



# Soins bucco-dentaires, antibioprophylaxie et risque d'endocardite infectieuse chez les patients porteurs de prothèses valvulaires

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# Infective endocarditis (IE)

- Rare but severe disease
  - in-hospital mortality rate  $\approx$  20% and 5-year mortality rate of 40%
- Oral streptococcal IE: responsible for 20-30% IE
- Prosthetic valve (PV) patients
  - At high risk of IE occurrence
  - At high risk of IE fatal outcome



# Oral streptococcal IE

- AB prophylaxis
  - recommended in most countries in PV pts
  - **No proof of AB prophylaxis effectiveness**
    - Neither a RCT, nor a prospective cohort study
    - Case-control studies with conflicting results
- Which is the culprit ?
  - Post dental procedure bacteremia ?
  - vs Everyday live bacteremia ?

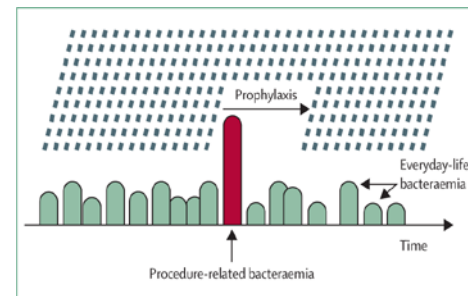


Figure 1: Current concept of the limited role of antibiotic prophylaxis against everyday versus procedures related bacteraemia  
Adapted from reference 15.

X. Duval et al. Lancet Infect Dis 2008

# Objectives

- To assess the relationship between invasive dental procedures and oral streptococcal IE
- To evaluate the role of antibiotic prophylaxis

2 designs

- ✓ a nationwide cohort study
- ✓ a case-crossover study

# Case Crossover study

- The “patient-case” is also his own “control”
- Comparison between exposure status immediately before the outcome (case period) with exposure in designated control period(s) earlier in time
- No bias related to the control group choice
- Particularly interesting in case of non measurable confusing factors between Case and controls (for ex dental hygiene)



- Conditions to be applicable:
  - rare event and acute event
  - intermittent exposure
  - no time-trend in exposure



met for IE

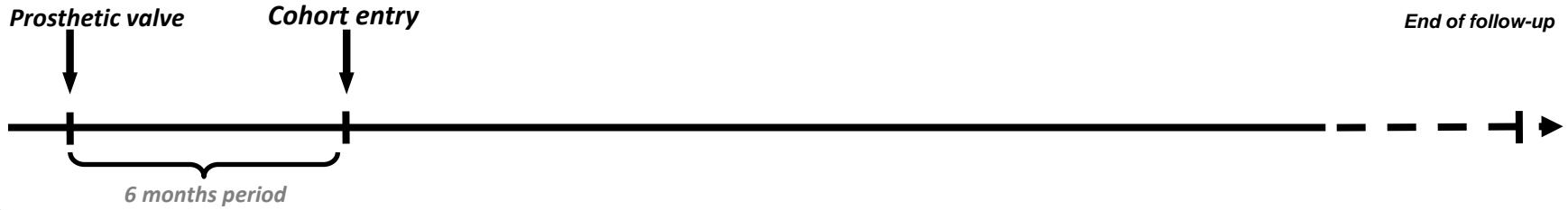
# Methods

French National health insurance database (SNIIRAM) linked with the national hospital discharge database (PMSI)

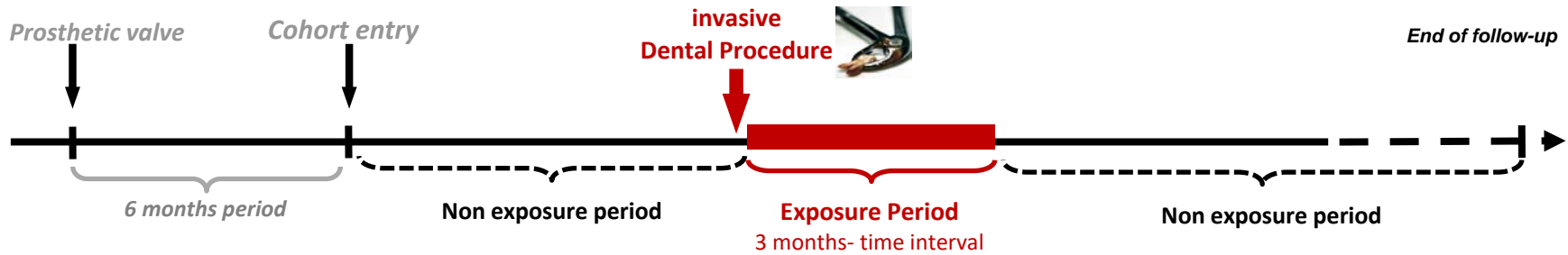
Make possible the identification of :

- Patients with prosthetic valves Jul 2008-Jul 2014 (CCAM)
- Dental procedures (invasives, non-invasives) (CCAM)
- Antibiotic prophylaxis through antibiotic reimbursement (ATC)
- Oral streptococcal IE episodes (combination of ICD 10 codes)

# Cohort study

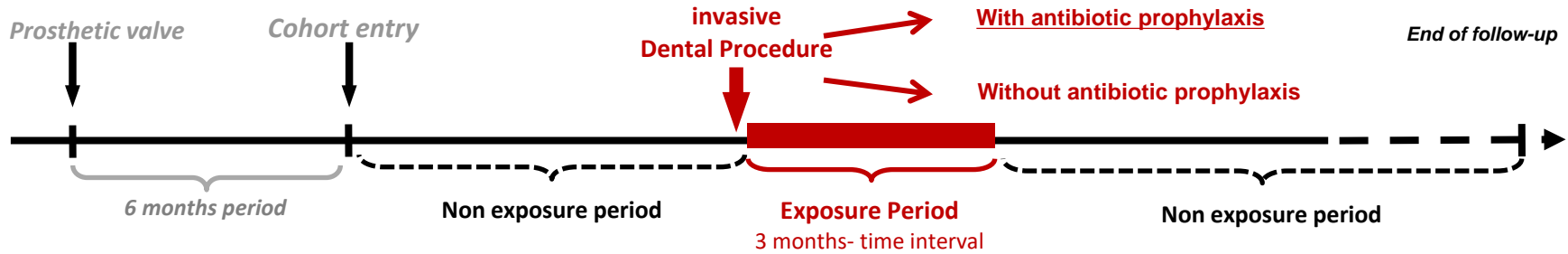


# Cohort study

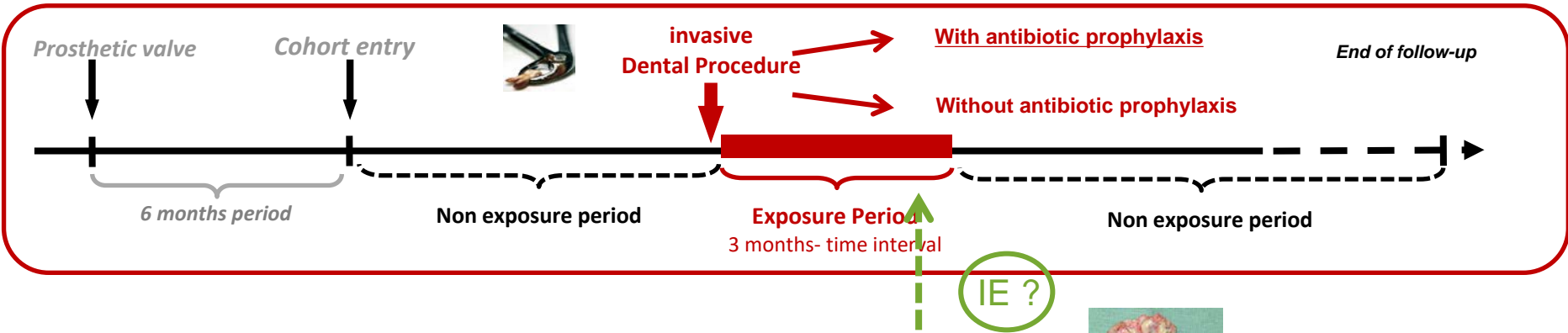




# Cohort study

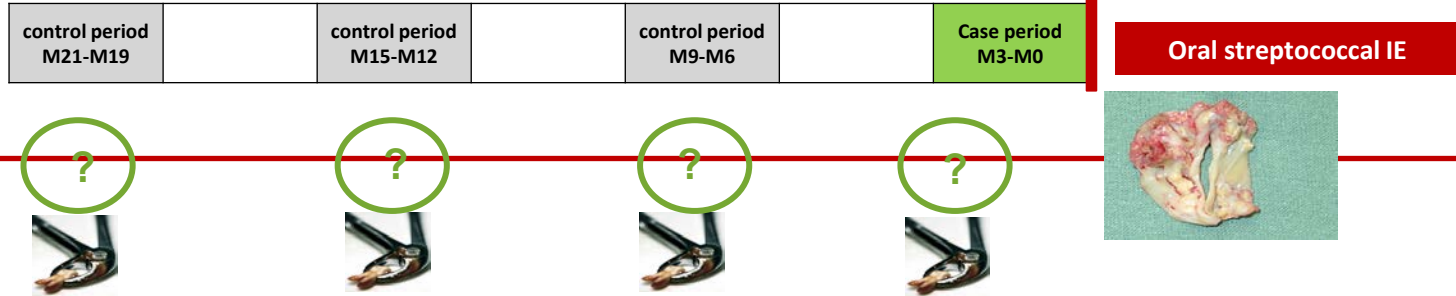


# Cohort study



- IE incidence in the 3 months following invasive dental procedures as compared to IE incidence outside this time window
- Poisson regression models to calculate the adjusted relative rates estimates of oral streptococcal IE with the different categories of exposure.

# Case crossover study



- **comparison of invasive dental procedure history**
  - in the 3 months preceding IE
  - as compared to historical periods in the same IE patients
- **Conditional logistic regression analysis to estimate the odds ratio in the case period, as compared with the matched control periods.**

# Results - cohort

- **Cohort Study:**
  - **138, 876** cardiac prosthetic valve individuals
    - 82 217 (59.2 %) were males
    - Median (Q1-Q3) age was 74 (63-80) years old
  - **285, 034** person-years
  - **267** oral streptococcal IE occurred

# Results - cohort

- Among the 138 876 PV patients of the cohort study:
  - 69 303 (49.9%) pts had  $\geq 1$  dental visit (median of 2.0 visits /pt/year)
  - During the follow-up period,
    - 396 615 dental procedures
      - 26% were classified as invasive procedures
      - AB prophylaxis dispensed in 50.1% of these invasive procedures
    - Cumulate exposure periods
      - 248 544 person-years for non-exposure period
      - 36 490 person-years for dental procedure period

# Results - cohort

## Cohort study: oral streptococcal incidence

- 94.6 per 100 000 PY (95%CI [82.5-106.6]) during the period of non-exposure to dental procedures

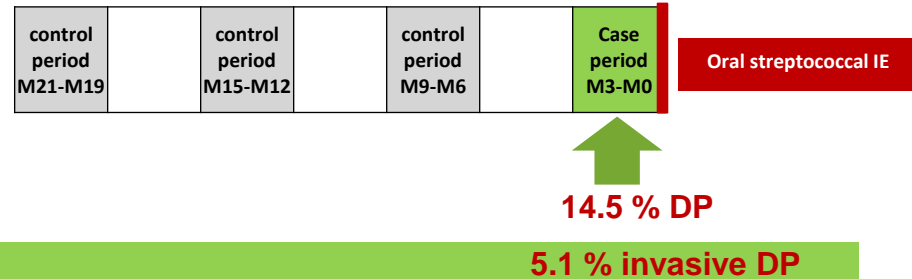
Versus

- 149.5 per 100 000 PY (95%CI [56.8-242.2]) within the 3 months following an invasive dental procedure without antibiotic prophylaxis

Fully adjusted RR: 1.57; 95%CI [0.90-2.53]; p: 0.08

# Results – case crossover

- **648 oral streptococcal IE**
  - 69.7% were male
  - median age : 77 years old



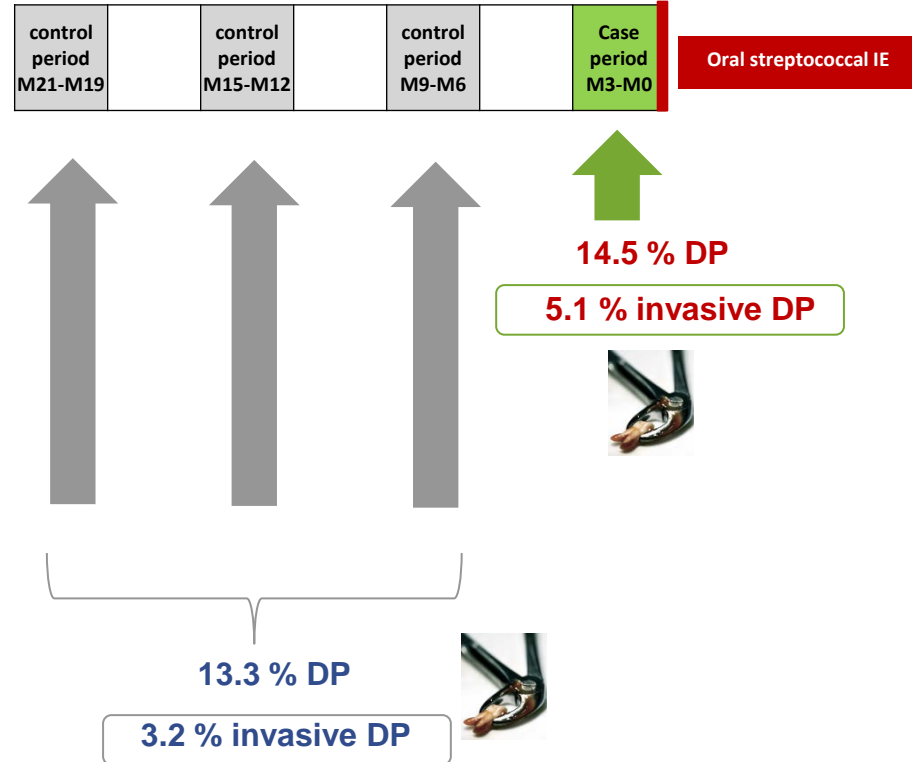
## Case period

- 94 / 648 (**14.5%**)  $\geq 1$  dental procedure during the 3 preceding months
  - 9.4% : non-invasive dental procedures
  - **5.1%** had an invasive dental procedure
  - effective antibiotic dispensed in 57.6%

# Results – case crossover

Control period

OR: 1.66; 95%CI [1.05-2.63]; p-value: 0.03





# Results Cohort – Case crossover

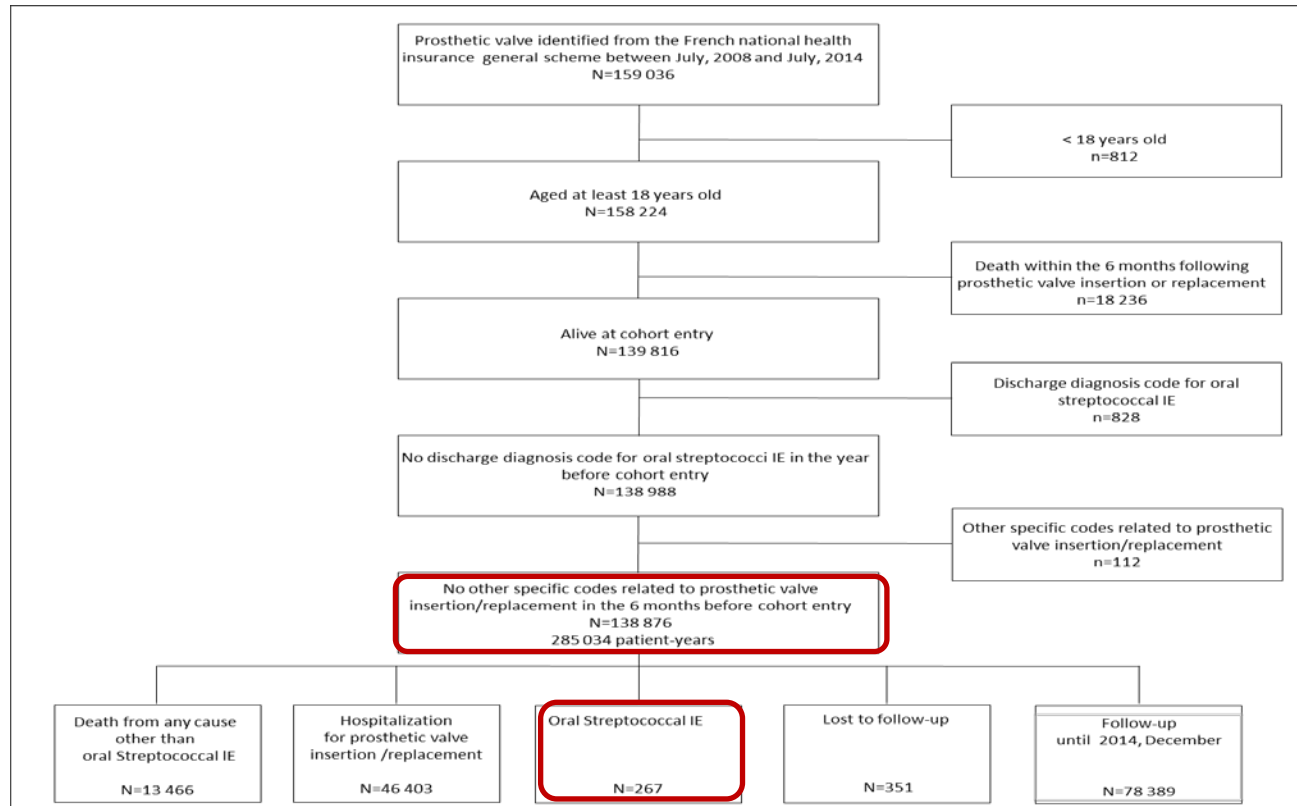
- Both give the same direction of effect  
Invasive Dental procedures may induce streptococcal IE in PV pts  
 $\approx$  5% of oral streptococcal IE in PV pts results from invasive dental procedures
- Potential for unmeasured confounding in the cohort study;
  - pooled data coming from a very heterogeneous population of patients in terms of
    - recourse to dental care (measured in our database)
    - and certainly in terms of dental hygiene and dental status (not measured in our database)
- Further research remains warranted (international collaborations)



**Merci à tooth de votre attention**



# Cohort Flow chart



**Crude Incidence Rates, Incidence Rates Ratio of oral streptococcal IE according to period of exposure, in the 138 876 patients of the cohort study 2008-2014**

Exposition	No. of patients 138 876	No. of dental procedures	PY	No. of oral strepto IE 267	Crude incidence rate of oral Strepto IE (per 100,000 person-years)	No. of oral strepto IE per 10,000 procedures	IRR (95 CI%)
<b>Non exposure period</b>	<b>138 846</b>		<b>248 544</b>	<b>235</b>			
<b>Total</b>	<b>33 181</b>	<b>103 463</b>	<b>11 811</b>	<b>14</b>			
<b>Invasive dental procedures period</b>							
<b>Total</b>	<b>53 443</b>	<b>293 152</b>	<b>24 679</b>	<b>18</b>			
<b>Non-invasive dental procedures period</b>							

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<b>Invasive dental procedures period</b>							
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Invasive dental procedures period							
<b>Total</b>	<b>53 443</b>	<b>293 152</b>	<b>24 679</b>	<b>18</b>	<b>72.94</b>	<b>0.6</b>	<b>0.77 (0.48 1.18)</b>
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Invasive dental procedures period							aRR : 1.25 (0.82-1.82)
<b>Total</b>	<b>53 443</b>	<b>293 152</b>	<b>24 679</b>	<b>18</b>	<b>72.94</b>	<b>0.6</b>	<b>0.77 (0.48 1.18)</b>
Non-invasive dental procedures period							aRR : 0.80 (0.56-1.12)

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Invasive dental procedures period	<b>Total</b>							
	without AP	21 471	51 183	6 688	10	149.53	2.0	1.58 (0.76 2.87)
	with AP	18 863	52 280	5 123	4	78.08	0.8	0.83 (0.24 1.99)
Non-invasive dental procedures period	<b>Total</b>							
	without AP	47 829	217 767	20 131	13	64.58	0.6	0.68 (0.36 1.16)
	with AP	19 428	75 385	4 548	5	109.94	0.7	1.16 (0.40 2.59)



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Invasive dental procedures period

Total

without AP

with AP

aRR : 1.57 (0.90-2.53)	1.58 (0.76 2.87)
aRR: 0.83 (0.33-1.69)	0.83 (0.24 1.99)

Non-invasive dental procedures period

Total

without AP

with AP

aRR : 0.70 (0.43-1.08)	0.68 (0.36 1.16)
aRR: 1.27 (0.40-2.59)	1.16 (0.40 2.59)

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# CASE-CROSSOVER

control period M21-M19		control period M15-M12		control period M9-M6		<b>Case period M3-M0</b>	Oral Streptococci IE N=648 patients
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Exposure to dental procedures according to the period of the 648 patients with oral streptococcal IE included in the Case-crossover study, 2009 to 2014

	n	%
<b>Case period M3-M0 (N=648)</b>		
<b>Non exposure</b>	554	(85.5)
<b>Invasive dental procedure</b>	<b>33</b>	<b>(5.0)</b>
<b>Non-invasive dental procedure</b>	<b>61</b>	<b>(9.4)</b>
<b>Control period M6-9, 12-15, 19-21 (N=1737)</b>		

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<b>Non-invasive dental procedure</b>	<b>61</b>	<b>(9.4)</b>
<b>Control period M6-9, 12-15, 19-21 (N=1737)</b>		
<b>Non exposure</b>	1507	(86.8)
<b>Invasive dental procedure</b>	<b>55</b>	<b>(3.2)</b>
<b>Non-invasive dental procedure</b>	<b>175</b>	<b>(10.1)</b>

# CASE-CROSSOVER

## Association between dental procedures and oral streptococcal infective endocarditis, case-crossover study, 2009-2014

		Odds Ratio	(95%CI)		p-value
Non exposure		1.00			
<b><i>Dental procedures model</i></b>					
Invasive dental procedures	1	1.66	1.05	2.63	0.03
Non-invasive dental procedures		0.98	0.70	1.36	0.16

# CASE-CROSSOVER

control period M21-M19		control period M15-M12		control period M9-M6		<b>Case period M3-M0</b>
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Oral Streptococci IE N=648 patients

Exposure to dental procedures according to the period of the 648 patients with oral streptococcal IE included in the Case-crossover study, 2009 to 2014

	n	%
<b>Case period M3-M0 (N=648)</b>		
<b>Non exposure</b>	554	(85.5)
<b>Invasive dental procedure</b>		
without antibiotic prophylaxis	14	(2.2)
with antibiotic prophylaxis	19	(2.9)
<b>Non-invasive dental procedure</b>		
without antibiotic prophylaxis	51	(7.9)
with antibiotic prophylaxis	10	(1.5)

<b>Control period M6-9, 12-15, 19-21 (N=1737)*</b>		
<b>Non exposure</b>	1507	(86.8)
<b>Invasive dental procedure</b>		
without antibiotic prophylaxis	25	(1.4)
with antibiotic prophylaxis	30	(1.7)
<b>Non-invasive dental procedure</b>		
without antibiotic prophylaxis	144	(8.3)
with antibiotic prophylaxis	21	(1.2)

# CASE-CROSSOVER

## Association between dental procedures and oral streptococcal infective endocarditis, case-crossover study 2008-2014

		Adjusted* Odds Ratio	(95%CI)		p-value
Non exposure		1.00			
<b><i>Dental procedures model</i></b>					
Invasive dental procedures	<b>1</b>	<b>1.66</b>	<b>1.05</b>	<b>2.63</b>	<b>0.03</b>
Non-invasive dental procedures		0.98	0.70	1.36	0.16
<b><i>Antibiotic prophylaxis dental procedures model</i></b>					
Invasive dental procedures without antibiotic prophylaxis	<b>2</b>	1.62	0.81	3.27	0.32
with antibiotic prophylaxis		1.69	0.93	3.06	0.19
Non-invasive dental procedures without antibiotic prophylaxis		0.99	0.69	1.42	0.29
with antibiotic prophylaxis		0.92	0.44	1.91	0.39