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Occupational exposure to plant protection products: Health effects and challenges

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Forum Medizin & Umwelt – Landhaus Solothurn – 23 Mai 2019



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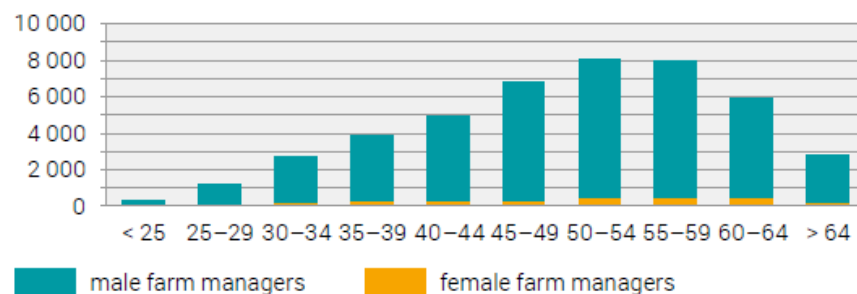
An overview of Swiss farming



Swiss farming

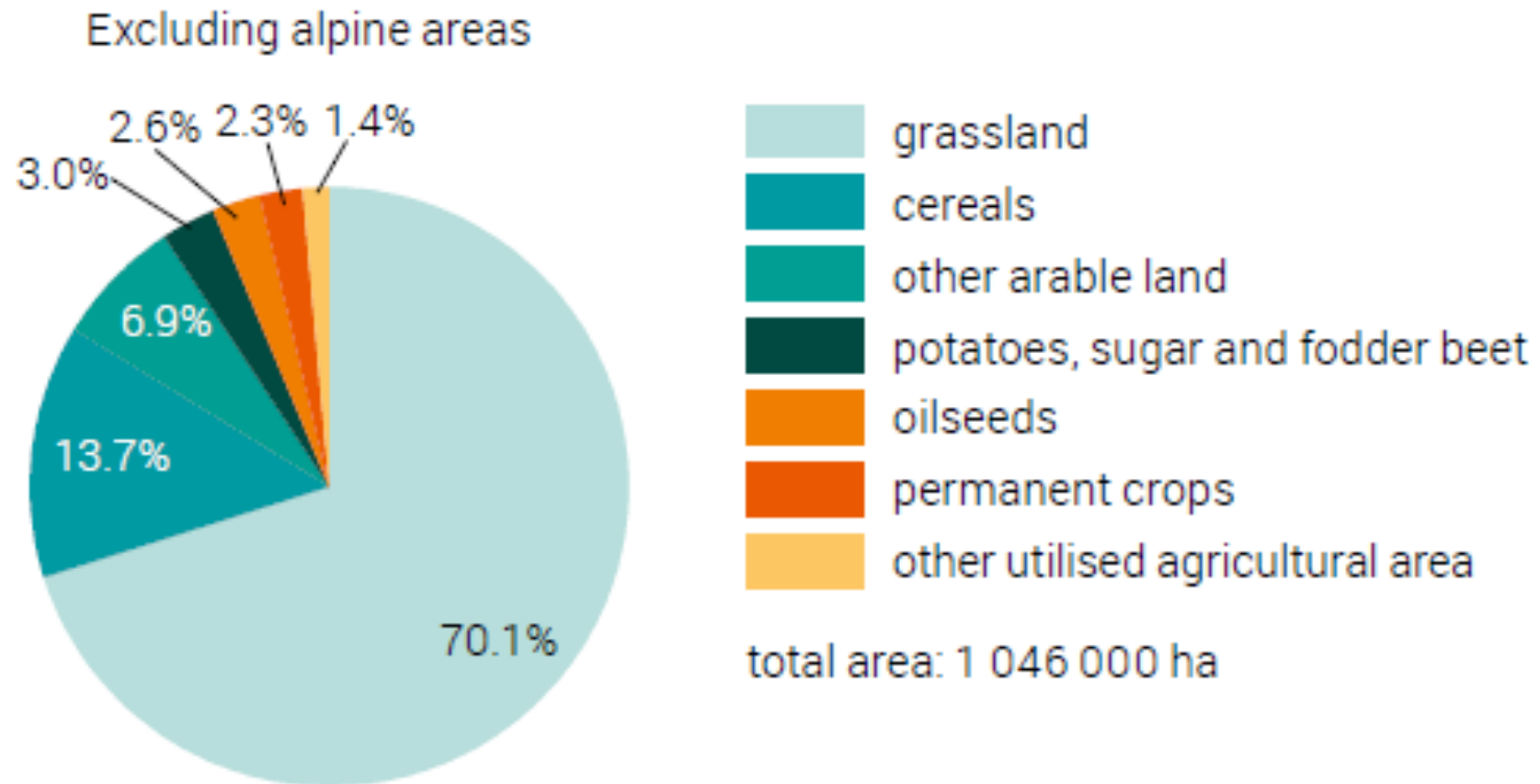
	2017	Organic farming
Number of farms	51'620	6'638 (12.9%)
Number of workers	153'864	20'590 (13.4%)
Agricultural area	1' 046'109 ha	151'404 ha (14.5%)
Agricultural area / farm	20 ha	23 ha
Average age of farm owners	52 years	-
Agricultural income / farm	64'300 CHF	-
Livestock farming	72%	-

Farm managers by age group¹, 2017



¹ Farm managers whose age is known (approx. 90%).

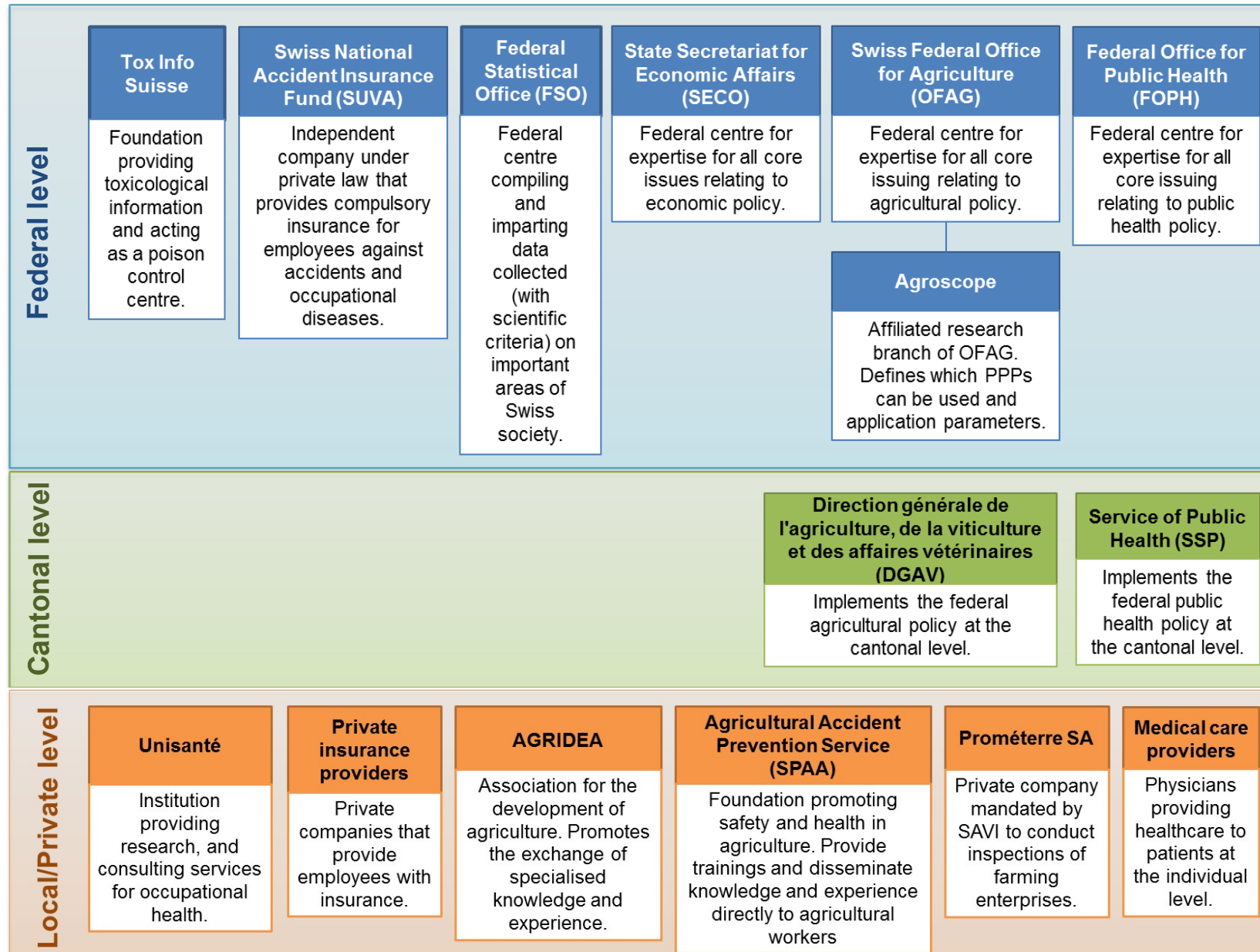
Use of utilized agricultural area (2017)



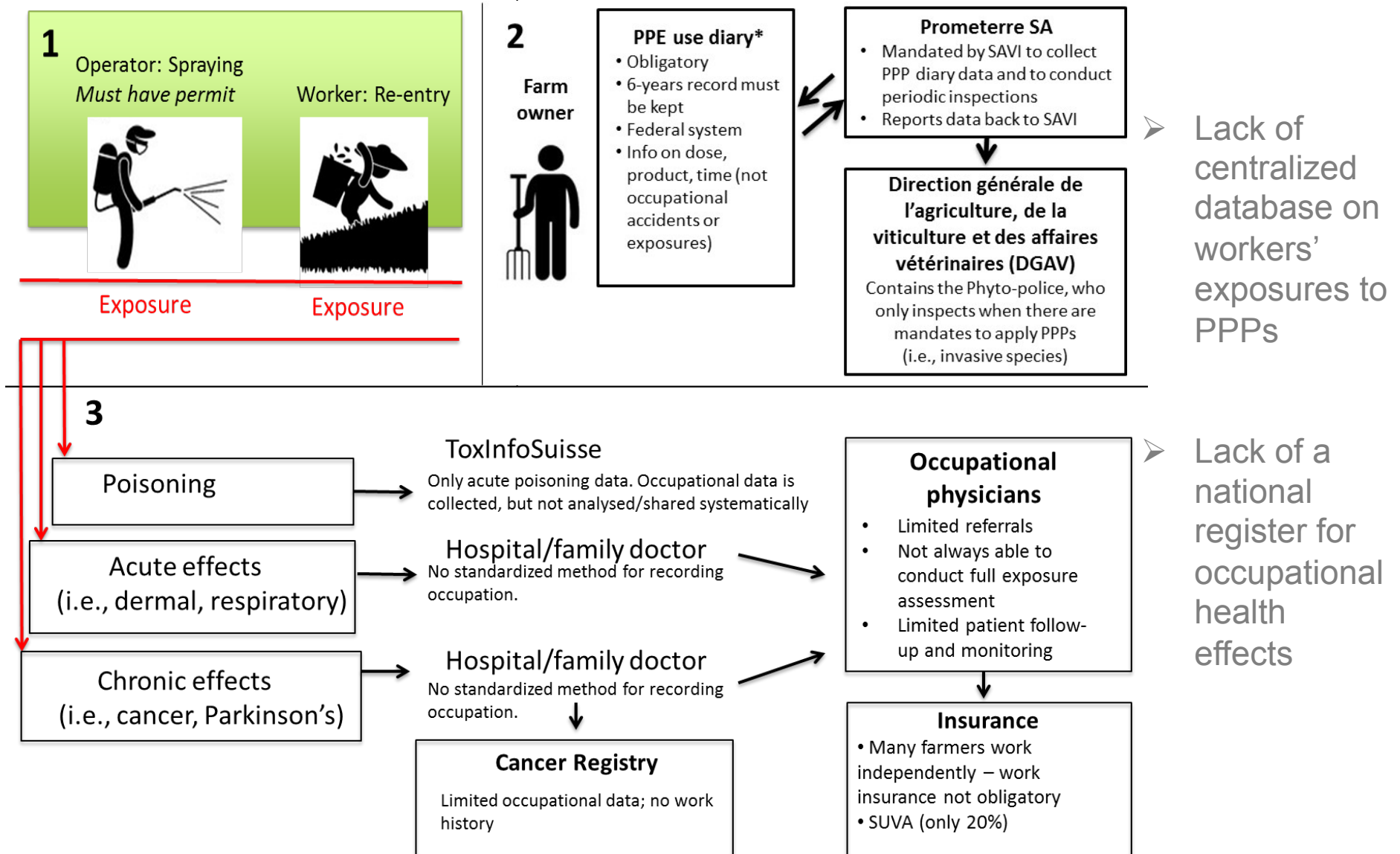
Health data and the Swiss system



Numerous stakeholders: lack of collaboration to share data



No health data center



Knowledge gaps

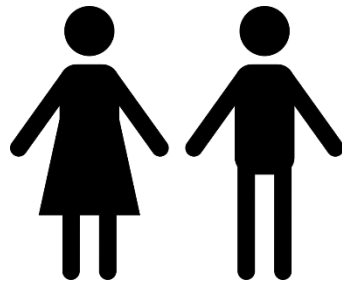
- 🍃 The lacuna of information:
 - 🌽 What are the incidence rates for pesticide-related disease among Swiss agricultural workers?
 - 🌽 How can we know if an occupational health risk exists among this population?
- 🍃 The potential reasons for the information gap:
 - 🌽 A neglect of workplace health indicators
 - 🌽 A problem of transparency and health information management
 - 🌽 A lack of connections between different health institutions regarding data sharing and monitoring

Occupational exposure to Plant protection products (PPPs)

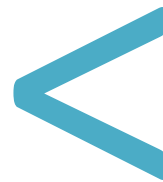


Pesticide exposure for the general population vs workers

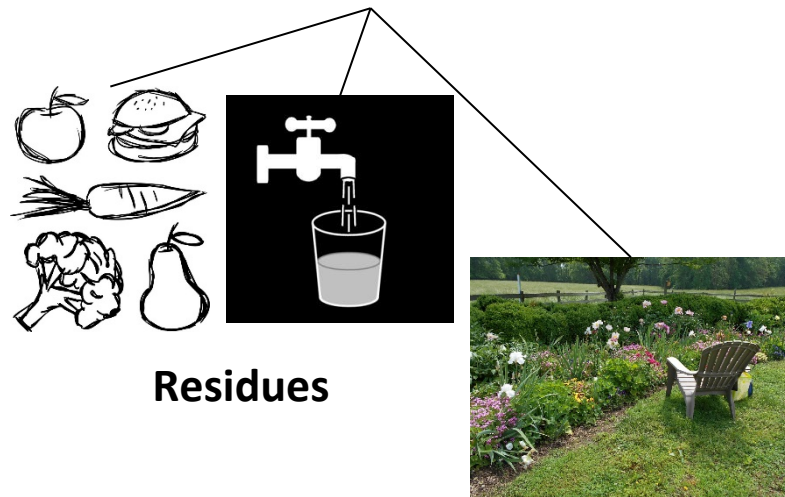
Exposure route:
≈ 90% dermal
≈ 10% inhalation



General population

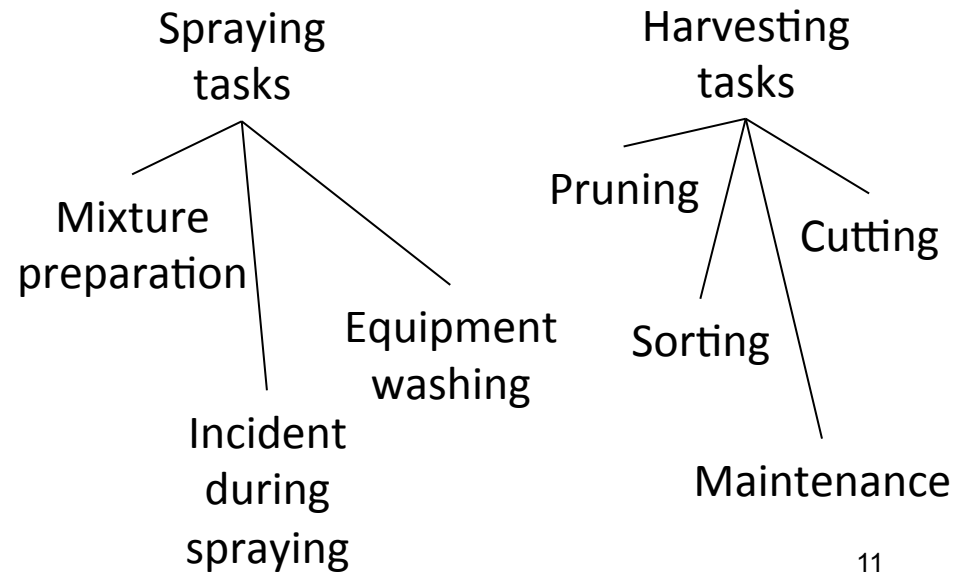


Workers



Residues

Bystanders



Highly exposed application tasks

A) Mixture preparation



Tasks: Storage room, weighing

Products: Powder, Liquid, Granule

Formulations: Active Ingredient (AI) + solvents, etc.



Tasks: Dilution, transfer to the tank, clean the material

B) Incidents during treatments / fill several times the tank



Tasks: Unblock/
Change spray nozzles



Tasks: Fill several times the tank depending on the material used to spray

C) Clean the treatment material and the personal protective equipment



SPAA 2018

Tasks: Clean all the material, the tank, PPE, remove working clothes

Highly exposed re-entry tasks

A) Crop Maintenance



Tasks : maintenance, cut, prune, sort, weed, etc.
Issues : Delay of ré-entry in the area after treatment, PPE

B) Plant sort



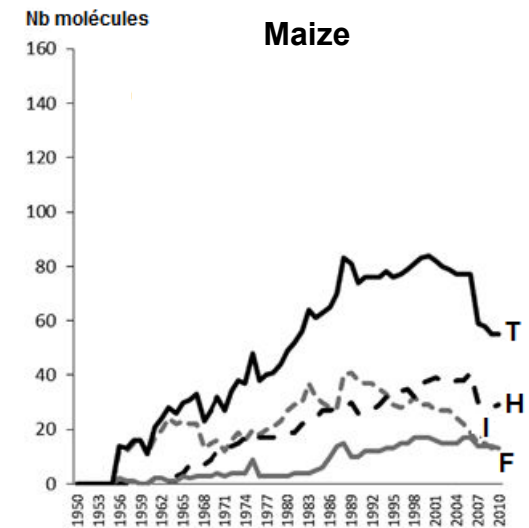
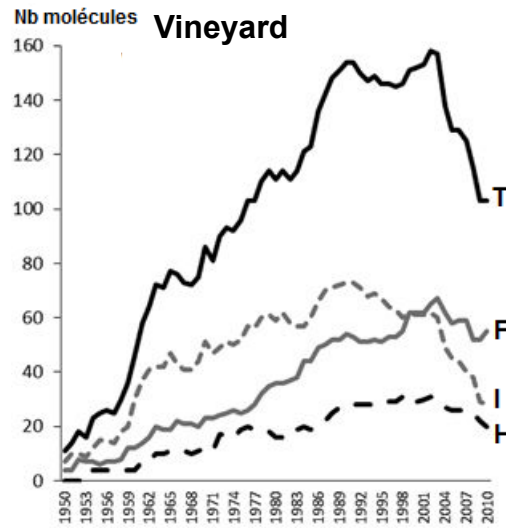
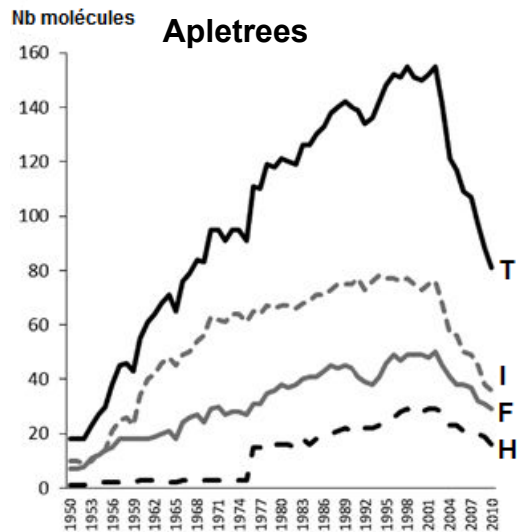
Tasks: Sort and remove weeds, verify the lack of diseases and/or pest

C) Harvesting, packaging



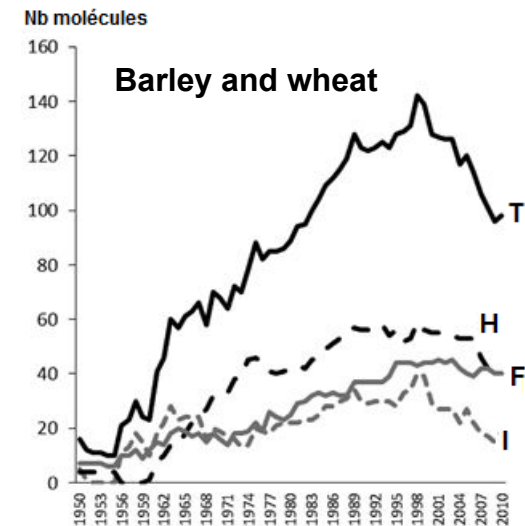
Tasks: harvest, sort, pack, etc.

Number of active substances used per year and per crop



Baldi et al. (2017) *Journal of Exposure Science and Environmental Epidemiology*

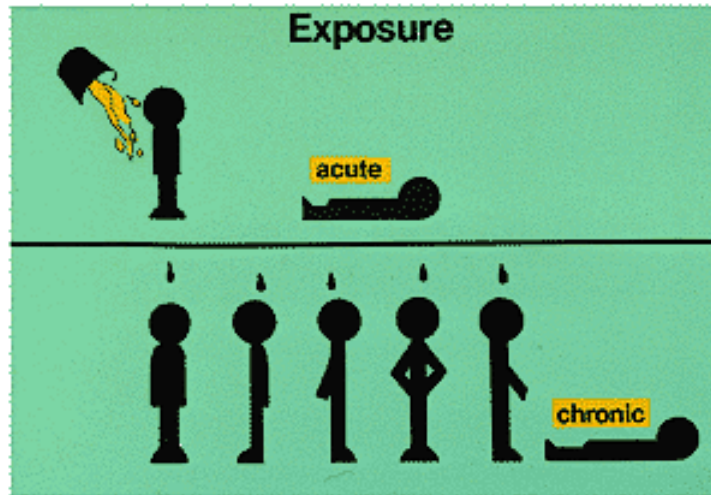
- 🍃 Multiple and repeated exposure
- 🍃 A large number of compounds
- 🍃 Lifetime exposure ...?



Potential health effects



Factors influencing toxicity



<https://popgreenland.wordpress.com/2016/12/12/negative-effects-related-to-pesticides/>

Generally well-known

Difficulty to link PPP exposure to specific health effects

Depend on the dose and route of absorption

Depend on chemical properties of compounds, metabolism, body distribution, ...

Exposure to mixture, other environmental toxicants, formulations, ...

Health effect types

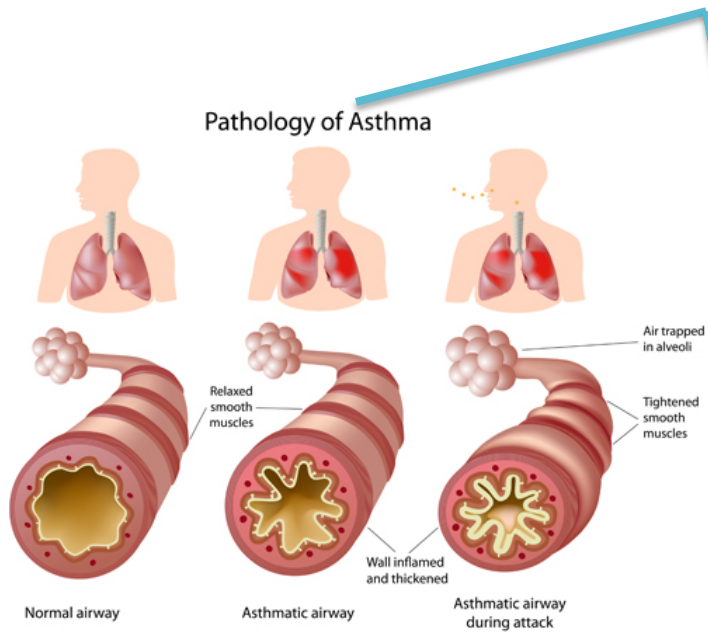


Acute, accidental poisonings : single and high dose

Acute/sub-chronic effects :
Dermal, respiratory

Chronic effects :
cancers,
neurodegenerative

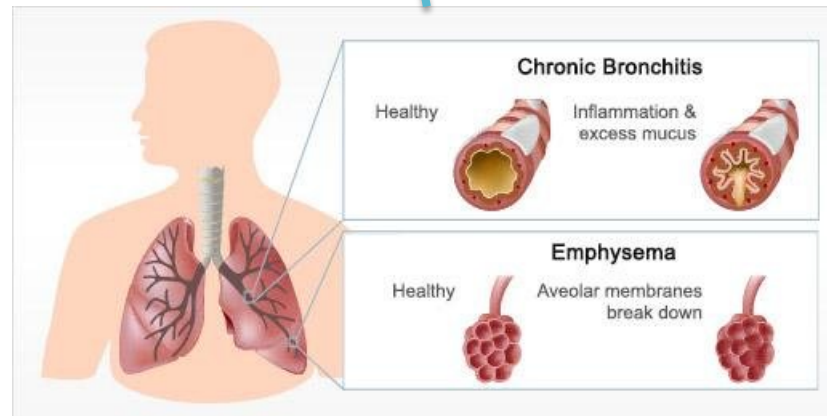
Respiratory and skin diseases



Irritation
(atopic dermatitis,
eczema, etc.)

Sensitization

Chemical burn



Chronic health effects: What do we know?



Epidemiology studies and cohorts: Limits

- Epidemiological studies have shown increasing evidence of a positive association between occupational exposure to PPPs and certain pathologies
- Significant challenge currently exists in regards to the interpretation of such studies, and the application of results into regulatory risk assessment
- Research is not often conducted with the aim to guide regulatory risk assessment. Prospective in nature – difficult to assess PPPs coming to the market, or that have recently entered

The agricultural cohorts around the world

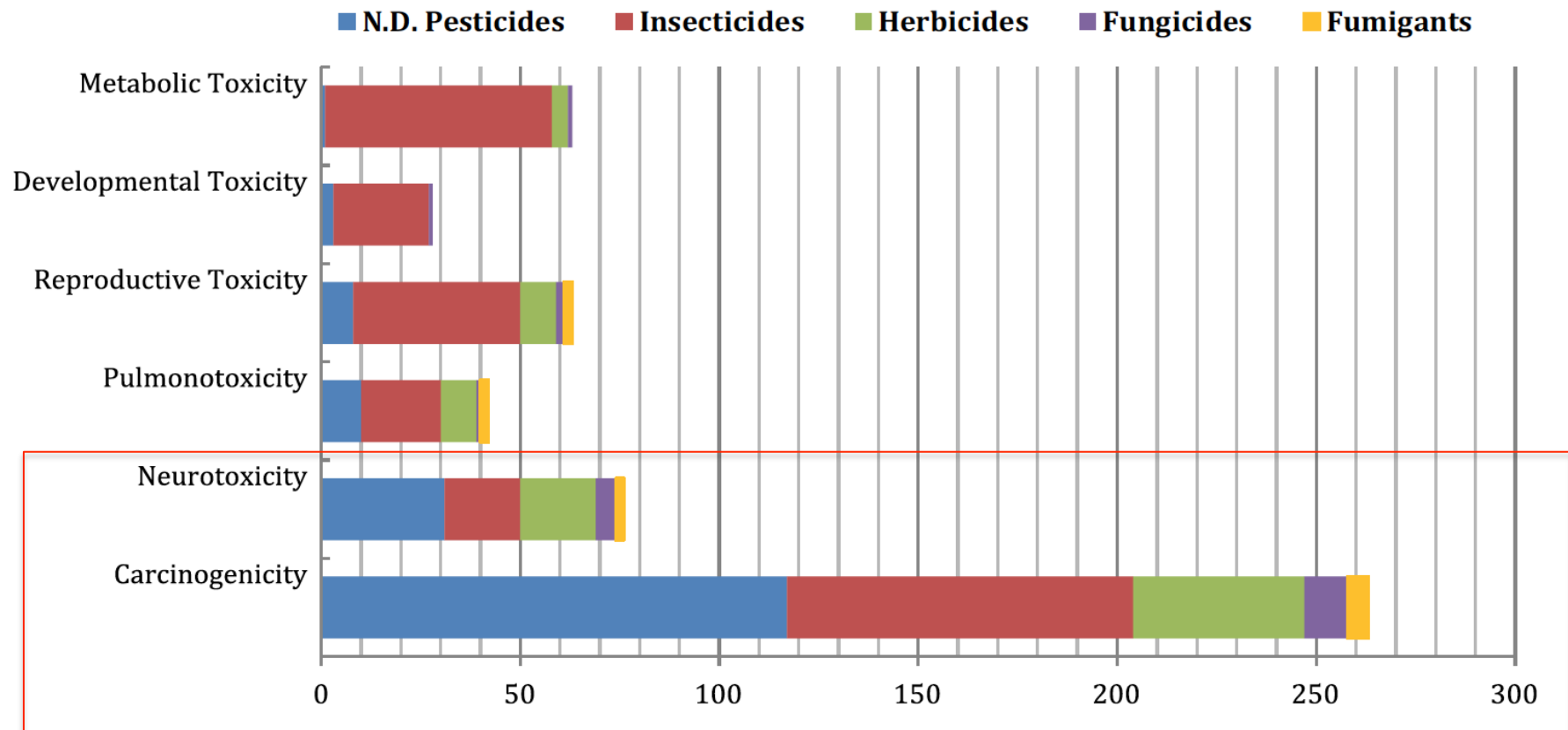
- 2010: the US National Cancer Institute and by the International Agency for Research on Cancer (IARC) initiated The Consortium for Agricultural Health Studies (AGRICOH). In 2016, 30 cohorts throughout the 5 continents
- 2013: European Food Safety Authority (EFSA) published a systematic review of all epidemiological studies published between 2006 and 2012
- 2013: the French National Institute of Health and Medical Research (INSERM) released a systematic literature review on the human health effects of PPP exposure, analyzing epidemiological and toxicological data published up to 2012, on specified health outcomes

Main outcomes from these cohorts

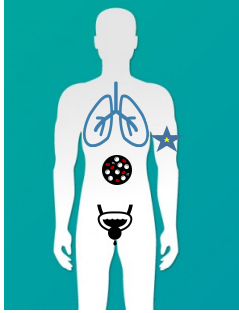
- It is accepted that agricultural populations present lower rates of mortality, for the main causes of death (cancer overall, cardiovascular diseases)
 - However, the analysis of the relationships of exposures and outcomes, protective actors, and risk factors showed:
Healthy worker effect and Overall healthier lifestyle
 - The healthy worker effect : self-selection of healthy workers into physically strenuous occupational such as farming and of unhealthy workers out (hypothesis since the 1980s)
 - Healthier lifestyle : decreased smoking (50% less), less alcohol consumption, more exercise, and healthier diet
- => ↓ risk cardiovascular diseases and some cancers (lung, bladder, pancreas, colon and rectum)

However, distinct chronic disease trends: Broad literature review

Mostafalou and Abdollahi (2017)



Schematic diagram showing the weight of evidence on the toxicities of pesticides.
Horizontal axis legend = Number of significant associations.



Presumption of associations between occupational exposure and health effects

Results from prospective cohort studies revealed that agricultural workers have an increased risk for:

- 8 cancer sites (Non-Hodgkin lymphoma, leukemia, lymphoma, multiple myeloma, prostate, testis, brain, melanoma)
- 3 neurodegenerative diseases (Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis)
- Cognitive or depressive disorders
- Effects on reproductive function (fertility, pregnancy and child development)

Strong presumptions of associations

Health outcome	Population with significant risk excess	Presumption strength	Numbers of analyzed studies
Parkinson's disease	Occupational and non-occupational exposure	++	7 meta-analysis + 1 prospective cohort
NHL	Farmers, operators, manufacturing plant personnel	++	6 meta-analysis + 1 prospective cohort
Multiple myeloma	Farmers, operators	++	6 meta-analysis + 2 prospective cohorts
Prostate cancer	Farmers, operators, manufacturing plant personnel	++	1 meta-analysis (2012, including 46 studies))

Institut national de la santé et de la recherche médicale (INSERM, 2013)

++: hypothesis supported by 3 mechanisms of toxicity (metabolism, mode of action, molecular pathways)

Moderate presumptions of associations

Health outcome	Population with significant risk excess	Presumption strength	Numbers of analyzed studies
Leukemia	Farmers, operators, manufacturing plant personnel	+	7 meta-analysis + 1 prospective cohort
Alzheimer's disease	Farmers	+	3 prospective cohorts
Cognitive disorders	Farmers	+	1 meta-analysis (>40 studies; mainly on OP insecticides)
Fertility and fecundability disorders	Occupational exposure	+	Several transversal studies

INSERM (2013)

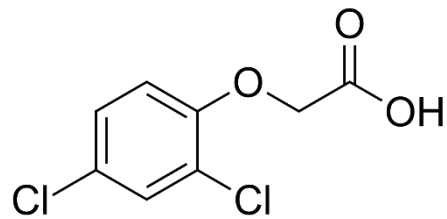
+ : hypothesis supported by at least one mechanism of toxicity (metabolism, mode of action, molecular pathways)

Weak presumptions of associations

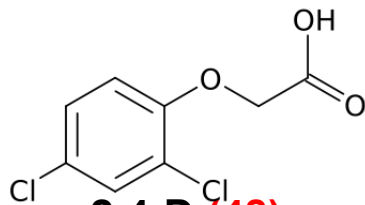
Health outcome	Population with significant risk excess	Presumption strength	Numbers of analyzed studies
Hodgkin lymphoma	Agricultural workers	±	4 meta-analysis + 1 prospective cohort
Testicular cancer	Agricultural workers	±	2 meta-analysis + several cohort studies + 1 case-control study
Brain cancer (glioma, meningioma)	Agricultural workers	±	3 meta-analysis + cohort studies + transversal studies
Melanoma	Agricultural workers	±	2 meta-analysis + several cohort studies + 1 case-control study
Amyotrophic lateral sclerosis	Farmers	±	2 meta-analysis
Anxiety, depression	Farmers, farmers with a history of acute poisoning, operators	±	1 case-control study + several transversal studies (mainly on OP insecticides)

Weak to moderate association with chronic health effects for 6 substances (number of formulations allowed in Switzerland)

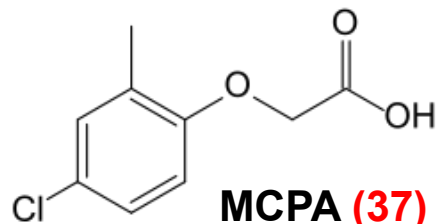
HERBICIDES



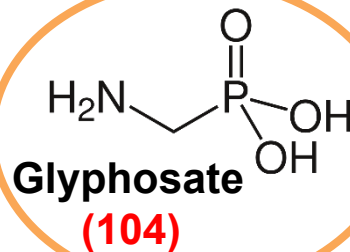
Mecoprop
(49)



2,4-D (48)



MCPA (37)
(2-methyl-4-chlorophenoxyacetic acid)



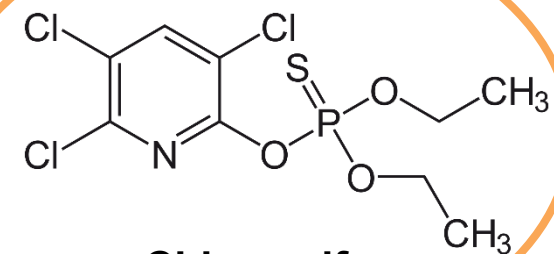
Glyphosate
(104)

NHL
(moderate)

Parkinson's disease
(weak)

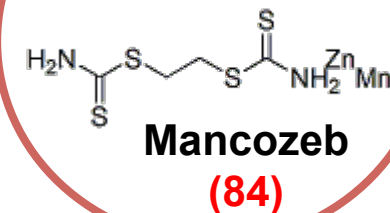
Hematopoietic cancers

INSECTICIDE



Chlorpyrifos
(15)

FUNGICIDE

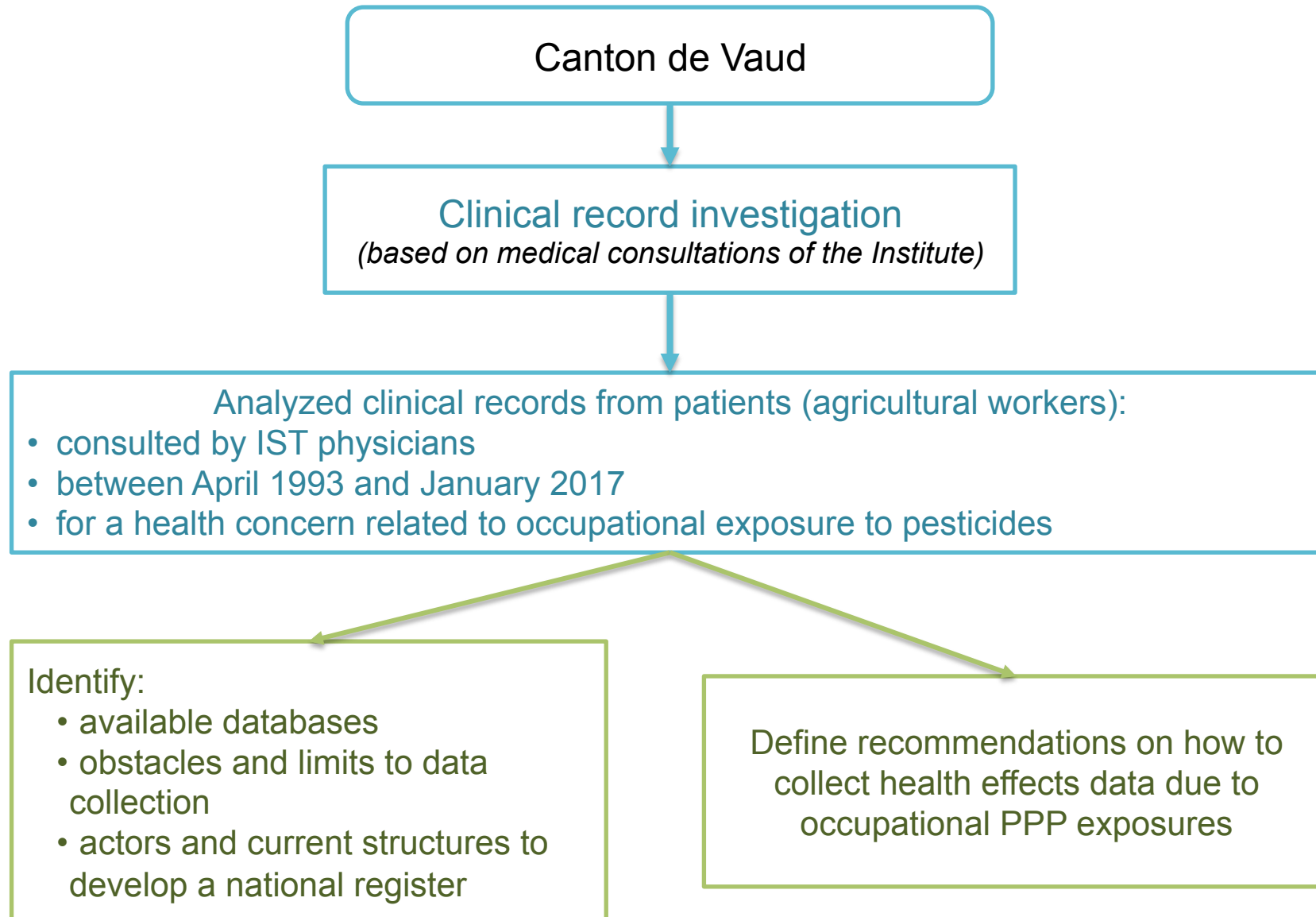


Mancozeb
(84)

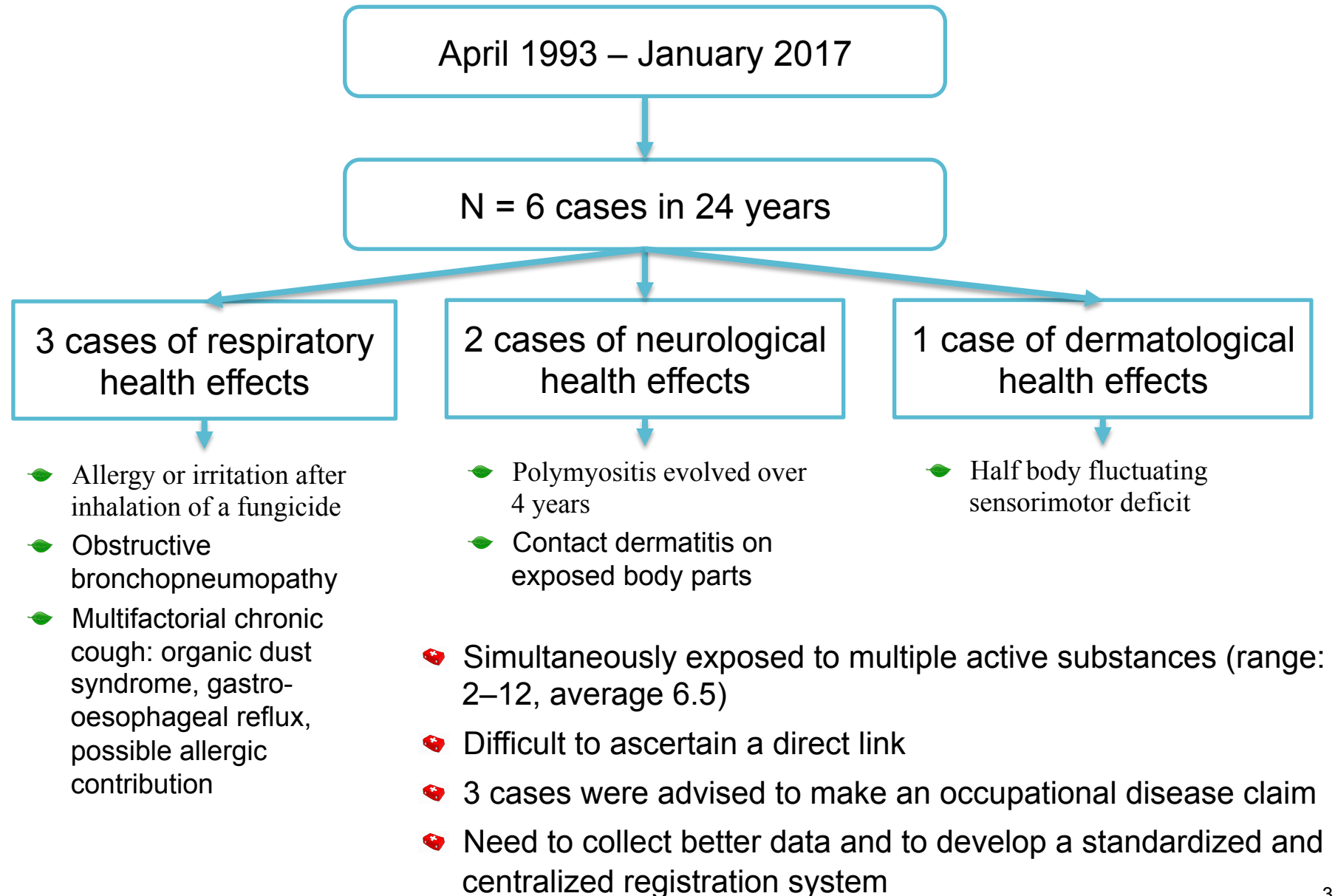
Exploratory data research for the canton of Vaud



Methodology



Clinical records



Conclusion



Limited data and 5 potential toxic substances

- Significant lack of data on the situation in Switzerland for occupational pesticide exposures and resulting health effects. Nevertheless, evidence from international studies provide a foundation of knowledge that can be applied for future investigations (e.g., pharmacovigilance programs)
- At least five active substances currently authorized and used in Switzerland that have a demonstrated moderate or strong association with chronic health effects



Extrapolation is not always suitable. The context and exposure data have to be considered!

Specific chronic diseases and increased risk to develop Parkinson's Disease

- Although the general health status of agricultural workers appears to be better than comparison populations, their occupational health appears to show distinct patterns of chronic disease trends.
 - Increased risk for PD, prostate cancer, Non-Hodgkin lymphoma, and multiple myeloma
- There is strong evidence in favour of a generic link between occupational exposure to pesticides and Parkinson's Disease (PD). Exposure to any pesticide involves a $\geq 50\%$ increased risk for developing PD

Recommendations: What do we need to do?



Improve health and safety for Swiss PPP users

- Exploit existing data sources to enhance knowledge on exposures
- Develop epidemiological research studies on pesticide-related health effects
- Emphasize occupational health among medical professionals
- Increase collaboration among stakeholders
- Increase focus on preventing chronic disease (described with a presumption link to pesticide exposures) and on monitoring the progression

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Thank you for your attention

Graczyk H, Hopf NB, Mediouni Z, Guseva-Canu I, Sanvido O, Schmid K,
Berthet A.

*Occupational exposure to plant protection products and health effects in
Switzerland: what do we know and what do we need to do?*

Swiss Med. Wkly. 2018, 48:w14610

