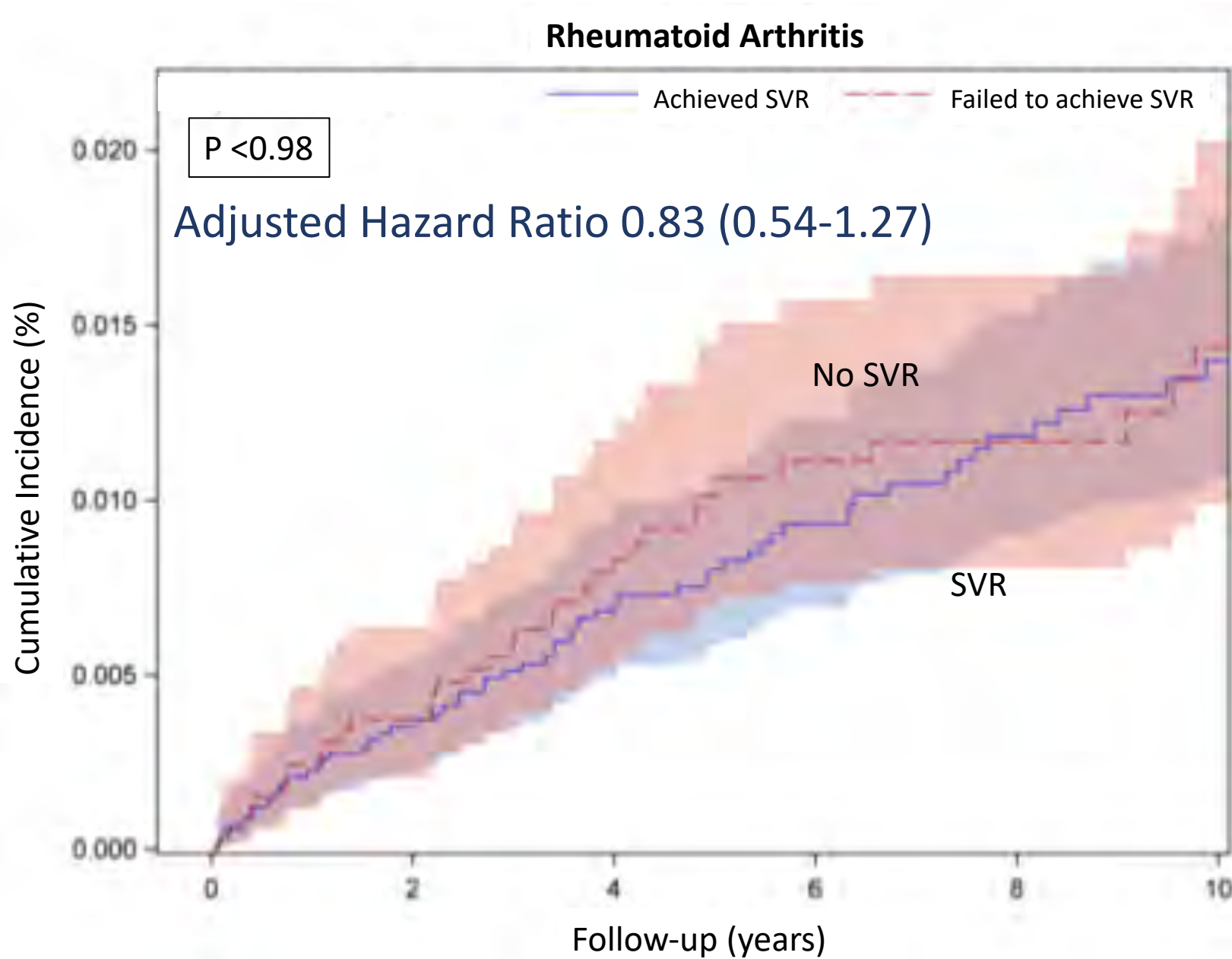


# Affect of SVR on Heart Disease

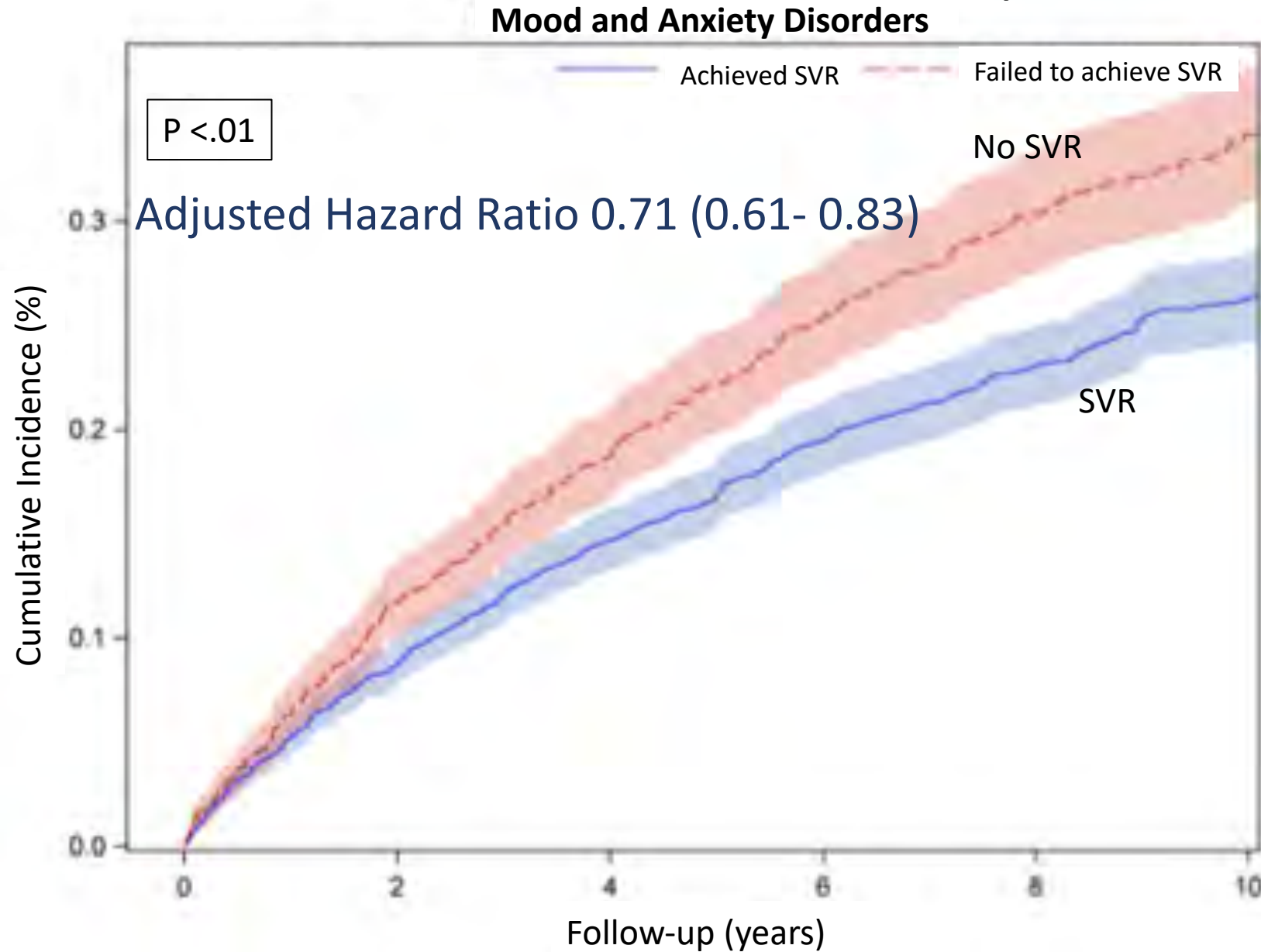




# Affect of SVR on RA



# Benefit of SVR on Mood and Anxiety



# Conclusion

- Reduced incidence of multiple but not all EHM
- Diabetes, CKD, or ESRD, stroke, and mood and anxiety disorders
- Reduction ranged between 29% ( mood and anxiety) and 52% renal disease



# EHM References – 2018 AASLD Abstracts

- Rossi, C et al. Sustained Virologic Response Reduces the Incidence of Extrahepatic Manifestations in Chronic Hepatitis C Infection, #148
- Butt, AA et al. Risk of Cardiovascular events after HCV treatment: Results from ERCIVES, # 1566
- Singer, A et al. Risk of Incident Diabetes in Hepatitis C Patients Following Completion of Direct-acting Antiviral Therapy,
- Evon, D et al. Improvement in Symptoms Shortly Following Viral Cure for Chronic Hepatitis C: A Large Multi-site Clinical Study, #149

# Evaluation and Certificates

- Please use the link or QR code below to complete the learner evaluation. This link will also be emailed to you within a few days. Please check your junk and spam email folders if you don't receive it.

<http://sgiz.mobi/s3/DecNW>

