

**Is there still validity to the Increased Mortality And Amputation Rates In Patients Receiving Paclitaxel Coated Devices:**

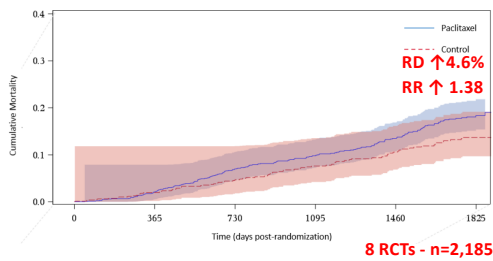
**Can we explain there signals in OLDER Studies and their DISAPPEARANCE in RECENT Data? – the case is NOT yet Fully Closed**

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**Conflicts of interest**

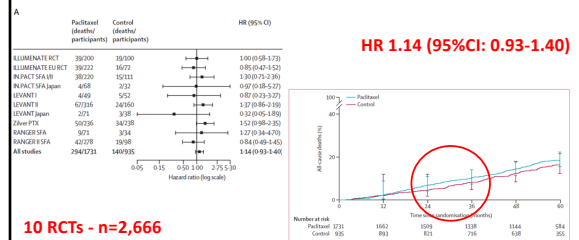
- Nothing to declare

**PTX: Original IPD Data meta-analysis**



Rocha-Singh K.J, et al. 2020 CIRCULATIONAHA.119.044697

**PTX: Updated industry IPD meta-analysis**



10 RCTs - n=2,666

(7 out 10 used low-dose 2.0µg devices)

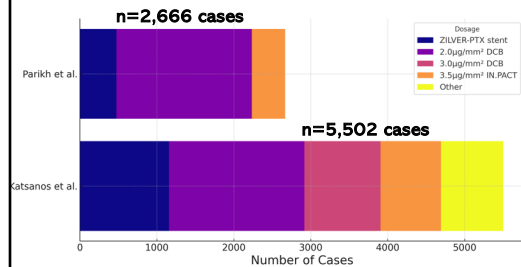
Parikh SA, et al. Lancet 2023

**Updated trial-level meta-analysis @2y**

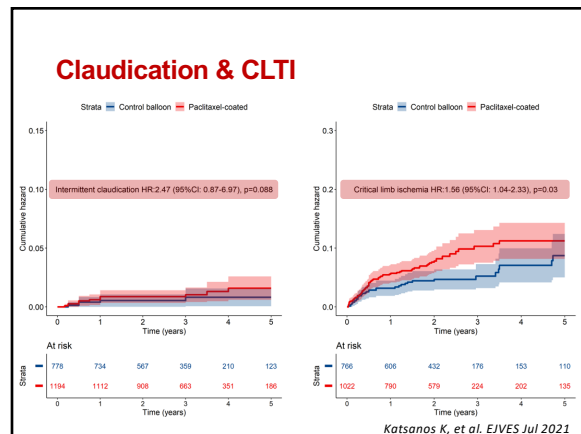
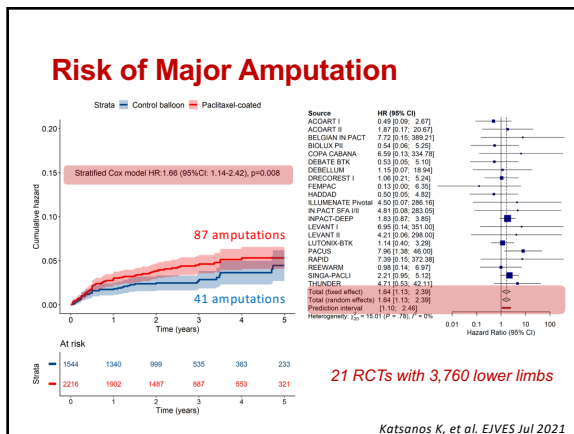
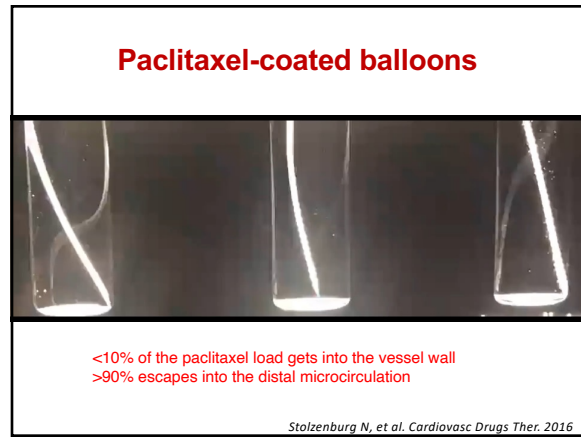
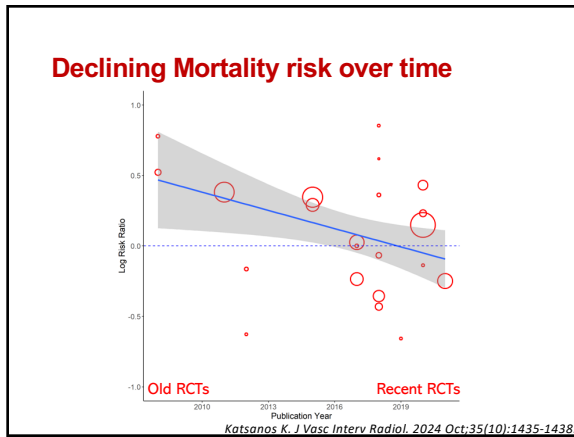
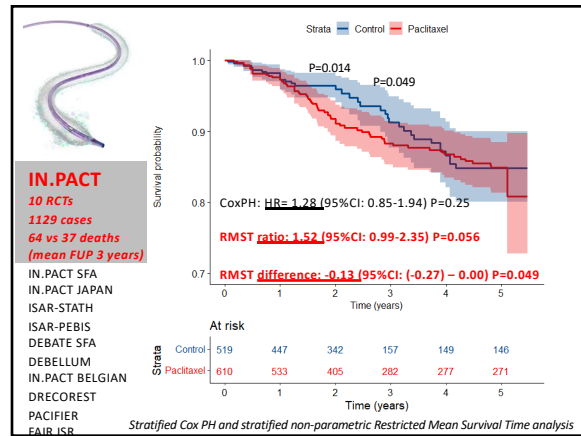
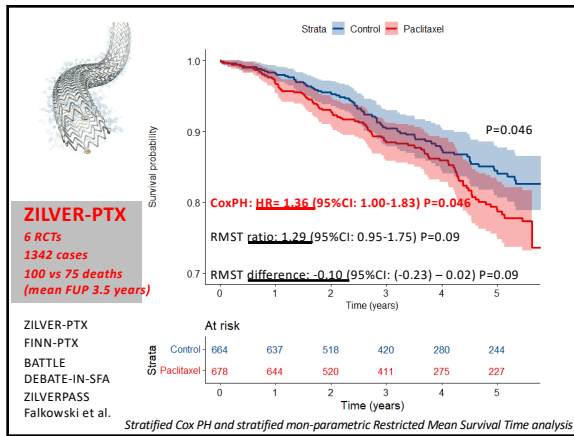
Study	Year	Paclitaxel Events	Paclitaxel Total	Control Events	Control Total	Risk Ratio	RR	95%-CI
FEMIPAC	2008	7	45	3	42		2.18	[0.60; 7.88]
TRINDOR	2008	7	48	5	54		1.98	[0.52; 6.64]
ZILVER-PTX	2011	19	302	7	177		1.59	[0.68; 3.71]
LEVANT 1	2012	4	49	5	52		0.85	[0.24; 2.98]
PACIFIER	2012	2	44	4	47		0.53	[0.10; 2.77]
IN PACT SFA	2015	16	220	1	111		8.07	[1.08; 62.09]
LEVANT 2	2015	21	316	7	162		1.52	[0.66; 3.50]
ILLUMINATE	2017	18	222	5	72		1.17	[0.45; 3.03]
ISAR-FEBIS	2017	3	28	0	29		7.25	[0.39; 134.09]
ISAR-STATH	2017	3	48	1	107		6.69	[0.71; 62.66]
ILLUMINATE pivotal	2017	16	200	10	100		0.96	[0.43; 1.86]
RAPID	2017	4	80	4	80		1.00	[0.26; 3.86]
ACCURATE 1	2018	8	96	6	95		1.32	[0.48; 3.65]
CONSEQUENT	2018	2	70	1	65		1.86	[0.17; 20.00]
FINIFTX	2018	3	23	1	18		2.35	[0.27; 20.72]
IN PACT SFA JAPAN	2018	4	66	1	29		1.70	[0.21; 15.05]
LUTONIX JAPAN	2018	2	71	3	38		0.36	[0.08; 2.04]
RANGIER I	2018	9	71	3	34		1.44	[0.42; 4.97]
EFFPAC	2018	1	85	2	86		0.51	[0.05; 5.48]
ORICOHEST	2018	8	29	4	28		1.93	[0.65; 5.70]
BIOFAC	2019	2	27	4	28		0.52	[0.10; 2.60]
BATTLE	2020	1	50	5	91		0.20	[0.02; 1.70]
COPA CABANA	2020	3	47	3	41		0.87	[0.19; 4.09]
ZILVERPASS	2020	14	100	8	100		1.75	[0.77; 3.95]
Fukushima et al	2020	6	126	4	130		1.55	[0.45; 5.35]
SWEDEPAD	2020	44	404	38	405		1.16	[0.77; 1.75]
RANGIER II	2021	15	278	3	98		1.76	[0.52; 5.95]
<b>Fixed effect model</b>		<b>244</b>	<b>3185</b>	<b>138</b>	<b>2317</b>		<b>1.32</b>	<b>[1.08; 1.62]</b>
<b>Random effects model</b>							<b>1.28</b>	<b>[1.04; 1.58]</b>
<b>Prediction interval</b>								<b>[1.05; 1.60]</b>

Katsanos K. J Vasc Interv Radiol. 2024 Oct;35(10):1435-1438.

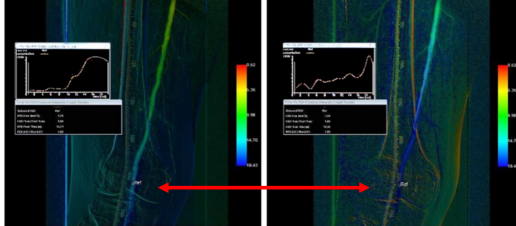
**Industry meta-analysis INCOMPLETE**



Katsanos K. J Vasc Interv Radiol. 2024 Oct;35(10):1435-1438.



### SLOW-FLOW after DCB application



Delayed SLOW-FLOW distal popliteal level after SFA high-dose DCB

Tang TY, et al. *Quant Imaging Med Surg.* 2022 Mar;12(3):2058-2065.

### Conclusions

1. No class effect for safety or effectiveness
2. RCT casemix & sample size differences between original and industry IPD analyses
3. CAREFUL: Mortality signal diluted from low-dose 2.0µg/mm<sup>2</sup> devices
4. Valid risk for amputations with paclitaxel DCBs in CLI patients

### Observational/administrative data

#### RCTs

- Randomized
- Controlled selection criteria
- Study specific interventions
- Hypothesis driven
- (Relatively) small population
- Fixed timeframe
- Powered

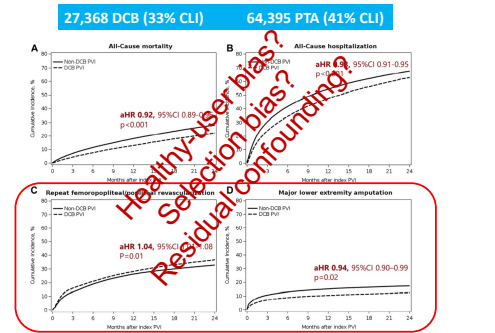
#### Real-world studies

- Observational
- No or broad selection criteria
- No study specific interventions
- Hypothesis generating
- Large population
- Long timeframe
- Flexible

>250,000 cases with paclitaxel devices in real-world mortality series

5,500 RCT cases (<2% of caseload)

### CMS: 91,763 cases @2 years



Weissler EH, et al. *JACC CI* 2020

### Observational amputation studies

#### XL-PAD study

Outcomes	DCB (n = 105)	Non-DCB (n = 222)	P-value
All-Cause Death <sup>a</sup>	3 (2.86%)	6 (2.70%)	0.9366
Target limb isoperthorization	17 (16.19%)	28 (12.61%)	0.2547
Target vessel revascularization	17 (16.19%)	26 (11.71%)	0.2039
Amputation			
Major	12 (11.43%)	9 (4.05%)	0.0112
Minor	16 (15.24%)	24 (10.81%)	0.2547

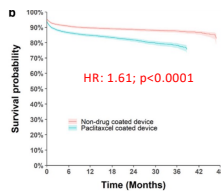
Notes: <sup>a</sup> Based on 327 patients.

Unadjusted outcomes

More amputations with DCB

Giannopoulos S, et al. *CRM* 2020

#### South Korea



	0	12	24	36	48
Non-drug coated device	6090	3620	2254	1057	
Paclitaxel coated device	6090	3030	1459	409	

Dai Sik Ka, et al. *Sci Rep* 2021

### Paclitaxel RCTs in PAD

	Claudication	CLTI
SFA	Efficacy <b>YES</b> Deaths <b>YES</b> Amputations ?	Efficacy ? Deaths <b>NO</b> Amputations <b>YES</b>
BTK	NA	Efficacy <b>NO</b> Deaths <b>NO</b> Amputations <b>YES</b>

**Paclitaxel dose (mg)**

Device	Size (DxL)	PTX (mg)	Relation
ELUVIA	6.0x120	0.4	•
ZILVER-PTX	6.0x120	1.1	•
LUTONIX	6.0x120	4.6	•
IN.PACT	6.0x120	8.4	•
Long lesions	>200mm	>20mg	•

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