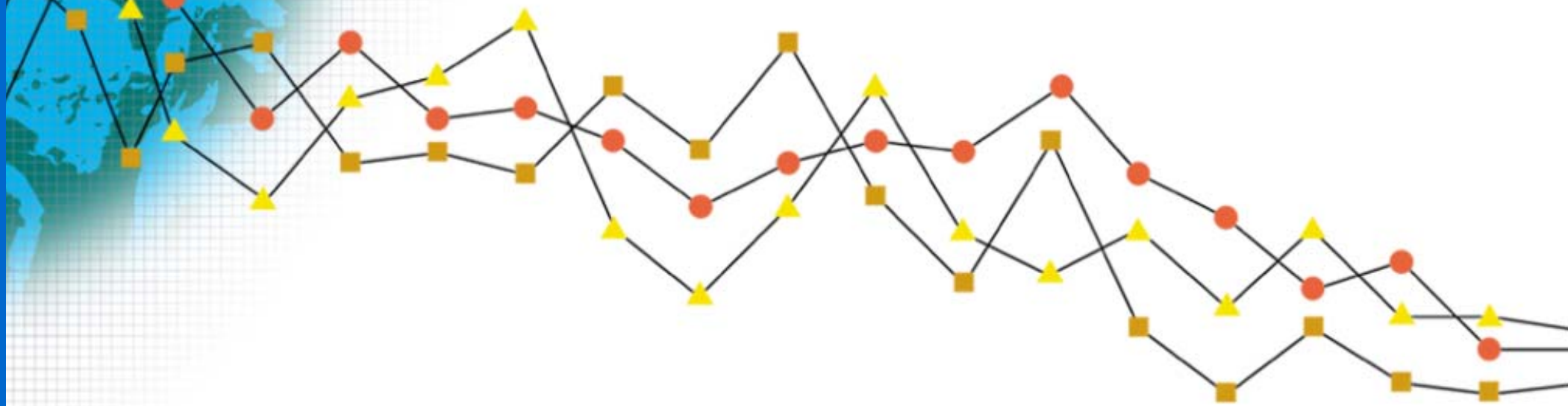
Mortality studies of phenoxy herbicide production workers

Symposium on Dioxin, Wellington, September 7 2005



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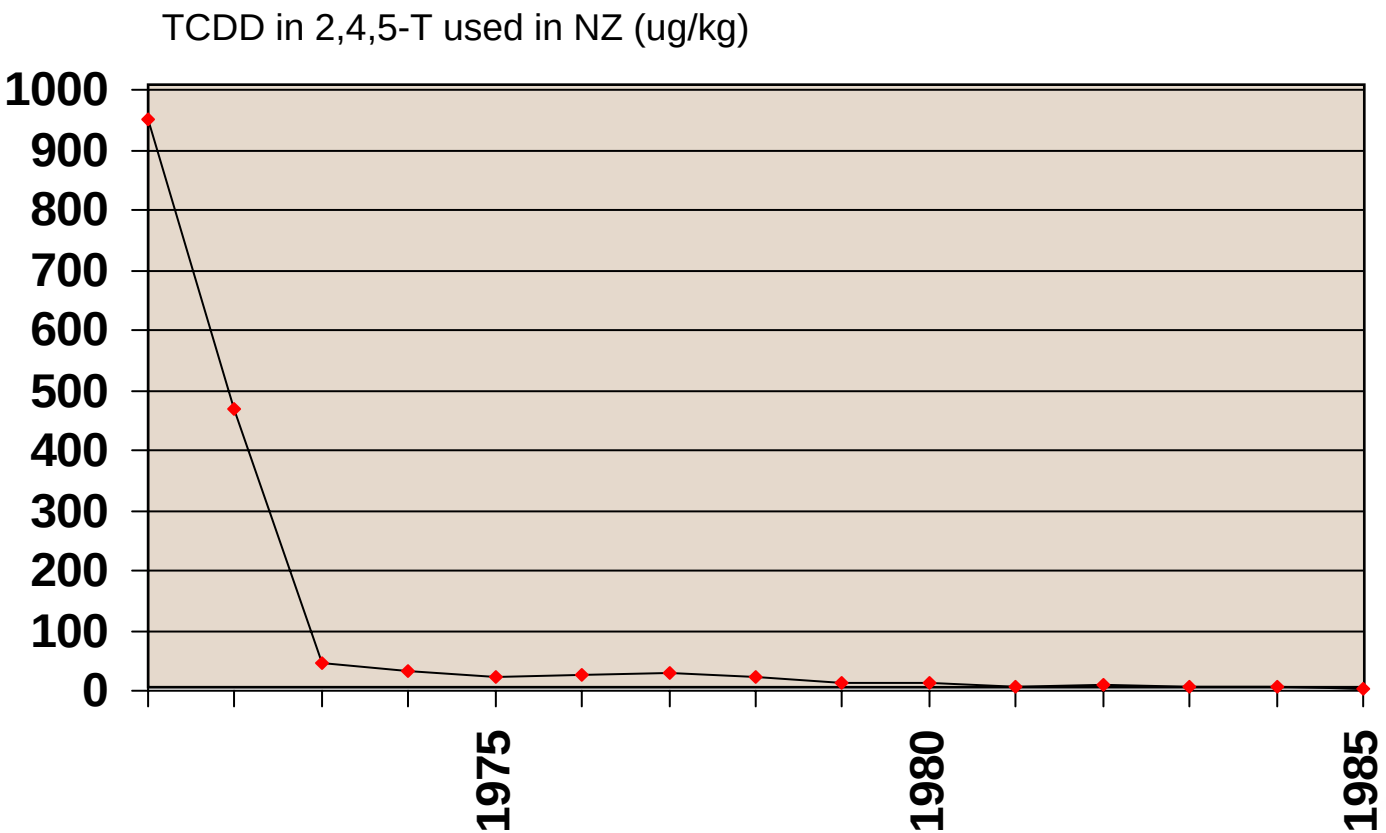
Use of phenoxy herbicides in New Zealand

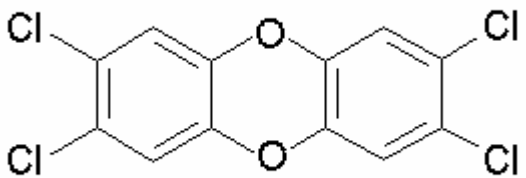
- 2,4,5-T has been used in New Zealand since **1948**
- Cheapest and most effective means to control **gorse and scrub**
- 1970-1980: 2,4,5-T represented the most widely used herbicide in NZ
- NZ has been described as the **heaviest user** of 2,4,5-T in the world

Production of phenoxy herbicides in New Zealand

- **1948:** start production of 2,4,5-T using imported TCP
- **1969:** start use trichlorophenol (TCP) plant
- **1977:** modifications in TCP production process
- **1982:** solvent extraction further reducing TCDD in product
- **1987:** production of 2,4,5-T ceased

TCDD in 2,4,5-T


TCDD in 2,4,5-T used in NZ (ug/kg)
1000
900
800
700
600
500
400
300
200
100
0
1975
1980
1985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NZ mortality study: History

- **1980:** IARC established an international cohort of producers and sprayers of phenoxy herbicides, included 36 cohorts from 12 countries

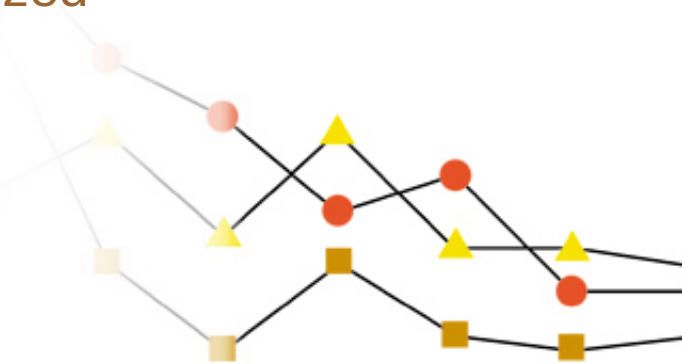
- This international study showed a **29%** overall increased risk in cancer for exposed

  (Kogevinas et al. Am J Epidemiol 1997;145:1061-75)

- Included **2 NZ** cohorts (producers and sprayers)

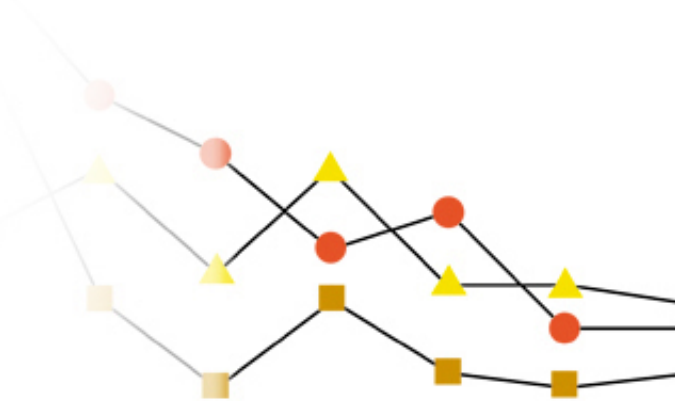
- In **2004** the New Zealand cohorts were individually analyzed

  ('t Mannetje et al. OEM 2005;62;34-30)



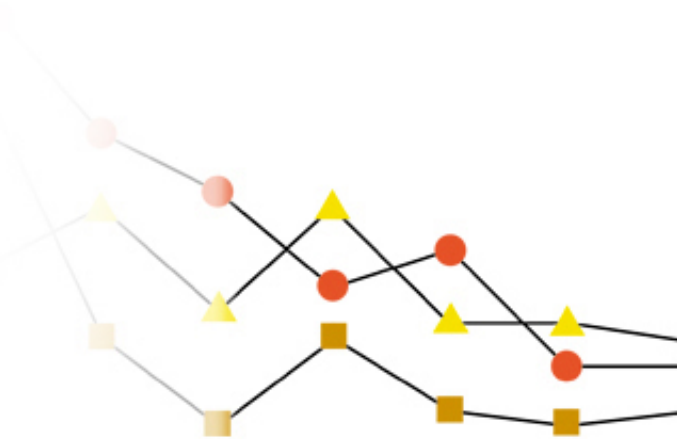
Methods of the study

- **1025** production workers (88% male)
- Employment records: worked for at least 1 month between **1969** and **1984**
- Based on department, 79% was evaluated to be **potentially exposed** to phenoxy herbicides and dioxins
- By end of follow-up: **122** had died (15%)
- Calculated **SMRs** (Standardized Mortality Ratio's)
- By comparing the **observed** number of deaths, with the **expected** number of deaths in the New Zealand population



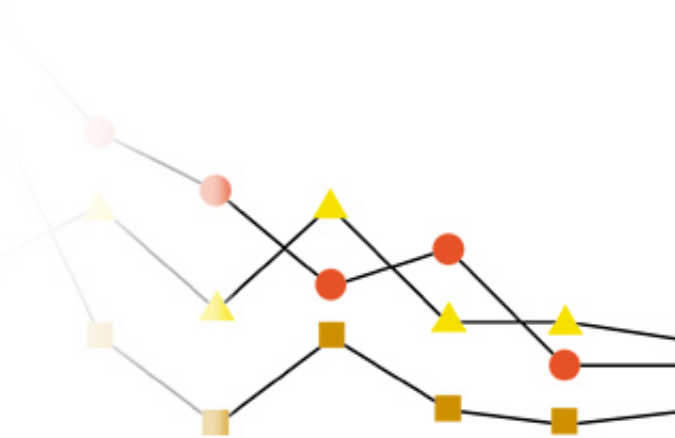
Results (1), by exposure status

	All cancer deaths			
	N	obs/exp	SMR	95%CI
exposed producers:	813	43/34.62	1.24	0.90-1.67
unexposed producers:	212	13/11.83	1.10	0.59-1.88



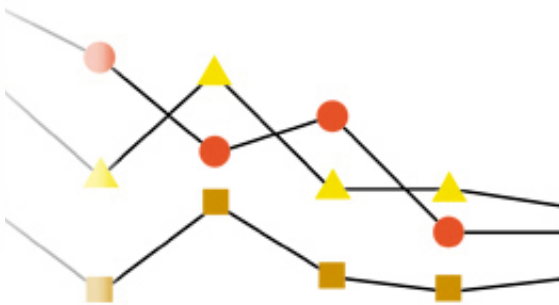
Results (2), by department

	All cancer deaths			
	N	obs/exp	SMR	95%CI
synthesis workers:	164	11/6.49	1.69	0.85-3.03
formulation and lab:	152	9/5.48	1.64	0.75-3.12
maintenance & waste:	169	10/6.86	1.46	0.70-2.68
packing & transport:	243	10/12.06	0.83	0.40-1.53
other exposed workers:	163	8/9.17	0.87	0.38-1.72



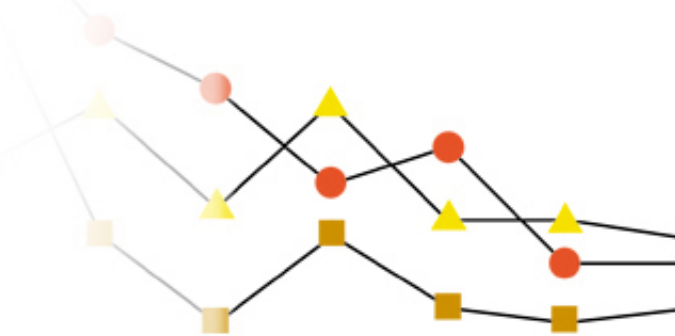
Results (3), by duration

	All cancer deaths			
	N	**obs/exp**	**SMR**	**95%CI**
synthesis workers:	**164**	**11/6.49**	**1.69**	**0.85-3.03**
0-5 year	(3620 py)	4/2.31	0.92	0.25-2.36
5-10 years		4/1.54	3.18	0.86-8.13
>10 years		3/0.89	3.37	0.70-9.85
test for linear trend			p=0.03	
formulation and lab:	**152**	**9/5.48**	**1.64**	**0.75-3.12**
0-5 year	(3652 py)	7/2.20	3.19	1.28-6.57
5-10 years		0/0.47	0.00	0.00-7.92
>10 years		2/2.82	0.71	0.09-2.56
test for linear trend			p=0.03	
maintenance & waste:	**169**	**10/6.86**	**1.46**	**0.70-2.68**
0-5 year	(3407 py)	6/3.90	1.54	0.56-3.35
5-10 years		2/1.22	1.63	0.20-5.92
>10 years		2/1.3	1.16	0.14-4.18
test for linear trend			p=0.76	



Remaining questions

- What were the **levels** of TCDD and other congeners in these workers?
- Did these levels differ between **departments**? What departments had the highest exposures?
- What was the influence of **duration** of employment? **Year** of employment?
- Were the workers exposed to **other agents** on the job, that could explain elevated cancer mortality?
- **Confounding:** to what extent can lifestyle factors, or other held jobs, explain the elevated cancer mortality?
- Do these workers have increased risk of **other health outcomes** associated with dioxin?



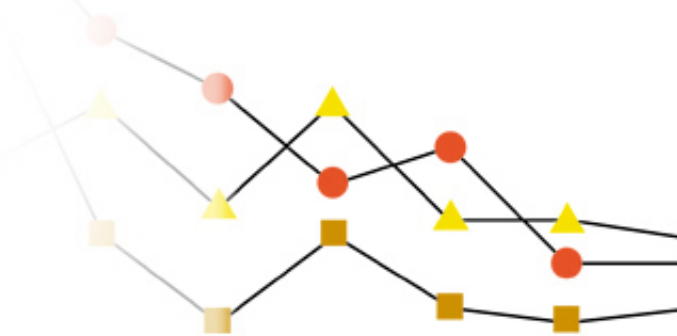
The new study, aims

1. To measure the **current dioxin levels** in the blood of the study participants

   re-analyse the whole cohort using this exposure information

2. To determine whether dioxin levels are associated with **adverse health effects** and **reproductive outcomes**

3. To study effects of dioxin at the **cellular level**



The new study, study population

Whole cohort
n=1025

Alive and living in New Zealand
n=629

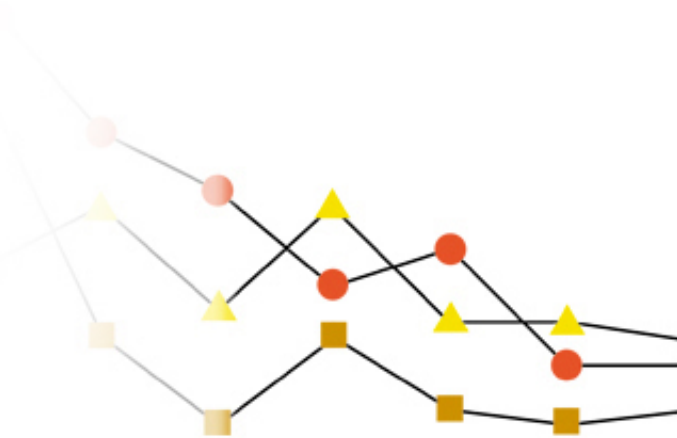
deceased
n=164

lost to follow up
n=232

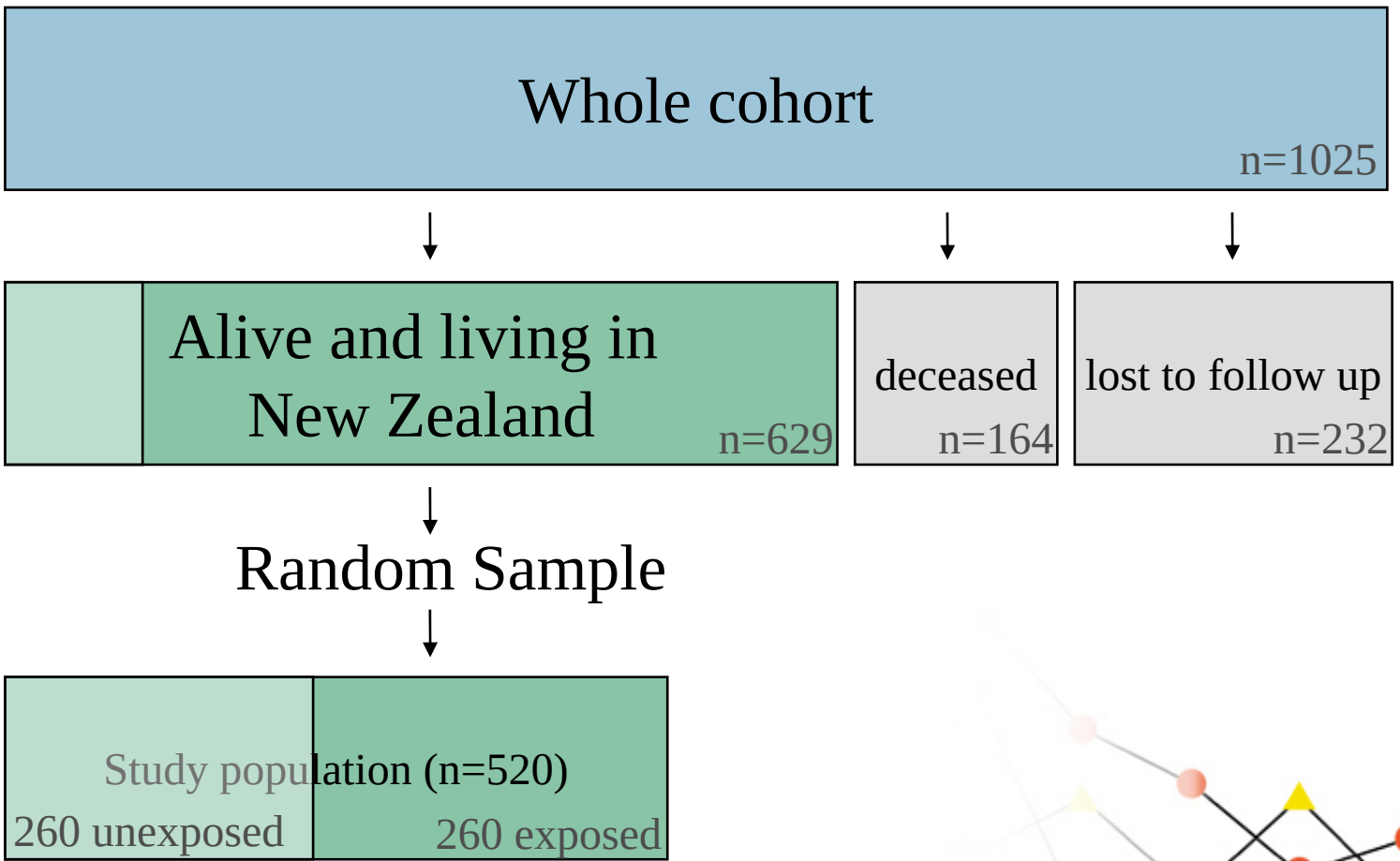
Random Sample

From PCP study
n=200

invitation health survey
n=320

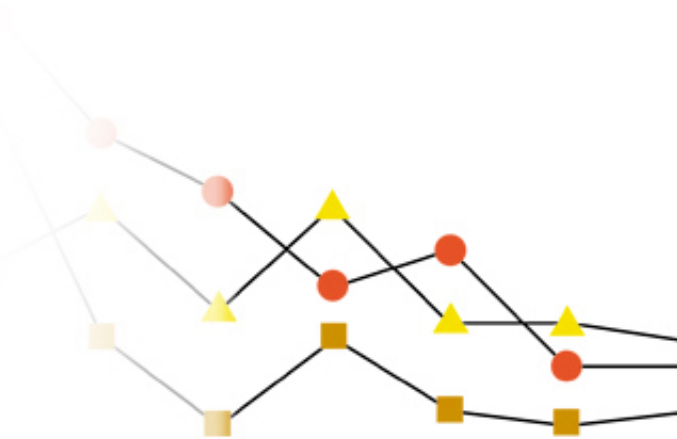


The new study, study population



New study: morbidity survey

- **Interview**
  - Lifetime work history & employment at IWD
  - Health, offspring
  - Lifestyle factors
- **Clinical examination**
  - Basic health parameters
  - Skin disease
  - Neurological symptoms
- **Blood taking**
  - Dioxins, levels
  - Blood glucose (diabetes)
  - Effects dioxin at the cellular level



Named investigators

- Dr Andrea ’t Mannetje - CPHR
- Dr Dave McLean - CPHR
- Tania Slater - CPHR
- Dr Evan Dryson - Department of Labour
- Dr Chris Walls - Department of Labour
- Professor Manolis Kogevinas - IMIM, Spain
- Professor Pier Bertazzi - EPOCA, Italy
- Dr Rod Lea - ESR
- Dr Barry Borman - Ministry of Health
- Dr Patrick O’Connor - MidCentral Health
- Professor Neil Pearce - CPHR