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 CE 91/414

1992 What pesticides are used in France ?

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

1993 Enrollment in AHS !

1995 Small cohort in Calvados area + genotoxicity biomarkers

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)

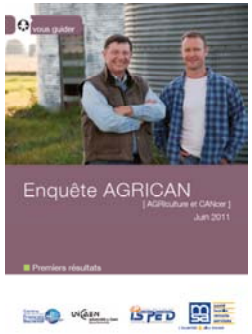
iii) Less studied population (women, farm workers…)

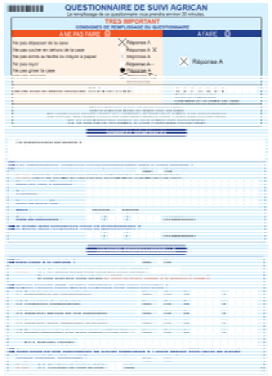
iv) Enough statistical power

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)

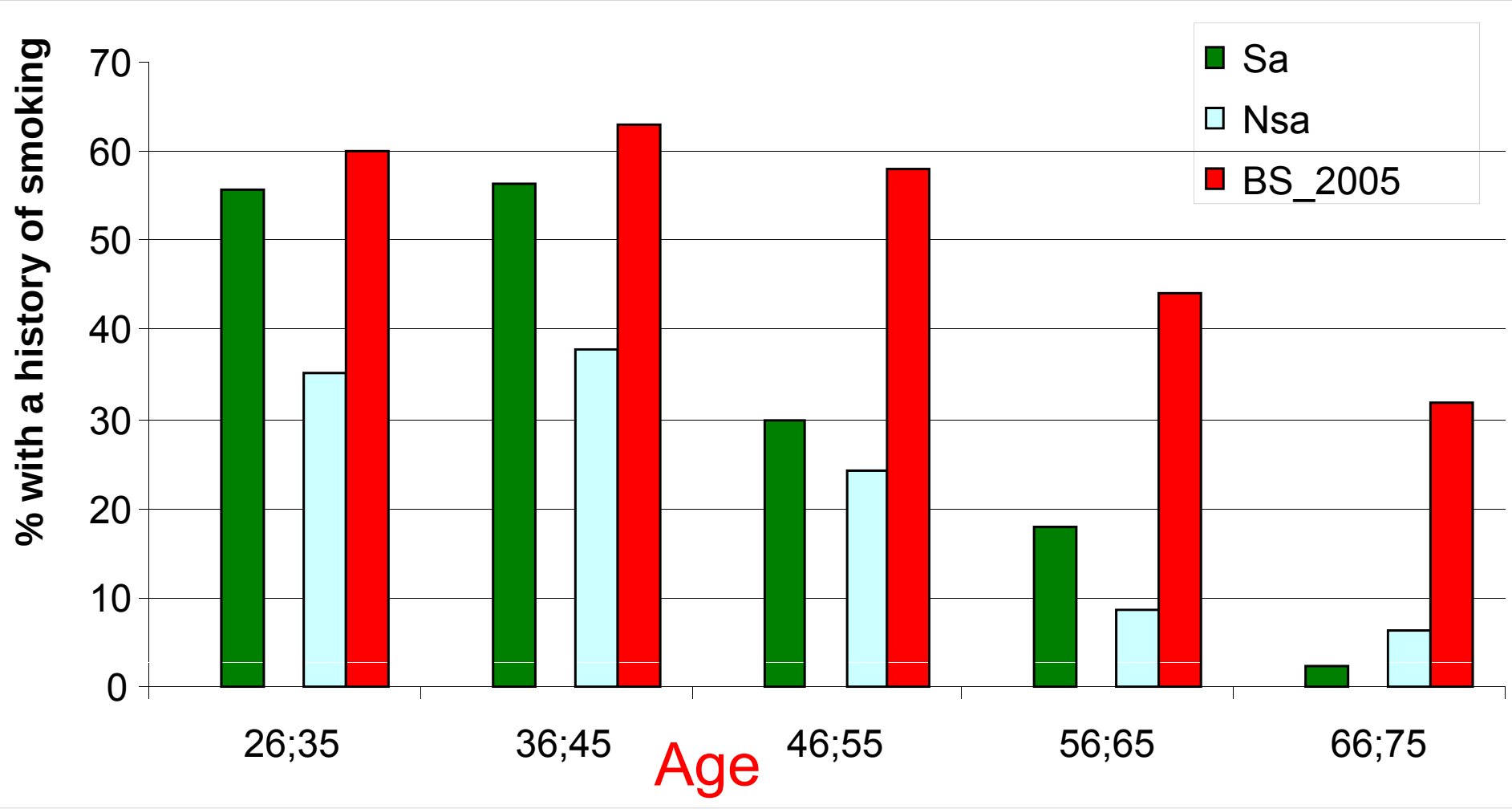
Mean duration of Work in agriculture= 28 years

Work in farms = 88%

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

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%)

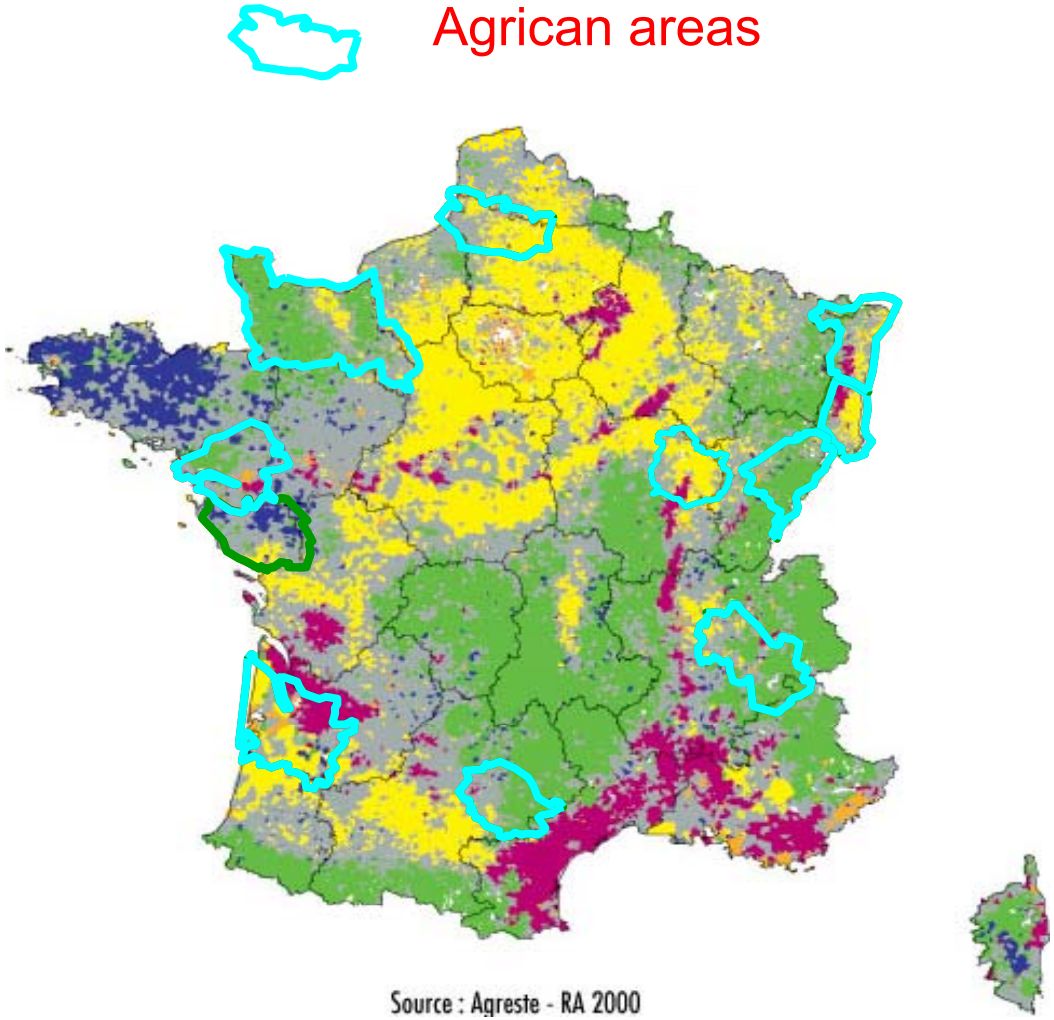
Greenhouses (<10%)

Rape (<10%)

Peas (<10%)

Sun flower (<10%)

Tobacco (<10%)

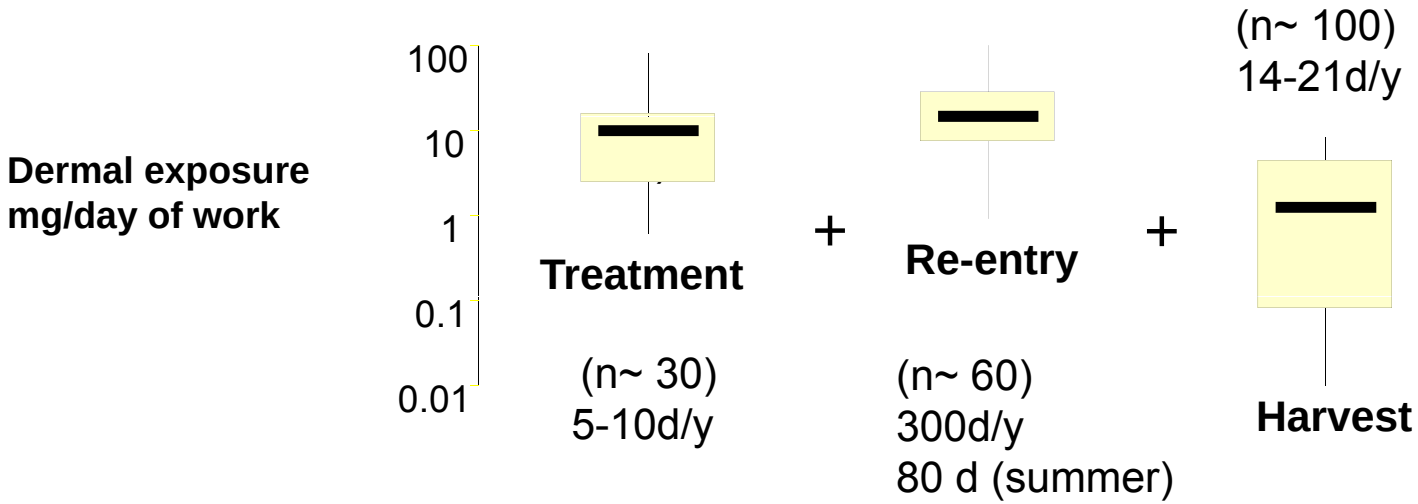


Levêque-Morlais et al. Int Arch Occup Environ Health 2014

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%**



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?)

Results on health: internal comparisons - 1

-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

…

Results on health: internal comparisons – 2
Lung cancers

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

- Agricultural activities at risk ?

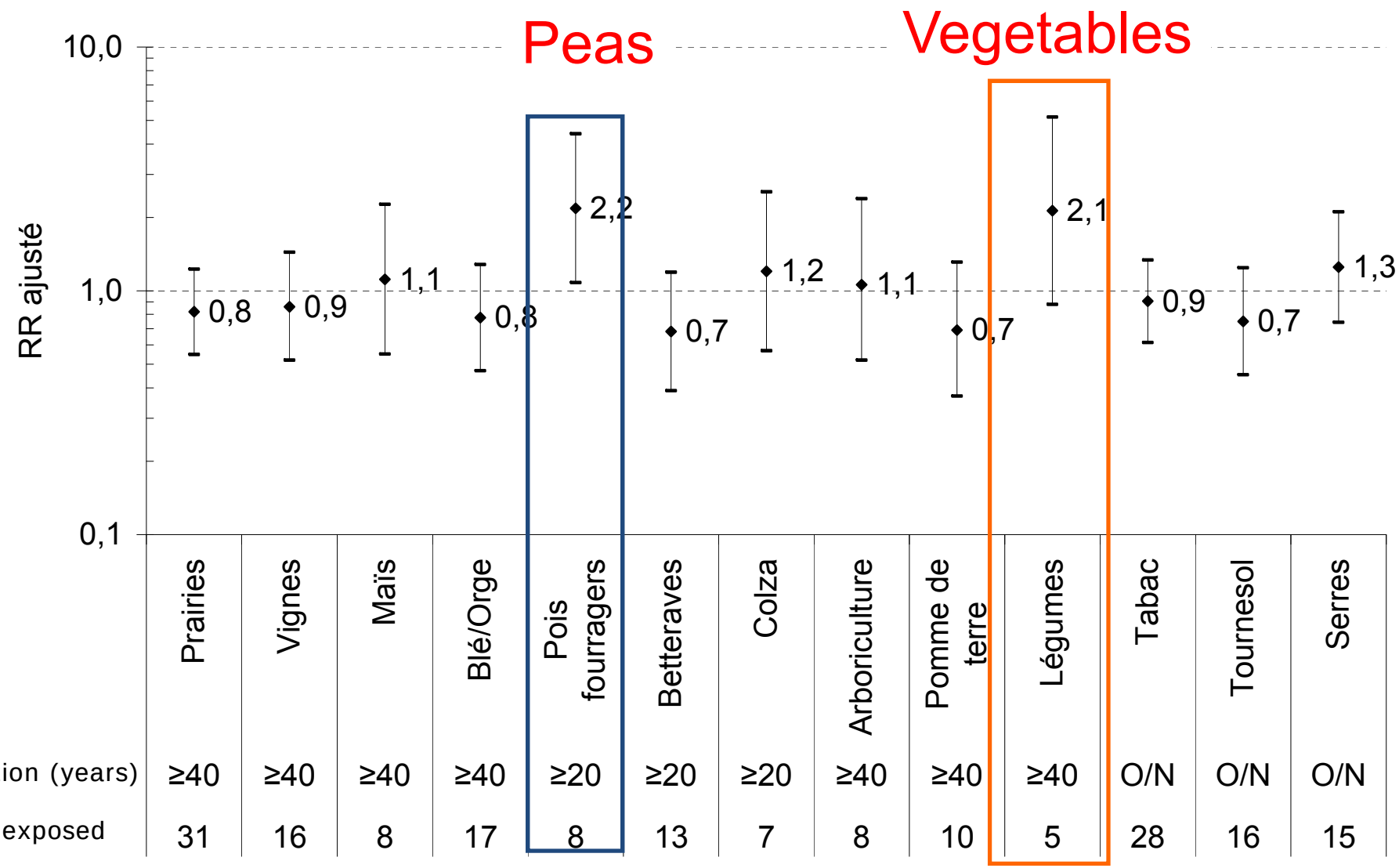
  Peas (harvest ?), fruit growing ? (cutting ?) vegetables (tasks ?)

- Agricultural activities with a decreased risk ?

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

Tual et al. In preparation (2015 ?)

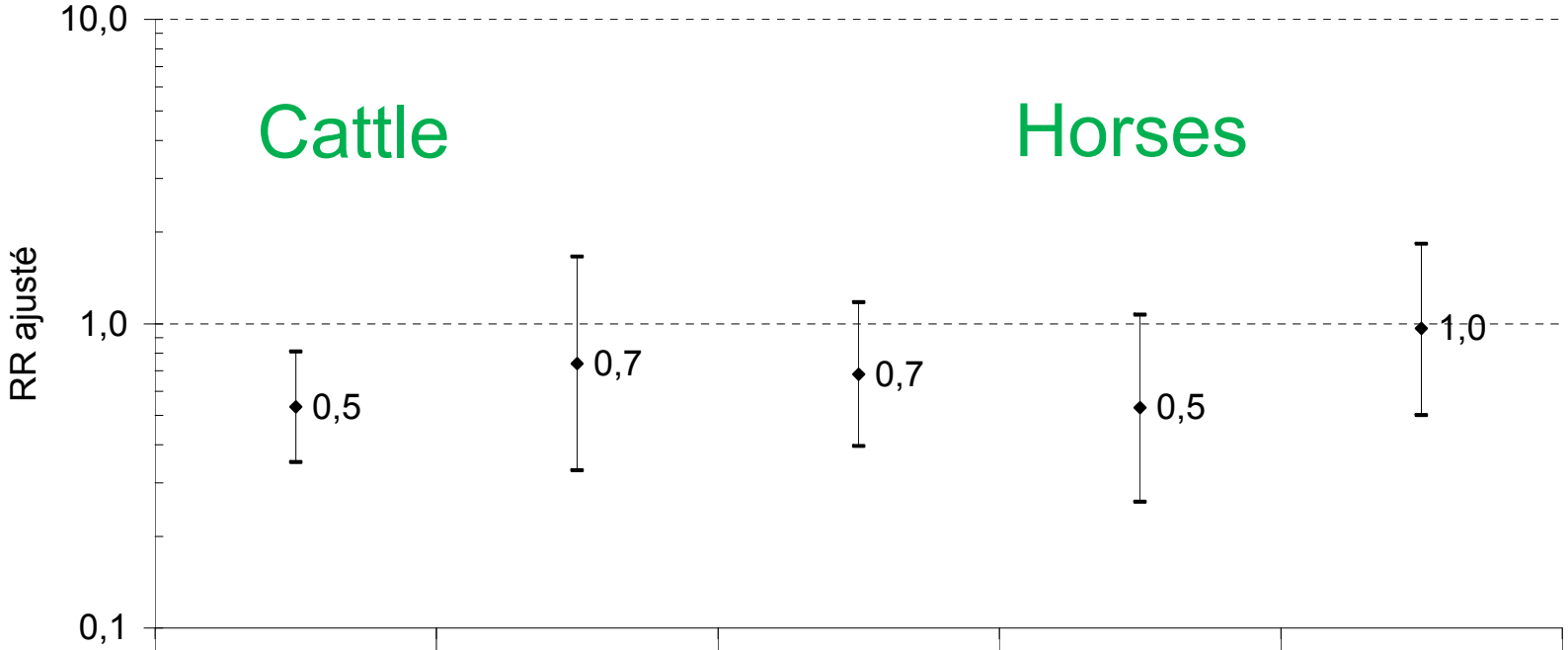
Results on health: internal comparisons – 3
Lung cancers



RR adjusted on smoking duration and age

Tual et al. In preparation (2015 ?)

Results on health: internal comparisons – 4
Lung cancers



	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

Tual et al. In preparation (2015 ?)

Results on health: internal comparisons – 5
Prostate cancers

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

- Agricultural activities at risk ?

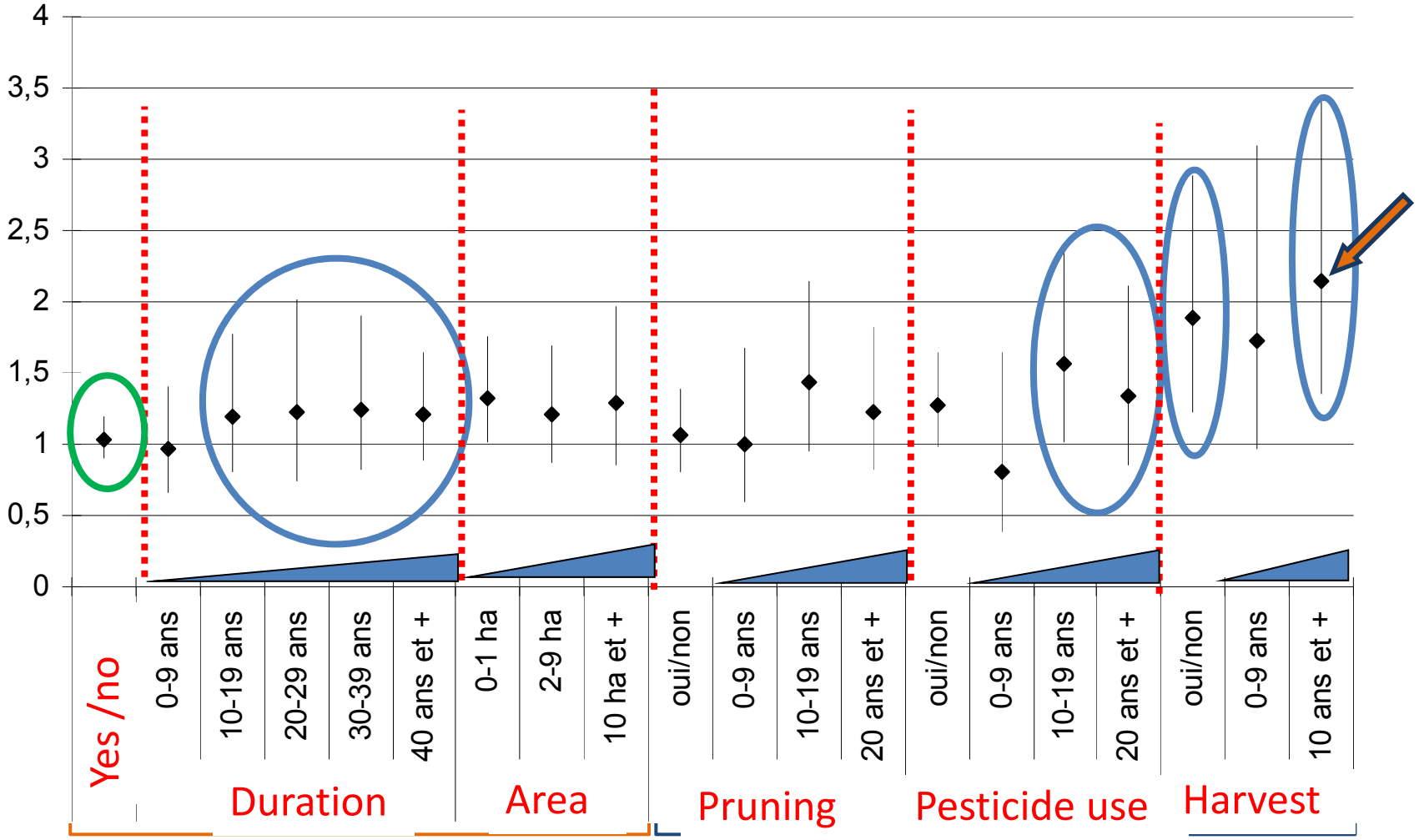
  Cattle growing (insecticide use ?), fruit growing (pesticides ? harvest ?) potatoes (pesticide use?), sunflower ? Tobacco production ?

- Agricultural activities with a decreased risk ?

  None

Lemarchand et al. In preparation (2015 ?)

Results on health: internal comparisons – 6
Prostate cancers – Fruit growing



RR adjusted on age

Lemarchand et al. In preparation (2015 ?)

= exposure

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…

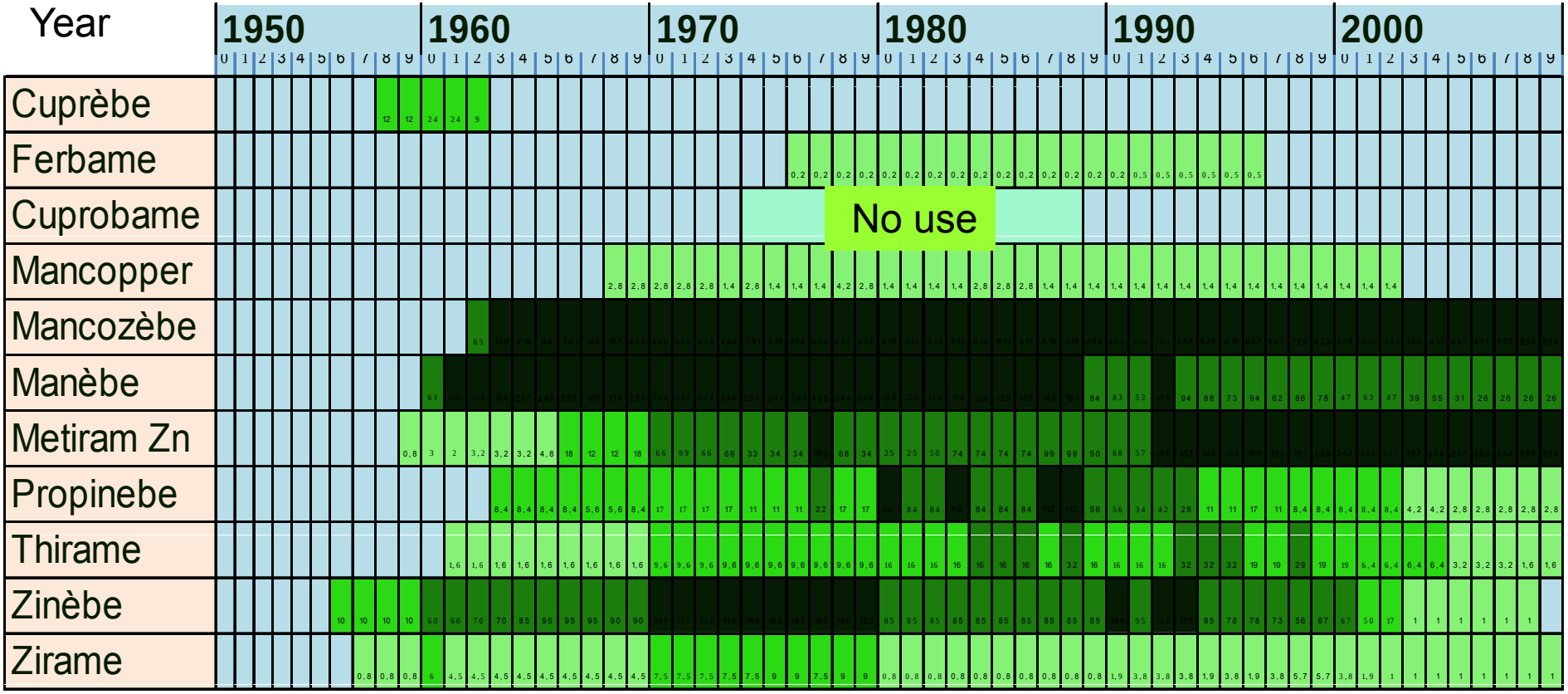
Strengths ?

- 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