Clinical outcome after bifurcation vs non-bifurcation stenting: a meta-analysis

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Aim of the Study

To overview, using a meta-analytic approach, the data collected so far in studies comparing the clinical outcome of patients undergoing PCI with DES implantation in coronary bifurcated lesions (**CBL**) and non-bifurcated lesions (**non-CBL**)

Study Design

- Systematic literature search to identify studies reporting the clinical outcome of patients undergoing DES implantation in **CBL** and **non-CBL**.

- Study characteristics were extracted and the left main (**LM**) patients constituted the main subset for subgroup analysis

- **Primary study end-point** was risk of **MACE** (composite of death, myocardial infarction, stent thrombosis and target vessel revascularization) at the longest available follow-up.

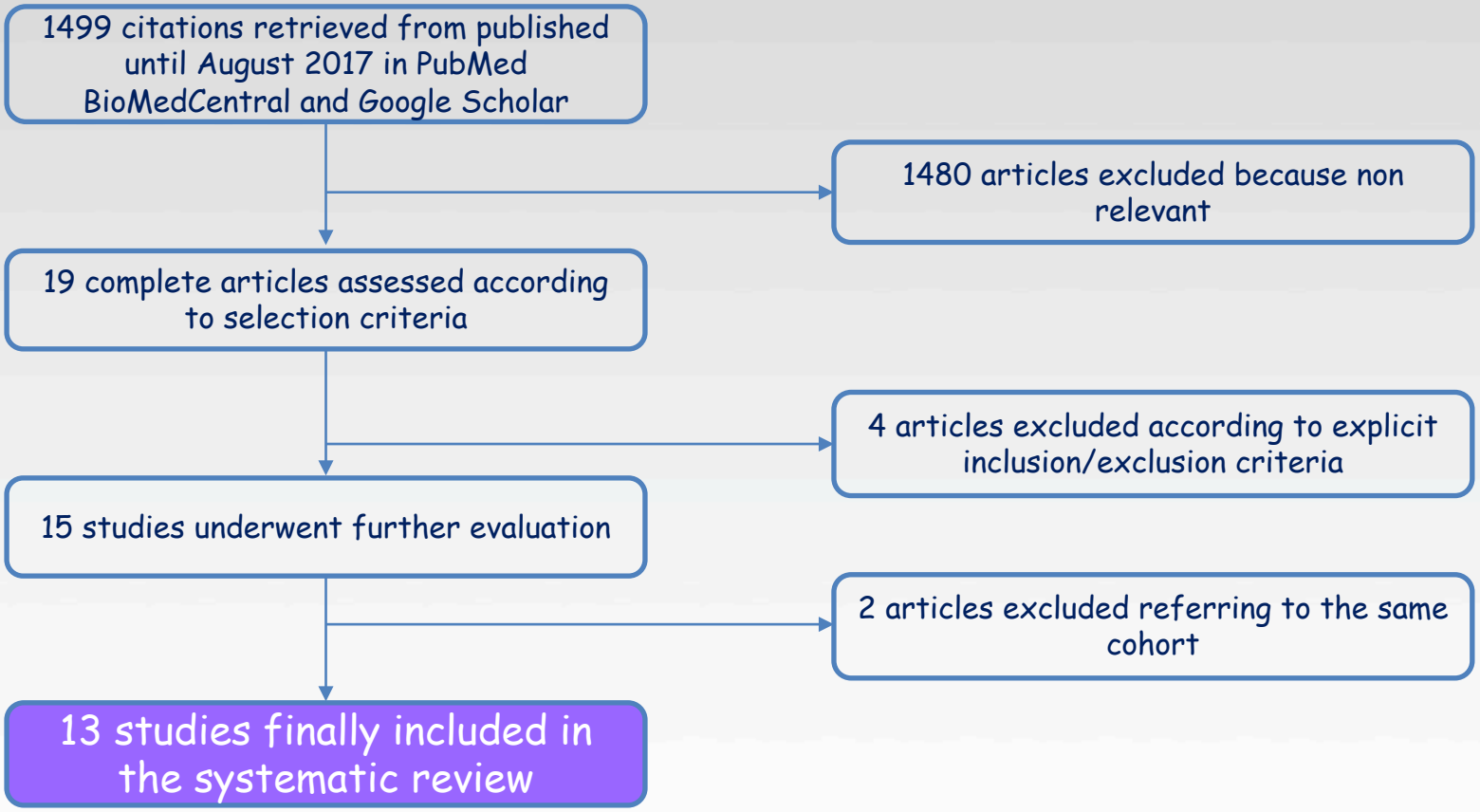
- Pooled estimates for odds ratios (**OR**) with 95% confidence intervals (CI) were computed according to random-effect methods

Study Group

Main co-investigators:

Umberto Annone, Lazzaro Paraggio, Fabrizio D'Ascenzo

Retrieved studies



Data on 23,891 patients were extracted (6,598 CBL vs. 17,363 non-CBL)

Study characteristics

Study	FU lenght (months)	DES	Double stenting rate in CBL arm (%)	Patients		Age (mean)		Diabetes (%)		Acute Coronary syndrome (%)		Target ULM(%)		Stent diameter (mm, mean)		Stent length (mm, mean)	
				Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL
LEADERS All Comers	60	Cypher (50.2%), Biomatrix Flex (49.8%)	27.5	1207	497	64.6	64.7	25.4	21.7	55.9	53.9	NA	NA	NA	NA	NA	NA
RESOLUTE All Comers + RESOLUTE International Registry	36	Resolute Integrity	31.4	2772	703	63.7	63.9	28.4	27	59.3	59.6	NA	NA	NA	NA	NA	NA
SPIRIT V	24	Xience V	NA	2156	492	62.7	62.9	31.1	25.7	11	14	0.9	3.1	NA	NA	NA	NA
ARTS II	36	Cypher	19	283	324	62.5	63.2	24.4	27.8	38.5	34.6	0	0	NA	NA	64.1	79.7
DUTCH PEERS	24	Resolute Integrity (50%), Promus Element (50%)	17.7	1346	465	64	63.8	17.9	17.8	60.5	53.1	NA	NA	NA	NA	28	36
TWENTE	36	Resolute Integrity (50,1%), Xience V (49,9%)	22.7	1029	362	64.3	64.3	22	20.7	51.1	52.7	NA	NA	NA	NA	30	40
Abdel-Wahab M et al	12	Taxus (55,1%), Cypher (44,9%)	NA	4312	814	65.2	64.9	32.1	29.5	44.4	40.7	1.9	9.3	3	3	18	18
ARRIVE registries	24	Taxus	NA	2698	575	63	63.3	29.8	29.4	0	0	0	3.1	3*	2.9*	21.6	26.8
DISTAL	24	Any DES	77.8	164	96	63	66	12.8	19.8	89	96.9	100	100	3.62	3.41	17.58	22.2
Barragan P et al	12	Cypher	48.6	84	143	66	69	25	27.3	40.5	38.5	100	100	3.3	3.2	11	17
Abdel Hakim DE et al	12	Any DES	10.7	496	150	59	59	22.1	24	100	100	NA	2.6	NA	NA	NA	16.2
DELTA registry	36	Cypher (54,6%), Taxus (44,3%), Resolute/Xience (1,1%)	40.7	482	1130	64.3	66.3	26.3	28.5	49.4	49.6	100	100	3.51	3.33	15.9	24.8
Palmerini T et al	24	Cypher (47%), Taxus (49,5%), other (3,5%)	41.3	334	777	71	71	31	29.4	59.5	53.9	100	100	3.49	3.27	11.7	18.6

Mean FU: 24 months

Study characteristics

Study	FU lenght (months)	DES	Double stenting rate in CBL arm (%)	Patients		Age (mean)		Diabetes (%)		Acute Coronary syndrome (%)		Target ULM(%)		Stent diameter (mm, mean)		Stent length (mm, mean)	
				Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL
LEADERS All Comers	60	Cypher (50.2%), Biomatrix Flex (49.8%)	27.5	207	497	64.6	64.7	25.4	21.7	55.9	53.9	NA	NA	NA	NA	NA	NA
RESOLUTE All Comers + RESOLUTE International Registry	36	Resolute Integrity	31.4	772	703	63.7	63.9	28.4	27	59.3	59.6	NA	NA	NA	NA	NA	NA
SPIRIT V	24	Xience V	NA	156	492	62.7	62.9	31.1	25.7	11	14	0.9	3.1	NA	NA	NA	NA
ARTS II	36	Cypher	19	283	324	62.5	63.2	24.4	27.8	38.5	34.6	0	0	NA	NA	64.1	79.7
DUTCH PEERS	24	Resolute Integrity (50%), Promus Element (50%)	17.7	346	465	64	63.8	17.9	17.8	60.5	53.1	NA	NA	NA	NA	28	36
TWENTE	36	Resolute Integrity (50,1%), Xience V (49,9%)	22.7	029	362	64.3	64.3	22	20.7	51.1	52.7	NA	NA	NA	NA	30	40
Abdel-Wahab M et al	12	Taxus (55,1%), Cypher (44,9%)	NA	312	814	65.2	64.9	32.1	29.5	44.4	40.7	1.9	9.3	3	3	18	18
ARRIVE registries	24	Taxus	NA	698	575	63	63.3	29.8	29.4	0	0	0	3.1	3*	2.9*	21.6	26.8
DISTAL	24	Any DES	77.8	164	96	63	66	12.8	19.8	89	96.9	100	100	3.62	3.41	17.58	22.2
Barragan P et al	12	Cypher	48.6	84	143	66	69	25	27.3	40.5	38.5	100	100	3.3	3.2	11	17
Abdel Hakim DE et al	12	Any DES	10.7	496	150	59	59	22.1	24	100	100	NA	2.6	NA	NA	NA	16.2
DELTA registry	36	Cypher (54,6%), Taxus (44,3%), Resolute/Xience (1,1%)	40.7	482	1130	64.3	66.3	26.3	28.5	49.4	49.6	100	100	3.51	3.33	15.9	24.8
Palmerini T et al	24	Cypher (47%), Taxus (49,5%), other (3,5%)	41.3	334	777	71	71	31	29.4	59.5	53.9	100	100	3.49	3.27	11.7	18.6

Double stenting rate in CBL: 19%

Study characteristics

Study	FU lenght (months)	DES	Double stenting rate in CBL arm (%)	Patients		Age (mean)		Diabetes (%)		Acute Coronary syndrome (%)		Target ULM(%)		Stent diameter (mm, mean)		Stent length (mm, mean)	
				Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL
LEADERS All Comers	60	Cypher (50.2%), Biomatrix Flex (49.8%)	27.5	1207	497	64.6	64.7	25.4	21.7	55.9	53.9	NA	NA	NA	NA	NA	NA
RESOLUTE All Comers + RESOLUTE International Registry	36	Resolute Integrity	31.4	2772	703	63.7	63.9	28.4	27	59.3	59.6	NA	NA	NA	NA	NA	NA
SPIRIT V	24	Xience V	NA	2156	492	62.7	62.9	31.1	25.7	11	14	9	3.1	NA	NA	NA	NA
ARTS II	36	Cypher	19	283	324	62.5	63.2	24.4	27.8	38.5	34.6	0	0	NA	NA	64.1	79.7
DUTCH PEERS	24	Resolute Integrity (50%), Promus Element (50%)	17.7	1346	465	64	63.8	17.9	17.8	60.5	53.1	NA	NA	NA	NA	28	36
TWENTE	36	Resolute Integrity (50,1%), Xience V (49,9%)	22.7	1029	362	64.3	64.3	22	20.7	51.1	52.7	NA	NA	NA	NA	30	40
Abdel-Wahab M et al	12	Taxus (55,1%), Cypher (44,9%)	NA	4312	814	65.2	64.9	32.1	29.5	44.4	40.7	9	9.3	3	3	18	18
ARRIVE registries	24	Taxus	NA	2698	575	63	63.3	29.8	29.4	0	0	0	3.1	3*	2.9*	21.6	26.8
DISTAL	24	Any DES	77.8	164	96	63	66	12.8	19.8	89	96.9	00	100	3.62	3.41	17.58	22.2
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Abdel Hakim DE et al	12	Any DES	10.7	496	150	59	59	22.1	24	100	100	NA	2.6	NA	NA	NA	16.2
DELTA registry	36	Cypher (54,6%), Taxus (44,3%), Resolute/Xience (1,1%)	40.7	482	1130	64.3	66.3	26.3	28.5	49.4	49.6	00	100	3.51	3.33	15.9	24.8
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CBL vs. non-CBL: Similar age, sex, diabetes rate, clinical history

Study characteristics

Study	FU lenght (months)	DES	Double stenting rate in CBL arm (%)	Patients		Age (mean)		Diabetes (%)		Acute Coronary syndrome (%)		Target ULM(%)		Stent diameter (mm, mean)		Stent length (mm, mean)	
				Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL	Non CBL	CBL
LEADERS All Comers	60	Cypher (50.2%), Biomatrix Flex (49.8%)	27.5	1207	497	64.6	64.7	25.4	21.7	55.9	53.9	NA	NA	NA	NA	NA	NA
RESOLUTE All Comers + RESOLUTE International Registry	36	Resolute Integrity	31.4	2772	703	63.7	63.9	28.4	27	59.3	59.6	NA	NA	NA	NA	NA	NA
SPIRIT V	24	Xience V	NA	2156	492	62.7	62.9	31.1	25.7	11	14	0.9	3.1	NA	NA	NA	NA
ARTS II	36	Cypher	19	283	324	62.5	63.2	24.4	27.8	38.5	34.6	0	0	NA	NA	NA	NA
DUTCH PEERS	24	Resolute Integrity (50%), Promus Element (50%)	17.7	1346	465	64	63.8	17.9	17.8	60.5	53.1	NA	NA	NA	NA	28	36
TWENTE	36	Resolute Integrity (50,1%), Xience V (49,9%)	22.7	1029	362	64.3	64.3	22	20.7	51.1	52.7	NA	NA	NA	NA	30	40
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Abdel Hakim DE et al	12	Any DES	10.7	496	150	59	59	22.1	24	100	100	NA	2.6	NA	NA	NA	16.2
DELTA registry	36	Cypher (54,6%), Taxus (44,3%), Resolute/Xience (1,1%)	40.7	482	1130	64.3	66.3	26.3	28.5	49.4	49.6	100	100	3.51	3.33	15.9	24.8
Palmerini T et al	24	Cypher (47%), Taxus (49,5%), other (3,5%)	41.3	334	777	71	71	31	29.4	59.5	53.9	100	100	3.49	3.27	11.7	18.6

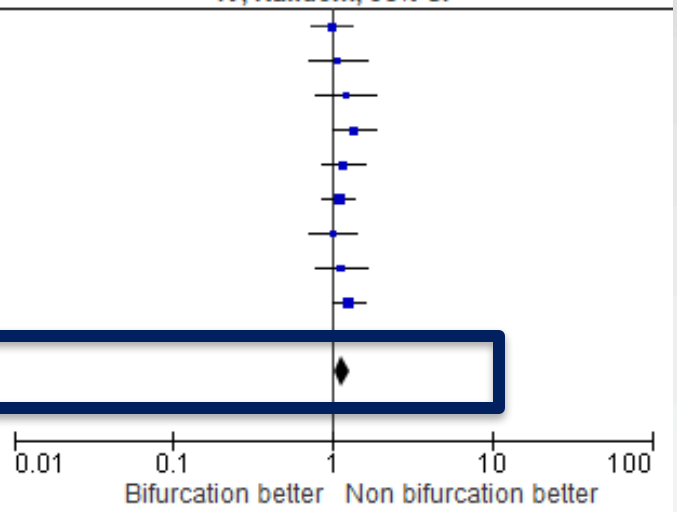
CBL vs. non-CBL: similar DES diameter (3 mm), slight longer DES length (24 vs. 19 mm)

MACE during the FU (all bifs)

Study or Subgroup	Non bifurcation Events	Non bifurcation Total	Bifurcation Events	Bifurcation Total	Weight	Odds Ratio (Non-event) IV, Random, 95% CI	Year
Abdel Hakim DE	285	4312	53	814	11.7%	0.98 [0.73, 1.33]	2008
Tsuchida K	45	283	55	324	5.8%	1.08 [0.70, 1.66]	2009
Abdel-Wahab M	97	496	34	150	5.5%	1.21 [0.77, 1.88]	2012
Diletti R	212	1838	58	385	10.9%	1.36 [0.99, 1.86]	2013
Dzavik V	207	2156	54	492	10.7%	1.16 [0.85, 1.59]	2013
Ferenc M	391	2772	107	703	19.9%	1.09 [0.87, 1.38]	2014
Lam MK	147	1021	52	360	9.2%	1.00 [0.71, 1.41]	2015
van der Hejiden LC	112	1346	43	465	7.9%	1.12 [0.78, 1.62]	2016
Grundeken MJ	270	1207	132	497	18.5%	1.26 [0.99, 1.60]	2016
Total (95% CI)		**15431**		**4190**	**100.0%**	**1.14 [1.03, 1.27]**	
Total events	1766		588				

Heterogeneity: Tau² = 0.00; Chi² = 3.53, df = 8 (P = 0.90); I² = 0%

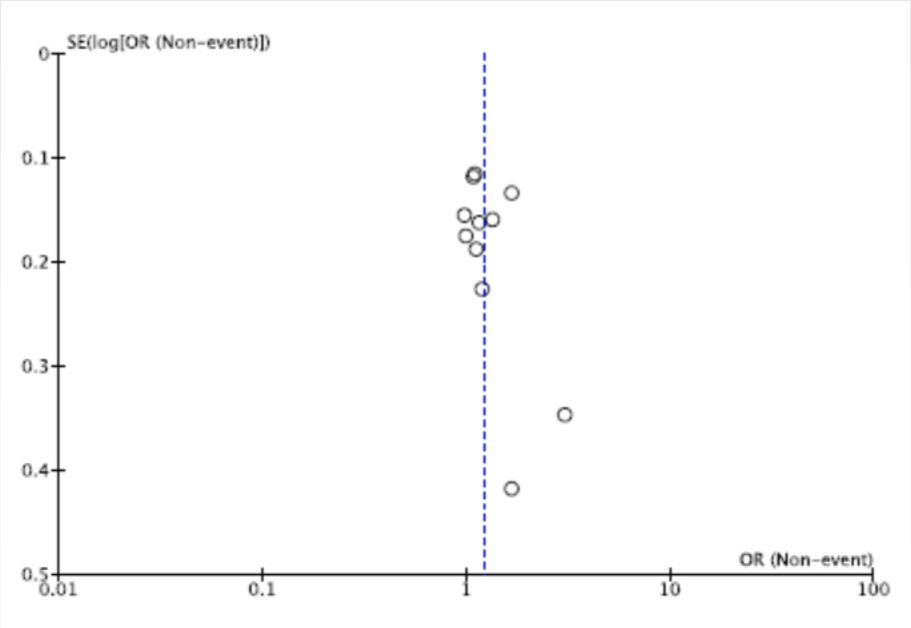
Test for overall effect: Z = 2.49 (P = 0.01)



Event	OR (95%CI) for CBL vs. non-CBL	P
MACCE	1.14 (1.03-1.27)	0.01
Death	1.05 (0.85-1.31)	NS
MI	1.42 (1.20-1.65)	<0.001
TVR	1.08 (0.92-1.27)	NS

MACE during the FU (all bifs)

Funnel plot



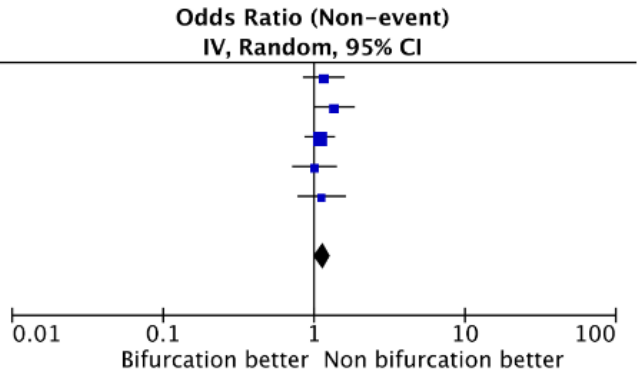
MACE during the FU (all bifs)

STUDIES USING 2nd GENERATION DES

Study or Subgroup	Non bifurcation Events	Total	Bifurcation Events	Total	Weight	Odds Ratio (Non-event) IV, Random, 95% CI	Year
Dzavik V	207	2156	54	492	18.2%	1.16 [0.85, 1.59]	2013
Diletti R	212	1873	58	392	18.6%	1.36 [0.99, 1.86]	2013
Ferenc M	391	2772	107	703	34.0%	1.09 [0.87, 1.38]	2014
Lam MK	147	1029	52	362	15.7%	1.01 [0.72, 1.42]	2015
van der Hejiden LC	112	1346	43	465	13.5%	1.12 [0.78, 1.62]	2016
Total (95% CI)		**9176**		**2414**	**100.0%**	**1.14 [1.00, 1.31]**	
Total events	1069		314				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.88$, df = 4 (P = 0.76); $I^2 = 0\%$

Test for overall effect: Z = 1.90 (P = 0.06)



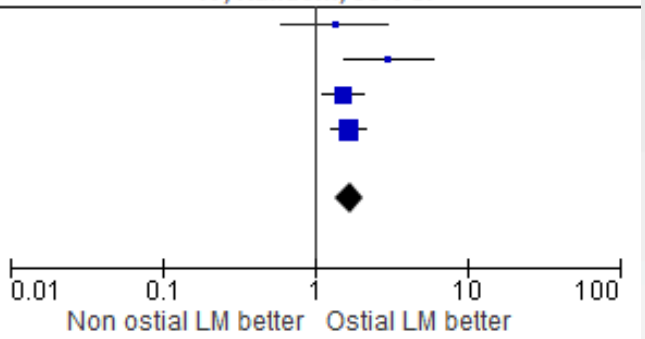
MACE during the FU (LM)

Distal left main vs. ostial/mid shaft

Study or Subgroup	Ostial LM Events	Ostial LM Total	Bifurcation Events	Bifurcation Total	Weight	Odds Ratio (Non-event) IV, Random, 95% CI	Year
Barragan	9	102	24	206	6.6%	1.36 [0.61, 3.05]	2008
Chen	17	164	25	96	9.2%	3.04 [1.55, 6.00]	2009
Palmerini	67	334	218	777	36.6%	1.55 [1.14, 2.12]	2009
Naganuma	92	482	322	1130	47.5%	1.69 [1.30, 2.19]	2013
Total (95% CI)		**1082**		**2209**	**100.0%**	**1.71 [1.38, 2.11]**	
Total events	185		589				

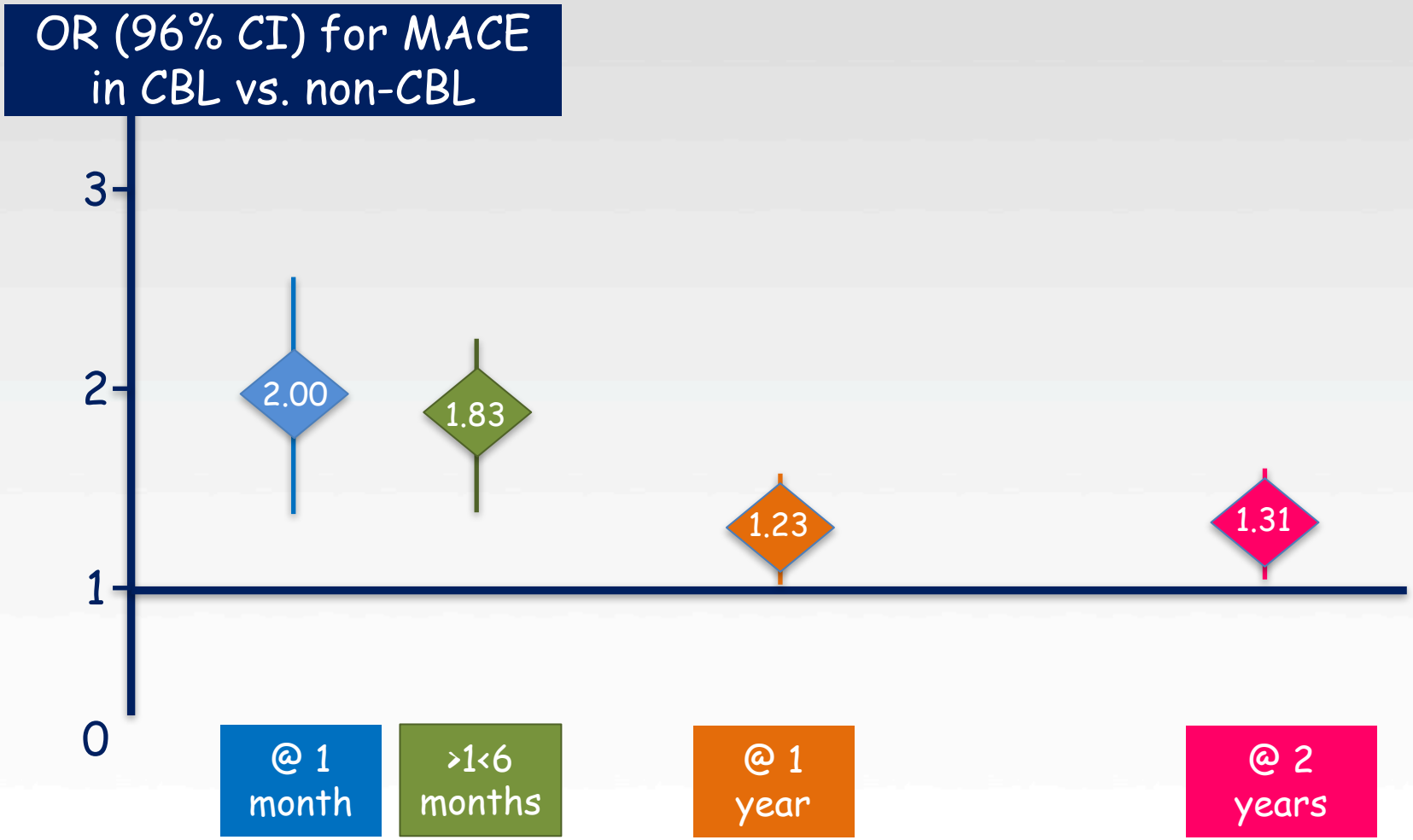
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.45$, $df = 3$ ($P = 0.33$); $I^2 = 13\%$

Test for overall effect: $Z = 4.94$ ($P < 0.00001$)

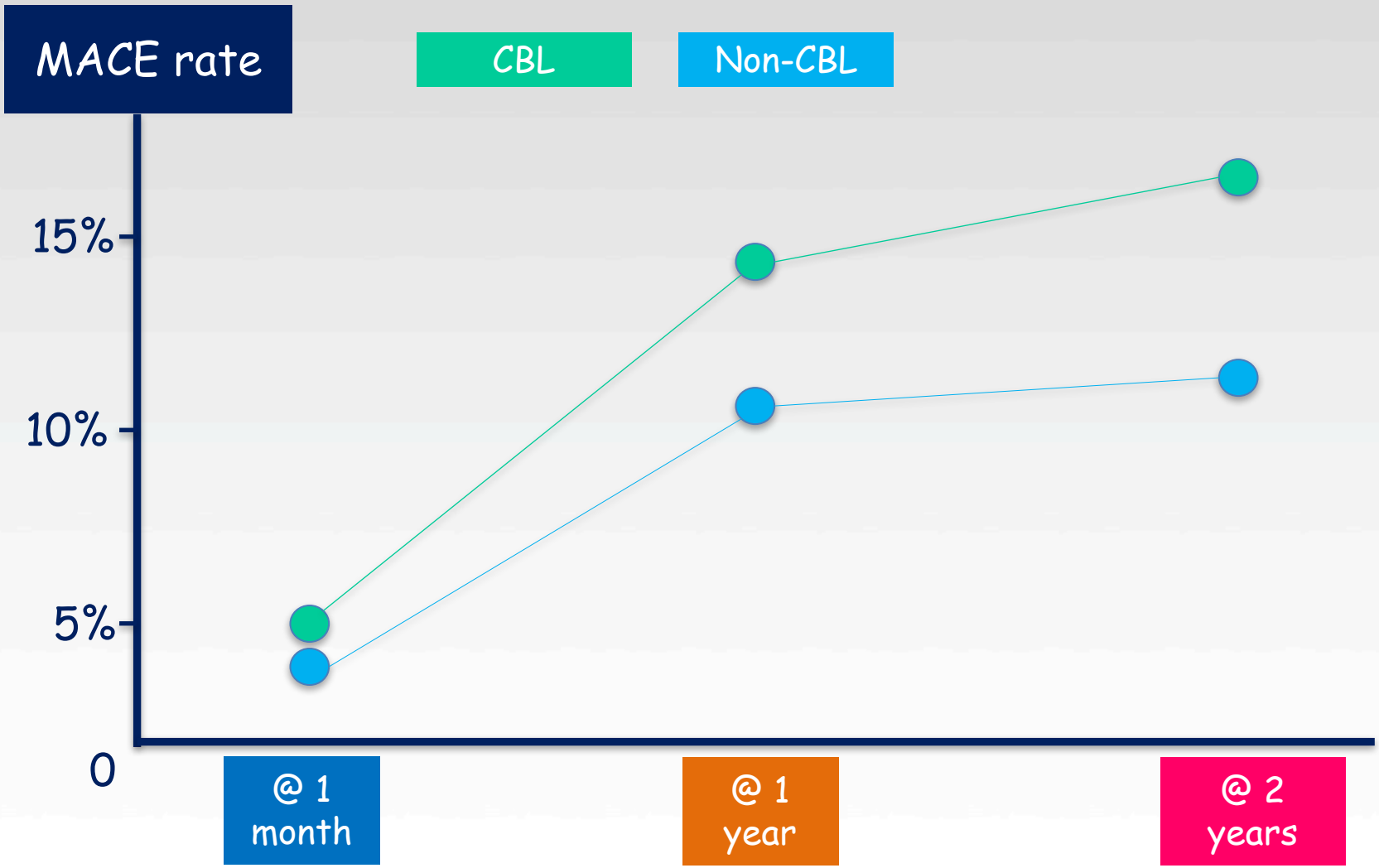


Event	OR (95%CI) for distal LM vs. non-distal LM	P
MACCE	1.71 (1.38-2.11)	<0.001
Death	0.77 (0.55-1.09)	NS
MI	0.92 (0.64-1.34)	NS
TVR	2.37 (1.85-1.27)	<0.001

MACE risk over time (all bif)



MACE events over time (all bif)



Conclusions

- Bifurcation stenting (LM included) in contemporary DES era is associated with increased risk of adverse events

- Such increased MACE risk is appreciable up to 2 years after successful DES implantation

- We have still lot to do for our patients!!!

Thanks for attention !!!