Cancers and agriculture in France, what are the current and expected short term lessons from the AGRICAN (AGRIculture & CANcer) cohort

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UMR 1086 « Cancers et Préventions »

Brief history on pesticides and cancers ?

1940s **Historical cohorts** (Arsenic compounds…)

1960s OCs in **human** tissues

1980s First **case-control studies**

1991

1992 What pesticides are used in France ?

1993

1995 Small cohort in Calvados area
+ genotoxicity biomarkers

CE 91/414

Some **French** Case-Control Studies
(Tricho., MDS, NHL…)

Enrollment in AHS !

Paquid and Phytoner cohorts

Main problem: exposure assessment !!

2000 Workshop in Bordeaux on Pesticide
Exposure Assessment

EUROPOEM

Field studies on pesticide exposure among users…
and for re-entry workers **PESTEXPO**

Algorithms in AHS

PESTIMAT matrix

2006 **Enrollment in AGRICAN cohort**

AGRICOH Consortium

2011 **Mortality** data from AGRICAN

Literature reviews (INSERM / EFSA)

2014 **Incidence** data from AGRICAN, **internal** analyses, **first follow-up**

AGRICAN cohort ?

Aims of AGRICAN:
- i) Cancer risk related with various agricultural activities
  (crops, livestock, various tasks)
- ii) Improvement of pesticide exposure assessment
  (direct and indirect exposure)
- iii) Less studied population (women, farm workers…)
- iv) Enough statistical power

Enrollment

- Adults
- From specialized health insurance (> 3 years)
- Living in one out of 11 areas (departement)

Pestimat / pestexpo

Follow-up Questionnaires + information n°2

2005   2007   2009 2011   2012   2014-2016

-**Vital** status (MSA, RNIPP): annual since **2009**
-**Causes** of **death** (CépiDC): annual since **2009**
-Place of **residence** (MSA, La Poste): annual since **2009**
-Agricultural **activities** (MSA since **2009**)
-**Cancer** diagnosis (FRANCIM, 18 registries): every 2 years since **2012**
- Follow-up **questionnaires:2014-2016**

Characteristics at enrollment-1
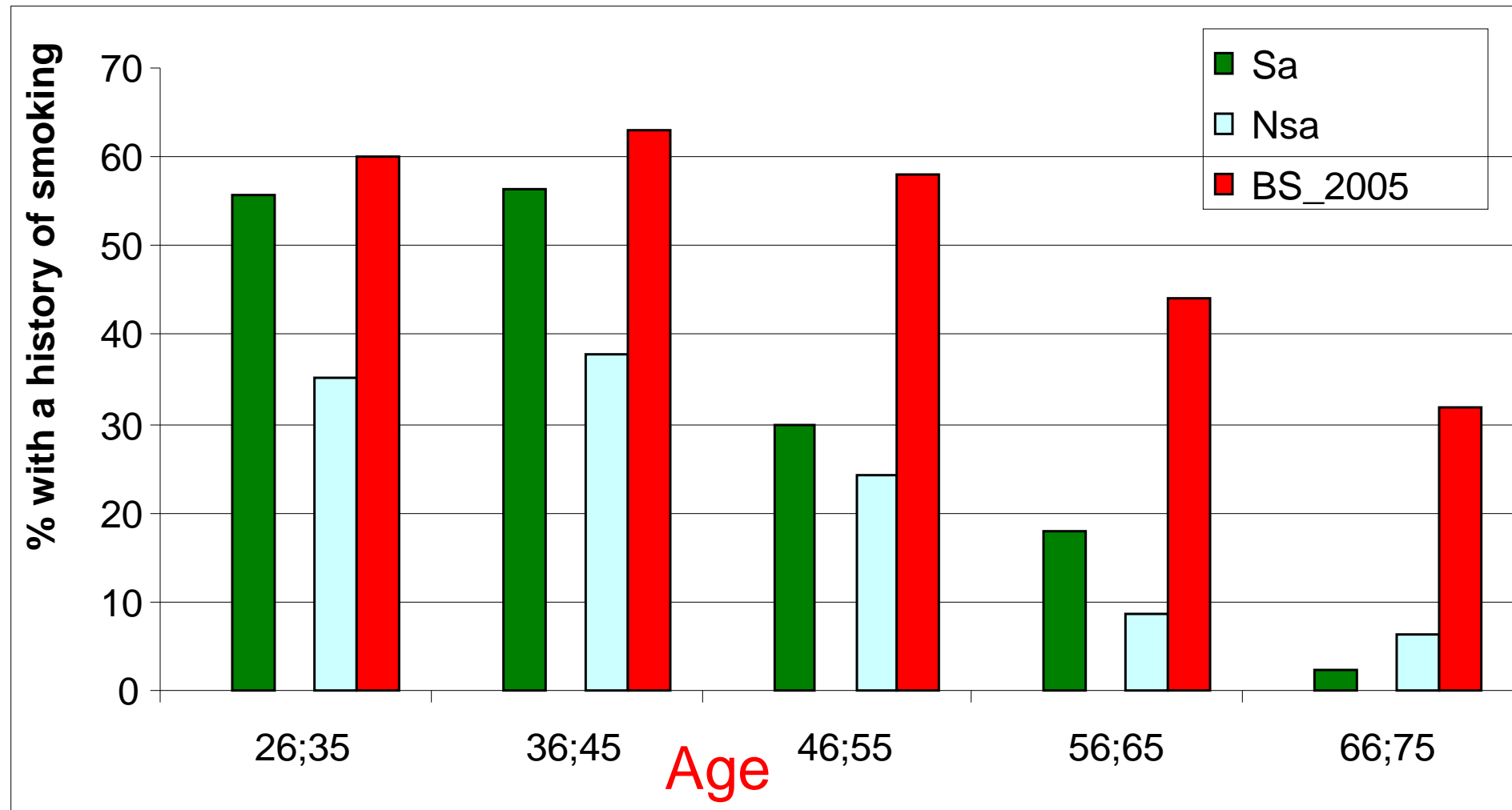
N=184,000

Women= 46%

Retired = 50%

Mean age= 64y (20 to 104 years old)

Mean duration of Work in agriculture= 28 years

Work in farms = 88%

Characteristics at enrollment -2
History of smoking among women

SA : Workers (including farm workers and other « agricultural » workers)
Nsa = farm owners at least part of their working life

Characteristics at enrollment -3
13 crops / 5 livestock (2 to 5 tasks)

Grassland (54%)

Wheat / Barley (41%)

Grapes (34%)

Corn (28%)

Potatoes (25%)

Beet (18%)

Fruit growing in field (18%)

Field vegetables (<10%)
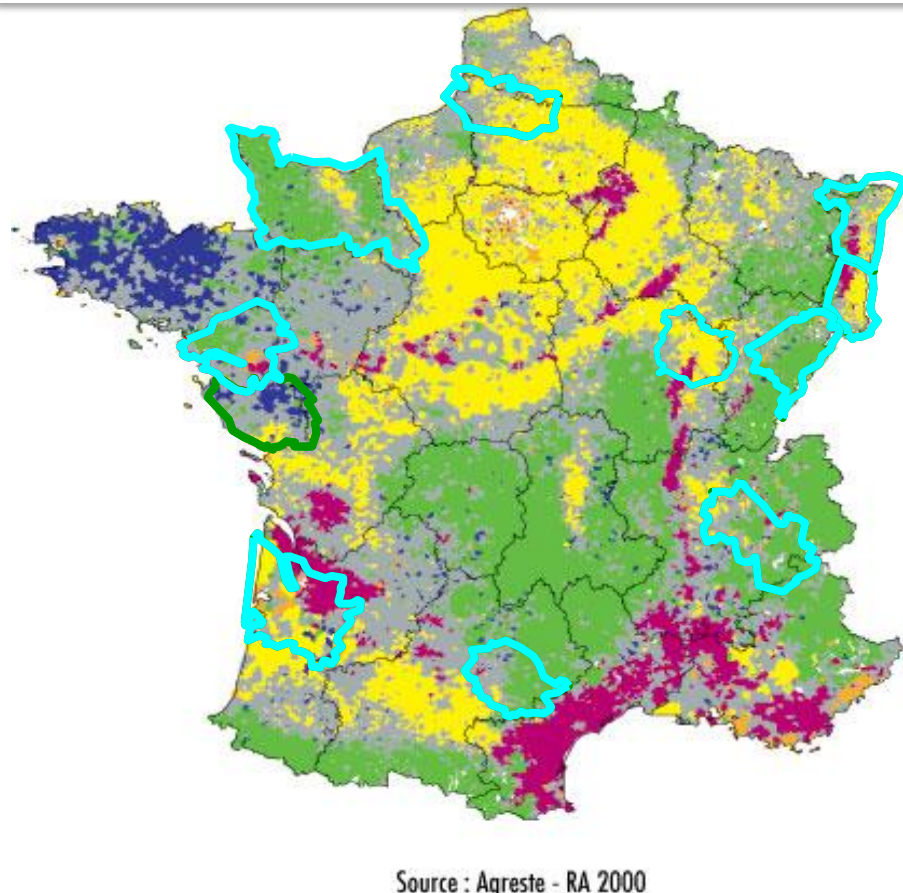
Greenhouses (<10%)

Rape (<10%)

Peas (<10%)

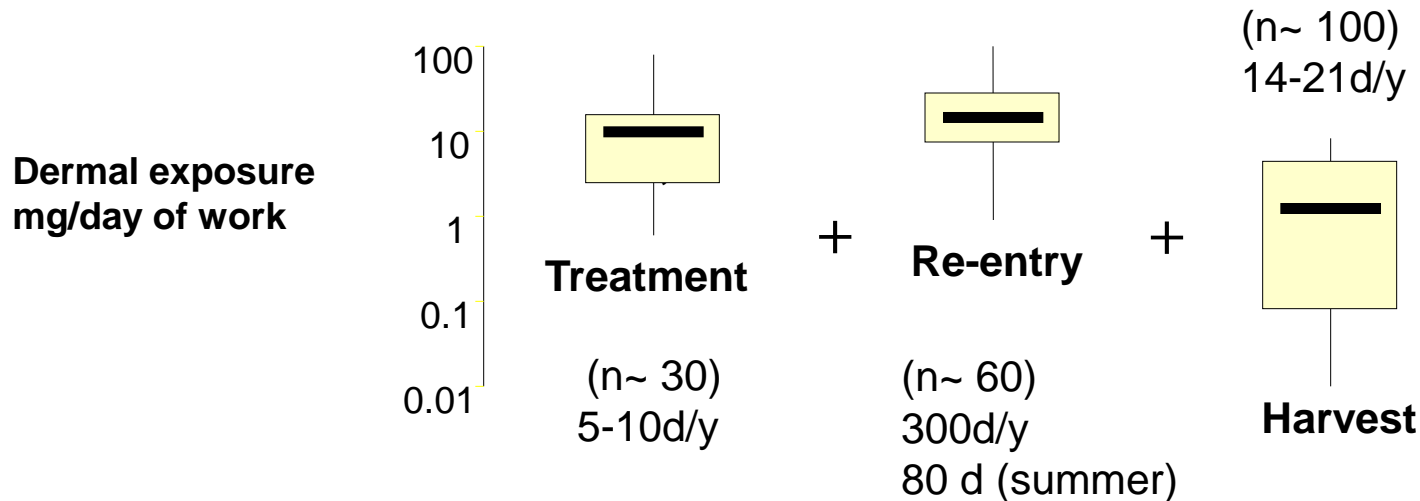Sun flower (<10%)

Tobacco (<10%)

Agrican areas

Source : Agreste - RA 2000

Levêque-Morlais et al. Int Arch Occup Environ Health 2014

Characteristics at enrollment -4

Pesticide exposure (direct and indirect)
On grapes by gender

	Women	Men
Indirect only (re-entry ± harvest)	**81%**	**31%**
Direct only (pesticide use)	**0.4%**	**2%**
Both direct and Indirect	**11%**	**60%**
Exposed ?	**92%**	**93%**

Dermal exposure mg/day of work

100

10

1

0.1

0.01

Treatment + **Re-entry** + **Harvest**

(n~ 30)
5-10d/y

(n~ 60)
300d/y
80 d (summer)

(n~ 100)
14-21d/y

Baldi et al. Environ Res 2014   Levêque-Morlais et al. Int Arch Occup Environ Health 2014

Results on health: comparison with general population - 1 Mortality data (2005-2010 period)

CANCERS	Men		Women	
* : p <0.05	N	SMR	N	SMR
Lip-Buccal-Pharynx (C00-C14)	63	**0.58***	9	**0.49***
Œsophagus	85	**0.60***	19	0.80
Stomach (C16)	123	**0.83***	59	0.94
Colon	241	**0.72***	172	**0.81***
Rectum	105	0.89	37	**0.56***
Liver and biliary tract (C22)	211	**0.73***	44	**0.64***
Pancreas (C25)	153	**0.77***	132	0.91
Lung (C33-C34)	455	**0.51***	101	**0.59***
Cutaneous Melanoma (C44)	38	0.98	24	1.02
Bladder (C67)	105	**0.61***	21	**0.52***
Hematological cancers	312	**0.89***	191	0.91
Prostate (C619)	429	**0.82***	-	
Breast (C50)	14	1.37	230	**0.71***

Decreased risk

To be confirmed

Levêque-Morlais et al. Int Arch Occup Environ Health 2014

Results on health: comparison with general population - 2 Cancer incidence data (2005-2009 period)

CIM-O_3	Men		Women	
* p< 0.05	N	SIR	N	SIR
All cancers	4,596	0.88*	2,259	0.89*
Lip	19	1.49	<5	NC
Buccal-pharynx	119	**0.56***	16	**0.41***
Œsophagus	91	**0.72***	13	0.64
Stomach	150	0.97	55	0.93
Colon	402	**0.87***	253	0.91
Rectum	262	0.98	101	0.80
Liver	157	**0.76***	27	0.75
Pancreas	112	**0.83***	91	0.91
Lung	372	**0.54***	89	**0.64***
Mesothelioma	11	**0.38***	5	0.79
Bladder	159	**0.62***	45	0.98

Decreased risk

To be confirmed

Lemarchand et al. In preparation (2015?)

Results on health: comparison with general population - 3
Cancer incidence data (2005-2009 period)

CIM-O_3	Men		Women	
* : p< 0.05	N	SIR	N	SIR
Cutaneous Melanoma	108	0,96	106	**1,26***
Brain	45	0,79	29	0,84
Thyroïd	25	0,78	63	1,02
Multiple myeloma	88	**1,26***	49	1,03
Non Hodgkin Lymphoma	395	1,07	210	0,98
Hodgkin Lymphoma	15	1,19	8	1,38
Acute Myeloïd Leukaemia	36	0,90	26	1,11
Testicular	8	0,57	-	
Prostate	1,668	0,96	-	
Breast	13	0,98	654	0,82
Ovary			91	1,03

Decreased risk   Increased risk

To be confirmed

Lemarchand et al. In preparation (2015?)
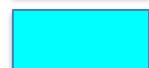
-Effect of activities, tasks (including pesticide exposure overall / activity) ?

-Effect of specific chemical families of pesticides (PESTIMAT) ?

a) Respiratory diseases
- Chronic Bronchitis
   (Tual et al., Annals Epidemiol 2013)
- Asthma
   (Baldi et al., Int J Hyg Environ Health 2014)

b) Cancers (on going)
- Lung (PhD Thesis S Tual, M Boulanger)
- Prostate / Breast (PhD Thesis C Lemarchand)
- Hematological cancers
   AGRICOH project / AGRICAN alone
- Bladder
- Brain
- Colo-rectal, pancreas, kidney
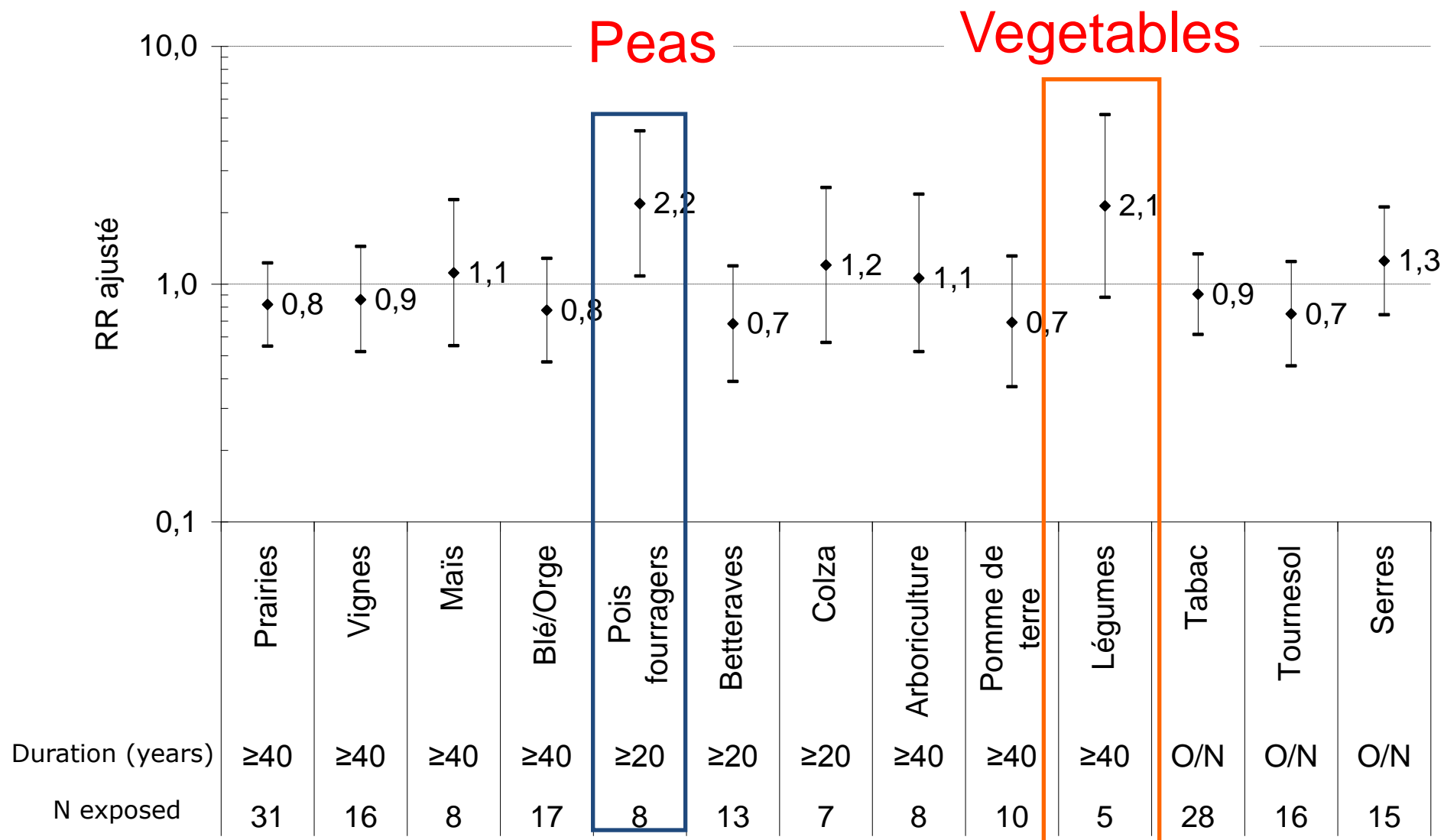…

- 388 lung cancer cases (2005-2009, +2010-2011 ?)

- Agricultural activities at risk ?

  Peas (harvest ?), fruit growing ? (cutting ?) vegetables (tasks ?)

- Agricultural activities with a decreased risk ?

  Cattle growing, Horses ?, milking on sheeps or goats?

Tual et al. In preparation (2015 ?)

Results on health: internal comparisons – 3
Lung cancers

RR adjusted on smoking duration and age

Tual et al. In preparation (2015 ?)

	Cattle		Horses		
	Bovins	Moutons/ Chèvres	Porcs	Chevaux	Volailles
Duration (years)	≥40	≥20	≥20	≥20	≥40
N exposed cases	29	6	14	8	10

RR adjusted on smoking duration and age

15
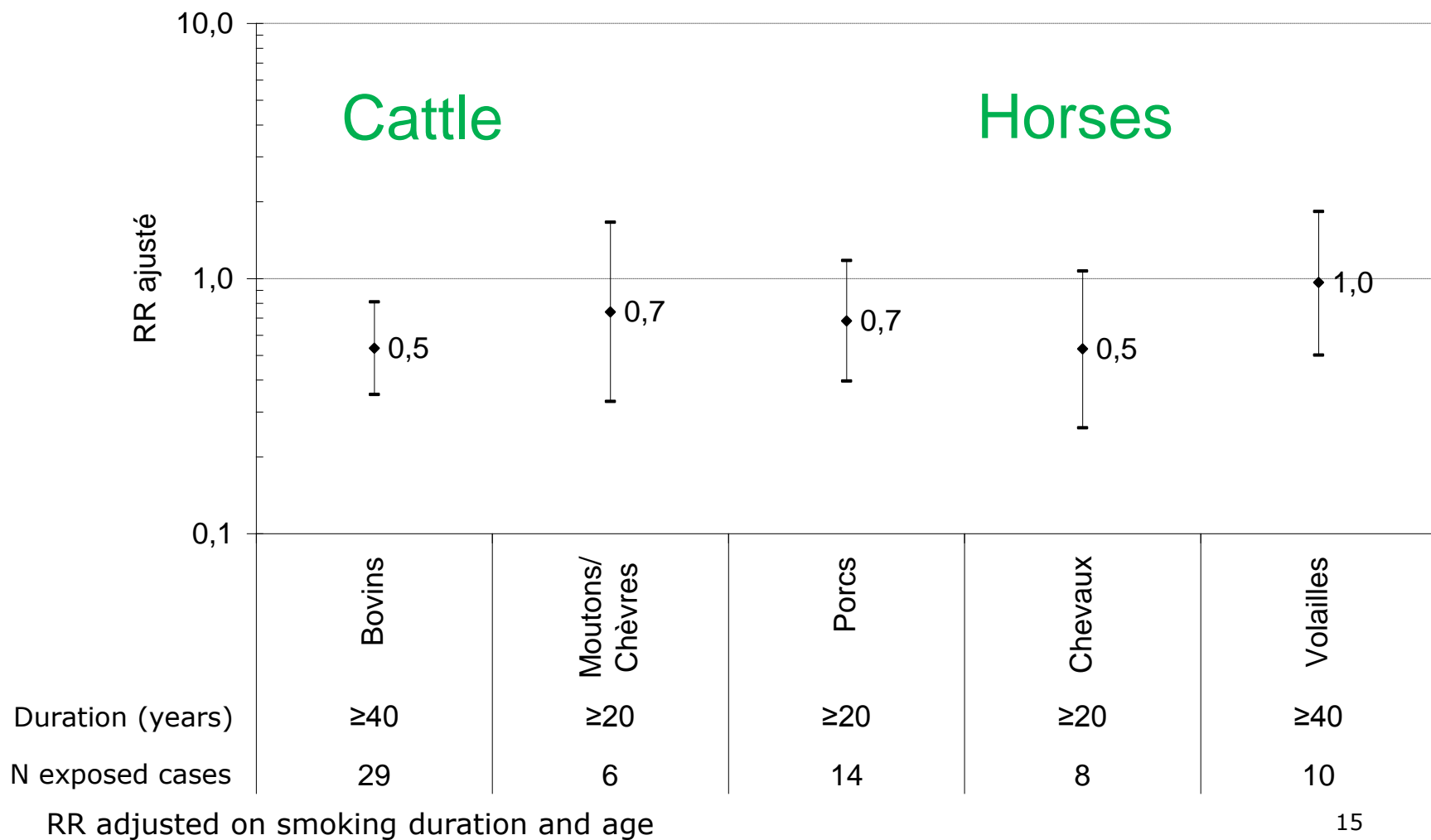
- 1,684 prostate cancer cases (2005-2009)

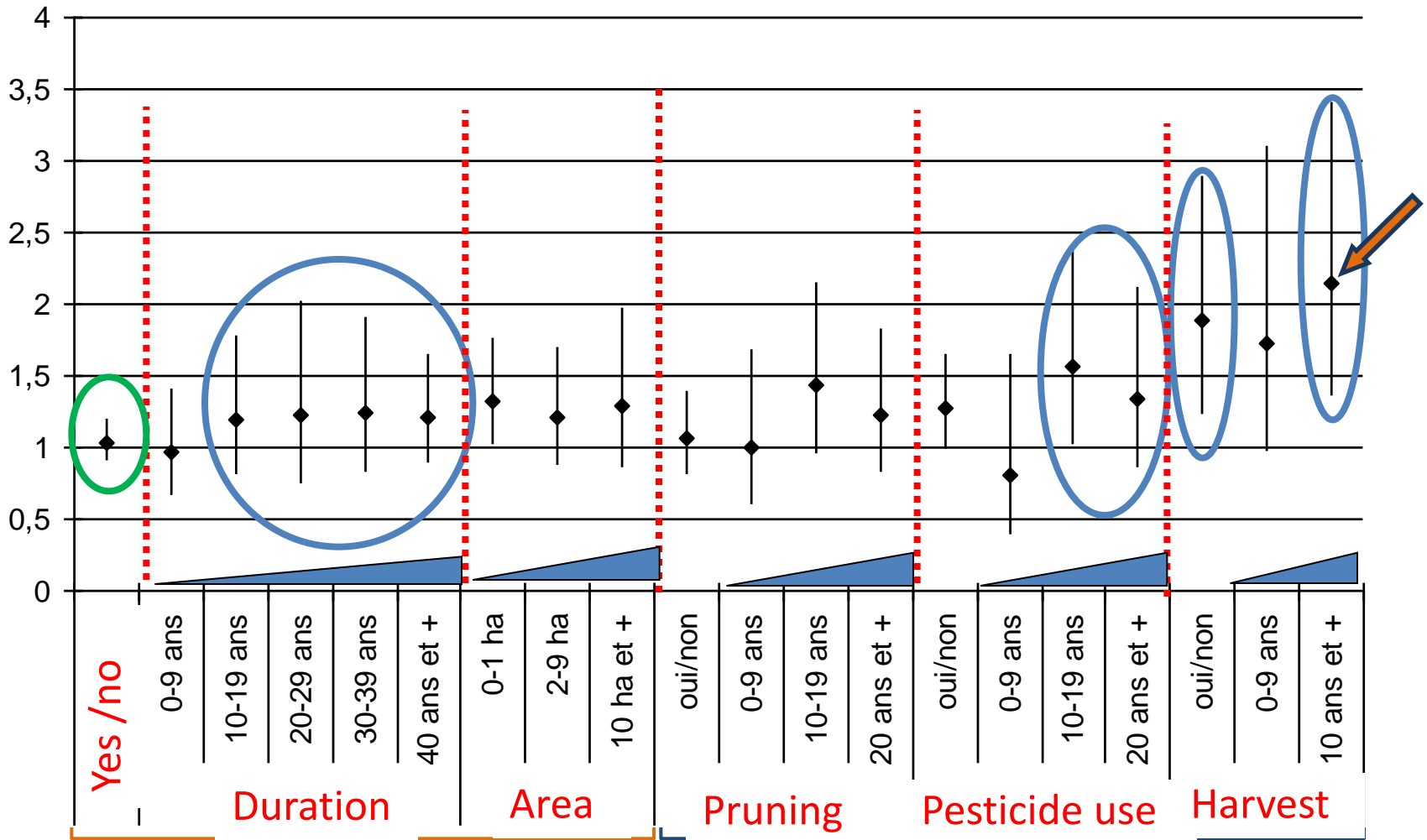- Agricultural activities at risk ?

  Cattle growing (insecticide use ?), fruit growing (pesticides ? harvest ?) potatoes (pesticide use?), sunflower ? Tobacco production ?

- Agricultural activities with a decreased risk ?

  None

Lemarchand et al. In preparation (2015 ?)
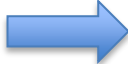
Results on health: internal comparisons – 6
Prostate cancers – Fruit growing

Lemarchand et al. In preparation (2015 ?)

Conclusion to date ?

Weaknesses (to date) ?

- Missing data (multiple imputation, improvement of data collection..)
- No results yet on the effect of specific pesticides (direct exposure)
- Effect of specific pesticides in re-entry tasks ?
- Interpretation of new findings on specific activities / tasks
    peas, cattle on lung cancers…

Strengths ?

- Large prospective cohort
- Many (all?) agricultural activities concerned in french context
- Detailed information on various tasks
- Many farm workers and women involved on farm tasks
- Possibility to improve exposure assessment (pestimat, follow up questionnaire)
- Other diseases followed

Pestimat crop exposure matrix
Dithiocarbamates fungicides on grapes (N=11)

Exposure indicator = Probability X Frequency X Intensity
Each year between 1950 to 2014…

first quartile of indicator   last quartile of indicator

Baldi et al. In preparation (2015 ?)

Collaborations:
LSTE, Francim, MSA
AGRICOH
Grants ?
Enrollment :
MSA, Ligue Contre le Cancer, ANSES, Conseil Régional Basse-Normandie,
ARC, Centre F Baclesse, Fondation de France, InCA,
Conseil Général du Calvados, UIPP
Follow up of health ?
MSA, Ligue Contre le Cancer, ANSES (ONEMA), Centre F Baclesse, UIPP
Phase 2 questionnaire ?
ONEMA, Ligue Contre le Cancer