

# Individual level meta-analysis integrating real world data and pivotal study on paclitaxel-containing devices and mortality

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# COI Disclosure

First Author : Hiroyoshi Yokoi M.D.

1.Consultation fees : none

2.Stock ownership/ Profit : none

3.Patent fees : none

4.Remuneration for lecture : COOK,Medotoronic,Bard,Boston

5.Manuscript fees: none

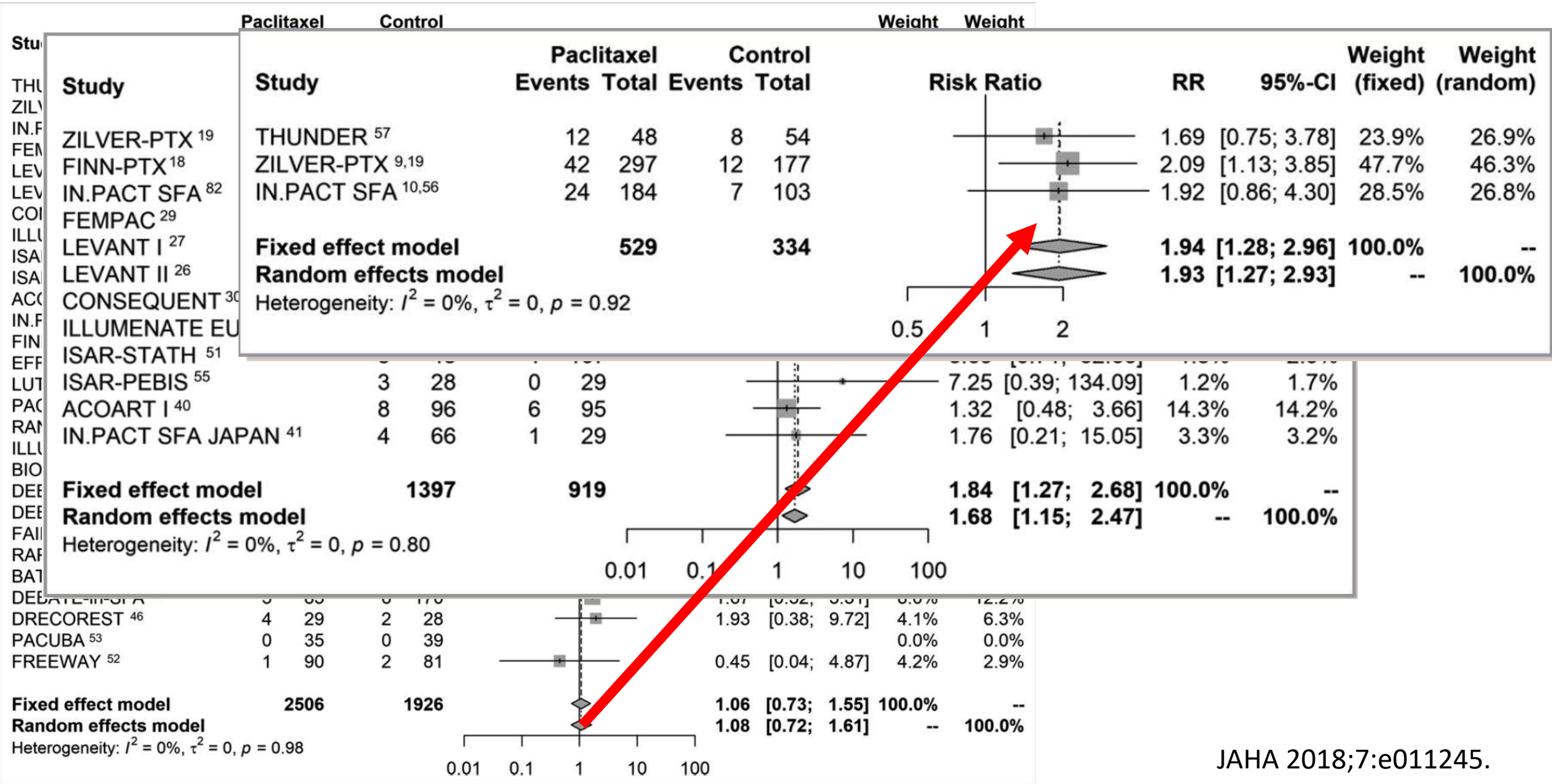
6.Trust research/ Joint research funds: none

7.Scholarship fund: none

8.Affiliation with Endowed Department : none

9.Other remuneration such as gifts : none

# A meta-analysis of Katsanos et al suggested the harmful effect of PTXD on long-term mortality



# Not conclusive



## Summary meta-analysis

Katsanos K, JAHA 2018

## Individual patient meta-analysis

VIVA group Circulation 2020

## Bayes Factor Meta-Analysis

JACC interv 2019

## Device specific meta-analysis

Dake MD et al. Cardiovasc Intervent Radiol 2019

Schneider PA et al. J Am Coll Cardiol 2019

Schneider PA et al. Catheter Cardiovasc Interv 2020

Gray WA et al. Circulation 2019

Ouriel K et al. JACC Cardiovasc Interv 2019

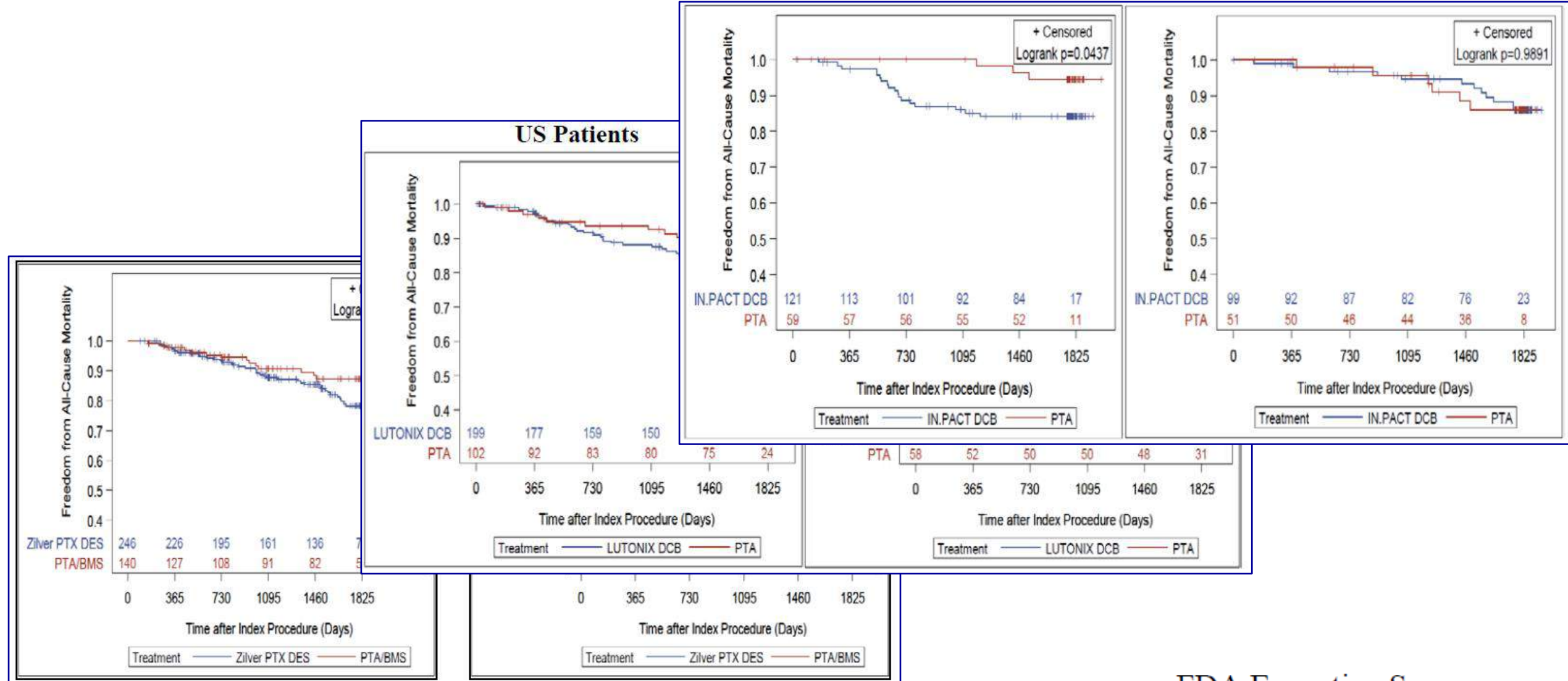
## RWD

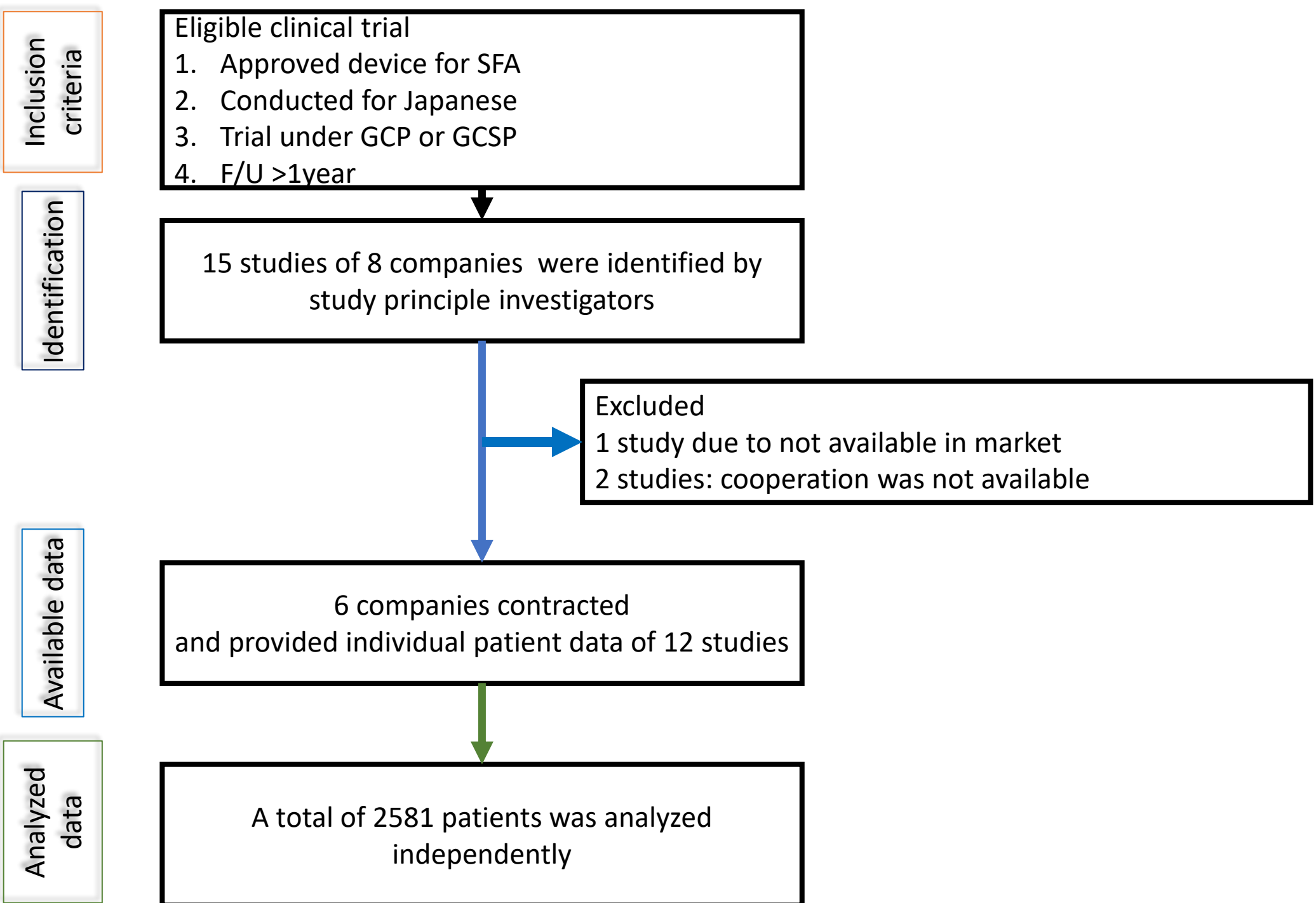
Freisinger E et al. Eur Heart J 2019

Secemsky EA et al. J Am Coll Cardiol 2019

Secemsky EA et al. JAMA Cardiol 2019

# Geographic factor: US vs outside of US patients



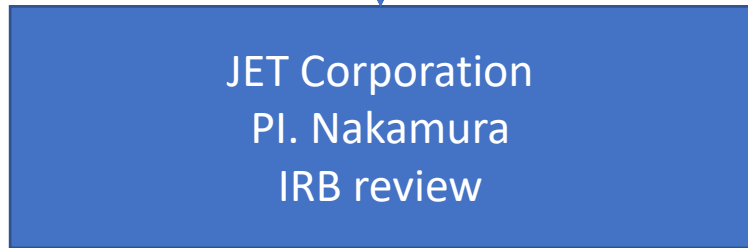


# Request of cooperation from MHW/PMDA

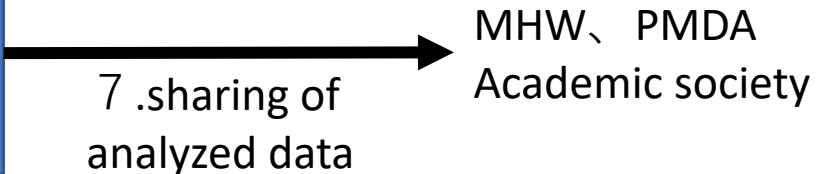


1. Confidentiality contract, data provision contract

2. provision of data catalog and masked data

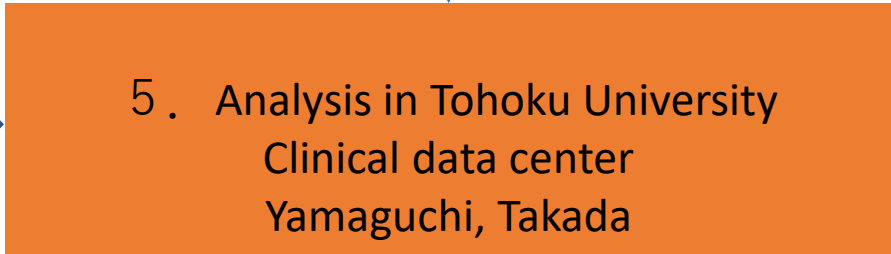
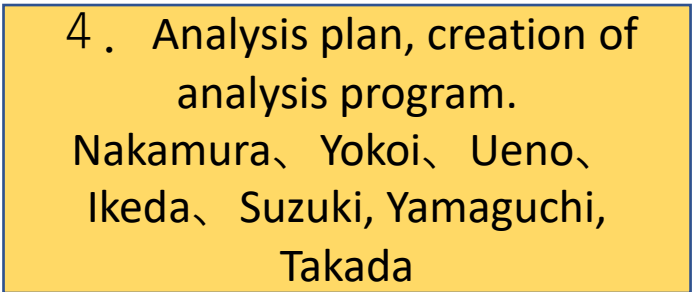


3. Data catalog and masked data



7. sharing of analyzed data

6. Feed back of analyzed data



# Method

- With the corporation of 6 companies that had Japanese clinical trial data on endovascular treatment for symptomatic superficial femoral artery (SFA) disease, individual data from all trials was integrated and a patient-level meta-analysis was conducted.
- This meta-analysis comprised of 1,389 cases of paclitaxel containing devices (PTXD: drug coated balloon: 388, drug eluting stent 1,001) and 1,192 cases of non- PTXD (bare metal stent 991, balloon angioplasty 201).
- A primary endpoint was all cause death and cumulative mortality was estimated by the Kaplan-Meier curve.
- Cox proportional hazard model was adopted to calculate hazard ratio and 95% confidence interval of PTXD versus non-PTXD.



# 12 trials 2581 cases : 6 RCT+6single arm study (1pivotal, 5PMS)

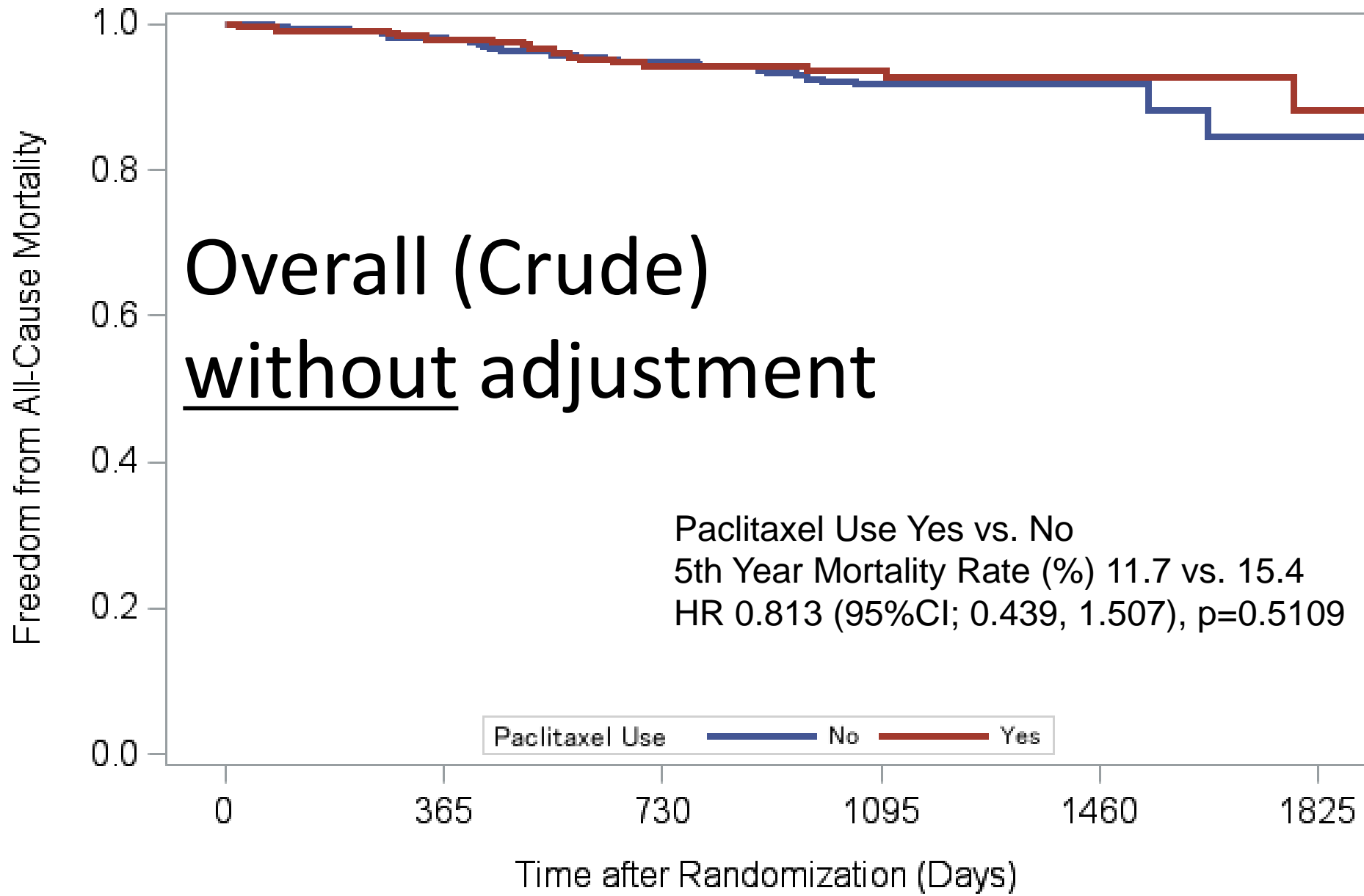
Name of trial	Device tested	Allocation of study	Enrollment (要確認)	Study design Allocation	Subjects included
<a href="#">NCT02574481</a>	Eluvia/Zilver PTX	DES/DES	Dec. 2015	Pivotal RCT 1:1	56/28
<a href="#">NCT00120406</a>	Zilver PTX	DES/Balloon	Jun.2007	Pivotal RCT 1:1	26/27
<a href="#">NCT02254837</a>		DES	May.2012	PMS	891
<a href="#">NCT01947478</a>	IN.PACT Admiral	DCB/Balloon	Sep.2013	Pivotal RCT 2:1	68/32
<a href="#">UMIN000030540</a>		DCB	Dec.2017	PMS	249
<a href="#">NCT01816412</a>	Lutonix	DCB/Balloon	Nov.2012	Pivotal RCT 2:1	71/38
<a href="#">UMIN000003291</a>	Misago	BMS/Balloon	April.2010	Pivotal RCT 1:1	50/51
<a href="#">UMIN000026875</a>		BMS	Jan.2013	PMS	292
<a href="#">UMIN000003928</a>	SMART	BMS/Balloon	Aug.2010	Pivotal RCT 1:1	52/53
NA		BMS	May.2013	PMS	317
<a href="#">NCT02254356</a>	Zilver Flex	BMS	May.2012	PMS	206
<a href="#">NCT01746550</a>	Life	BMS	Sep.2012	Pivotal	74

**PTXD 6 trials、 non-PTXD 6 trials**

RCTs

552 cases

(PTX249 vs Non-PTX 303 )



No	303	286	264	112	26	16
Yes	249	243	212	102	23	15

# Cox proportional hazard model

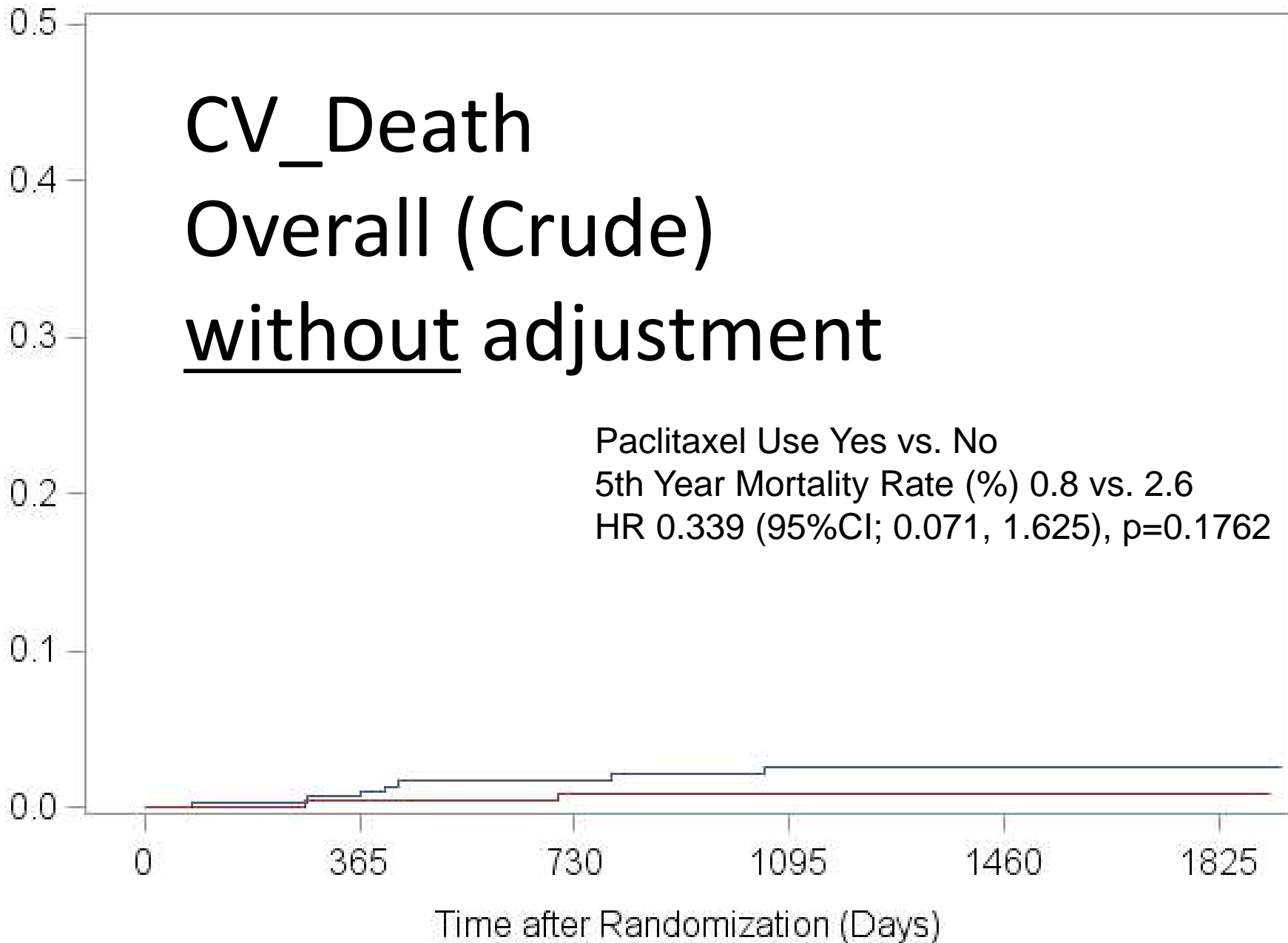
<b>Size</b>	<b>No. of death</b>	<b>HR</b>	<b>95% CI</b>	<b>P-value</b>
550	42	1.01	0.39-2.61	0.98

Model : Study, Age, Gender, HT, Hyperlipidemia, DM, Rutherford分類, Smoking

# CV\_Death Overall (Crude) without adjustment

Cumulative Incidence

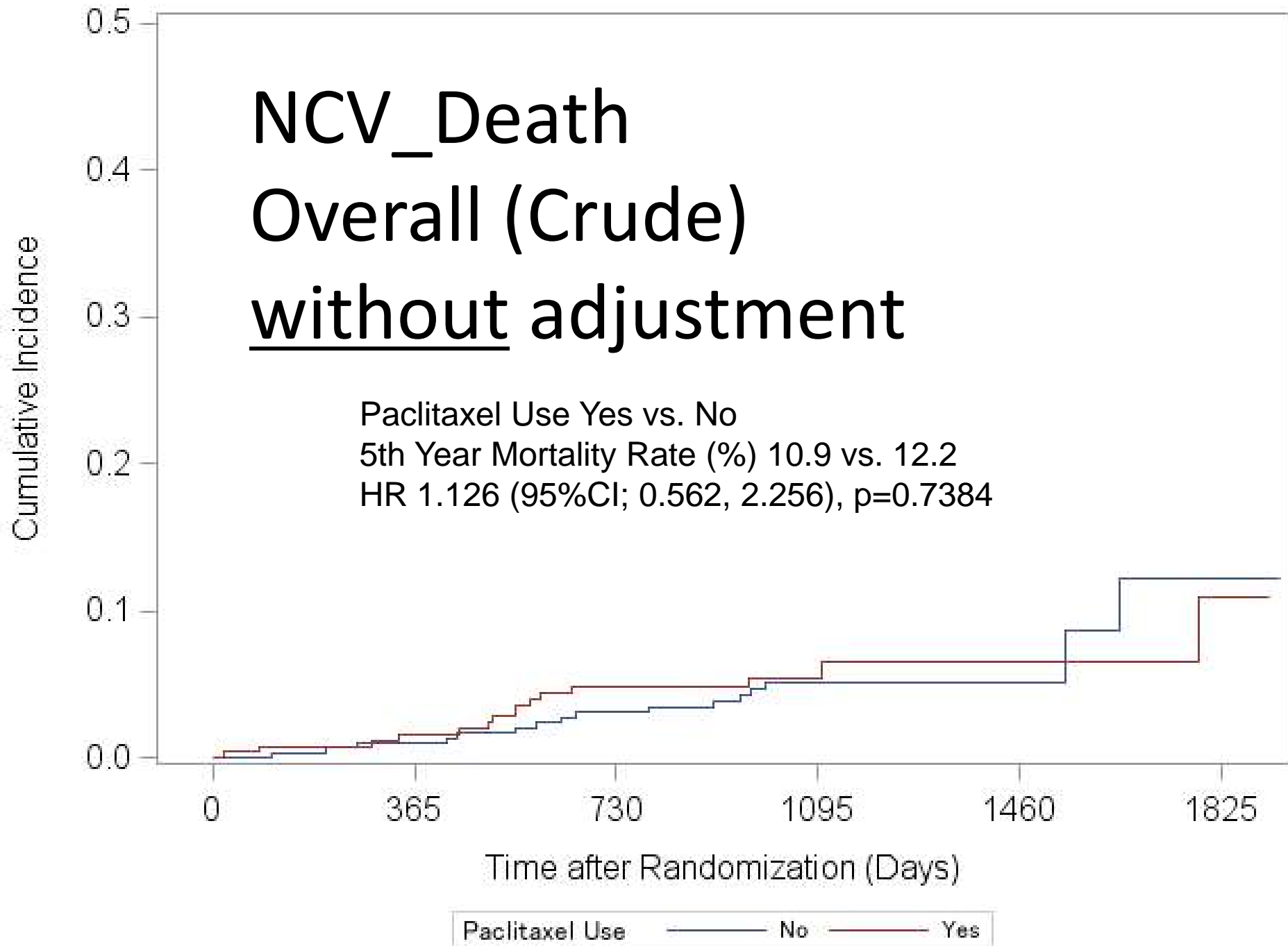
Paclitaxel Use Yes vs. No  
5th Year Mortality Rate (%) 0.8 vs. 2.6  
HR 0.339 (95%CI; 0.071, 1.625), p=0.1762



Paclitaxel Use — No — Yes

# NCV\_Death Overall (Crude) without adjustment

Paclitaxel Use Yes vs. No  
5th Year Mortality Rate (%) 10.9 vs. 12.2  
HR 1.126 (95%CI; 0.562, 2.256), p=0.7384

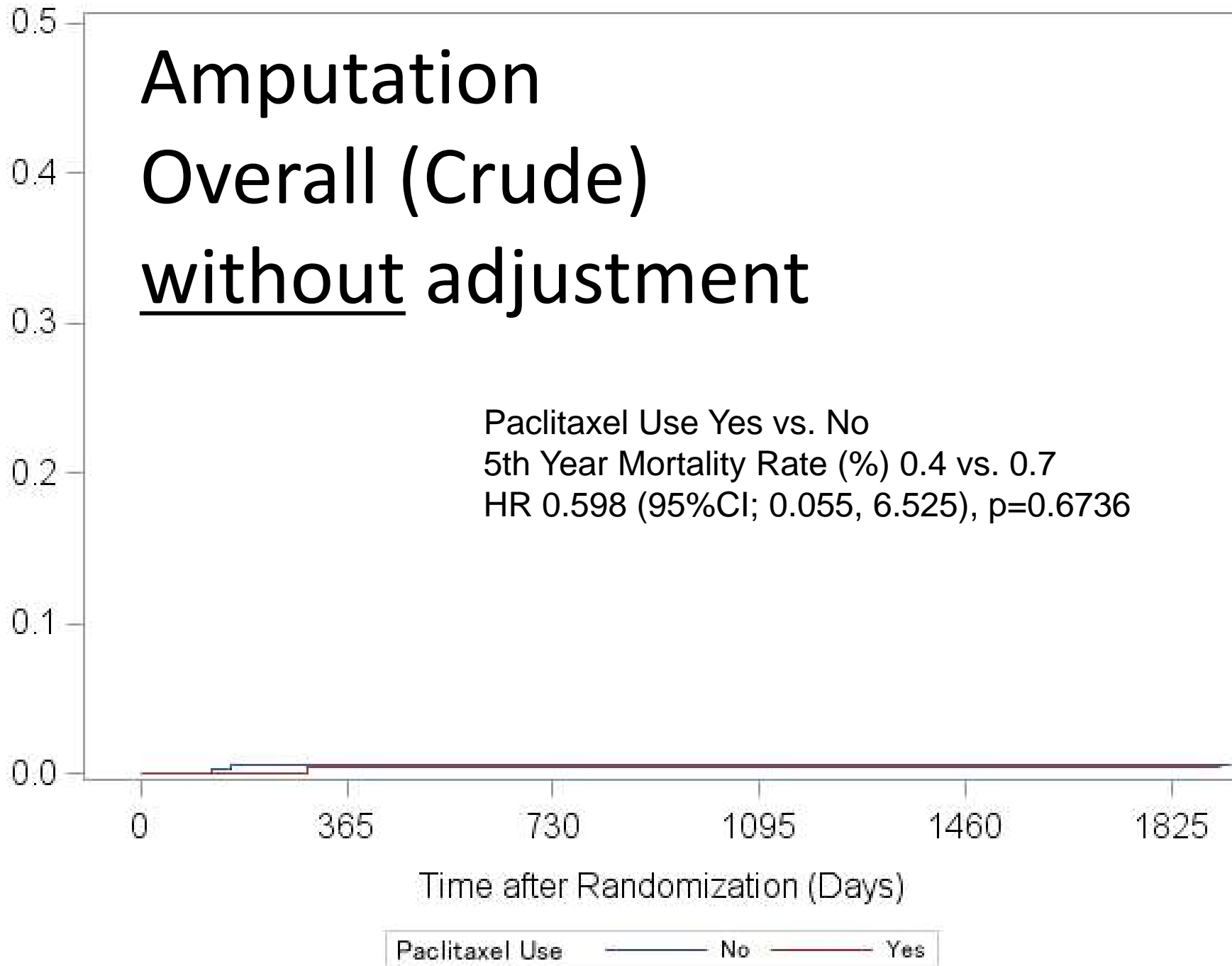


# Amputation Overall (Crude) without adjustment

Paclitaxel Use Yes vs. No  
5th Year Mortality Rate (%) 0.4 vs. 0.7  
HR 0.598 (95%CI; 0.055, 6.525), p=0.6736

All 3  
Major 0  
Minor 2  
Unknown status 1

Cumulative Incidence

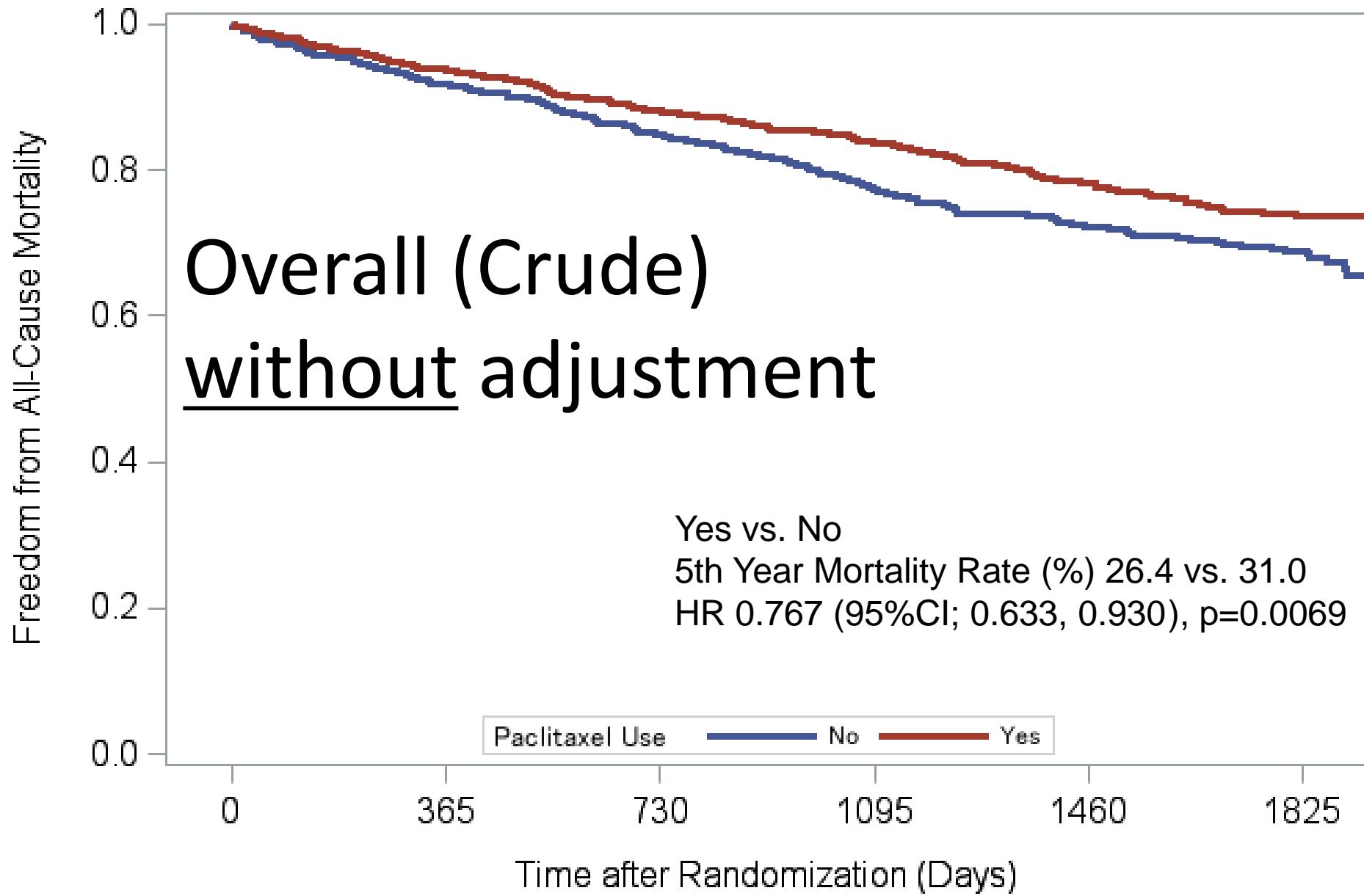


Single arm study

2029 cases

(PTX 1140 vs Non-PTX 889)





No	889	734	620	457	293	175
Yes	1140	931	671	565	467	224

<b>Model</b>	<b>Size</b>	<b>No. of death</b>	<b>HR</b>	<b>95% CI</b>	<b>P-value</b>
Model 1	1984	411	0.83	0.68-1.01	0.07
Model 2	1882	391	0.89	0.72-1.08	0.23
Model 3	1231	215	1.04	0.7-1.54	0.84

Model 1: Age, Gender, HT, Hyperlipidemia, DM

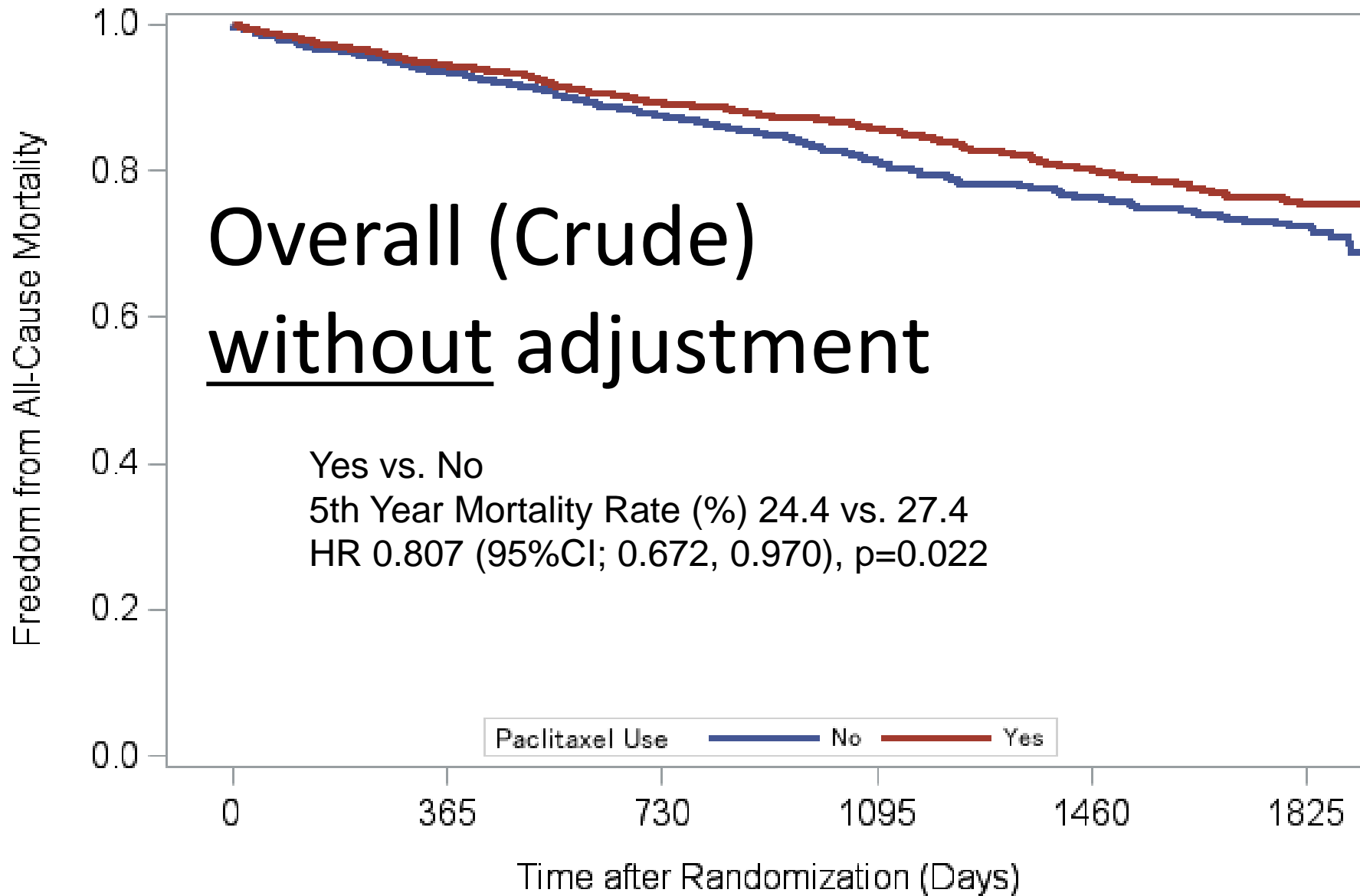
Model 2: Age, Gender, HT, Hyperlipidemia, DM, Rutherford

Model 3: Age, Gender, HT, Hyperlipidemia, DM, Rutherford, Dialysis, Smoking, CAD

RCT+Single arm study

2581 cases

(PTX 1389 vs Non-PTX 1192)



No	1192	1020	884	569	319	191
Yes	1389	1174	883	667	490	239

<b>Model</b>	<b>Size</b>	<b>No. of death</b>	<b>HR</b>	<b>95% CI</b>	<b>P-value</b>
Model 1	2460	438	0.96	0.38-2.43	0.93
Model 2	2434	433	0.99	0.39-2.53	0.98
Model 3	2296	404	1.01	0.39-2.57	0.99

Model 1: Study, Age, Gender, HT, Hyperlipidemia, DM, Dialysis

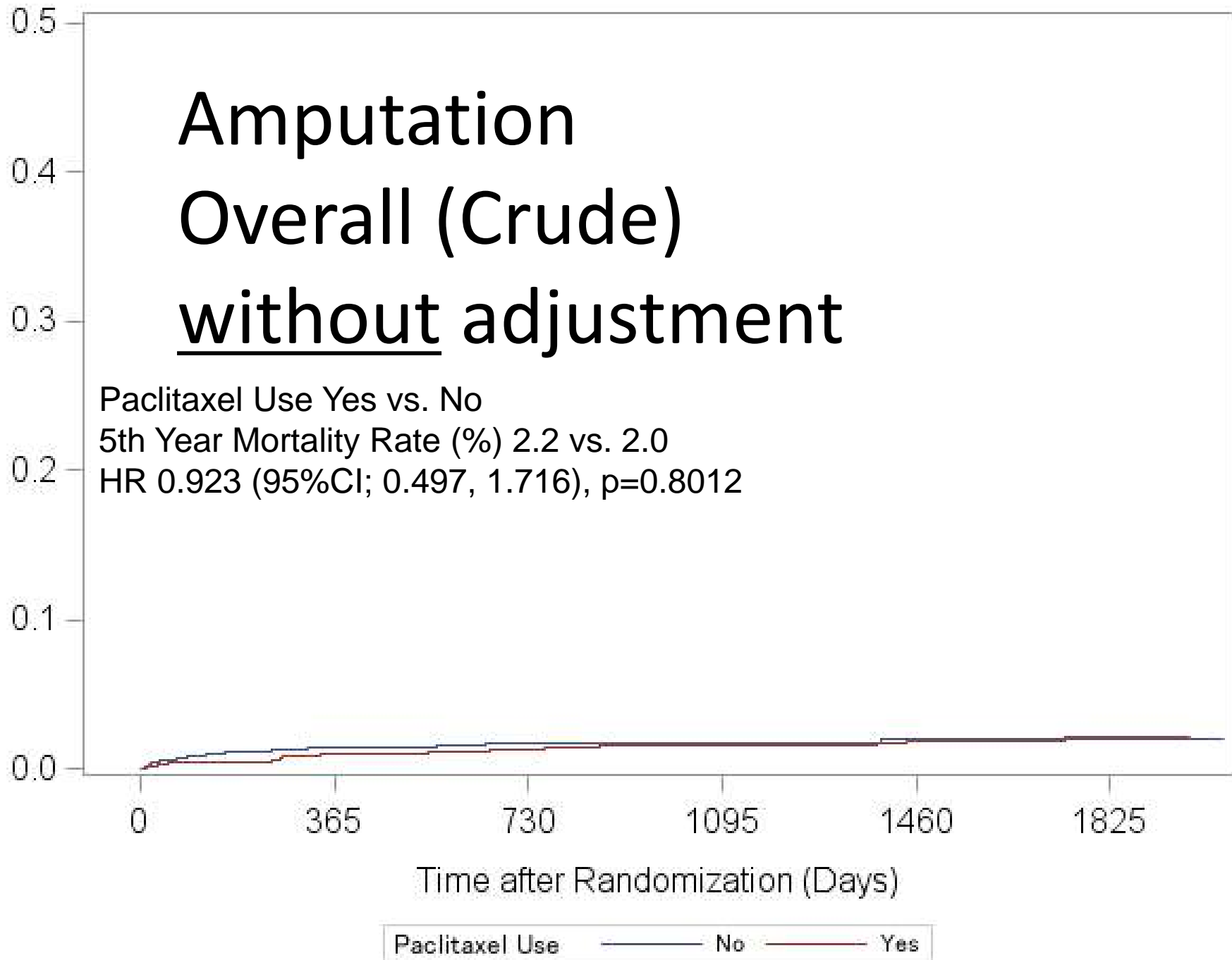
Model 2: Study, Age, Gender, HT, Hyperlipidemia, DM, Rutherford

Model 3: Study, Age, Gender, HT, Hyperlipidemia, DM, Rutherford, Dialysis, Smoking

# Amputation Overall (Crude) without adjustment

Paclitaxel Use Yes vs. No  
5th Year Mortality Rate (%) 2.2 vs. 2.0  
HR 0.923 (95%CI; 0.497, 1.716), p=0.8012

Cumulative Incidence



## In summary

*This individual meta-analysis of a wide range of SFA patients did not demonstrate significant difference in 5year mortality between PTXD and non PTXD.*

