The Health and Occupation Research Network
THOR (UK & Republic of Ireland)

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Methodologies to identify work-related diseases:
Review of sentinel and alert approaches

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v3
To outline and discuss, with reference to THOR:

- The drivers for sentinel approaches / monitoring systems

- An outline description of relevant THOR schemes and methods, with illustrations (limited to chemicals in this presentation) of:
  - sentinel monitoring
  - alert function

- Consideration of strengths / weaknesses,
  - obstacles, challenges,
  - and potential solutions

- The link with prevention

- Open debate
Drivers for THOR sentinel approaches/monitoring systems and alerts for new work-related diseases (WRDs)

- Original drive was to estimate incidence (and trends in incidence) of WRDs (funded by the UK Health and Safety Executive.)

However this evolved to incorporate sentinel approaches to detect new causes of WRDs, with a view to generating alerts, further investigation and prevention.

- Need to keep up with the EU (e.g. for the Republic of Ireland’s Health and Safety Authority)

- Physicians’ motivation and perceived needs are crucial to THOR’s success:
  – especially occupational physicians, respiratory physicians and dermatologists
The Health and Occupation Research Network (THOR)

• Research & surveillance ‘medical observatory’ - originally for measuring the incidence and determinants of occupational disease / WRDs (but later extended e.g. sentinel reporting, sickness absence burden)

• Started in UK with 1st scheme in 1989: SWORD

• Currently >1000 doctors participate in UK & ROI reporting incident cases (either every month or as a sample for 1 random month p.a.)
  -> Hence estimate of annual cases

• Reports from clinical ‘system’ specialists account for an estimated 5,000 new UK cases of work-related ill-health per annum.

• Reports from OPs and GPs account for a further estimated 10,000 UK cases per year
The Health and Occupation Reporting (THOR) network

- **SWORD**
  - Surveillance of Work-related & Occupational Respiratory Disease
  - Chest Physicians

- **EPIDERM**
  - Occupational Skin Surveillance
  - Dermatologists

- **MOSS**
  - Musculoskeletal Occupational Surveillance Scheme
  - Rheumatologists

- **OPRA**
  - Occupational Physicians Reporting Activity
  - Occupational Physicians

- **THOR-GP**
  - THOR in General Practice
  - General Practitioners

- **THOR-EXTRA***
  - Special reports outside the Incidence Sampling Frame, &/or extra data

- **SIDAW**
  - Surveillance of Infectious Diseases At Work
  - Consultants in Communicable Disease Control

- **SOSMI**
  - Surveillance of Occupational Stress and Mental-illness
  - Psychiatrists
Surveillance networks

Example

General Practitioners

The Health and Occupation Research Network in General Practice

THOR-GP

(Map shows GB only
But reporters also in Ireland)
The work-related ill health
Sentinel surveillance pyramid

- Specialist diagnosis
  - THOR-GP
  - THOR
- Recognised in primary care
- Unrecognised in primary care
- Symptomatic health effects
  - Self reported WRI
- Asymptomatic health effects
Incidence rate per 100,000 persons employed for work-related musculoskeletal, mental, skin and respiratory ill-health (2006 to 2009) as reported by clinical specialists, GPs & self-reports.
Specific features of THOR that make it work with regard to the identification of new WRDs

• Generally highly motivated participating physicians nurtured by:
  – Generic feedback (quarterly report)
  – Specific feedback (answers to queries)
  – Consultation (advisory meetings etc)
  – Continuing Professional Development esp. EELAB (Electronic, Experiential Learning, Audit and Benchmarking)

• Particularly good for respiratory and skin disease
  – System specialists
  – Occupational Physicians
  – (GPs)
THOR-extra

Same doctors in THOR schemes which measure incidence but for:

- Reporting sentinel cases outside the usual incidence sampling period
- Detailed exposure and other data collection (e.g. non-occupational)
Dermatitis – from trends in incidence to finding new causes

Incidence trends overall

> Trends with specific work practices, or

> Trends for specific classes of agents

> New causes
Relative risk by year (2015=1) (95% CI) of contact dermatitis as reported to EPIDERM (dermatologists) and OPRA (occ. physns.)

**Estimated annual change (1996-2015)**

- **EPIDERM**: -3.8% (95% CI: -4.3%, -3.3%)
- **OPRA**: -7.4% (95% CI: -8.8%, -6.0%)

**Estimated annual change (2006-2015)**

- **EPIDERM**: -3.9% (95% CIs: -5.3%, -2.4%)
- **OPRA**: -2.9% (95% CI: -6.5%, +0.8%)
Trends in Irritant Contact Dermatitis attributed to hand hygiene in healthcare workers

Incidence rate ratio relative to 1997

- Healthcare workers; hand hygiene
- Healthcare workers; infection control agents (right)
- Wetworkers; all agents (right)
- Other workers; all agents (far right)
- Hand rub reported (aggregated)

# Work and Methyl(chloro)isothiazolinones

Average annual percentage change in reported incidence in work-related contact dermatitis attributed to MCI/MI and or MI, 1996-2012

<table>
<thead>
<tr>
<th>Group</th>
<th>Total number actual cases</th>
<th>Average annual percentage change and 95% confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal care exposures</td>
<td>136</td>
<td>+3.8% (-0.3 to 8.0)</td>
</tr>
<tr>
<td><strong>Healthcare workers</strong></td>
<td>63</td>
<td>8.1% (2.1 to 14.4)</td>
</tr>
<tr>
<td>Beauty workers (including nail technicians)</td>
<td>25</td>
<td>6.6% (-2.2 to 16.2)</td>
</tr>
<tr>
<td>Hairdressers</td>
<td>48</td>
<td>1.5% (-4.7 to 8.1)</td>
</tr>
<tr>
<td>Detergent exposures</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Cleaners</td>
<td>10</td>
<td>Insufficient numbers for analysis</td>
</tr>
<tr>
<td>Industrial exposures</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>Painters (or paint mentioned as a causal agent)</td>
<td>15</td>
<td>Insufficient numbers for analysis</td>
</tr>
<tr>
<td><strong>Manufacturing</strong></td>
<td>118</td>
<td>6.3% (1.8 to 10.9)</td>
</tr>
<tr>
<td>Other (range of occupations)</td>
<td>79</td>
<td>Insufficient numbers for analysis</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>358</td>
<td>4.1% (1.4 to 6.9)</td>
</tr>
</tbody>
</table>

Relative rates by year (95% CI) of Allergic Contact Dermatitis reported by dermatologists attributed to fragrance versus not attributed to fragrances (all occupations)

<table>
<thead>
<tr>
<th>Group</th>
<th>Attributed to fragrances</th>
<th>Not attributed to fragrances</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health and social care</td>
<td>0.4 (-2.6, 3.6)</td>
<td>-8.3 (-9.9, -6.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beauty</td>
<td>3.1 (-0.2, 6.5)</td>
<td>1.4 (-0.5, 3.2)</td>
<td>0.193</td>
</tr>
<tr>
<td>Food</td>
<td>1.3 (-3.1, 5.9)</td>
<td>-3.7 (-6.1, -1.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>All industry</td>
<td>1.1 (-0.8, 3.0)</td>
<td>-5.5 (-6.2, -4.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*p Test to see if trends (fragrance v not fragrance) are statistically, significantly different
Preliminary analysis of number of actual cases of Allergic Contact Dermatitis by fragrance ‘type’, reported by dermatologists to EPIDERM, 1996-2015

Each case may be attributed to more than one agent
*e.g. cinnamyl alcohol, cinnamaldehyde
Lyral is Hydroxymethylpentylcyclohexene-carboxaldehyde

n = 808
Cases reported via report card or webform

Data coded (occupation, industry, substance etc.) by 2 project assistants

Coding discrepancies reconciled by a third party

Each quarter new cases are scanned for substances of interest (possible novel causes or workplaces, unusual clusters etc)

Highlighted in quarterly report

Contact physician who reported the case for further details

Action taken on cases thought significant

Reporters of similar cases put in contact with each other

List of cases of possible interest reviewed by specialist research occupational physician

Increasing the signal of THOR reports
Examples of ‘new’ WRD identified in THOR - 1

‘New’ = new causal agents + rare + new{agent+job/task+agent}

Skin:

• Allergic contact dermatitis in veterinary laboratory worker using limonene for histopathology

• Dermatitis caused by isocyanate exposure in vehicle paint sprayers

• Contact urticaria from cannabis exposure in a forensic scientist

Systemic / skin:

• Scleroderma caused by perchlorethylene in a factory worker in the manufacture of chemical and chemical products
Cases of occupational *asthma* attributed to latex exposure reported to SWORD (1991-2014)
Extracts of example of hierarchy of searching

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>Agent</th>
<th>Job / task</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASTHMA</td>
<td>Diisocyanates</td>
<td>Car spray painter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glueing ***</td>
</tr>
<tr>
<td></td>
<td>Flour</td>
<td>Baking</td>
</tr>
<tr>
<td></td>
<td>Denatonium***</td>
<td></td>
</tr>
<tr>
<td>PNEUMOCONIOSIS</td>
<td>Silica</td>
<td>Stone mason</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemical engineer***</td>
</tr>
<tr>
<td>BRONCHIOLITIS ***</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*** = Special focus? new disease or? new cause
Examples of ‘new’ WRD identified in THOR - 2

‘New’ = new causal agents + rare + new{agent+job/task+agent}

Lung:

• Chemical **pneumonitis** caused by silicone waterproofing spray in boat repair

• **Alveolitis** from spraying fabric protector (? silicone) in furniture manufacturer

• **Lipoid pneumonia** from spray mount glue in a graphic designer

• Non-malignant **pleural disease** in process operator exposed to marinite (? cryptic asbestos)

• **Bronchiolitis** (? ketone peroxides) in boat laminator

• **Asthma** caused by heated triglycidyl isocyanurate (TGIC), a hardening agent used in powder paints.

• Asthma / Type 1 allergy due to denatonium benzoate in a nurse testing PPE for bio-protection

• Asthma from cyanoacrylates in forensic fingerprint specialists*

• Asthma from isocyanates in funeral wreath manufacturers*

(* disproportionality analysis by Prof Bonneterre)
Example of corroborating evidence: Quantitative Structure Activity Relationships (QSARs)

QSAR = a statistical analysis of chemical substructures associated with biological activity.

![Internal Validation Graph](image)

- Controls: n=301
- Asthmagens: n=78

Hazard Scale:
- 0.1
- 0.2
- 0.3
- 0.4
- 0.5
- 0.6
- 0.7
- 0.8
- 0.9
- 1.0
Corroboration by QSAR of THOR reports of occupational asthma due to novel agents

**Denatonium (benzoate)** (CAS 86398-53-0)

Hazard Index = 0.92

![Denatonium structure](image)

**Thiamine** (CAS no.59-43-8)

Hazard Index = 0.95

![Thiamine structure](image)
Alert function of the THOR schemes/ systems

THOR information given to HSE e.g. on specific hazards in:
• hairdressing,
• car manufacture / repair,
• metal working fluids,
• silica in new contexts

But: debate about the requisite level of proof and legal aspects
(we cannot disclose information which could identity the reporting physician, patient or workplace)

Improvements could be achieved by:
• Pooling with other systems (EU wide)
• Regular use of disproportionality metrics (as per RNV3P)
• Assumption by another body e.g. HSE (UK), or EU-OSHA of the final alert action and any associated legal responsibility
The link with prevention

• Need to validate / corroborate novel causes:
  – expert review,
  – collation of cases / case finding, (national / international)
  – other approaches e.g. Other data mining, QSARs

• Alerting HSE and other stakeholders – promoting vigilance

• But legal considerations - cautious and slow approach

• Preventive campaigns for employers and employees
  e.g. In hairdressers (skin), vehicle manufacture / repair (lung)

• Possible recommendation of less risky options e.g. substitutes
Summary: From sentinel surveillance to dissemination of ‘alert’

THOR reporting through random or core sampling

THOR Extra – extra data or reporting outside the sampling frame

Ad Hoc HSE requests

THOR research fellow data analysis & screen

Regular quarterly compilation of new / uncommon causes

Specialist academic occupational physician screening

Quarterly report, BECK report

Ad Hoc reports to HSE

Advisory committee discussion

Reporters

Sharing with HSE
Obstacles facing alert and sentinel approaches/monitoring systems for the identification of new WRDs

- Reporting fatigue, time pressure on physicians – need to maintain motivation
  - Balance against -
- Limits to data collection e.g. detail on exposure, case management
- Works well for respiratory and skin disorders, but not so well for other organ systems / diseases
- Need to undertake further evaluations
- Funding challenges
- Pooling of data and expertise needed
  - work for more international collaboration (e.g. Modernet),
  - with systematically applied methods
Acknowledgements

- All participating physicians
- Funding bodies: UK HSE, ROI HSA, EU-COST etc

- Thank you for your attention

www.coeh.man.ac.uk/thor

www.agius.com/raymond