Cleaning agents and disinfectants as irritants and sensitizers

(including in swimming pools)

- Catalysing the discussion -

Raymond Agius, Melanie Carder, Louise Hussey, Martin Seed

Centre for Occupational & Environmental Health

The University of Manchester

http://www.medicine.manchester.ac.uk/oeh/thor

6th Jack Pepys workshop

Toronto, Canada

Friday 13th May 2016

Cleaning agents and disinfectants as irritants and sensitizers

(including in swimming pools)

Objectives:

- To share UK epidemiologic data derived from clinical practice showing the reported magnitude of the problem

- To present a simple chemical taxonomy, to help in the classification of causes, understanding of mechanisms and potential for prevention

- To explore whether 'Structure Activity Relationships' may help categorise the agents into those which are 'classical' sensitisers and others presumably 'irritant' in character

Some UK data from
## The Health and Occupation Research network (THOR):

SWORD: chest physicians

OPRA: occupational physicians

Notes:

- Data from specialists is usually from the 'apex' of the surveillance pyramid and are therefore likely to under-estimate the incidence when compared to population based surveys

- The data may be biased e.g. towards cases perceived to be more severe, or requiring special investigation

- Data from occupational physicians show a higher incidence rate but the denominator is very patchy (e.g. most of health care, no beauticians)

- Data are as yet unpublished – happy to share in the workshop, Outwith the workshop for the next five slides you can quote **the bold underlined 'take home' text**

Number of actual cases of work-related respiratory disease attributed to cleaning agents, reported by chest physicians to SWORD (1989-2015) and occupational physicians to OPRA (1996-2015)
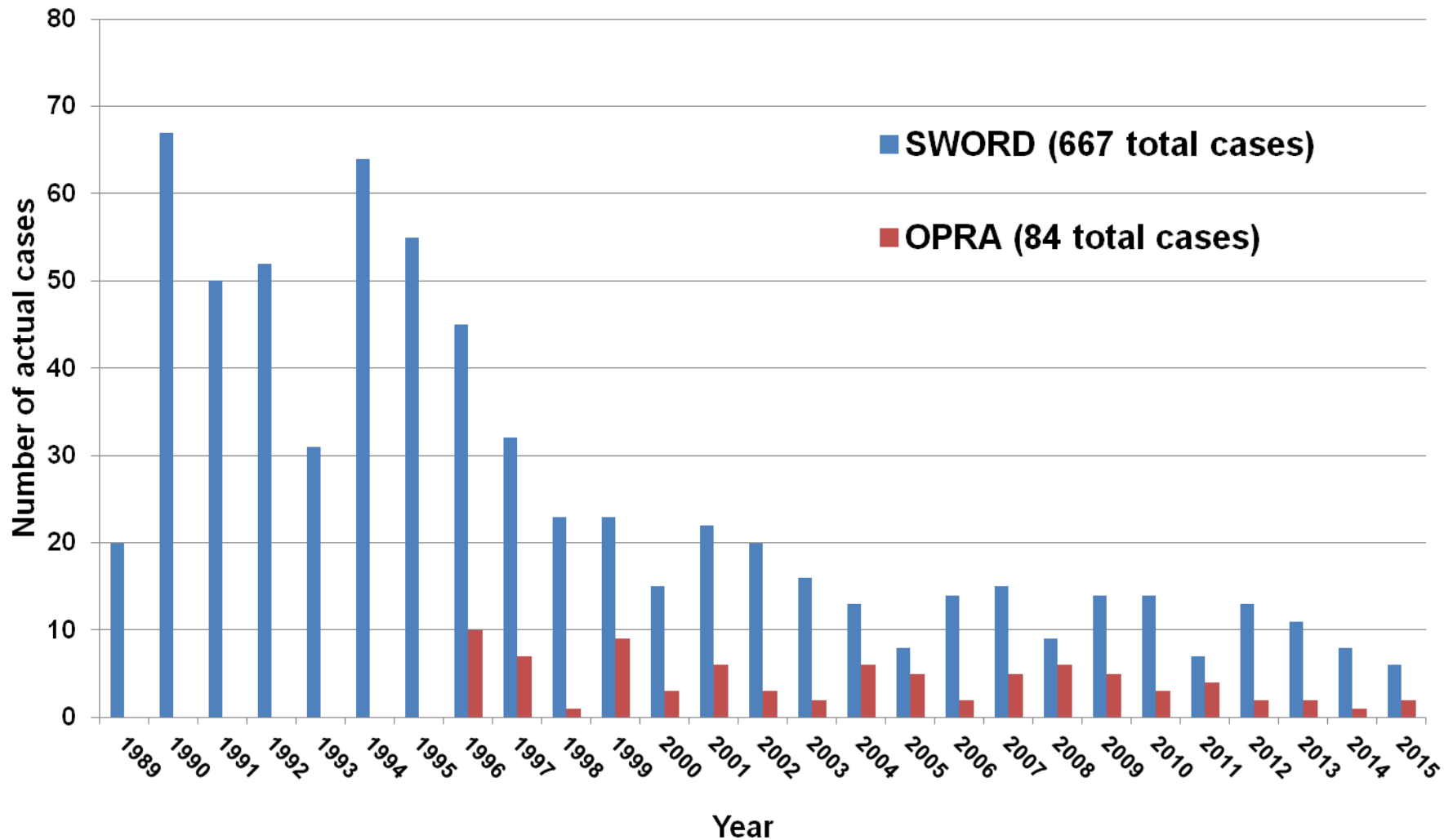
Relative incidence rates by year (2014 estimate = 1), with 95% confidence intervals (MultiLevel Model) of work-related respiratory disease* attributed to cleaning agents, as reported by chest physicians to SWORD
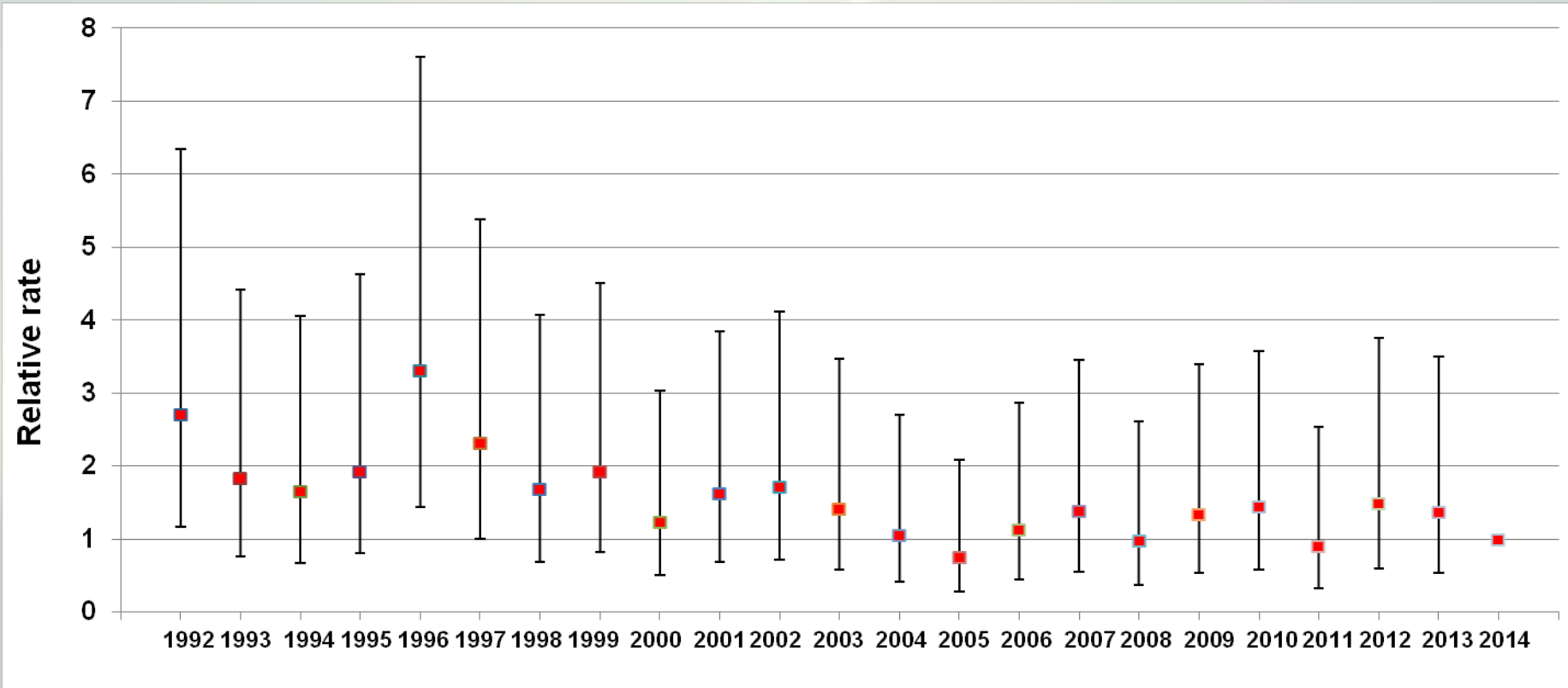
Estimated annual change (1992-2014)

Cleaning agents: -4.5% (95% CIs: -6.9, -2.0)

All other agents: -5.9% (95% CIs: -6.8, -5.1)

*excluding asbestos related diseases: mesothelioma, NMPD, pneumoconiosis, lung cancer

The gradual decline in reported incidence of occupational lung disease attributed to cleaning agents and disinfectants appears no different from the trend for all other comparable agents

All cleaning agents by occupational group (10 highest ranked in case numbers), reported by chest physicians to SWORD (1989-2015)

(SOC 2000 code) description	Actual cases	Annual average incidence rate per 100,000 employed*
(3211) **Nurses**	200	3
(9233) **Cleaners**	132	2
(6211) **Sports and leisure assistants**	32	5
(6111) Nursing auxiliaries and assistants	29	<1
(8111) Food, drink and tobacco process operatives	22	1
(9139) Labourers in process and plant operations n.e.c.	18	2
(8129) Plant and machine operatives n.e.c.	14	1
(5431) Butchers, meat cutters	13	1
(9234) **Launderers, dry cleaners, pressers**	12	7
(3111) Laboratory technicians	11	1
All other occupations	184	<1
Total	667	<1

*Rates based on estimated cases, accounting for sampling ratio, mid-point LFS (2002)data applied as the denominator

All cleaning agents by industry, (10 highest ranked in case numbers) reported by chest physicians to SWORD (1989-2015)
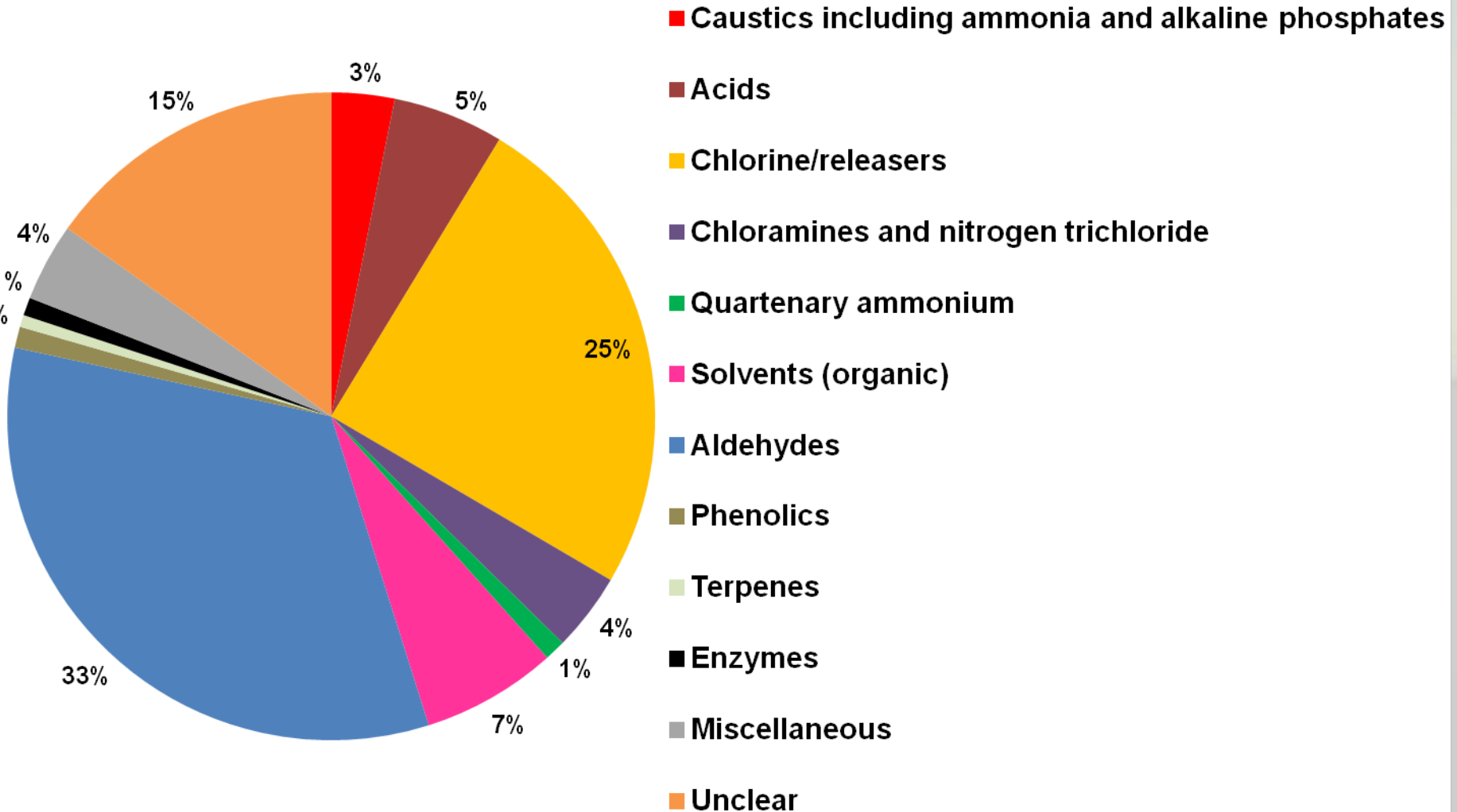
(SIC 2007 code) description	Actual cases	Annual average incidence rate per 100,000 employed*
(86-88) Human **health** and social work activities	318	0.8
(10) **Manufacture of food products**	49	0.7
(93) Sports activities and amusement and recreation activities	40	0.4
(85) Education	38	0.1
(81) **Services to buildings** and landscape activities	25	0.6
(84) Public administration and defence	24	0.1
(96) **Other personal service activities**	24	0.6
(20) Manufacture of chemical and chemical products	10	0.2
(1) Crop and animal production	7	0.3
(45) Wholesale and retail trade; repair of motor vehicles and motorcycles	6	0.3
All other industries	126	0.1
Total	667	0.2

*Rates based on estimated cases accounting for sampling ratio, mid-point LFS (2002)data applied as the denominator

Actual cases of reported to SWORD, 1989-2015, categorised by agent group.

Note: About one third are attributed to aldehydes; and another third to chlorine, chlorine releasing agents, or products thereof e.g. chloramines.

N = 667

Pie chart percentages: 3%, 5%, 25%, 4%, 1%, 7%, 33%, 1%, 1%, 4%, 15%

Legend:
- Caustics including ammonia and alkaline phosphates
- Acids
- Chlorine/releasers
- Chloramines and nitrogen trichloride
- Quartenary ammonium
- Solvents (organic)
- Aldehydes
- Phenolics
- Terpenes
- Enzymes
- Miscellaneous
- Unclear

Taxonomy of the main agents:

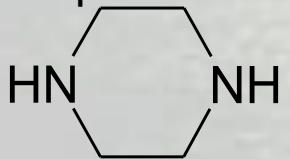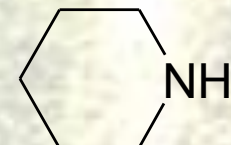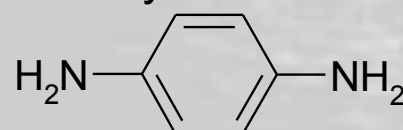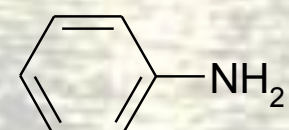| Chemical 'class'	Possible implications
Extremes of pH: acids and bases	Irritant / corrosive rather than sensitising in sensu strictu
Chlorine: direct release / related	'RADS' very well recognised, but also sensitisation where N-Cl
Quaternary ammonium	Specific sensitisation well recognised
Organic solvents	Generally unlikely sensitisers (but some e.g. unsaturated probably are)
Aldehydes	Specific sensitisation well recognised, but they are intrinsically irritant too
Phenolics and Terpenes	Probably both 'irritant' and sensitising
Enzymes	Specific and potent sensitisation well recognised

Quantitative Structure Activity Relationships
- Generic concepts

Relating the structure of an organic low molecular weight chemical to the likelihood of it causing occupational asthma:
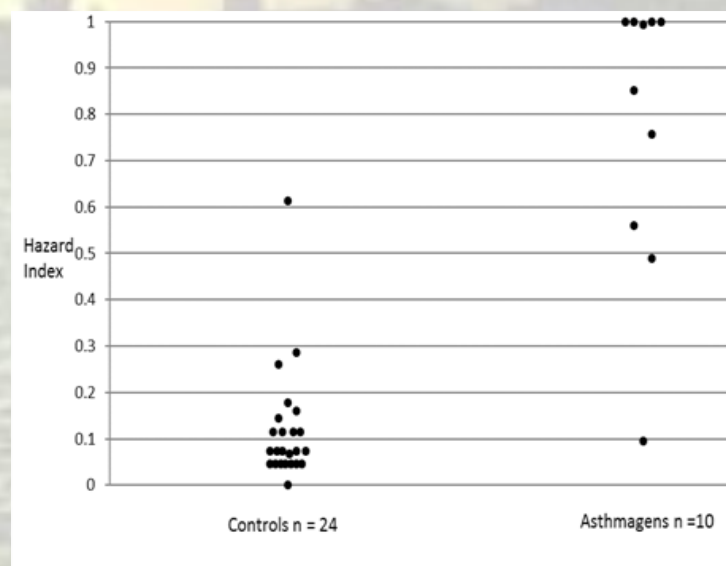
Hazard Index scale of 0 (exceedingly unlikely) to 1 (most likely)

Several papers e.g. Jarvis et al 2005, 2015. Latest model:

Sensitivity: 90%, Specificity: 96%, Area under ROC curve: 0.95

Asthmagenic	Non-asthmagenic
Ethylenediamine	Ethylamine
$H_2N-C-C-NH_2$ (with H_2 H_2)	$H_3C-C-NH_2$ (with H_2)
Piperazine	Piperidine
HN ⬡ NH	⬡ NH
P-Phenylenediamine	Aniline
H_2N-⬡$-NH_2$	⬡$-NH_2$

2nd external validation – latest QSAR model

Quantitative Structure Activity Relationships (QSAR)
- Applied to cleaning agents, disinfectants etc

The five most frequently reported specific Low Molecular Weight (<1000D) organic compounds in our 'cleaning agents etc' dataset, showing our occupational asthma Hazard Indices using the 2005 and 2015 QSAR logistic regression equations

Chemical name	THOR Actual cases	HI 2005 (cut point 0.5)	HI 2015 (cut point 0.39)
Glutaraldehyde	217	0.82	0.6
Dichloroisocyanurate	30	0.85	0.49
Perchloroethylene	19	0.01	0.07
Formaldehyde	18	1	1
Peracetic acid	10	0.03	0.07

Conclusions

- The incidence of occupational asthma attributed to cleaning and allied agents as reported by chest physicians and occupational physicians is less than that suggested from data 'lower down the surveillance' pyramid

- The temporal trends are consistent with a gradual decline in reported incidence but need to be interpreted carefully

- The data permit ranking of incidence by industry sectors, as well as by job.

- Aldehydes and chlorine releasing agents are the two largest specific categories of causal agents

- It is possible to classify the causal agents by virtue of their chemical structure. Structure-activity relationships are consistent with two types of mechanisms: asthmagenesis by 'classical' sensitisation, and by 'irritancy'

- These data may assist in mechanistic understanding, diagnosis, prediction and prevention

Thank you

- Thank you for listening, and in anticipation of a lively discussion.

- Acknowledgements are due to the funders: UK Health and Safety Executive, EU-COST, Colt Foundation et al

- Special thanks to the thousands of physicians (particularly respiratory and occupational, but also GPs and dermatologists) who participate in THOR

- Thanks also to many other UK and overseas colleagues