MR. MARKOV AND THE WIZARD OF ROSS

OR

HOW TO ASSESS HEART VALVE DEFECTS WITHOUT CRYSTAL BALL

Select 74, December 2011

Dr. Karsten Filzmaier

Munich RE

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Evidence based underwriting

- Mortality after aortic valve surgery - the Wizard of Ross improves prognosis
- Mortality of aortic valve stenosis - how Mr. Markov unravels the mystery

Critical Illness claims handling of “heart valve surgery”

- Are we prepared for the future ? - let’s have a look into the crystal ball

Going to the bar after the lecture and have some drinks ?

- Do it and your heart will love you ! - an evidence based excuse

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MORTALITY AFTER AORTIC VALVE SURGERY

NEW TYPES OF SURGERY – BETTER PROGNOSIS ?

Aortic Valve

The aortic valve regulates the blood flow between the left ventricle and the Aorta

It works like a reed valve:

- permitting the blood to be pumped into the aorta during systole
- prevents a backflow of blood into the left ventricle during diastole

Aortic valve orifice: 3-4 cm^2

Aortic Valve Surgery
- Indications -

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< 70 years	> 70 years
Bicuspid aortic valve (50%)	Degenerative (48%)
Rheumatic fever (25%)	Bicuspid aortic valve (27%)
Degenerative (18%)	Rheumatic fever (23%)
Other reasons (7%)	Other reasons (2%)

Developing countries: rheumatic fever main cause in all age groups

Aortic Valve Surgery
- Bicuspid Valve -

Bicuspid aortic valve (BAV)´:

- Two leaflets instead of the normal three
- ~ 1-2% of the population, male : female = 2 : 1
- May cause no problems, but….

  ….. is often associated with preterm valve degeneration and ….

  ….. results in aortic valve stenosis, aortic valve regurgitation or both

Aortic Valve Surgery
- Bicuspid Valve -

Recent studies: BAV is not a simple valve condition

BAV appears to be a genetically based connective tissue disorder, which affects the aortic valve, but also the aorta and other organs, including:

- Thoracic aortic dilation, aneurysm, or dissection
- Coarctation of the aorta
- Kidney or liver cysts
- Scoliosis and flexible joints
- Intracranial aneurysm

Currently there are no tests capable of determining who will experience progressive aortic valve failure or aortic aneurysm and who will not.

Traditional Aortic Valve Replacement
- Types of surgery -

Mechanical valves:

Advantage: man-made material and very durable = last forever

Disadvantage: There is a tendency for blood to clot on mechanical valves (thrombus formation) = need for anticoagulation forever

Traditional Aortic Valve Replacement
- Types of surgery -

Bioprosthetic (or biological) valves:

Valves of animals (e.g. pigs) which undergo chemical procedures to make them suitable for implantation in the human heart

Advantage: no anticoagulation = valves are mimicking human tissue

Disadvantage: Not as durable as mechanical valves = need for reoperation

Traditional Aortic Valve Replacement
- Valve related complications -

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Risk of…..	Complication	Mechanical Valve	Bioprosthetic Valve
Thrombus formation	Stroke, renal infarction	high	low / moderate
Bleeding	Intracranial haemorrhage, gastric bleedings	high	low
Reoperation	Stroke, renal failure	Very low	Very high
Endocarditis	Brain abscess, reoperation, sepsis	increased	increased

Traditional Aortic Valve Replacement
- Valve related complications -

Valve replacement is associated with a considerable risk for valve associated complications.

Nevertheless, you can live a normal life and be sportive, successful, fertile and…..

……the strongest man in universe !!

Arnold Schwarzenegger:

- Born with bicuspid aortic valve
- Bioprosthetic aortic valve since 1997
- September 1997: his wife Maria Shriver gave birth to his son Christopher
- October 1997: his housemaid Patty Baena gave birth to his son Joseph
- Governor of California 2003 – 2011

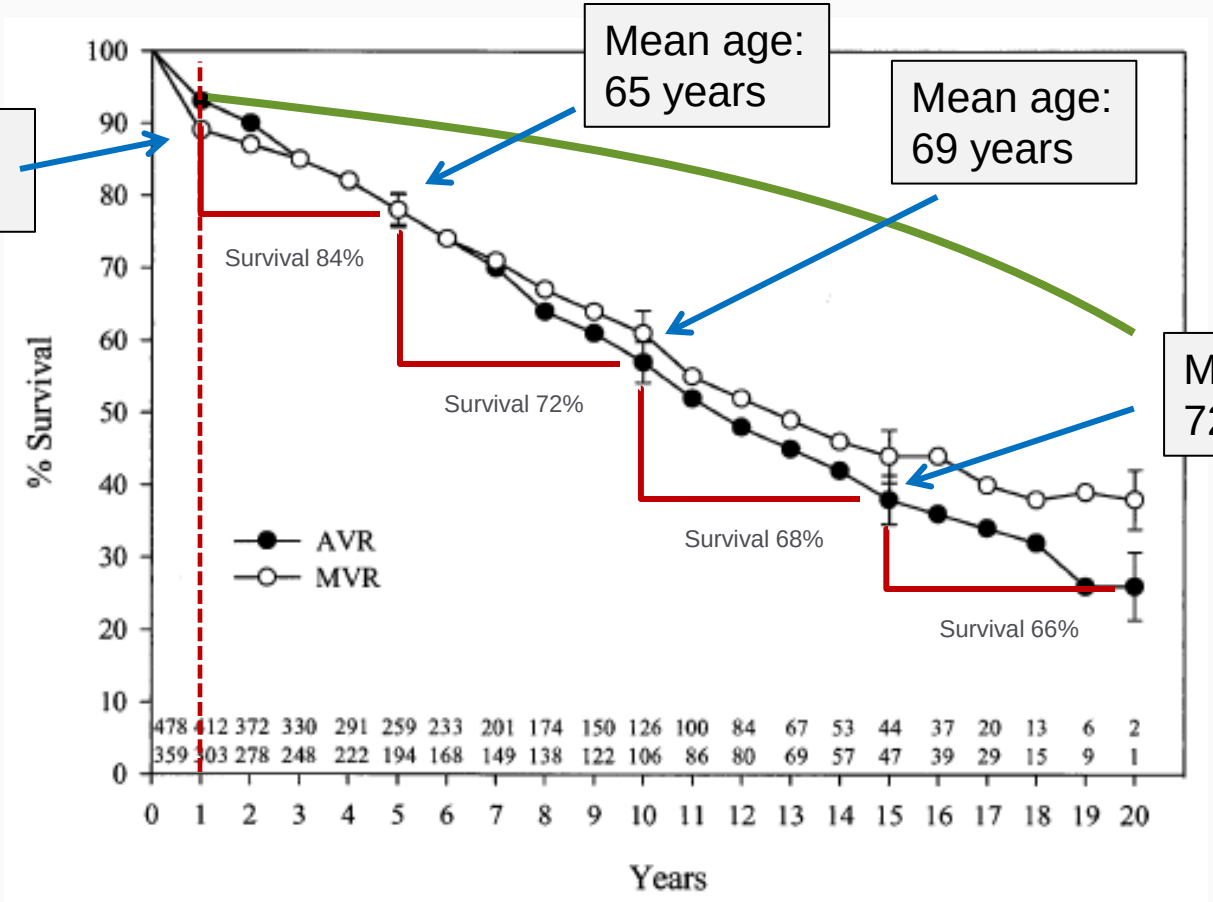
Traditional Aortic Valve Replacement
- Long term prognosis **mechanical valve** -

Mean age: 61 years

Mean age: 65 years

Mean age: 69 years

Mean age: 72 years



1 – 5 years = 112 % e.m.

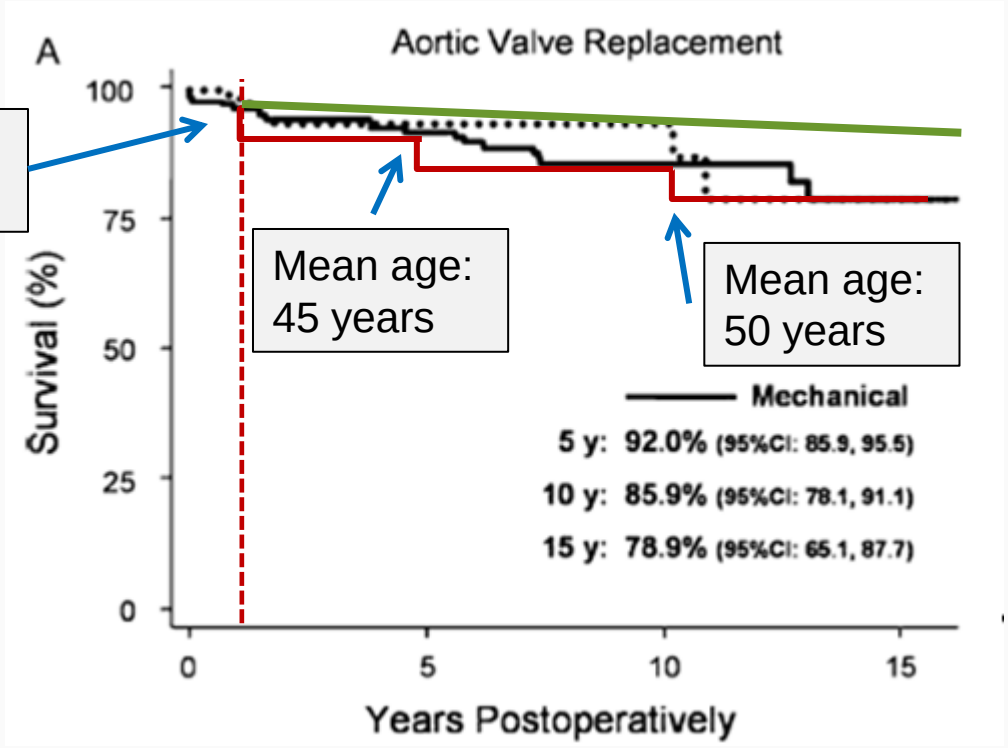
5 – 10 years = 112 % e.m.

10 – 15 years = 78 % e.m.

>15 years = 53 % e.m.

John S. Ikonomidis et al.: „Twenty-year experience with the St Jude Medical mechanical valve prosthesis" Journal of Thoracic and Cardiovascular Surgery 2003;126:2022-2031

Traditional Aortic Valve Replacement
- Long term prognosis **mechanical valve** -



1 – 5 years = 268 % e.m.

> 10 years = 191 % e.m.

5 – 10 years = 201 % e.m.

Marc Ruel et al.: „ Long-term outcomes of valve replacement with modern prostheses in young adults" European Journal of Cardiothoracic Surgery 2005;27:425-433

Traditional Aortic Valve Replacement
- Long term prognosis **bioprosthetic valve** -

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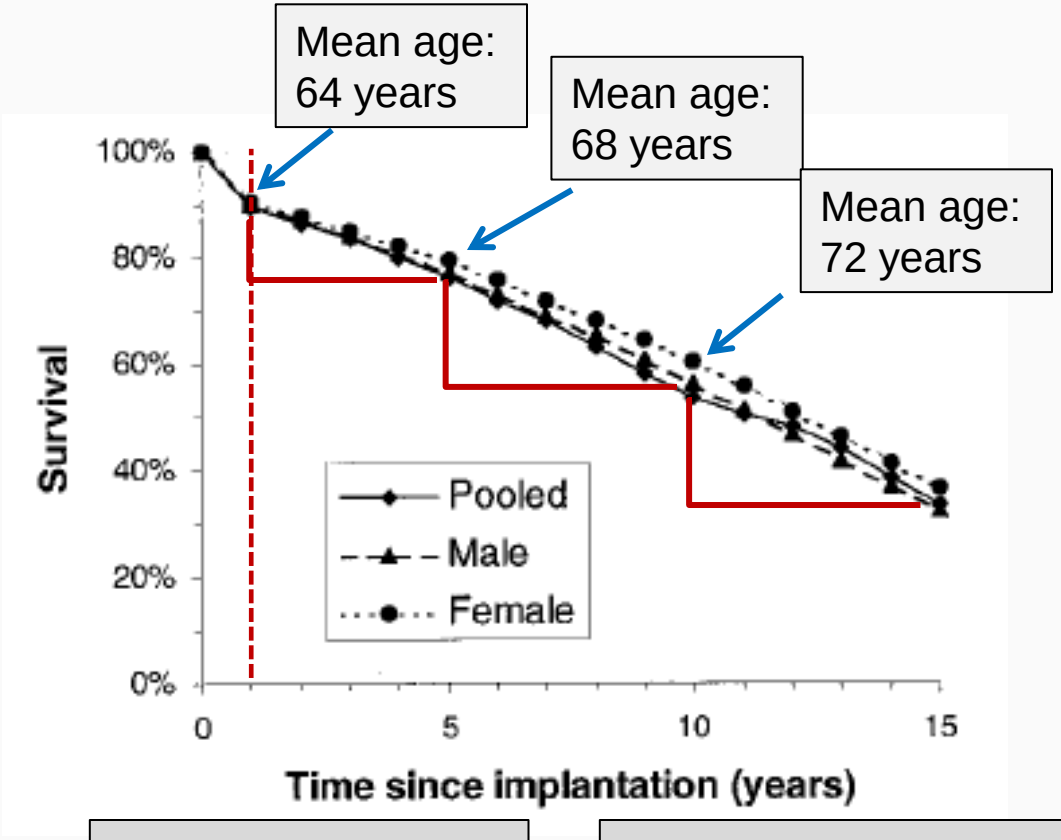

1 – 5 years = 140 %

10 – 15 years = 105 %

5 – 10 years = 113 %

J.P.A. Puvimanasinghe et al.: „Prognosis After Aortic Valve Replacement With a Bioprosthesis Predictions Based on Meta-Analysis and Microsimulation" Circulation 2001;103;1535-1541

Ross Procedure
- Revival of an old idea ? -

The Ross procedure is named after Dr. Donald Ross, a pioneer in cardiac surgery in the UK

He proposed it in 1962 and first performed it in 1967

Procedure:

1. The patient's own pulmonary valve (the "autograft") is used as a replacement for the diseased aortic valve
2. The pulmonary valve is replaced with a donor tissue valve ("homograft")

After being “forgotten”, the numbers of Ross procedures performed have increased significantly during the last 15 years

Ross Procedure
- Revival of an old idea ? -

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Advantages:

Optimal haemodyamics:

The pulmonary valve “mimics” the intrinsic structural characteristics of the native aortic valve, resulting in optimal hemodynamic function

No anticoagulation:

Autograft is living tissue native to the patient = no need for anti-coagulation

The valve grows as the patient grows:

The autograft also demonstrates the potential for growth, which has proven to be a distinct advantage for children and young adults

Ross Procedure
- Revival of an old idea ? -

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Disadvantages:

General:

Single valve disease treated with a two valve procedure

Technical complexity:

More complex than a standard aortic valve replacement = only surgeons with experience/good technical skills will produce good results

Longer surgery:

Longer intraoperative clock-time and time on heart-lung machine

Ross Procedure
- Revival of an old idea ? -

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Indication:

- Infants/children (“growing valve”)
- Young adults with need for excellent haemodynamics (athletes)
- Young women with possible future pregnancy (no anticoagulation)
- Middle aged / older adults ??

Ross Procedure
- Studies -

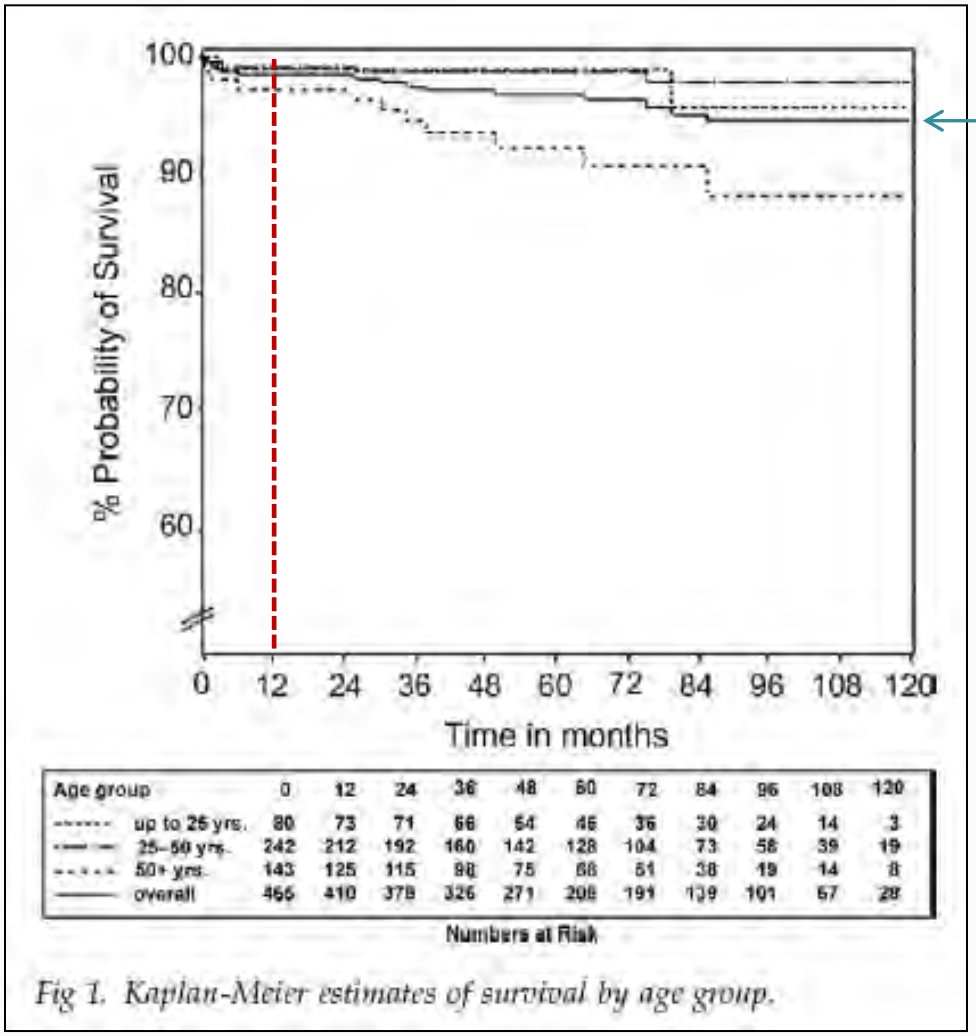

Fig 1. Kaplan-Meier estimates of survival by age group.

overall

Extramortality:	
< 25 years	328 %
25-50 years	127 %
> 50 years	84 %
Overall	143 %

Jürgen O. Böhm et al.: „ A Single-Institution Experience With the Ross Operation Over 11 Years" The Annals of Thoracic Surgery 2009;87:514-520

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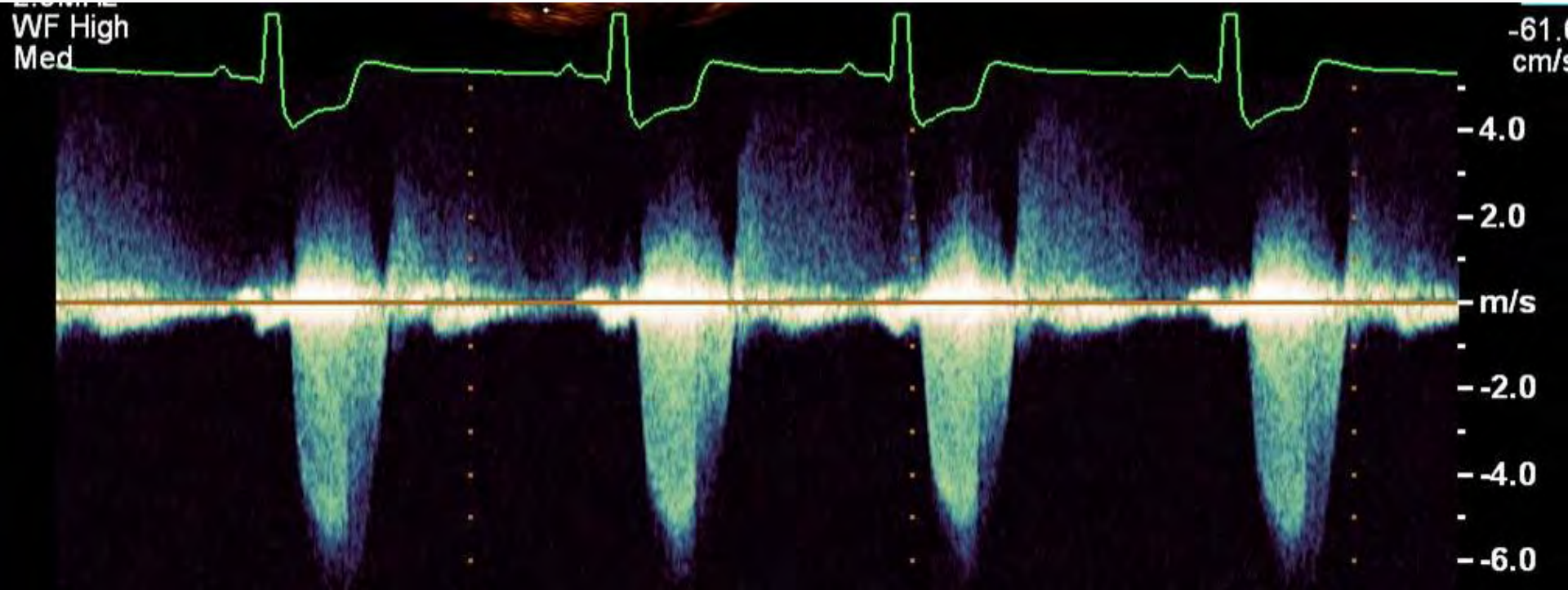
MORTALITY OF AORTIC VALVE STENOSIS

CRYSTAL BALL VERSUS MARKOV MODEL



Aortic Valve Stenosis

Aortic valve stenosis is narrowing of the aortic valve due to various reasons

It is the most frequent heart valve defect

The left ventricle has to increase its pressure to pump a sufficient amount of blood through the narrowed orifice

The left ventricle *compensates* by thickening of its muscle walls (hypertrophy) in order to increase its pumping pressure

Aortic Valve Stenosis
- Natural Course -

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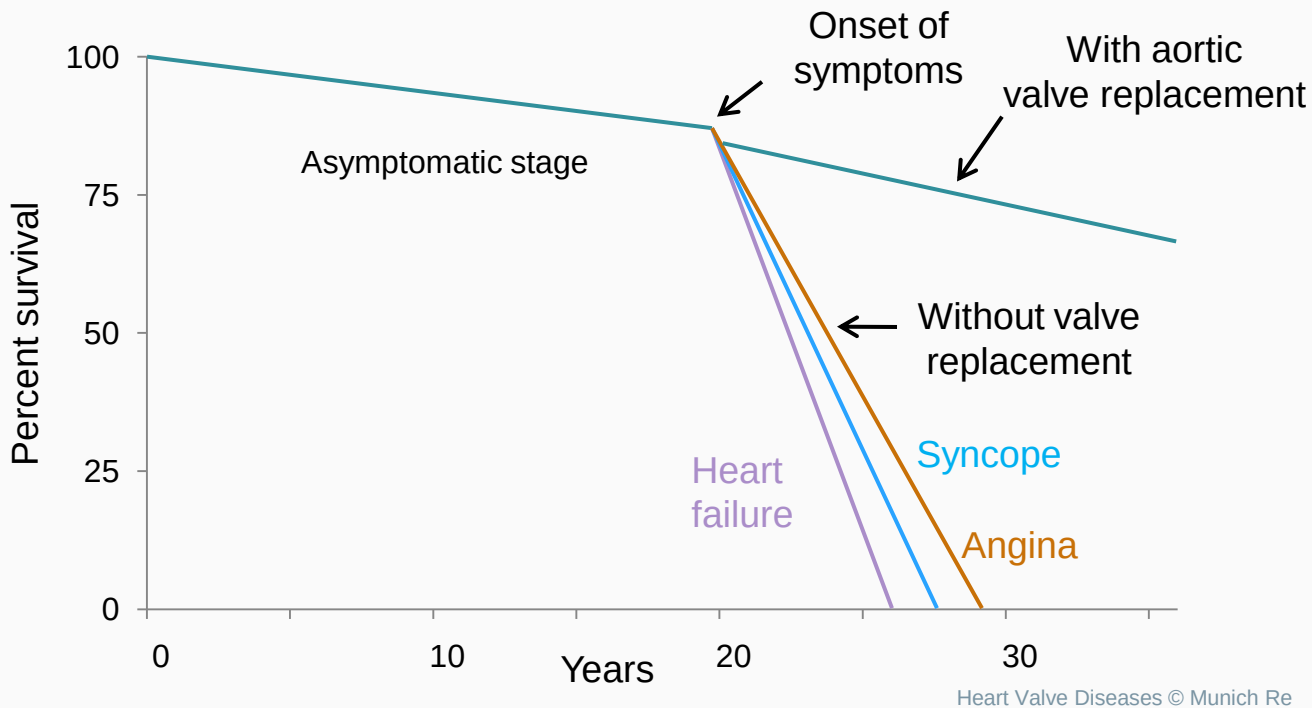
"Compensated" left ventricle = asymptomatic patient

The duration of the asymptomatic period is correlated to the speed of progression to severe aortic valve stenosis

The development of symptoms indicates a "decompensation" of the left ventricle, which is associated with very poor prognosis.



Aortic Valve Stenosis
- Natural Course -

Conclusion:

Severe aortic valve stenosis is usually progressive and heart valve surgery is necessary within some years in most cases

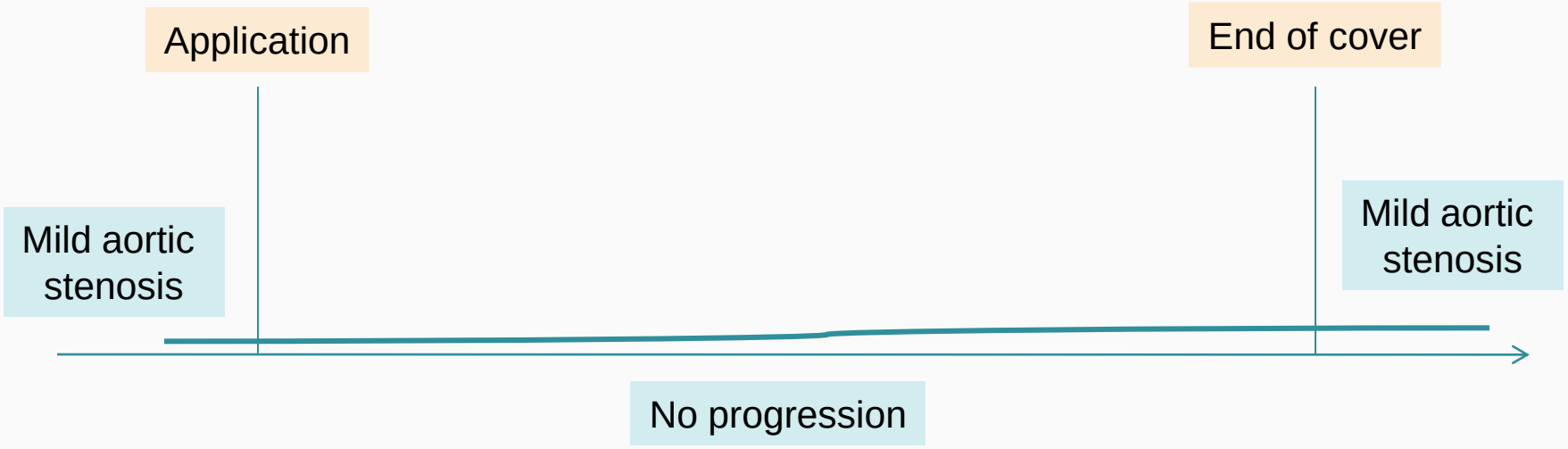
The natural course of a mild to moderate aortic valve stenosis is very difficult to predict

Risk assessment of mild to moderate aortic valve stenosis is challenging

Aortic Valve Stenosis
- Natural Course -

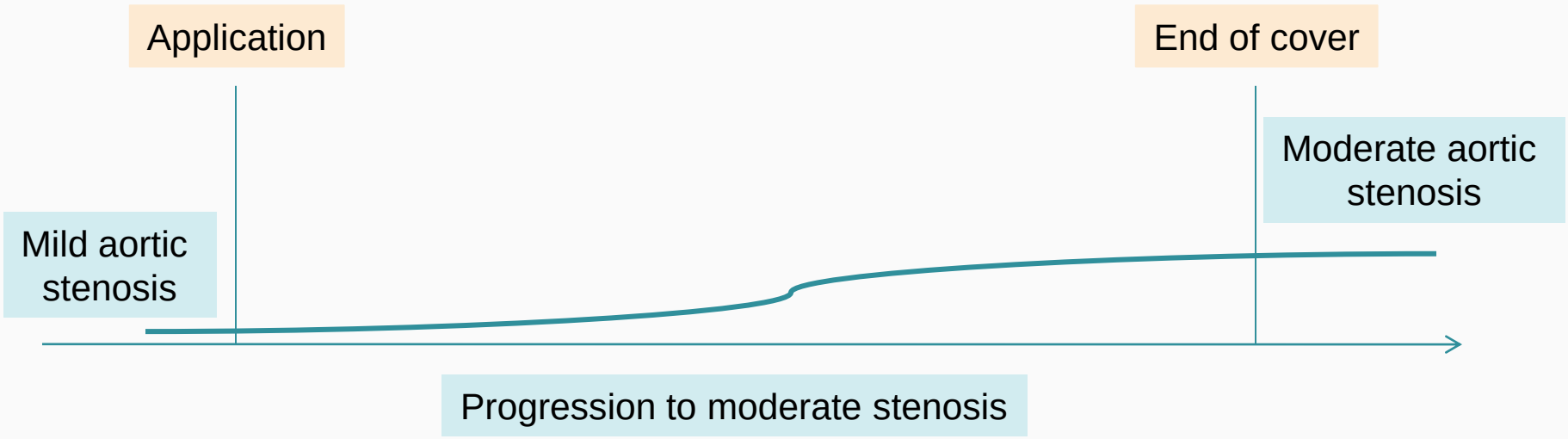
Hypothetical course of a 40 year old applicant with mild aortic valve stenosis

Scenario 1:



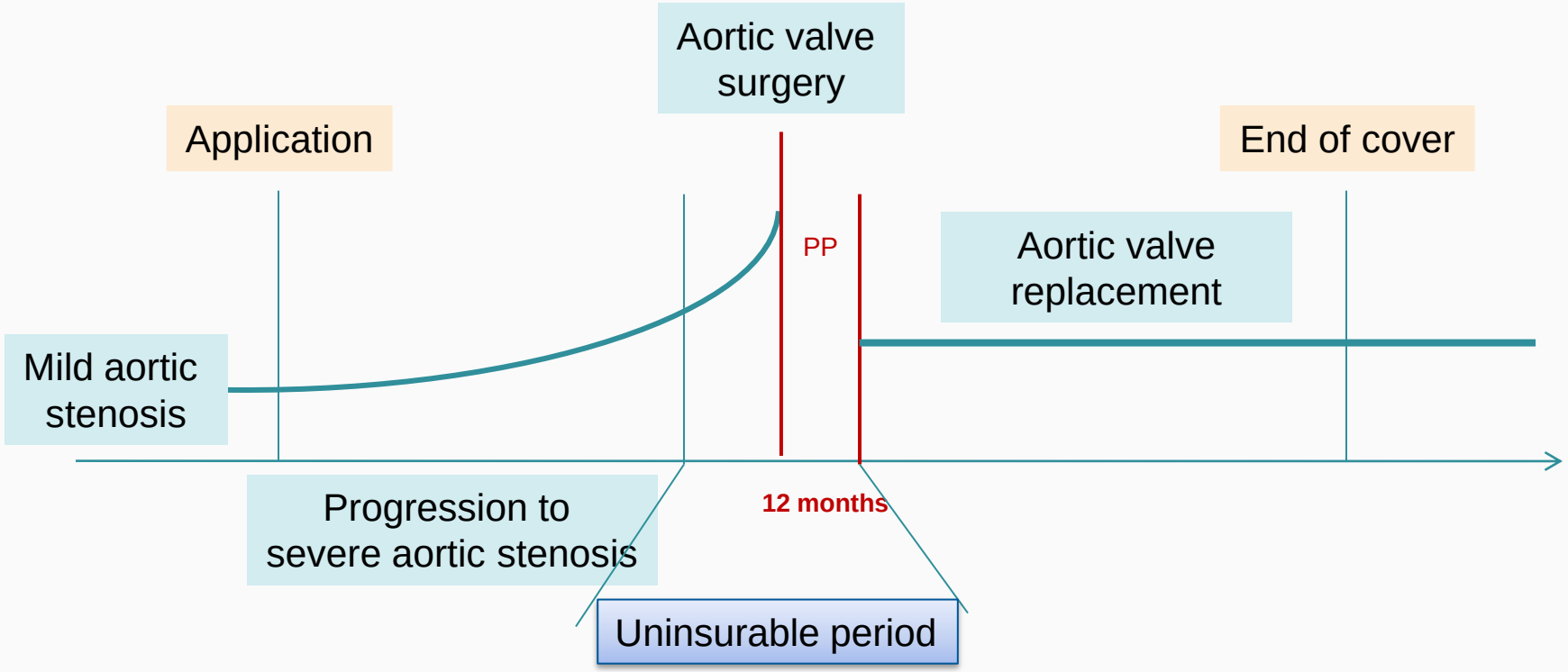
Aortic Valve Stenosis
- Natural Course -

Scenario 2:



Aortic Valve Stenosis
- Natural Course -

Scenario 3:



Aortic Valve Stenosis
- Available Studies -

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Available Studies for mild/moderate aortic valve stenosis:

Table 1 Clinical outcomes in adults with asymptomatic mild to moderate aortic stenosis

Study	Selection criteria	*n*	Mean age	Subgroups	Follow-up (years)	Event-free survival
Horstkotte 1988[1]	Cath for other reasons	[illegible]	?	Mild AS (AVA >1.5 cm^2)		92% at 10 years
	Cath for other reasons	[illegible]		Mod AS (AVA 0.8–1.5 cm^2)		80% at 10 years
Kennedy 1991[2a]	Cath AVA 0.7–1.2 cm^2	28	67±10	AVA 0.92±0.13 (0.7=1.2)	2.9	72% at 4 years
Seattle AS Study 1997[3b]	Abnormal valve with V_{max} ≥2.6 m/s	97	63±16	V_{max} <3 m/s (*n*=29)	2.5±1.4	84±16% at 2 years
				V_{max} 3–4 m/s (*n*=68)		66±13% at 2 years
Rosenhek 2004[5]	Aortic stenosis with V_{max} 2.5–3.9 m/s	176	58±19	Overall	4±1.6	75±3% at 3 years
				V_{max} <3 m/s		89±4% at 3 years
				V_{max} 3–4 m/s		70±4% at 3 years
				No or mild valve Ca^{++}		90±4% at 3 years
				Mod-severe valve Ca^{++}		61±7% at 3 years

AS=aortic stenosis; AVA=aortic valve area; Cath=cardiac catheterization; Mod=moderate; Ca^{++}=calcification; V_{max}=maximum aortic stenosis jet velocity.

[a] Only the asymptomatic patients are shown.
[b] Only the subgroups with mild-moderate aortic stenosis (defined as an aortic jet velocity <4.0 m/s are shown).

Solution:

a) looking into a crystal ball

b) using a mathematical model

Aortic Valve Stenosis
- Markov-Model -

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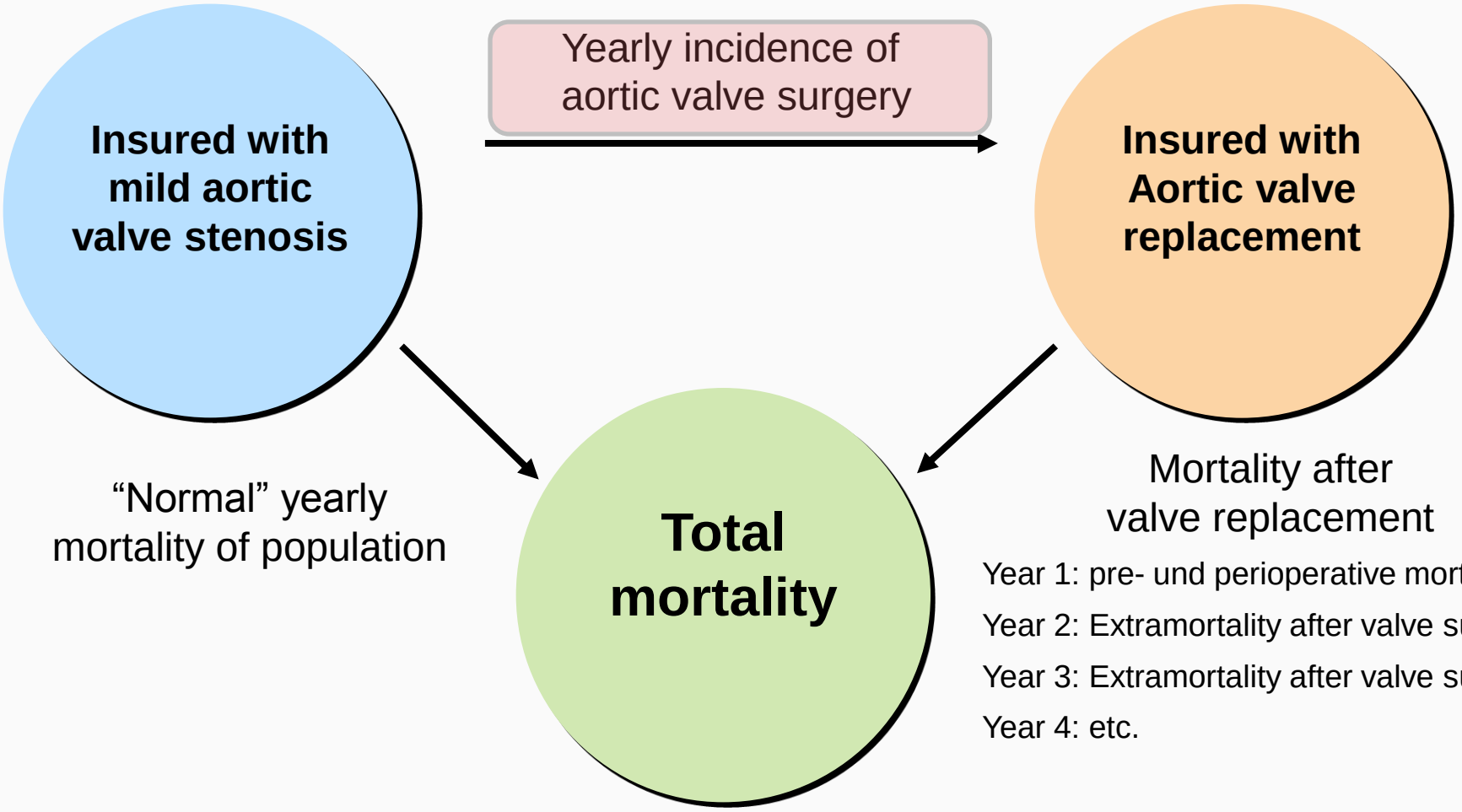
A Markov-Model models the state of a system with a random variable that changes through time:



Aortic Valve Stenosis
- Incidence of Aortic Valve Surgery in Mild Aortic Valve Stenosis-

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100 % mild
aortic valve stenosis

After 25 years:
38 % mild aortic valve stenosis
24 % moderate aortic valve stenosis
38 % severe aortic valve stenosis or surgery

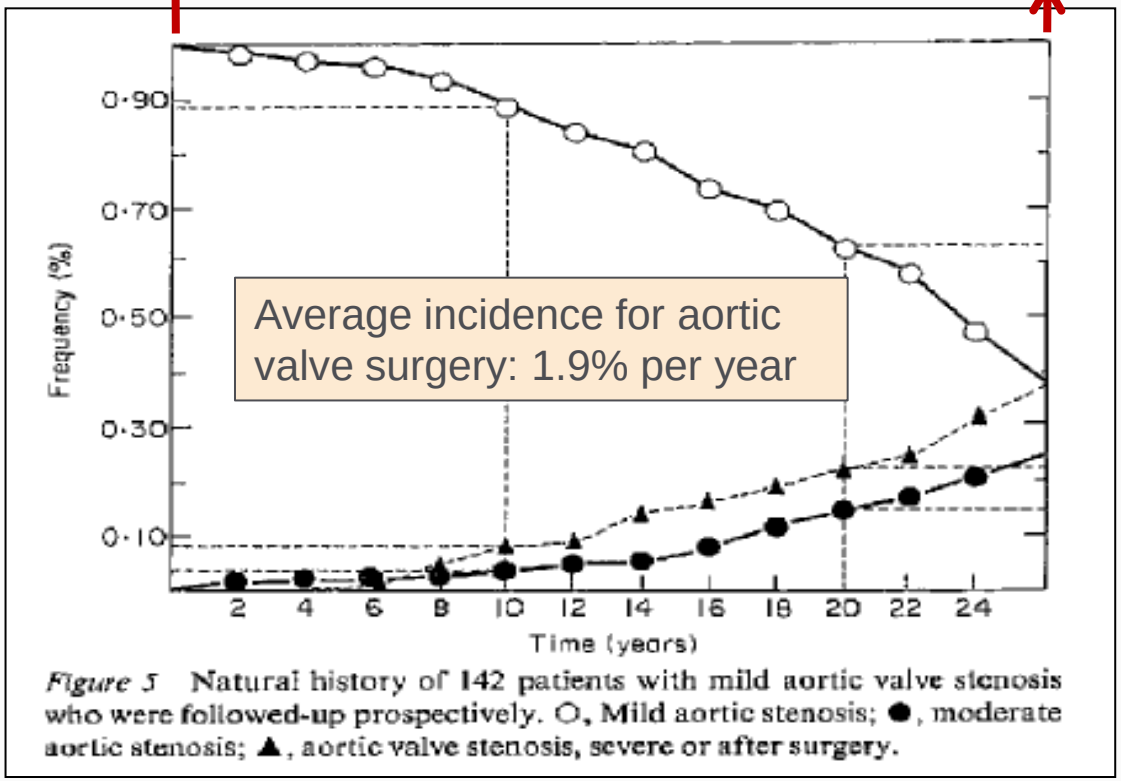
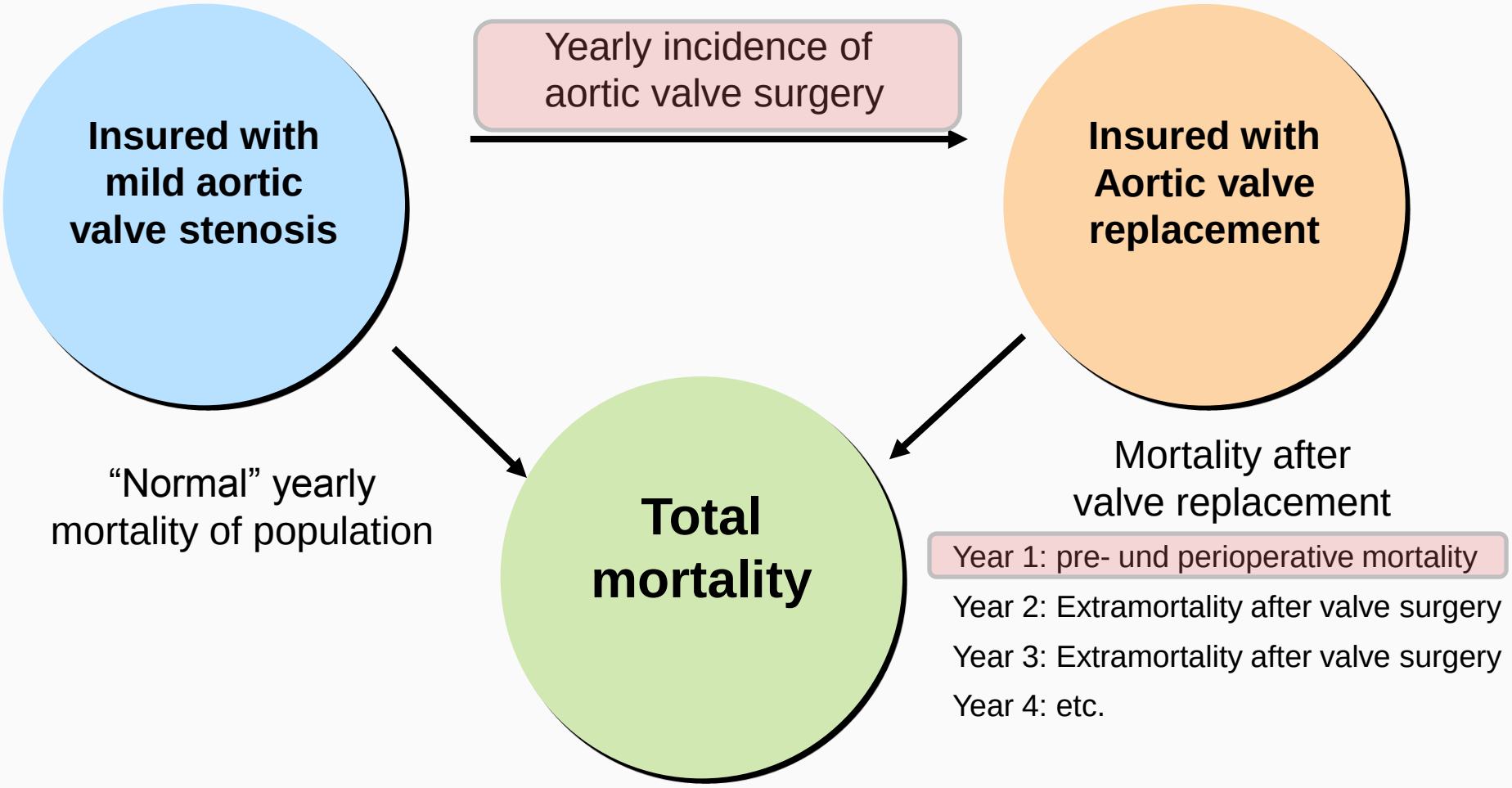


Figure 5 Natural history of 142 patients with mild aortic valve stenosis who were followed-up prospectively. ○, Mild aortic stenosis; ●, moderate aortic stenosis; ▲, aortic valve stenosis, severe or after surgery.

D. Horstkotte et al.: „The natural history of aortic valve stenosis“ European Heart Journal 1988;9:57-64

Aortic Valve Stenosis
- Markov-Model -



Aortic Valve Stenosis
- Pre- and Perioperative Mortality -

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Perioperative mortality depends on:

1) Age

2) Comorbidities

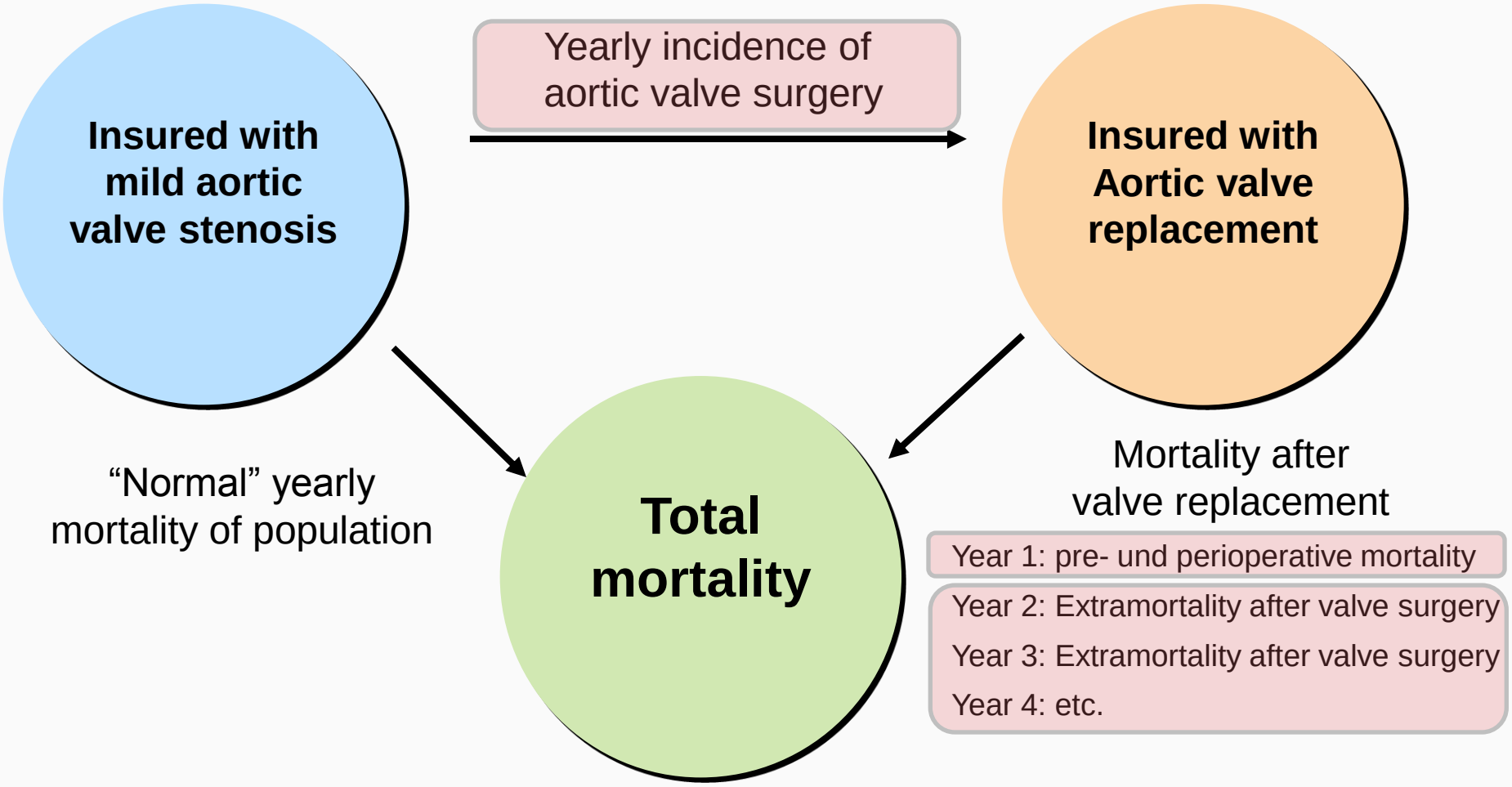
3) Type of valve surgery: bioprosthetic, mechanical, Ross-Procedure etc.

Average perioperative mortality in available studies: 2.5 - 6%

Average preoperative mortality in available studies: ~ 1.5%

Mortality numbers will be even lower in a typical insurance population, as applicants with severe comorbidities will not pass the underwriting process.

Aortic Valve Stenosis
- Markov-Model -



Aortic Valve Stenosis
- Yearly Extramortality of Aortic Valve Replacement -

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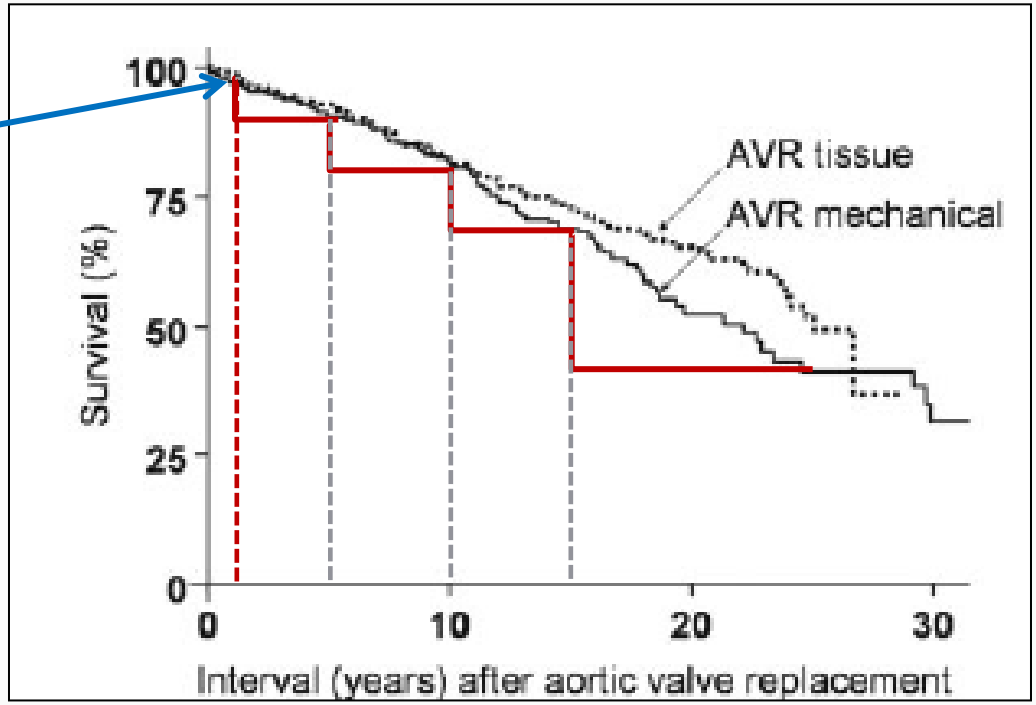
Age:
50 years



1 – 5 years = 183 % e.m.

10 – 15 years = 138 % e.m.

5 – 10 years = 173 % e.m.

>15 years = 119 % e.m.

Marc Ruel et al.: „Very Long-Term Survival Implications of Heart Valve Replacement With Tissue Versus Mechanical Prostheses in Adults <60 Jahrs of Age" Circulation 2007;116 [suppl I]:I-294–I-300

Aortic Valve Stenosis
- Extramortality Calculated by Markov-Model -

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Extramortality of mild aortic valve stenosis

Age	Incidence of valve surgery (per year)	Pre- and perioperative mortality	Extramortality with valve replacement (per year)	**Total extramortality (Markov-Model)**
21-30 years	1.9%	4%	300%	**130%**
31-40 years	1.9%	4%	250%	**82%**
41-50 years	1.9%	5%	225%	**56%**
51-60 years	1.9%	6%	200%	**34%**
> 60 years	1.9%	6%	175%	**23%**

Summary

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Aortic valve replacement:

Standard aortic valve replacement is associated with moderate to high e.m.

Gender: no difference in prognosis

Ross procedure is a promising alternative and associated with better outcome, especially in younger individuals

Mild to moderate aortic valve stenosis:

No available studies for an evidence based calculation of prognosis

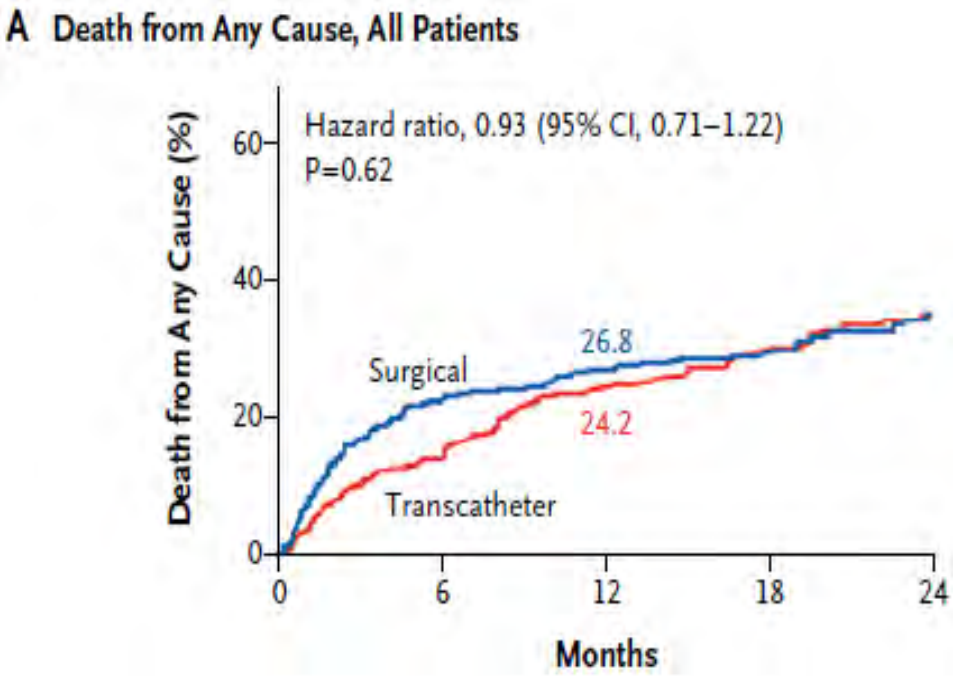
With a Markov-Model a calculation of mortality and morbidity is possible

All variables of the model are evidence based

CI CLAIMS HANDLING OF “HEART VALVE SURGERY”

ARE WE PREPARED FOR THE FUTURE ?

Medical Progress
- Transcatheter aortic valve replacement (TAVI) -



PARTNER A Study:

- Published June 2011
- 699 patients <u>suitable for surgery</u>
- Mean age 84 years
- Same survival after 2 years

Craig Smith, Principal Investigator (Columbia University, New York, USA):

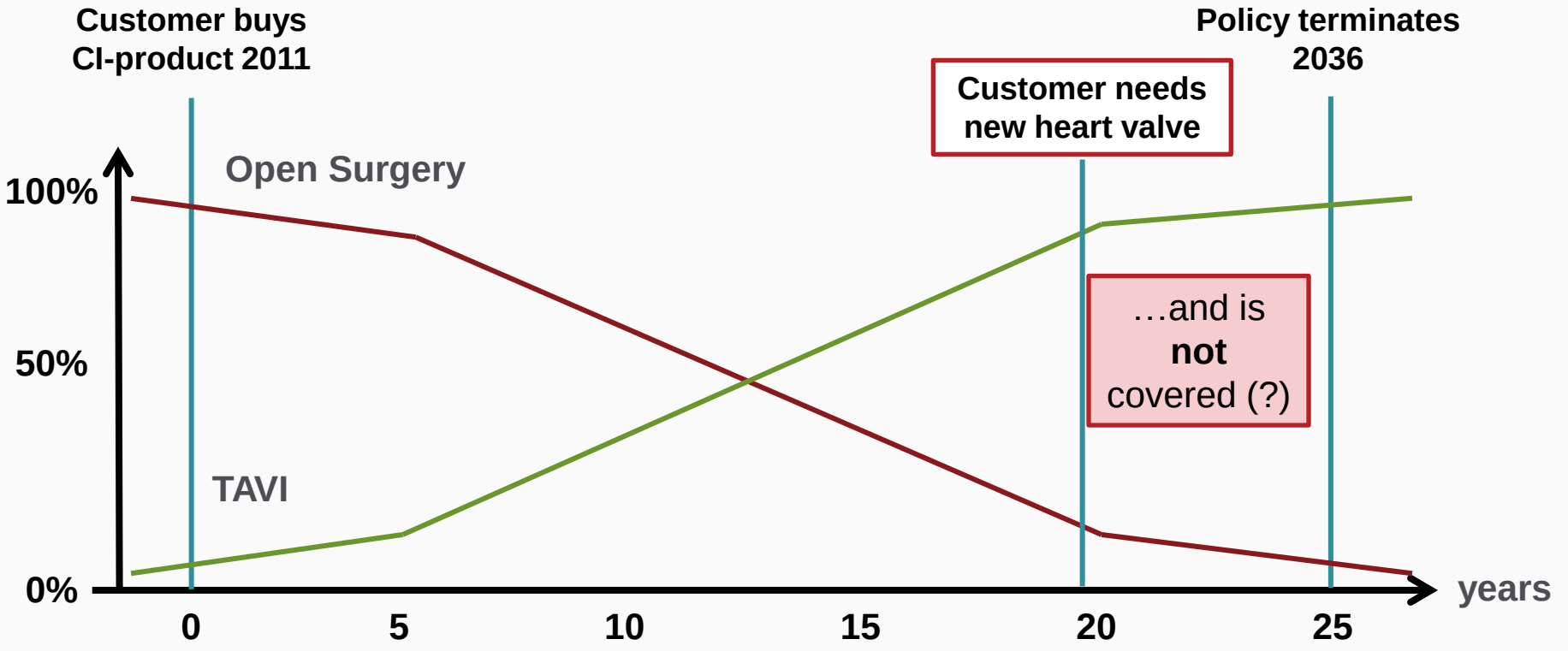
"This study introduces a new era in interventional cardiology"

*" ... Future clinical trials should include **patients with low surgical risk**"*

CI pricing and claims handling
- Risk of change -

Heart valve replacement or repair – *with surgery to divide the breastbone*

The undergoing of surgery requiring median sternotomy (surgery to divide the breastbone) on the advice of a Consultant Cardiologist to replace or repair one or more heart valves.



CI pricing and claims handling
- Risk of change -

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- Modern treatment = no pay out
- Old fashioned (inferior ?) treatment = pay out
- Insurance companies will have credibility problem
- Consumers will not accept this = call for consumer rights
- Most likely judges will be more on the consumer side

Possible consequences:

New procedure „only“ replaces old procedure = no change in incidence rates

New procedure will extend surgical indication = increase in incidence rates

Our expectation

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TAVI will revolutionize the treatment of aortic valve defects

The actual CI definition will be challenged and maybe “overruled” by the legislation, if TAVI becomes standard treatment

TAVI will mainly replace open surgery in younger age groups = CI pricing unaffected in CI products with end age 65

TAVI will widen the indication in the elderly (comorbidities) = pricing of CI products with end age > 65 and health products will be affected

TAVI should be included into a revised CI definition for heart valve surgery

A lot of cardiac surgeons may need occupational redeployment

GOING TO THE BAR AFTER THE LECTURE ?

AN EVIDENCE BASED EXCUSE

	Cardiovascular disease mortality (n=21 studies, 1 184 956 subjects)	Coronary heart disease	
		Incident (n=29 studies, 549 504 subjects)	Mortality (n=31 studies, 1 925 106 subjects)
Active drinkers *v* non-drinkers:			
Least adjusted models	0.84 (0.75 to 0.95) (11)	0.73 (0.65 to 0.82) (14)	0.80 (0.70 to 0.91) (10)
Most adjusted models	0.75 (0.70 to 0.80) (21)	0.71 (0.66 to 0.77) (29)	0.75 (0.68 to 0.81) (31)
Active drinkers *v* lifetime abstainers	0.82 (0.78 to 0.86) (9)	0.73 (0.61 to 0.88) (9)	0.75 (0.66 to 0.85) (7)
Former drinkers *v* non-drinkers	1.48 (1.23 to1.79) (6)	1.10 (0.91 to 1.33) (8)	1.31 (1.02 to 1.68) (6)
Alcohol intake (g/day) *v* none:			
<2.5	0.71 (0.57 to 0.89) (7)	0.96 (0.86 to 1.06) (6)	0.92 (0.80 to 1.06) (6)
2.5–14.9	0.77 (0.71 to 0.83) (15)	0.75 (0.65 to 0.88) (9)	0.79 (0.73 to 0.86) (18)
15–29.9	0.75 (0.70 to 0.80) (13)	0.66 (0.59 to 0.75) (15)	0.79 (0.71 to 0.88) (15)
30–60	0.85 (0.73 to 0.98) (10)	0.67 (0.56 to 0.79) (9)	0.77 (0.72 to 0.83) (12)
>60	0.99 (0.84 to 1.17) (6)	0.76 (0.52 to 1.09) (9)	0.75 (0.63 to 0.89) (9)

Alcohol and Cardiovascular Mortality

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February 2011: "Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis"

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Paul E Ronksley et al.; British Medical Journal 2011;342:d671 (Published 22 February 2011)

Alcohol and Cardiovascular Mortality

"With respect to public health messages, there may now be an impetus to better communicate to the public that alcohol, in moderation, may have overall health benefits that outweigh the risks in selected subsets of patients"

Prescription:

ASA 100	1-0-0
Metoprolol 50	1-0-0
HCT 25	1-0-0
Captopril 25	1-0-1
Pint	0-0-1

Strategies for the Prevention of MI

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February 2011: "Public health importance of triggers of myocardial infarction"

Trigger for heart attack	Odds ratio	Population-attributable fractions
Anger	3.1	3.0%
Cocaine	23.7	1.0 %
Sex	3.1	2.2 %
Exhaust fumes, traffic noise	2.9	7.36 %

TS Nawrot et al.; Lancet 2011 Feb 26;377(9767):732-40

<u>You can help reduce the burden of myocardial infarction by 7 %, if you:</u>

a) **Use your car** and never get angry, no more drugs, no sex

or

b) **Go by bike** and let your emotions rip, use drugs, practice free love

THANK YOU VERY MUCH FOR YOUR KIND ATTENTION

AND A MERRY CHRISTMAS TO ALL OF YOU

Dr. Karsten Filzmaier

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