Universiteit Utrecht

**Faculty of Science**
**Departement Pharmaceutical Sciences**

# Potential economic impact of probiotics in respiratory tract infections”

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# Disclosures

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- Director Public Health & Scientific Relations, Danone Company
- Chair of INPHORM, a working group of Health Technology Assessment international (www.HTAi.org)
- IDF – ILSI Liaison Officer

# Burden of common RTIs

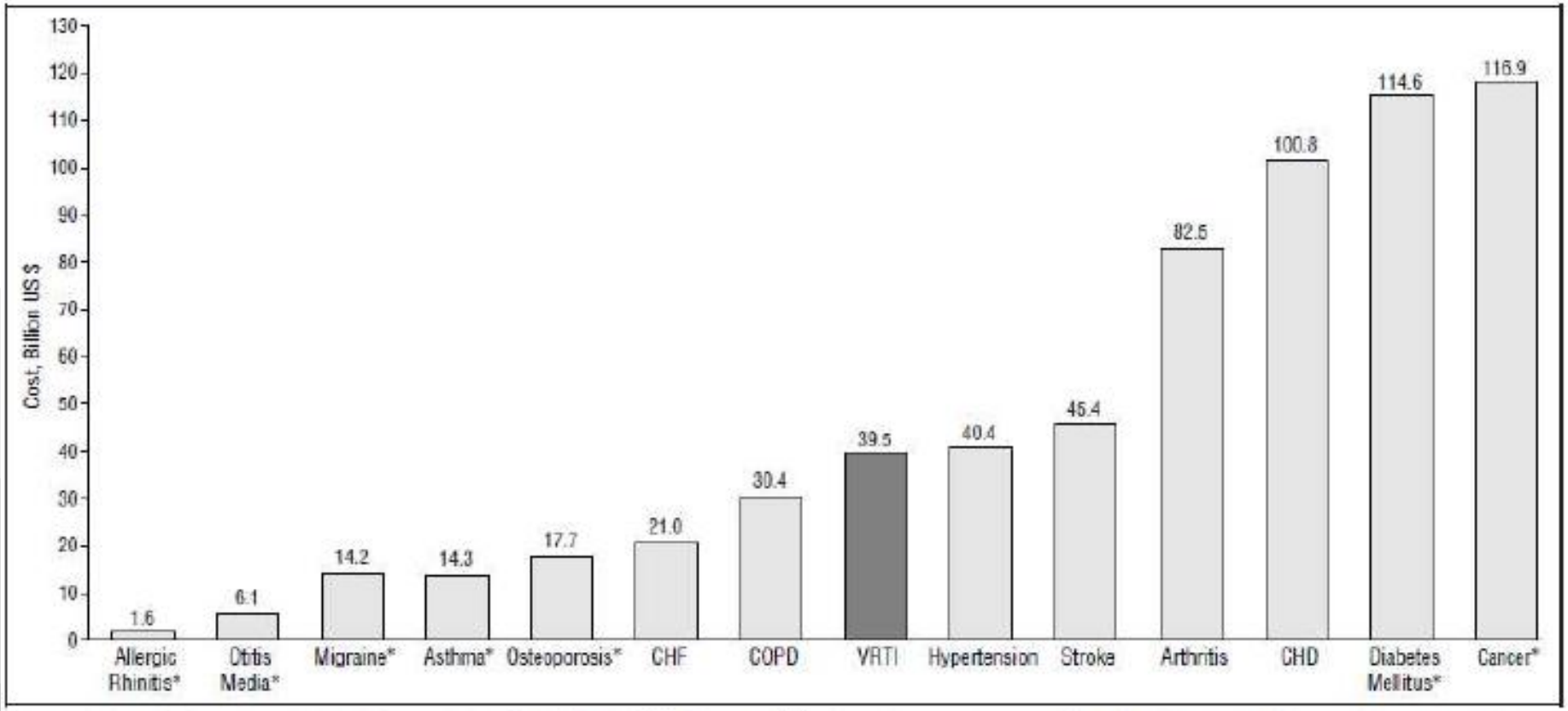



**Figure 4.** Cost of illness for selected diseases in the United States.[41-43] The asterisk indicates that costs were adjusted to the year 2001, assuming an annual inflation rate of 4%. CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; VRTI, viral respiratory tract infection; and CHD, coronary heart disease.

*Arch Intern Med 2003;163:487-494*

# Effect of probiotics on common respiratory tract infections

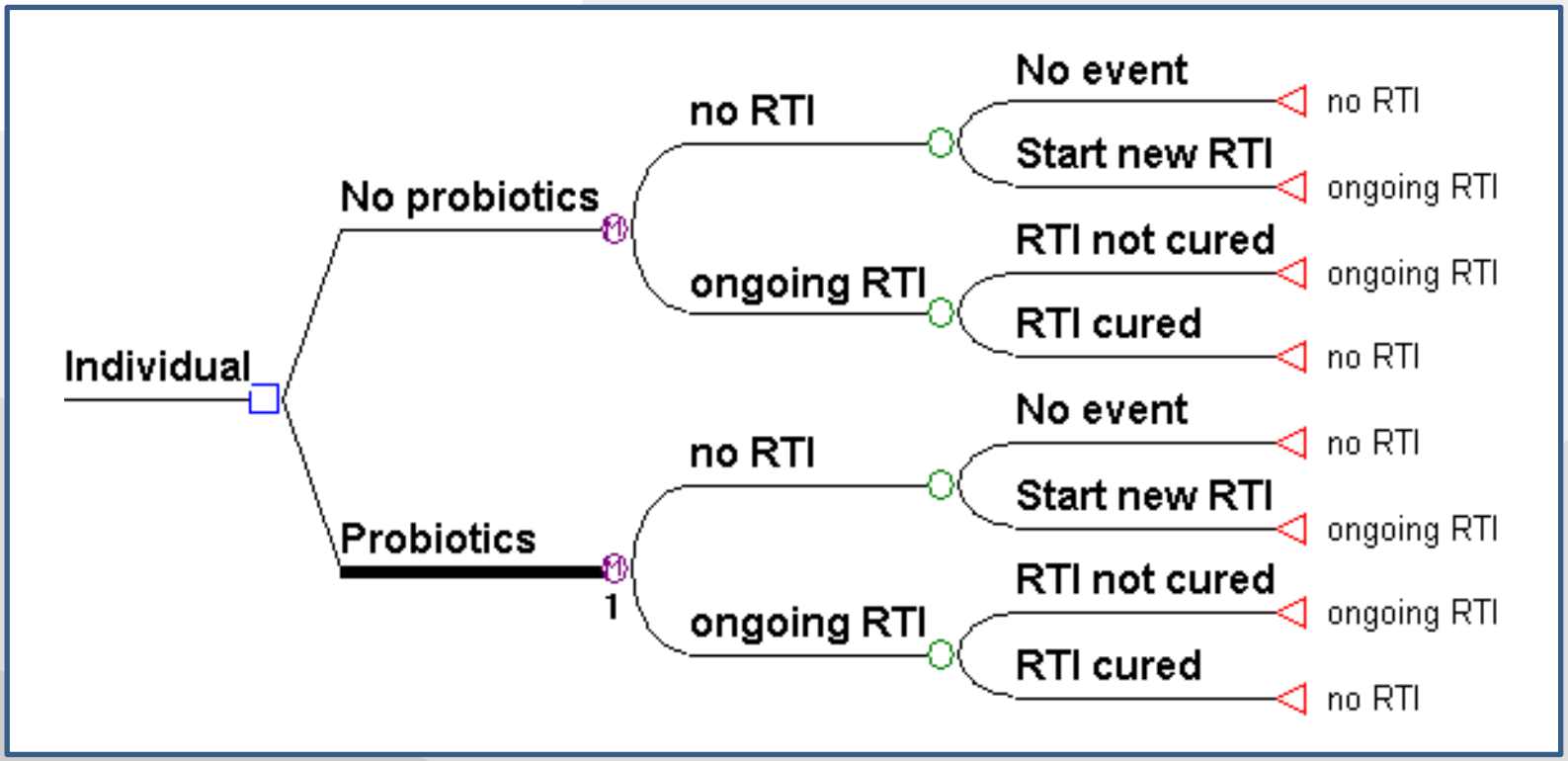
Recent systematic reviews have reported a positive effect of probiotics, specifically *Lactobacillus* and *Bifidobacterium* strains, in reducing the duration or incidence of acute respiratory infections in -otherwise healthy- children and adults

We hypothetized that reducing the duration or incidence of CRTI will influence health care utilisation and associated expenditures.

The purpose of our study was to assess the cost consequences of the beneficial effect of probiotics in CRTI.

# Methodology

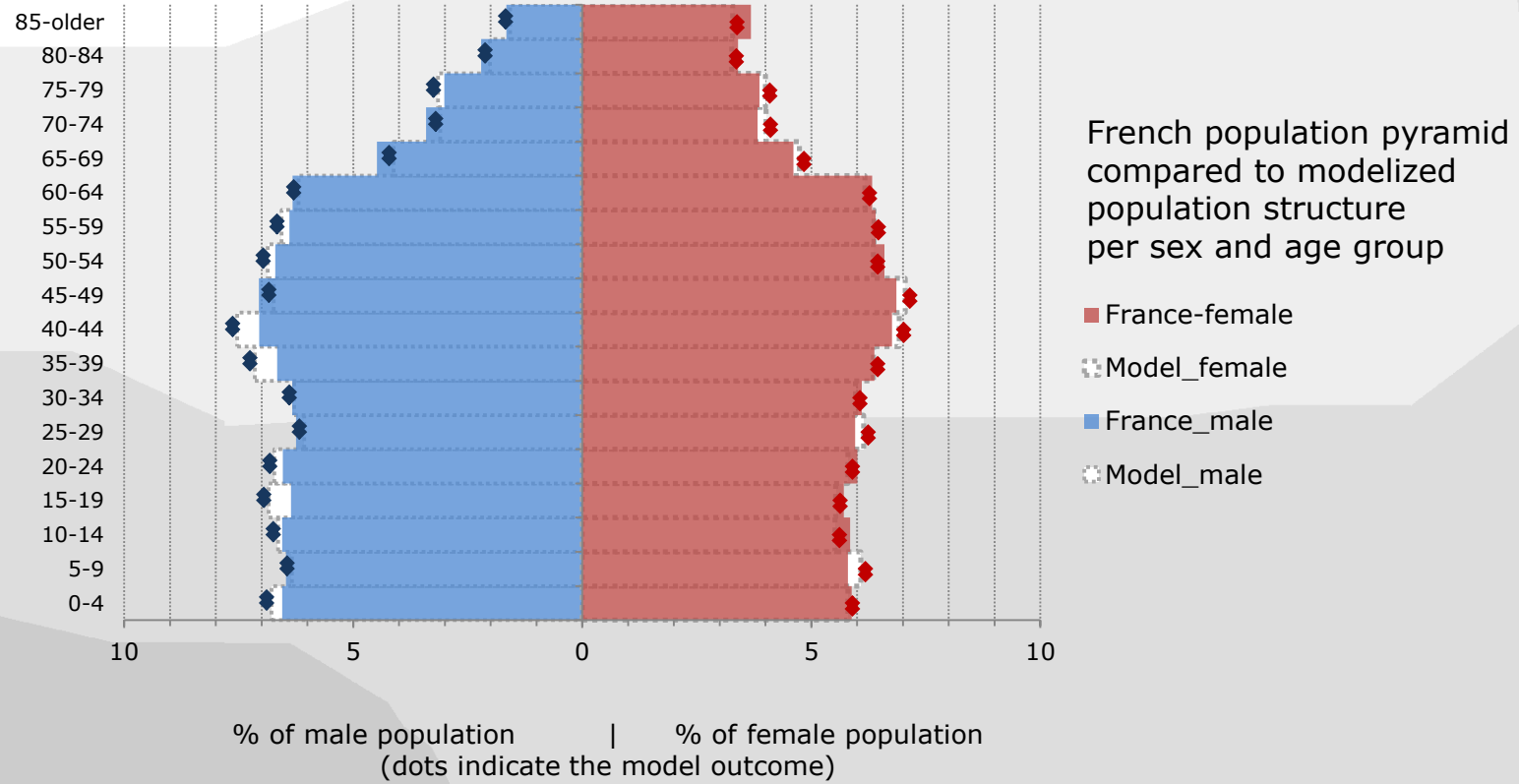
A model was constructed using decision analytical techniques



# Probiotic model

## Population

The population was representative of the French population (Eurostat - http://epp.eurostat.ec.europa.eu/)



# Probiotic model

**Population**
The population was representative of the French population (Eurostat - http://epp.eurostat.ec.europa.eu/)

**Comparison -** The comparator of probiotics was no probiotics

**Perspective -** National Health System, Society and Family (restricted to medical direct and indirect costs)

# Data input

**Clinical outcomes**

- YHEC meta-analysis
- Cochrane meta-analysis

**Epidemiological data**

- Sentinelles (French GP network)

**Resources utilisation** (costs)

- Medical honoraria
- Antibiotics
- Non-antibiotic drugs prescribed
- Sick leave days - EcoGrippe (http://www.grog.org/documents/jour_2007/Ecogrippe.pdf)

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# Clinical Outcomes

**Analysis 2.1. Comparison 2 ITT analysis: Probiotics versus placebo: prescribe antibiotics for acute URTIs, Outcome 1 The number of participants who used antibiotics.**

Review: Probiotics for preventing acute upper respiratory tract infections

Comparison: 2 ITT analysis: Probiotics versus placebo: prescribe antibiotics for acute URTIs

Outcome: 1 The number of participants who used antibiotics

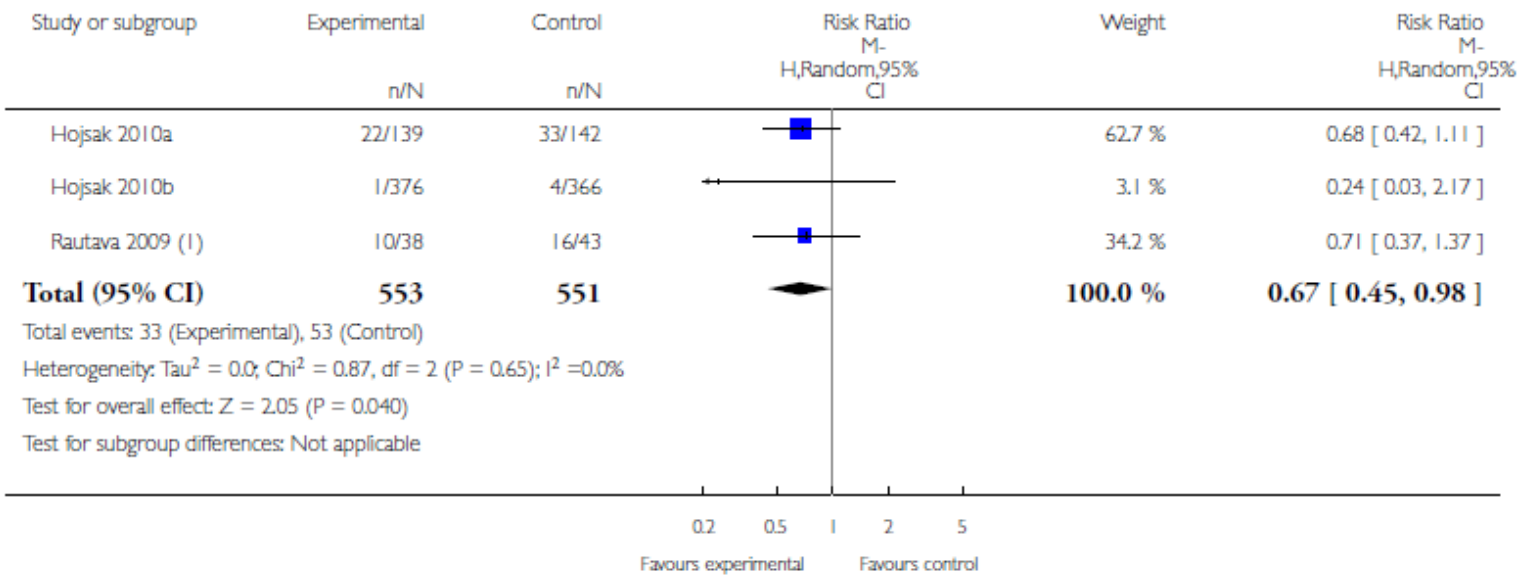
| Study or subgroup | Experimental n/N | Control n/N | Risk Ratio M-H,Random,95% CI | Weight | Risk Ratio M-H,Random,95% CI |
|---|---|---|---|---|---|
| Hojsak 2010a | 22/139 | 33/142 | | 62.7 % | 0.68 [ 0.42, 1.11 ] |
| Hojsak 2010b | 1/376 | 4/366 | | 3.1 % | 0.24 [ 0.03, 2.17 ] |
| Rautava 2009 (1) | 10/38 | 16/43 | | 34.2 % | 0.71 [ 0.37, 1.37 ] |
| **Total (95% CI)** | **553** | **551** | | **100.0 %** | **0.67 [ 0.45, 0.98 ]** |

Total events: 33 (Experimental), 53 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.87$, df = 2 (P = 0.65); $I^2 = 0.0\%$

Test for overall effect: Z = 2.05 (P = 0.040)

Test for subgroup differences: Not applicable



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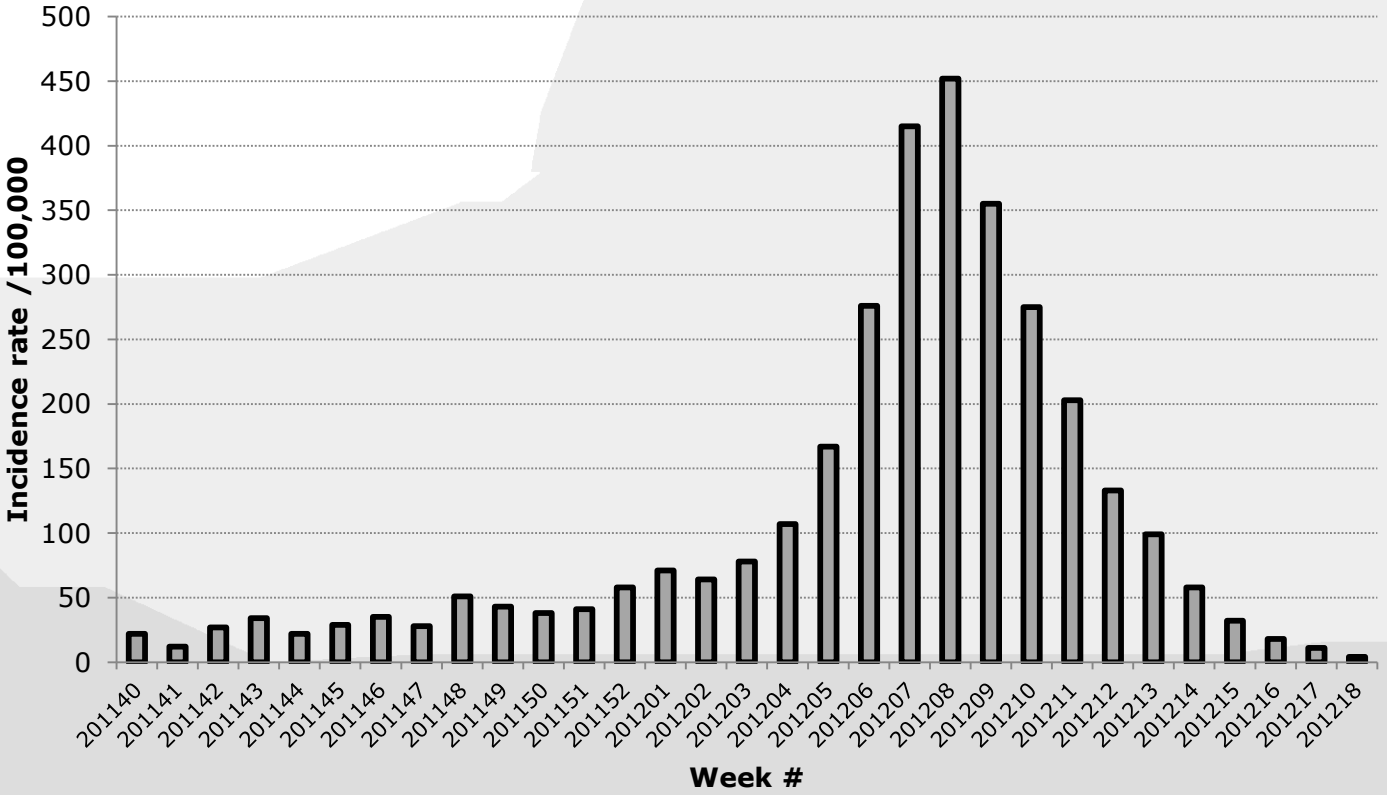
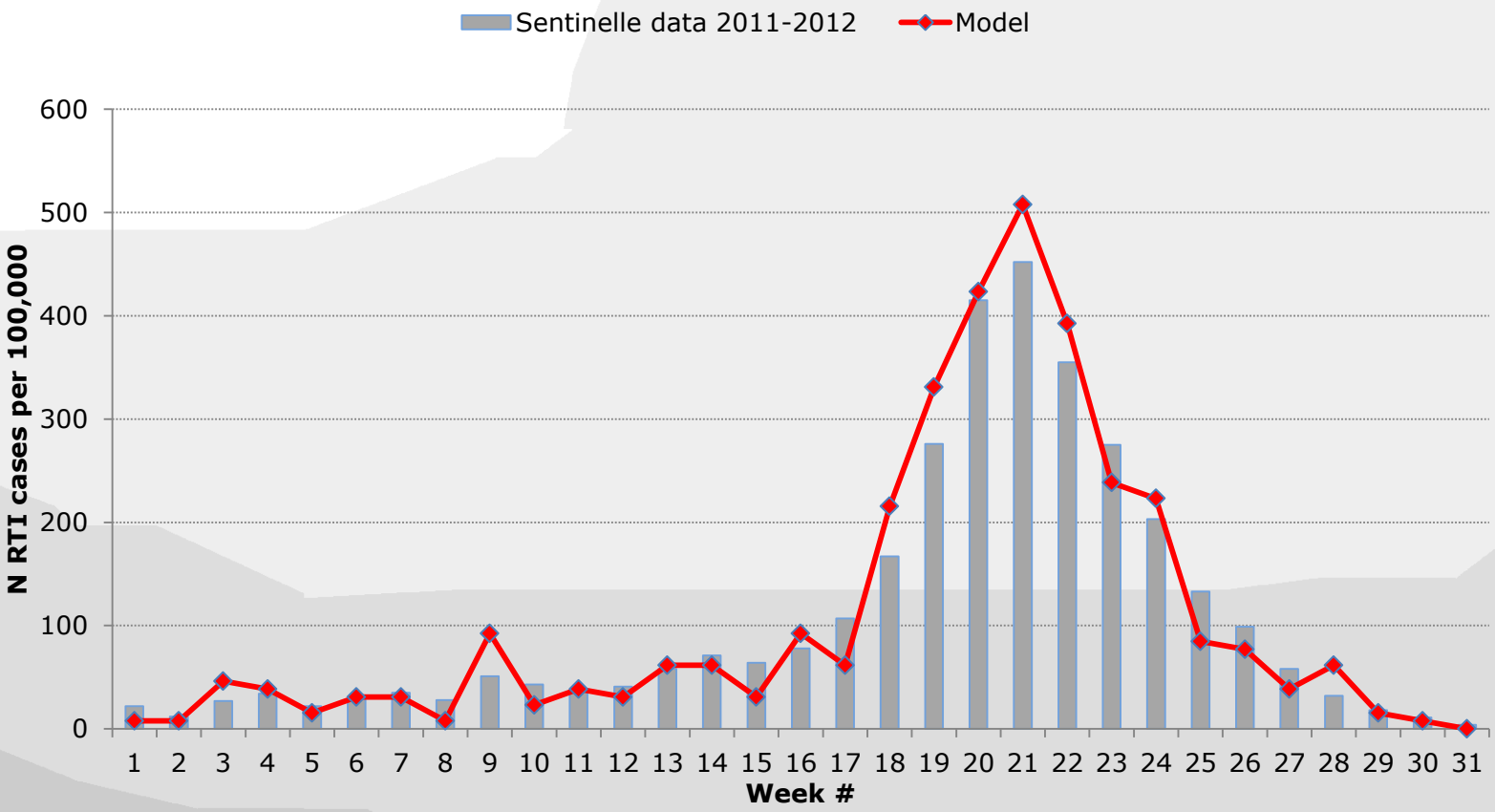
# Epidemiological data

Sentinelles
Réseau Sentinelles




CRTI weekly incidence over all ages (for 100 000 inhabitants for the period of 10/2011-05/2012)

# The model allowed to closely reproduce the weekly incidence of CRTI in the French population

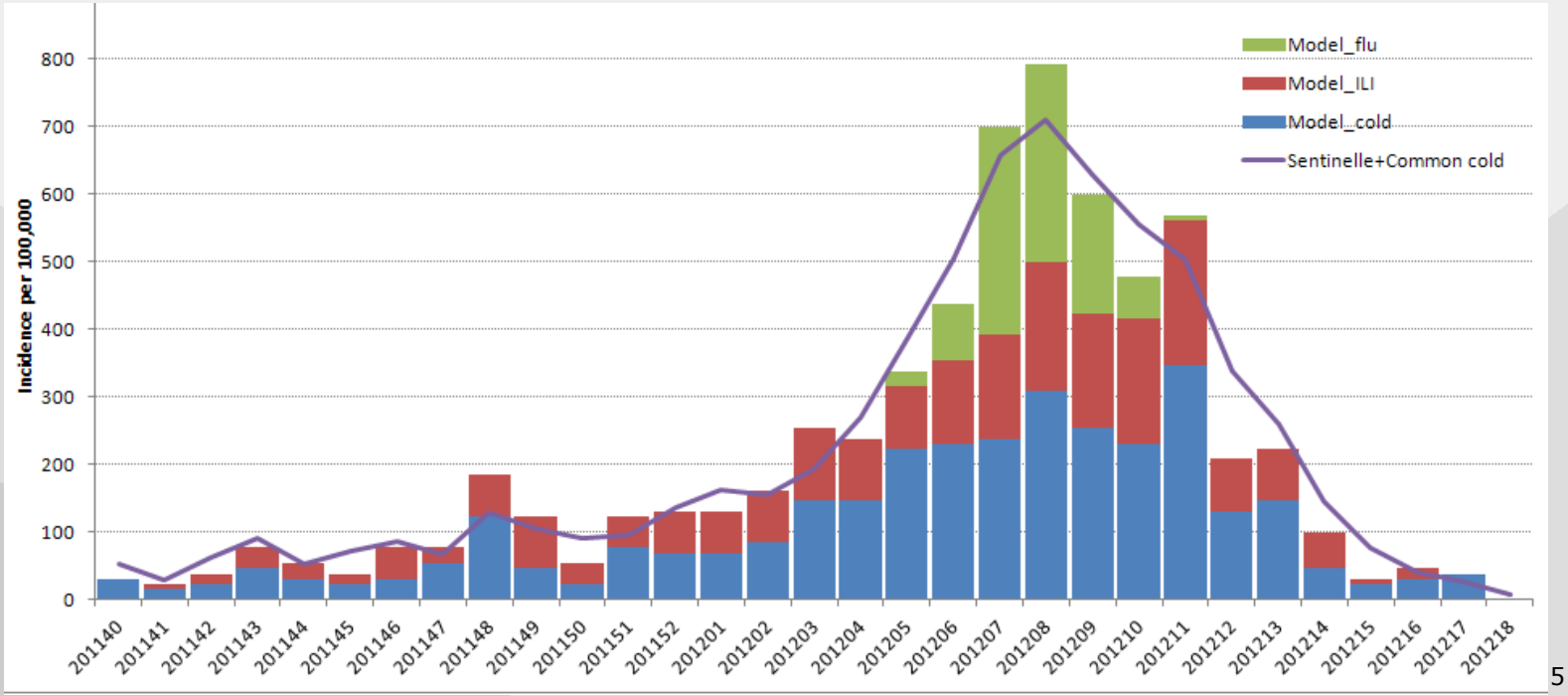



CRTI weekly incidence per age group (2011-2012)

# Common respiratory tract infections

International literature provided the weekly incidence for each type of CRTI and allowed to determine

- the proportion of true flu (virally documented) vs ILI among the total number of cases reported
- the ratio ILI/CC
- per age group and as diagnosed by GPs



# Scenario 1 - YHEC

The first scenario analysis showed that the effect of probiotics on a reduced duration of CRTI would yield

- 2.4 million fewer days with CRTI
- 291,000 antibiotic courses
- 581,000 sick leave days

**Associated cost savings from the Public Payer perspective**
Euro 2012, population aged 3-79, sampling rate 1/1000 (N=59,300)

| | Probiotics | No probiotics | Difference |
|---|---|---|---|
| **NHS - YHEC** | | | |
| Cost visits | 72,356 | 72,356 | 0 |
| Cost antibiotics | 1,718 | 2,564 | -846 |
| Cost sick days | 35,454 | 49,255 | -13,801 |
| **Total cost** | 109,528 | 124,175 | **-14,647** |

# Scenario 2 - Cochrane

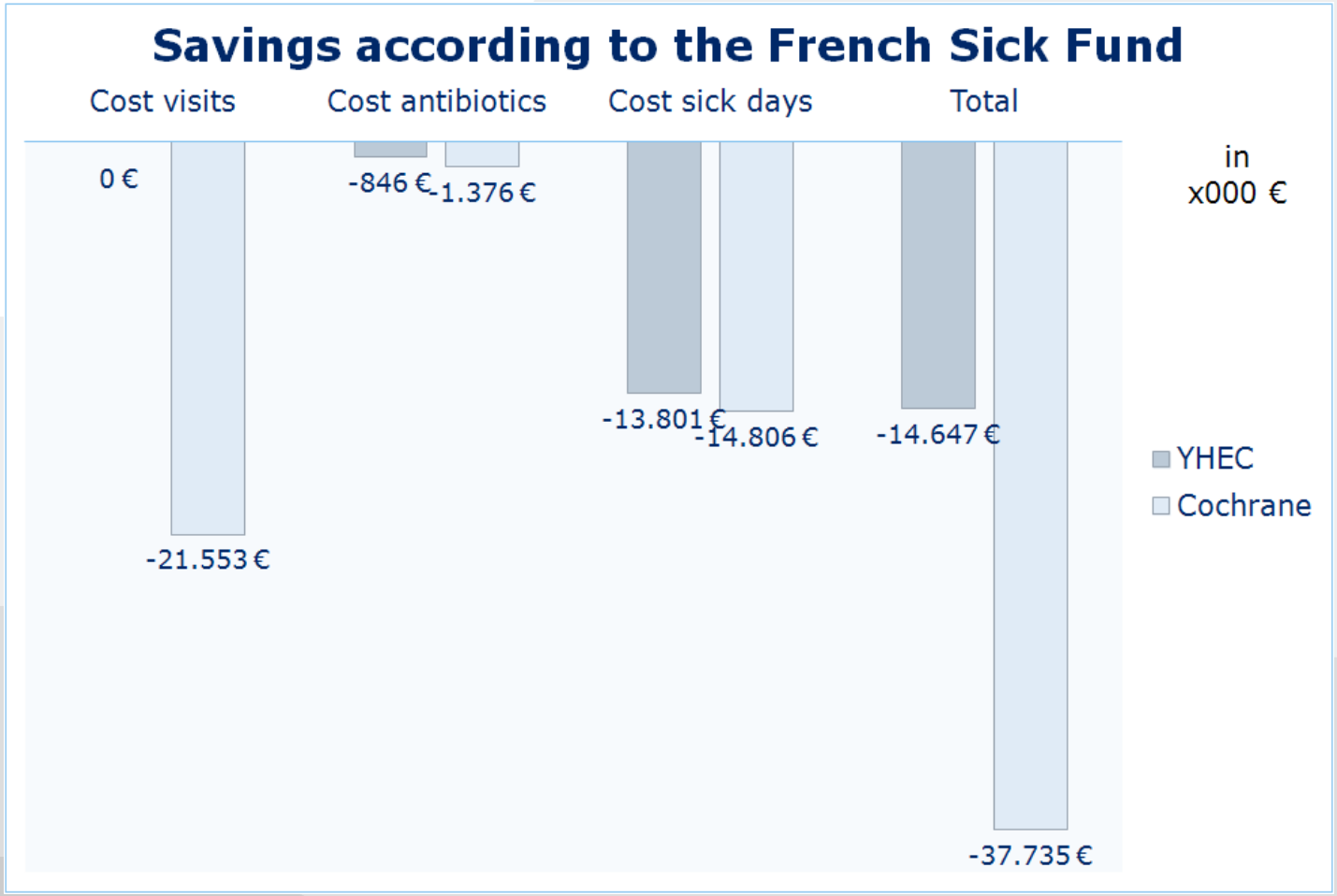
Applying the Cochrane data on CRTI incidence with probiotics, results show the following savings

- 6.6 million CRTI days
- 473,000 antibiotic courses were avoided
- the number of working days lost was reduced by 1,5 million sick leave days

**Associated cost savings from the Public Payer perspective**
Euro 2012, population aged 3-79, sampling rate 1/1000 (N=59,300)

| | Probiotics | No probiotics | Difference |
|---|---|---|---|
| **NHS – Cochrane** | | | |
| Cost visits | 51,247 | 72,8 | -21,553 |
| Cost antibiotics | 1,239 | 2,615 | -1,376 |
| Cost sick days | 36,128 | 50,934 | -14,806 |
| **Total cost** | 88,614 | 126,349 | **-37,735** |

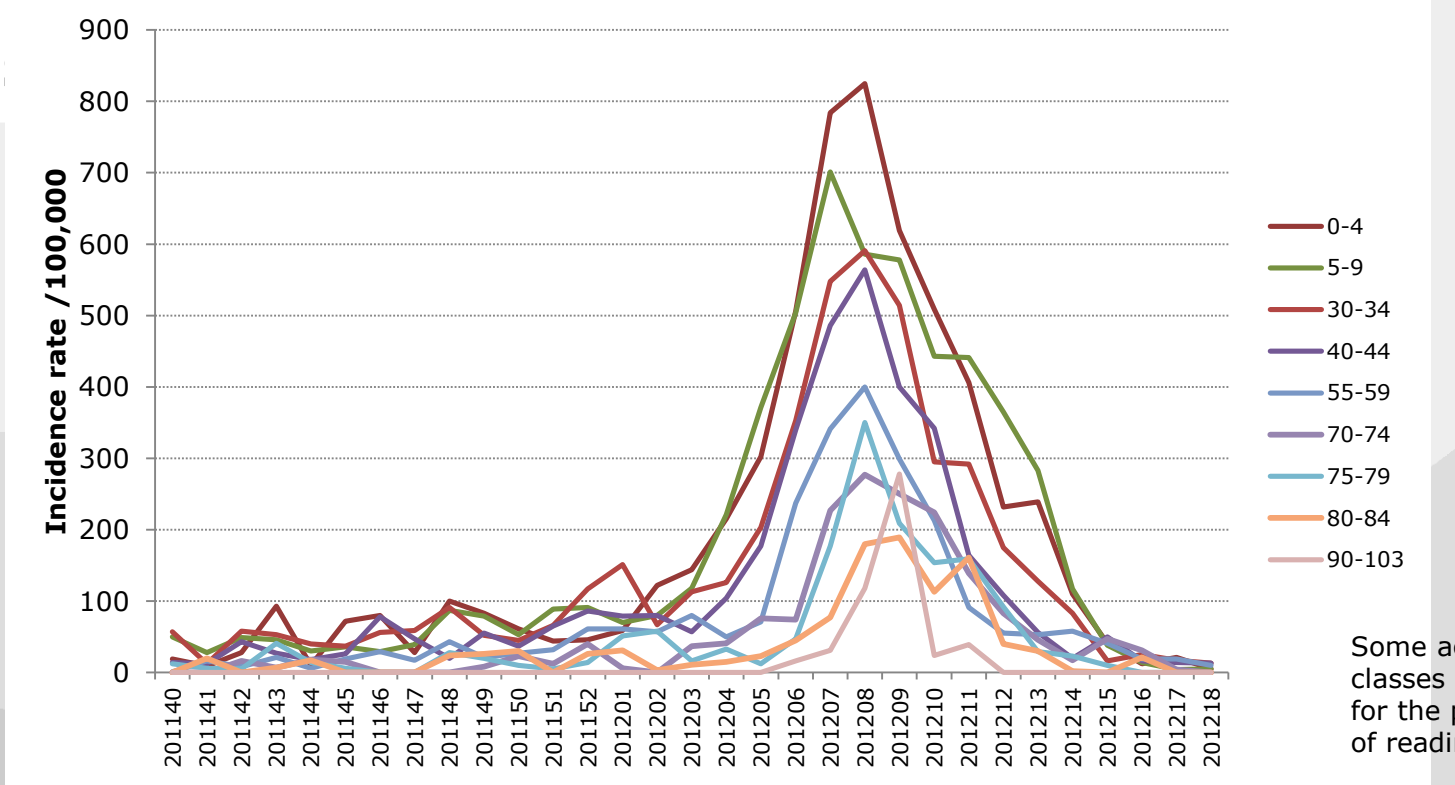
# Overall outcomes



# Risk factors

**Risk factors => individuals are more prone to RTIs**

**Age**



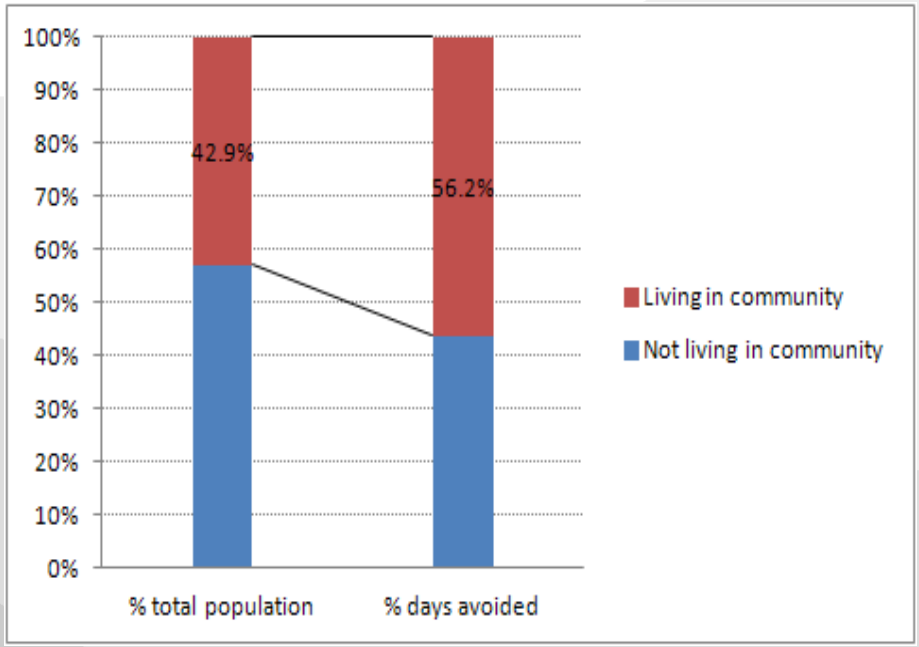

Some age classes deleted for the purpose of readiness

RTI weekly incidence per age group (2011-2012)

# Risk factors – application of relative risk

**Risk factors were implemented while keeping the incidence rates unchanged at a national level => the exemple of**

**Living in a community setting**




**Scenario 1 – general population**

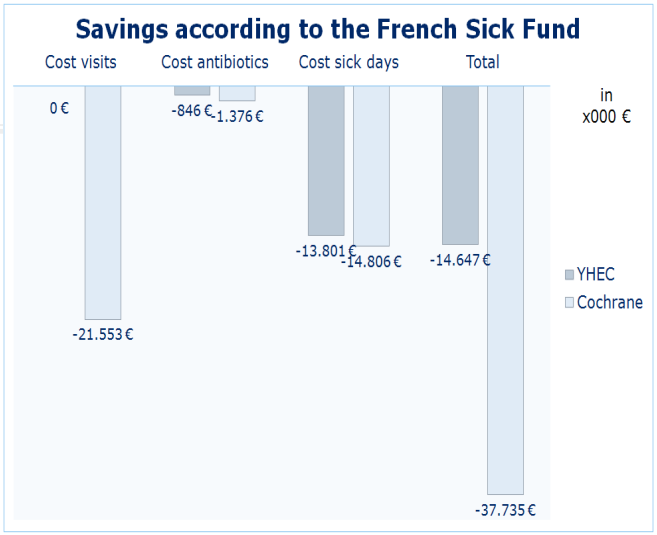
## Scenario 1

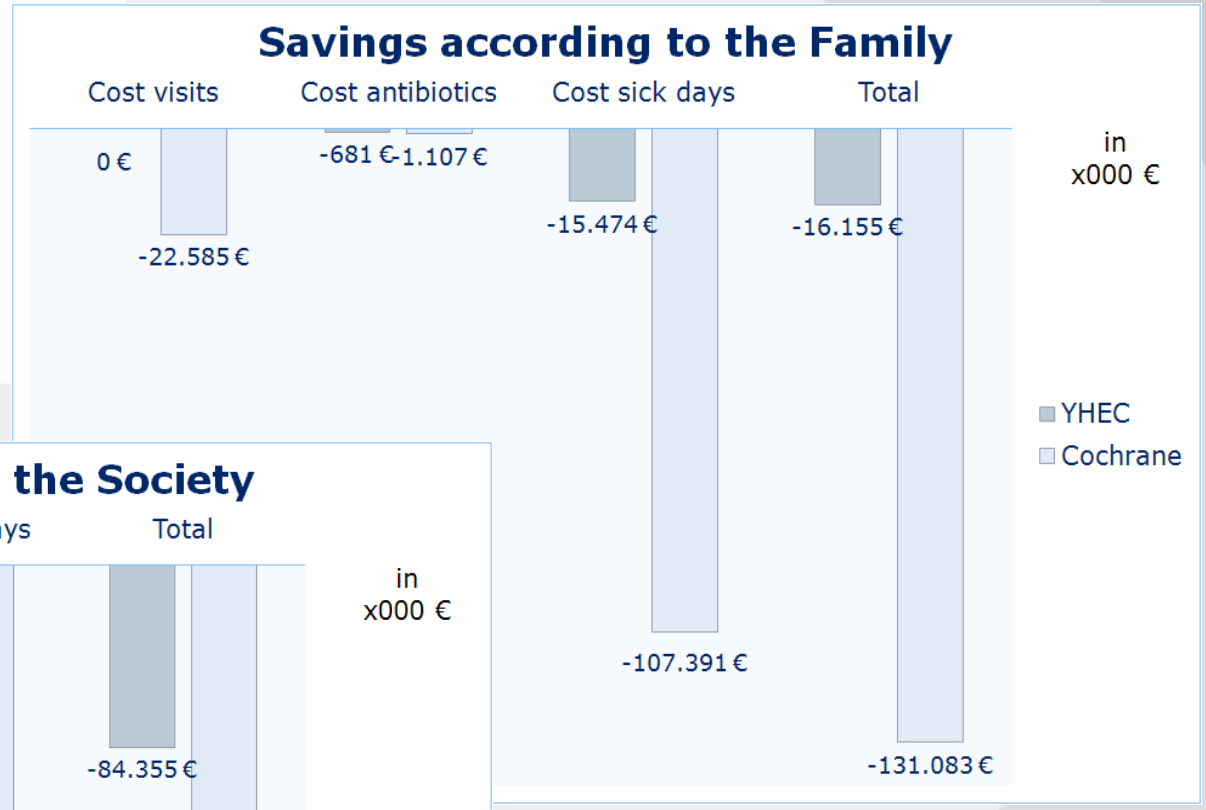
| *Model N (% total) =28,067 (42.9%)* | *Probiotics* | *No probiotics* | *Difference (% of total)* |
|---|---|---|---|
| **Cost honoraria** | 106,438 | 106,390 | 48 (100%) |
| **Cost AB** | 1,802 | 2,687 | -886 (48.4%) |
| **Cost sick days** | 280,757 | 331,090 | -50333 (52.2%) |
| Total cost | **388,997** | **440,167** | **-51170 (52.1%)** |

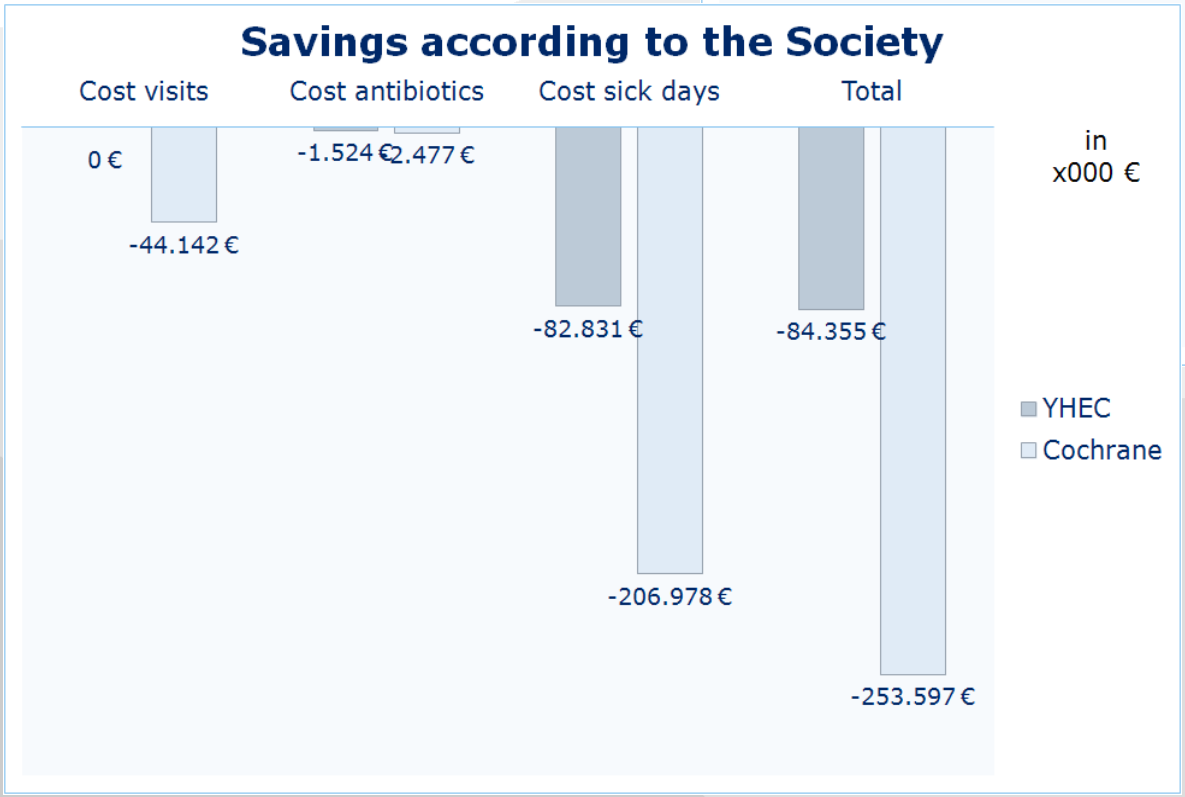
## Scenario 2

| *Model N (% total) =28,067 (42.9%)* | *Probiotics* | *No probiotics* | *Difference (% of total)* |
|---|---|---|---|
| **Cost honoraria** | 78,555 | 106,390 | -27835 (55.6%) |
| **Cost AB** | 1,323 | 2,687 | -1364 (48.5%) |
| **Cost sick days** | 241,921 | 331,090 | -89169 (47.3%) |
| Total cost | **321,799** | **440,167** | **-118368 (49.1%)** |

# Other perspectives



# Limitations

- The model covers only CRTI patients who consulted their GP (estimated at 1% of the total number of cases)
- The winter season studied (2011-2012) was associated with a low incidence rate of ILI
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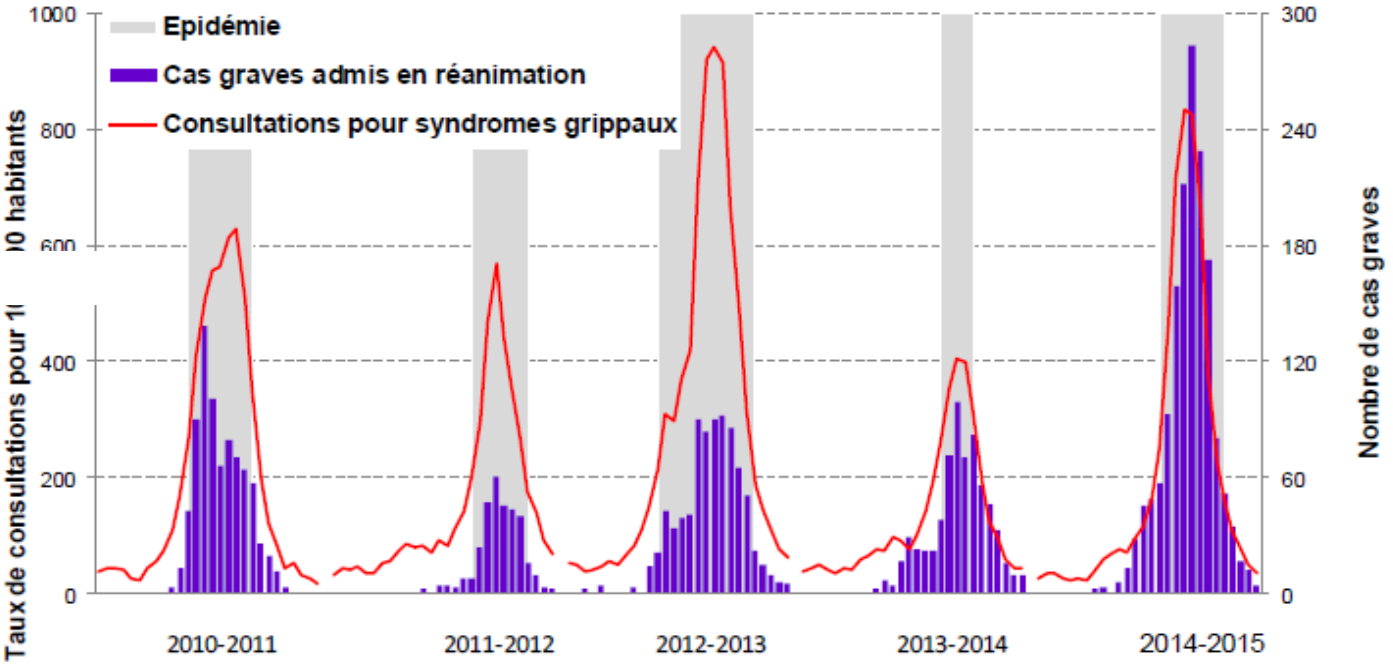
**| Figure 2 |** Taux hebdomadaire d'incidence des consultations pour syndromes grippaux et du nombre de cas graves en réanimation, semaines 40/2010 à 15/2015, en France métropolitaine



# Conclusion

The effect of probiotics on CRTI

- Can be associated with a substantial reduction of the economic burden of this very common health concern
- May contribute in preserving sustainable health care systems

**Probiotics should be taken into consideration for population-oriented strategies aiming to prevent and reduce seasonal respiratory tract infections and related costs**

# Acknowledgments

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