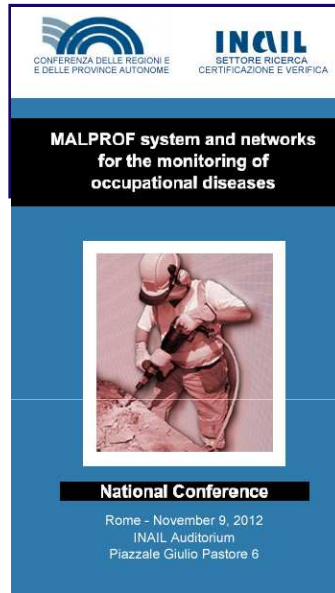



MALPROF / INAIL Conference – Rome, 9th November 2012



CONFEDERAZIONE DELLE REGIONI E DELLE PROVINCE AUTONOME

INAIL
SETTORE RICERCA
CERTIFICAZIONE E VERIFICA

**MALPROF system and networks
for the monitoring of
occupational diseases**



National Conference
Rome - November 9, 2012
INAIL Auditorium
Piazzale Giulio Pastore 6

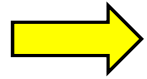
Searching for *NEW* occupational diseases (OD) with a dual approach: clinical watch system & data mining analyses

Vincent Bonneterre, on behalf of the RNV3P and MODERNET



MODERNET
Monitoring trends in Occupational Diseases
and new and Emerging occupation Risks

What are new Occupational Diseases? (1/2)



1/ New « disease x exposure » couples

- **SPAIN & ALGERIA 1992** : Ardystil syndrom or « textile sprayer's lung »: 15 cases of interstitial lung diseases in textile printing (7 death). related to spraying Acramin-FWN (polyamidamine)
 - First publications in Spanish : 1994-1995, first publication in English : Thorax 1996; 51(1):94-5 / Eur Respir J 1998;11:265-71 / Eur Respir J 1999;13:940-1

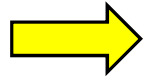
 - **USA 1997-8** : Nylon flock Workers Lung Disease
 - Kern. Ann Intern Med 1998;129:261-272 // Eschenbacher. Am J Respir Crit Care Med 1999, 159, 2003-8 // Kern. Chest 2000,117, 1,251-9

 - **USA 2002**: Bronchiolitis obliterans in popcorn-factory workers
 - NJEM 2002;347:1980-82 / JOEM 2002;44:216-218

 - **JAPAN 2003** : Interstitial pulmonary disorders in indium-processing workers (Indium Tin Oxide ITO)
 - *Eur Respir J* 2005;25(1):200-4 // *Eur Respir J* 2007, 29:317-324

 - **USA 2007**: Progressive inflammatory neuropathy among swine slaughterhouse.
 - CDC MMWR 2008;57:122-124
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What are new Occupational Diseases? (2/2)



2/ New « disease x exposure x *occupational setting* » associations...

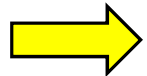
= « Old friends in *new places* » (Axel Wannag)

- USA 2009: Angiosarcoma of the liver in hairdressers and barbers due to former use of vinyl chloride propellant in hair spray
 - Infante PF. Int J Occup Environ Health. 2009;15(1):36-42.

 - SPAIN, ITALY, FRANCE 2009: Occupational asthma IgE mediated due to *Chrysonilia sitophila* in coffee industry.
 - S : Monzón S et al. Allergy. 2009;64(11):1686-7
 - I : Heffler E. Ann Allergy Asthma Immunol. 2009;102(2):168-9
 - F : Francuz. Clinical and Vaccine Immunology, Oct 2010:1645-46
-

What can be said about new OD highlighting?

- These kind of examples are not thought to be identified by compensation schemes as these ones produce data about a limited list of OD after scientific and social consensus
- **Historically**, new OD were first highlighted by organ-specialists physicians /surgeons... or workers themselves



1. There is a need to organise a VIGILANCE system for Occupational Diseases = system trying to capture potential new cases, assess their relevance, and disseminate the information, accordingly to the level of proof, severity of the disease, public health concern, etc.
2. Now that Occupational Medicine is well developed -and that OD specialists and OD centres exist- it's our responsibility to build such a system

What about Vigilance in other health fields?

- Ex: Pharmacovigilance

- developed at national and international levels
 - *a priori evaluation* of drug side-effects (pre-marketing studies, including human data)
 - *a post-marketing surveillance system* (spontaneous reporting of adverse effects)
 - experts forums to discuss issues identified as raising concerns
 - data mining tools trying to highlight early « Signals » ... also used in toxicovigilance
 - *SIGNALS = « reported information on a possible relationship between an adverse event and a drug, of which the relationship is unknown or incompletely documented previously » (WHO)*
-

To start building a EU-wide OD vigilance system is one of « Modernet » aims

Modernet? (cf presentation of action's Chair: Raymond Agius)

- « Monitoring OD and new Emerging Risks NETwork »
- Primarily collaborative network of OD centres and academic centres involved in research on OD. Extended to participants of 16 countries thanks to a EU-COST funding
- « Disease first approach »

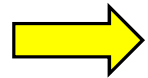
How? – By identifying « early signals » from

1. Clinical watch system
2. Data mining tools

... and assessing their relevance with common expertise

Clinical Watch system

- Such a system has recently been built in France from the network of OD centres (rnv3p)
 - Several cases described
 - ALERT: asthma x bronchitis related to formaldehyde among hairdressers using some « brasilian smoothing » products)
 - 2 in progress (Extrinsic alveolitis in a manicurist exposed to EMA, Asthma and coffee machines maintenance workers (mold *Chrysonilia sitophilia*)
 - Other discussed
- Several discussed at Modernet level
 - + decision to have higher sensibility for Nanoparticles and endocrine disruptors



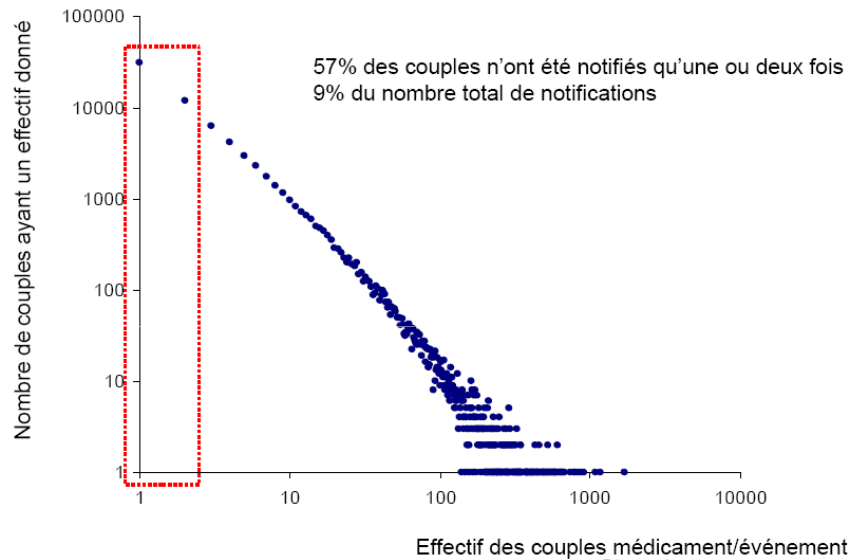
You might be the first physicians to face these cases and raise the hypothesis of work-relatedness. Take contact with one of the Italian OD specialist members of Modernet (Claudio Colosio, Stefano Mattioli, Pierrluigi Cocco) + MALPROF

Data Mining?

- = to systematically mine **already existing databases** that might capture these cases trying to identify early signals about potentially new OD, not otherwise identified
 - Especially look at new associations...
 - Disease x exposure // Disease x occupation // Disease x activity sector
 - Disease x exposure x occupation... etc
 - That might be reported only a few times
 - And which are generating a signal of disproportionality in the database
-

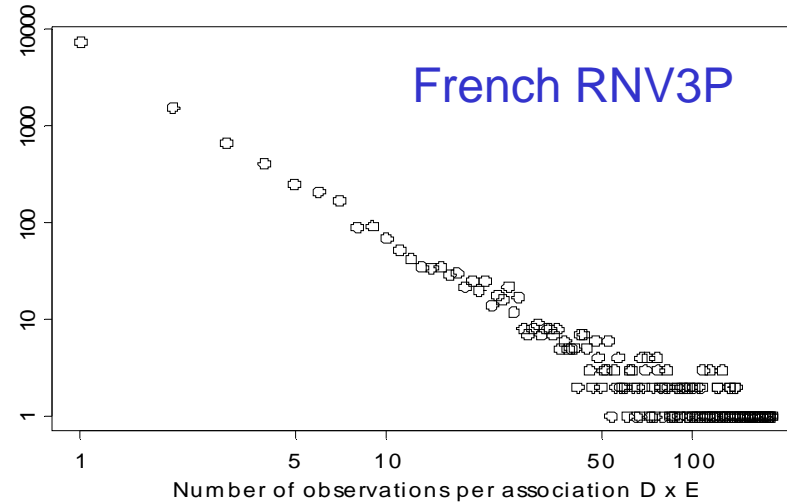
How frequently are associations reported in these databases?

French Pharmacovigilance database

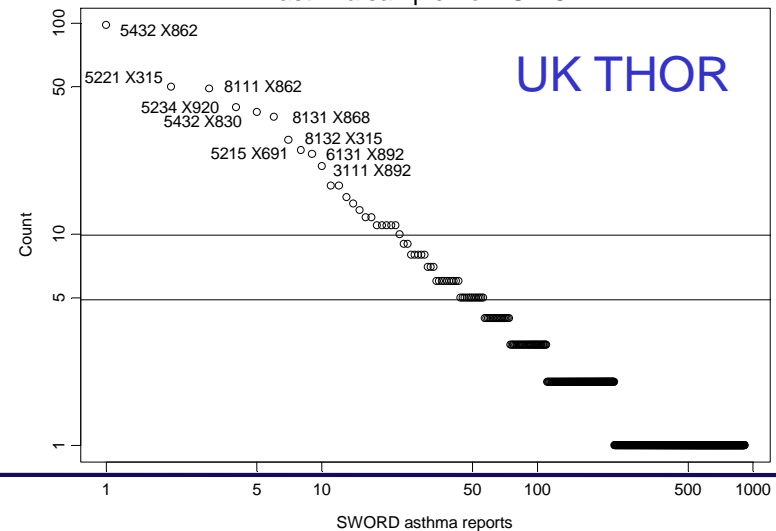


Shall we search also for any useful information in these low-reported associations? Why? How? What kind of results could be expected?

D x E associations according to their number of observations



Counts of the (Occupations x Agents) associations in asthma sample from SWORD

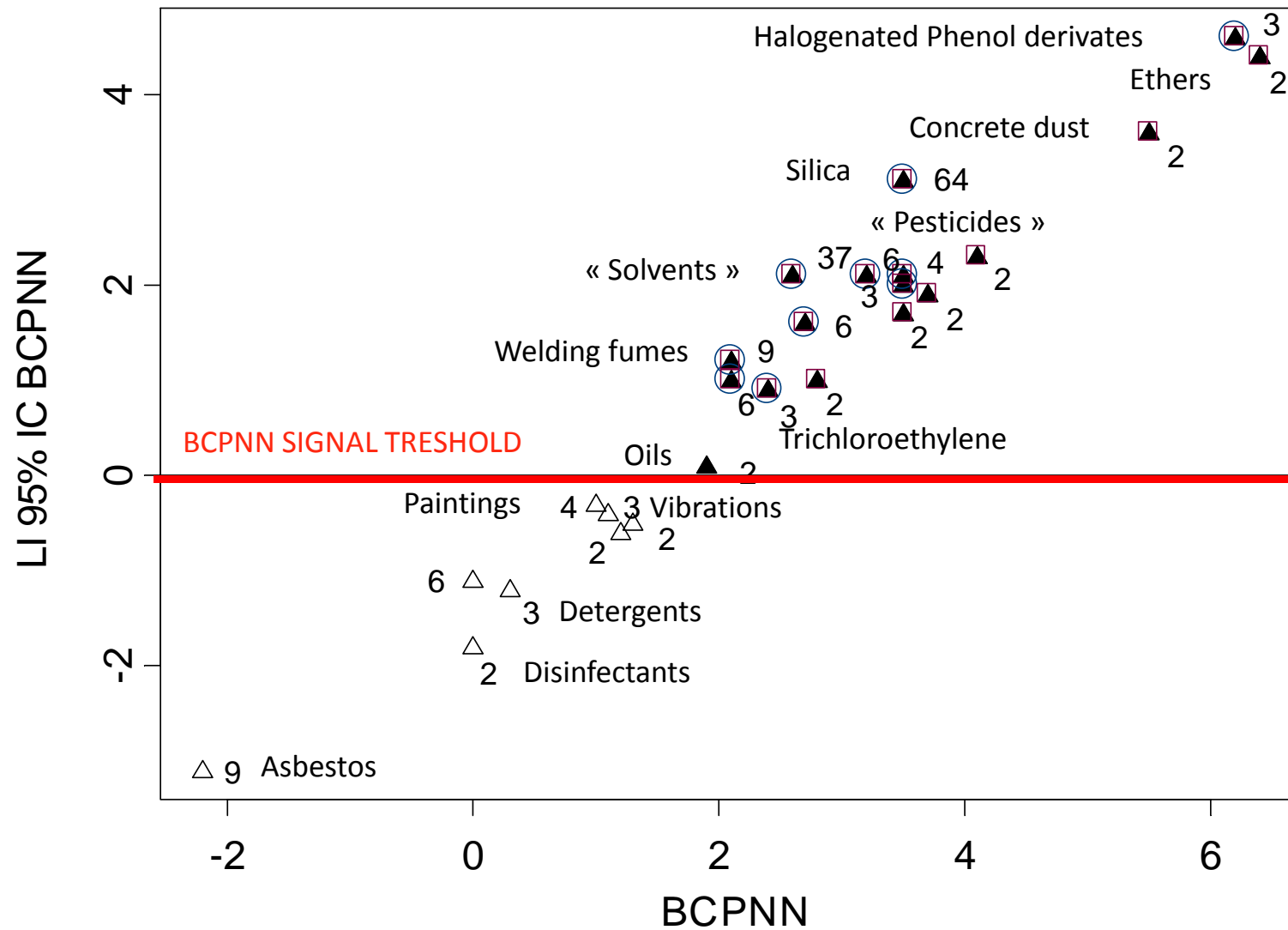


What kind of information are we supposed to find?

False positive: Wrong codes use, bias in referrals,... ☹️

might be interesting for quality procedures, but it is not our objective yet

- Unique situations in unique workplaces 😊
 - Potentially interesting for a detailed knowledge, or case-reports, but not to be prioritized for preventive purposes
 - **New occupational situation at risk** 😊
 - Before being reported about ten times, a new situation at risk (ex for asthma) will be reported once or twice: **We might find clues about early interesting signals we would like to identify**, which would help save months or years to identify such a situation, make early warning about it, and take preventive steps.
 - Need to integrate the time (and geographical) dimensions
-



RNV3P DATA. “Systemic Scleroderma (ICD10 “M34” as main diagnosis) x Exposure” associations reported twice ore more, their number of reports, their BCPNN measures whether they generate a signal (solid triangles) or not (empty triangles), and overlap with PRR signals (PRR1 in blue circles and PRR2 in red squares).

Hypotheses generation is just the beginning...

Later on, evidence contained in a signal will depend from :

- Quantitative strength of the association
- Most of all, by other data assessed by experts ++:
 - Consistency of the exposure-response relationship
 - Biological plausibility
 - Experimental findings
 - Possible analogies
 - Nature & Quality of the Data

Bonneterre et al. [Sh@w](#) 2012;3:92-100. [Occup Environ Med](#) 2010 ;67(3):178-186; [Occup Environ Med](#) 2008 ; 65(1):32-7

Conclusion: motivation within Modernet to start building a vigilance system dedicated to the capture of early signals regarding new OD

SCENHIR « 8 reasons for past failure »

« There are a number of reasons why an emerging issue was not identified at an appropriate time or its potential effects were not properly considered, namely: »

- 1. Inadequate monitoring/surveillance resulting in a failure to detect the presence of a disease and/or agent at an early stage.*
- 2. Failure to make important relevant information available to the risk assessors/risk managers.*