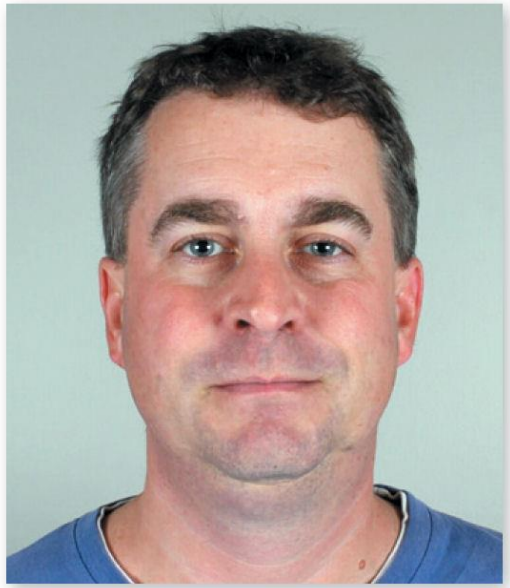

Dr Chris Lewis

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Saturday, June 10, 2017

14:10 - 14:35 How to Reduce Lung Disease and its Impacts

Supported by:

TUAPAPA PŪKAHUKAHU LUNG FOUNDATION New Zealand

MSD

Pfizer

How to reduce lung disease and its impacts

Dr Chris Lewis

Respiratory Physician

Auckland District Health Board

TUAPAPA PŪKAHUKAHU

LUNG FOUNDATION

New Zealand

Disclosures

I have previously received

- honoraria for participating in advisory boards for MSD in 2016 and 2017, and for Pfizer previously
- sponsorship from Olympus for travel and accommodation to attend the ANZIP (interventional pulmonology) meetings in Australia in 2015 and 2016
- Travel sponsorship and speaker fees from AstraZeneca
- Speaker fees from GSK

Preventing lung disease

- Starts *in utero*
- Childhood
  - Access to appropriate healthcare
  - Healthy living environment (warm, not overcrowded, no passive smoke, low pollution, childhood vaccinations)
- Good diet
- Not starting smoking
- Smoke cessation
- Vaccination

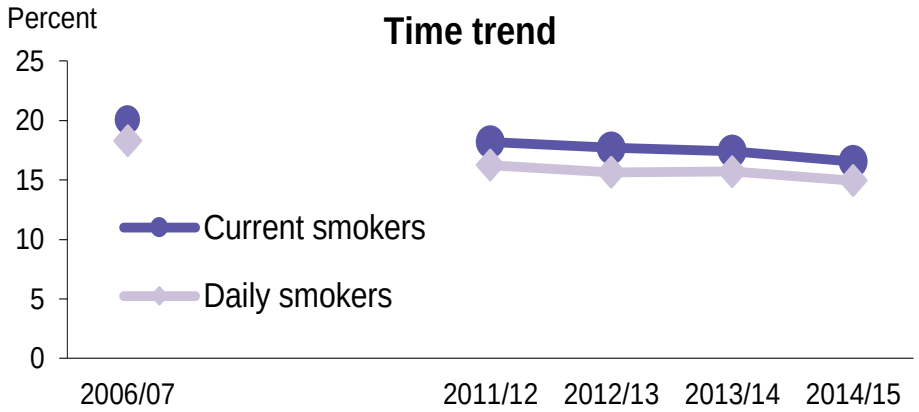
Smoking and tobacco control

- Never start
  - Vast majority of smokers start aged under 25, most as “children”
  - Most state that they regret starting smoking, if asked

- Smoke cessation
  - Best interventions still only have success rate of around 25% at 1 year
  - Although even “brief advice” successful in 10%

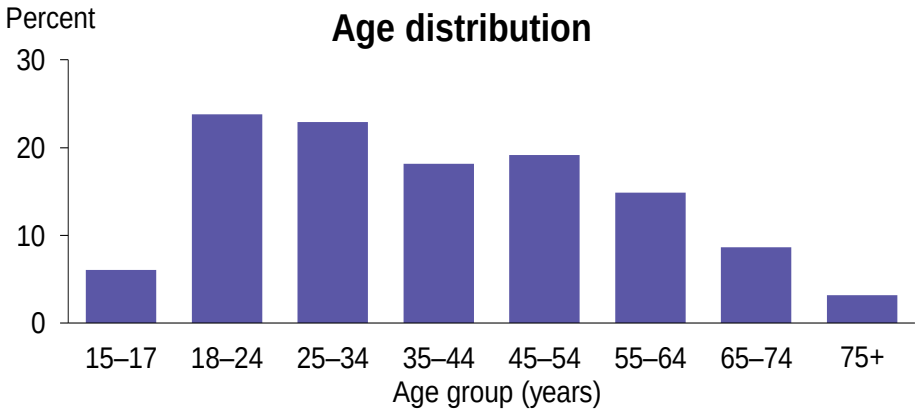
Box 2: Adults who are current smokers (smoke at least monthly) and time trend for adults who are daily smokers, 2014/15

The prevalence was **16.6%**
which is an estimated
605,000 adults



Adjusted rate ratio	
Men vs women	1.2 *
Māori vs non-Māori	2.7 *
Pacific vs non-Pacific	1.4 *
Asian vs non-Asian	0.3 *
Most vs least deprived	3.1 *

* There is a statistically significant difference between the two groups.



Aspire 2025

- Aim to eliminate tobacco from NZ by 2025
  - Supported by National government / John Key
- Smoking rates are gradually falling
- Plain packaging legislation in progress
- Gradually rising taxes / cost
- Political will ?fading and short on detail

www.aspire2025.co.nz

Respiratory disease in New Zealand

- Asthma
- COPD
- Lower respiratory tract infections and pneumonia
- Lung cancer
- Bronchiectasis
- (SLEEP APNOEA)

Asthma

- Affects 1 in 9 adults in NZ, and 1 in 7 children
- 460,000 NZers in total
- Women > men; Maori and NZ Euro > PI and Asian people
- 68 deaths from asthma in 2006, 57% in age > 65
- Hospitalisations highest in 2-16 year olds
- 4,618 hospitalisations in 2011-2 (increased from previous)
- Economic costs of asthma estimated at $825 million per year in late 1990s ($700m of which were non-medical costs)

“Difficult asthma”: assessment

- Is it definitely asthma?
- Is it asthma plus something else?
- Is the patient taking their treatment correctly?
- Is the patient taking their treatment at all?
  - Unintentionally not?
  - Intentionally not? Patient or parent?
- In “difficult asthma” clinics, roughly 20-25% genuinely have “difficult asthma”

Is it Asthma?

NOT ASTHMA

- COPD
- Bronchiectasis
- Upper airways disease
- Gastroesophageal reflux
- Central tumours
- Foreign bodies
- Hyperventilation

ASTHMA PLUS

- Bronchiectasis
- Upper airways disease
- Gastroesophageal reflux
- ABPA
- Occupational asthma
- NSAIDs and asthma
- Churg-Strauss syndrome
- Hyperventilation

Source: Prof Neil Barnes

Features that increase the probability of asthma

- More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough particularly if symptoms
  - worse at night and morning
  - occur with allergen, exercise or cold air
  - after aspirin or β blocker
- History of atopic disorder
- Family history of asthma/atopic disorder
- Wheeze on auscultation
- Unexplained low PEF or FEV_1
- Unexplained blood eosinophilia

Source: Prof Neil Barnes

Features that lower the probability of asthma

- Prominent dizziness, light-headedness, peripheral tingling
- Productive cough in the absence of wheeze or breathlessness
- Repeatedly normal examination when breathless
- Voice disturbance
- Symptoms only with colds
- Significant smoking history(>20 pack years)
- Cardiac disease
- Normal PEF or FEV_1 when symptomatic

Source: Prof Neil Barnes

Asthma: purism v pragmatism

Terrible paradox!

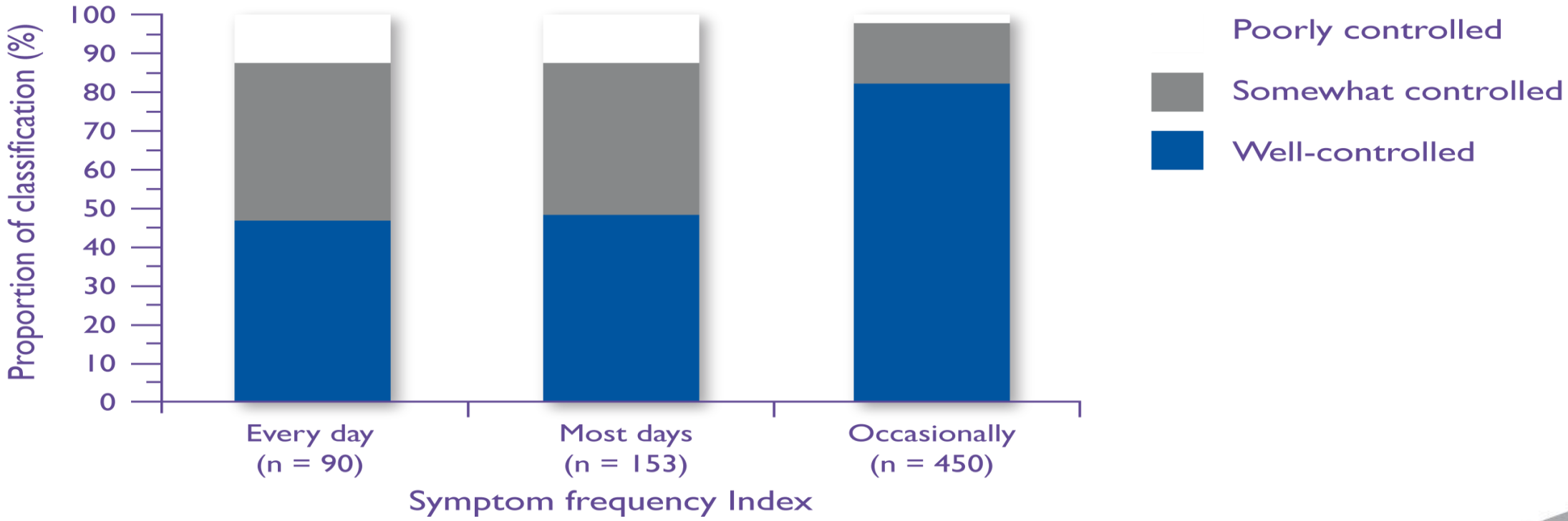
- Poor control of asthma is common
- Patients (and sometimes doctors) overestimate level of asthma control
- Treatments are now very effective
- But patients often don’t take them!

Asthma control

- Symptoms are the “tip of the iceberg” of airway inflammation and hyperresponsiveness
- Tools to measure asthma control can help unmask poor control
- Research trials giving treatment to give good asthma control (as per GINA guidelines) show high levels of achievement of this

Patients overestimate their level of control

Self-assessed asthma ‘control’ in adults in the last 4 weeks by symptom frequency index.*



* Participants were asked, ‘Overall, how well would you say your asthma has been controlled in the last 4 weeks?’

Adapted from Marks et al. *Respirology*. 2007

Prescription Filling and Healthcare Utilisation

Prescription filling

	<50% ICT n=63	>50% ICT n=119	p value
Sex M/F	16/47	53/66	0.02
Admissions in last 12 months	25%=3	10%=3	0.02
	5%=2	9%=2	
	18%=1	16%=1	
	52%=0	65%=0	
Nebuliser	31(49%)	35(29%)	0.01
Total SABA nebules	99	42	0.03

Gamble et al AJRCCM 2009

Oral Steroid Adherence in “Difficult Asthma” clinic

	Nonadherent n=23	Adherent n=26
Blood plasma prednisolone µg/L	ND	194+/-160
Blood plasma cortisol nmol/L	212+/-116	ND

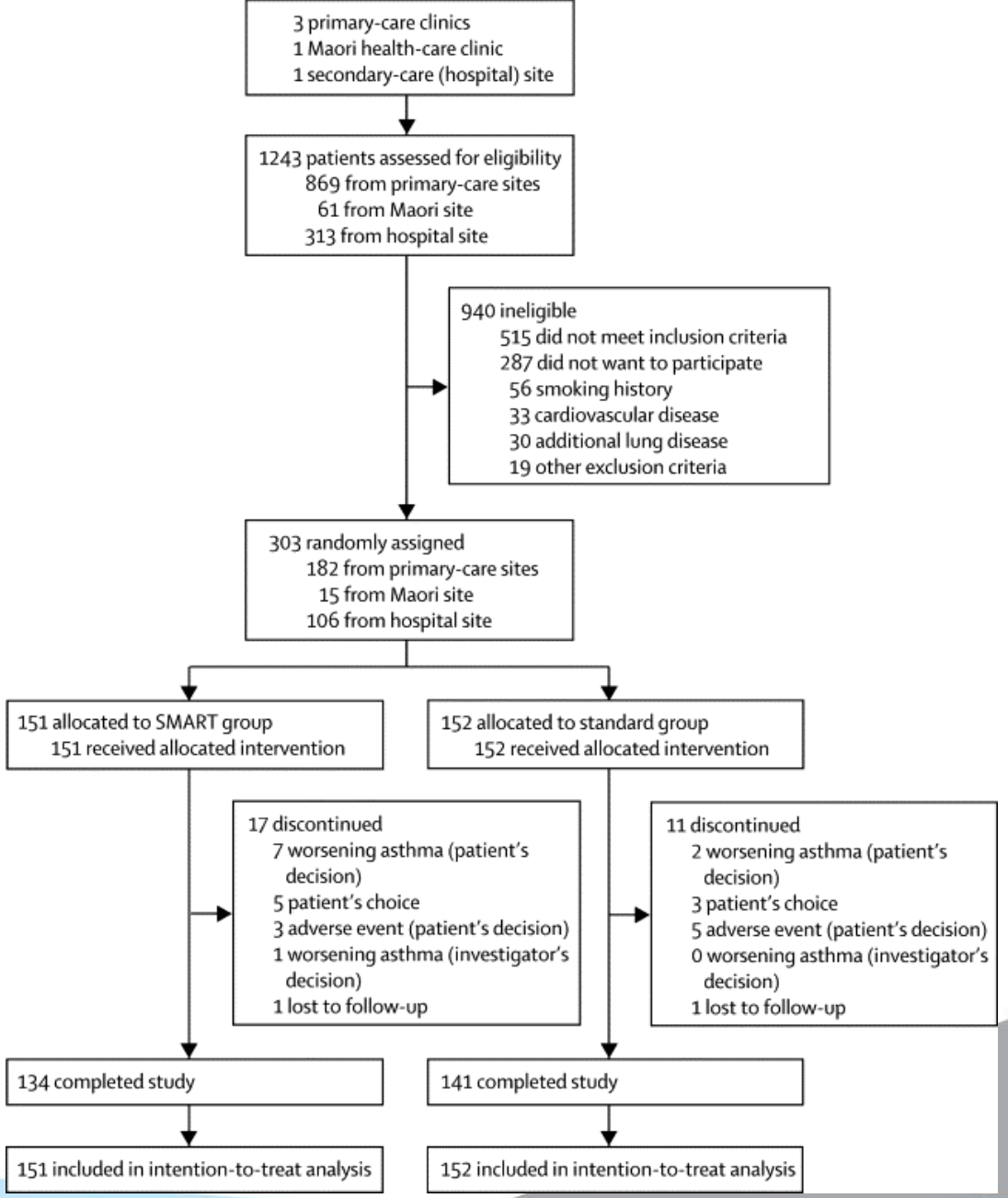
Gamble et al AJRCCM 2009

Single inhaler as maintainence and reliever therapy (SMART)

- Patients often perceive their reliever medication (a bronchodilator) to be the most effective
- Would it be better to add inhaled steroid to extra puffs of reliever medication, to treat the underlying inflammation?
- Note the phrase “maintenance and reliever”!
- Lots of industry funded studies on this, but criticised
  - Exclusion of “higher risk” patients who use a lot of beta-agonist
  - Dosing criticisms

Efficacy and safety of maintenance and reliever combination budesonide–formoterol inhaler in patients with asthma at risk of severe exacerbations: a randomised controlled trial

Mitesh Patel, Janine Pilcher, Alison Pritchard, Kyle Perrin, Justin Travers, Dominick Shaw, Shaun Holt, Matire Harwood, Peter Blackt, Mark Weatherall, Richard Beasley, for the SMART Study Group



	SMART group (n=151)	Standard group (n=152)	Relative risk (95% CI)	Relative rate (95% CI)*	p value
Primary outcome					
At least one high-use episode of medication	84 (56%)	68 (45%)	1·24 (0·99–1·56)	–	0·058
At least one high-use episode (adjusted for budesonide-formoterol use in excess of maintenance in the standard group)	84 (56%)	94 (62%)	0·90 (0·74–1·09)	–	0·27
Secondary outcomes†					
High use of medication					
Number of days of high use	5·1 (14·3)	8·9 (20·9)	–	0·58 (0·39–0·88)	0·01
Number of days of high use in participants with at least one high-use episode‡	9·1 (18·2)	19·9 (27·7)	–	–	–
Number of days of high use without medical review in participants with at least one high-use episode‡	8·5 (17·8)	18·3 (24·8)	–	0·49 (0·31–0·75)	0·001
Marked overuse of medication					
At least one episode of marked overuse	54 (36%)	56 (37%)	0·97 (0·72–1·31)	–	0·85
Number of days of marked overuse	2·6 (10·2)	4·8 (14·9)	–	0·56 (0·35–0·88)	0·013
Number of days of marked overuse in participants with at least one marked overuse episode§	7·4 (16·0)	13·1 (22·3)	–	–	–
Extreme overuse of medication					
At least one episode of extreme overuse	41 (27%)	40 (26%)	1·03 (0·71–1·50)	–	0·87
Number of days of extreme overuse	1·6 (6·7)	2·9 (12·2)	–	0·56 (0·34–0·91)	0·02
Number of days of extreme overuse in participants with at least one extreme overuse episode¶	5·8 (11·9)	11·0 (22·1)	–	–	–
Underuse of maintenance budesonide-formoterol‖					
At least 1 day with zero actuation	120 (79%)	126 (83%)	0·96 (0·86–1·07)	–	0·45
Number of days with zero actuation	23·9 (32·6)	33·6 (42·8)	–	0·72 (0·55–0·95)	0·022
At least 1 day with zero or one actuation	129 (85%)	132 (87%)	0·98 (0·90–1·08)	–	0·72
Number of days with zero or one actuation	28·8 (35·4)	36·9 (44·6)	–	0·80 (0·62–1·03)	0·087
At least 1 day with two or less actuations	143 (95%)	150 (99%)	0·96 (0·92–1·00)	–	0·052
Number of days with two or less actuations	61·3 (47·4)	70·6 (51·0)	–	0·89 (0·76–1·05)	0·19

Data are number (%) or mean (SD), unless otherwise indicated. SMART=Single combination budesonide-formoterol inhaler Maintenance And Reliever Therapy. *Weighted as part of the analysis and might be numerically different from the values calculated from the tabulated means. †Analysis of the relative rates of days of overuse was calculated by use of Poisson regression with an offset for the treatment exposure; the results of the analysis suggested overdispersion, which was adjusted with a dispersion term. ‡84 participants in the SMART group and 68 in the standard group. §54 participants in the SMART group and 56 in the standard group. ¶41 participants in the SMART group and 40 in the standard group. ‖Analysis of the relative rates for days of underuse was calculated by use of Poisson regression with an offset for the logarithm of the treatment exposure; the variable days of underuse was overdispersed and was corrected with a deviance-based term.

Table 2: **Medication use in the SMART and standard groups**

Bottom line messages

- Fascinating insight into patient behaviour, medication use, use of asthma action plans
- SMART protocol was as safe as standard, even though treatment was often not used as prescribed in either group
- Steroid exposure was equivalent (more inhaled in SMART, more oral in standard treatment)
- Fewer exacerbations with SMART
- No difference in ED visits and hospitalisations

The way forward?

Do we accept patient behaviour, and treat accordingly?

- Is this “SMART” approach the most appropriate in asthma?
- Role of other inhalers with LABA with rapid onset of effect?
- Would ICS/SABA combination work?

Would more effective education work, or be better?

- Open discussion about adherence – is this possible? Should all inhalers be microchipped?!
- What about effective, once daily inhalers? Would these improve adherence, particularly unintentional non-adherence?

What on earth can we do about intentional non-adherence??

COPD

- Affects in 1 in 15 NZers over age 45
- Prevalence in Maori twice that of other ethnicities
- NZ has the second highest rate of hospitalisations due to COPD in the OECD
- 30 day re-admission rate 17.9%; length of stay 4.2 days

Treatment

- Stop smoking!
- Pulmonary rehabilitation – the most effective treatment?

Effect Size of Interventions: Health Related Quality of Life

Intervention	HRQL; Change in Total SGQ Score.
<u>DRUGS</u> LABA	- 2.3 *
LABA + ICS	- 2.9 *
LABA + Tio vs Tio	- 1.6 *
LABA + Tio + ICS vs Tio	- 2.5 *
<u>Non-Pharmacologic Interventions</u> Rehabilitation	- 6.1 *
Smoking Cessation	- 2.9 to -11

LABA = Long-acting B agonist
ICS = Inhaled corticosteroid
Tio = Tiotropium

(* based on results of Cochrane Reviews)
Slide courtesy of Prof John Kolbe

COPD: prevent harm and treat comorbidities

- Increasingly clear link between inhaled steroids and pneumonia risk
  - Consider stopping or stepping down (especially if milder disease on spirometry, no or never asthma, few exacerbations or little prednisone use)
- Comorbidities:
  - Anxiety and depression
  - Osteopenia and osteoporosis
  - Malnutrition
  - Cardiac disease (more pts with COPD die of this than the COPD)
  - Lung cancer

COPD: statins

- Link between statin use and better COPD outcomes in cross-sectional observational studies
- ?direct effect on statins on lung inflammation in COPD
- STATCOPE study: no effect of statins in COPD patients without cardiac disease or risk factors
- What does this tell us?
  - Cardiac risk factors and disease prevalent in COPD
  - Optimising / treating this with statins improves outcomes
  - ?a marker of good care

Bronchiectasis

Clinical estimates of prevalence are 272-341 per 100,000

- Auckland bronchiectasis clinic population
  - Maori and Pacific over-represented, NZ Euro underrepresented
  - This persisted even when allowing for socio-economic status
  - Lung function did not show an accelerated decline in any group

- Rejuvenation of interest worldwide
  - New treatments: macrolides, mucolytics, inhaled antibiotics

Pneumococcal pneumonia and invasive disease

Recommendations

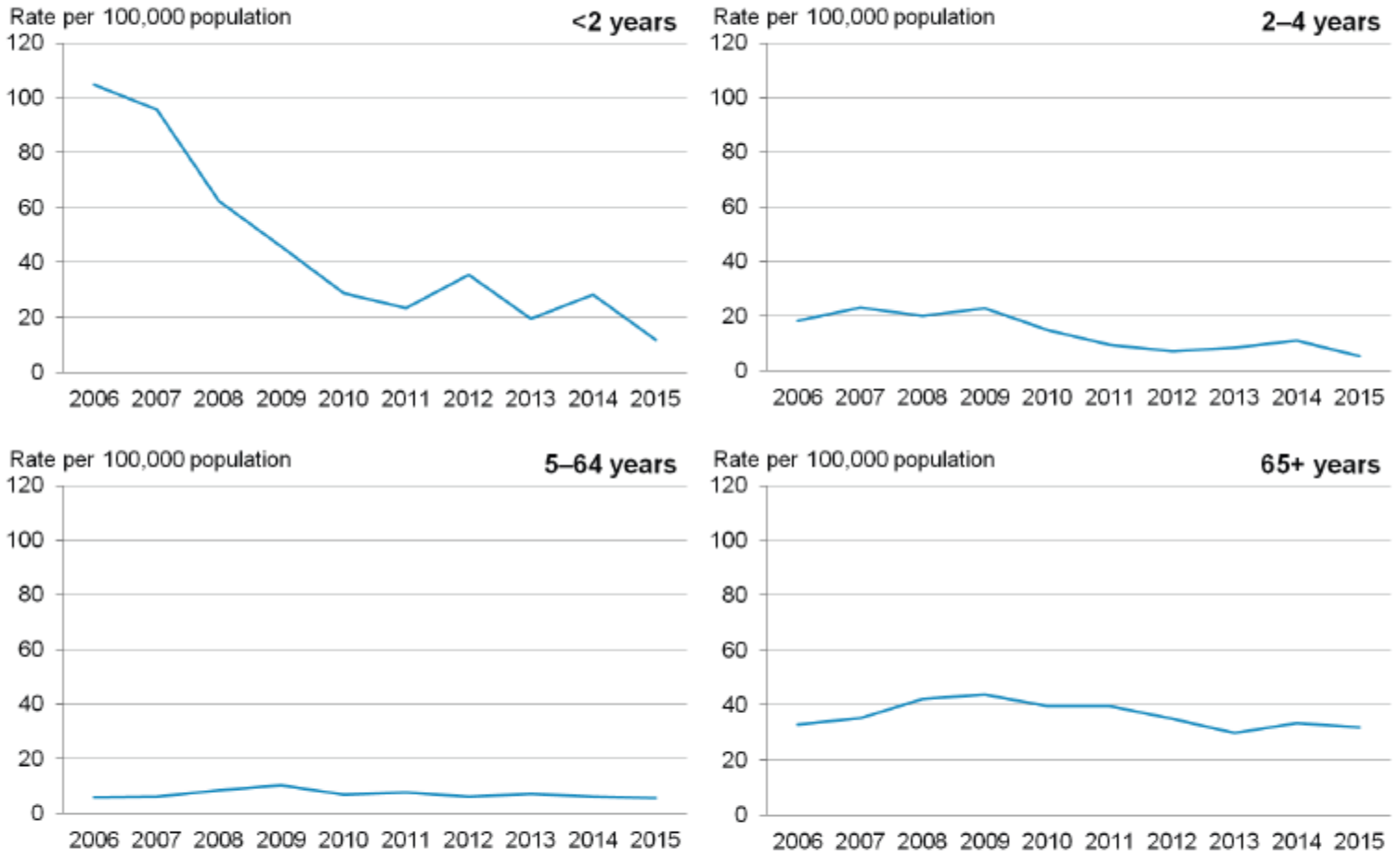
PCV13 and 23PPV are recommended but not funded for the following individuals:

- immune-competent adults (aged 18 years and older)at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic heart, renal, liver or **pulmonary disease**, diabetes or alcoholism)
- adults with cerebrospinal fluid leak
- Immunocompromised adults at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin's disease)
- individuals of any age who have had one episode of IPD
- **smokers**

Adults aged 65 years and older with no other risk factors

- Give one dose of PCV13 followed at least eight weeks later with 23PPV (not funded)

Figure 15.1: Rate per 100,000 of invasive pneumococcal disease by age group and year, 2006–2015



Notes:

PCV7 was introduced in 2008, PCV10 in 2011 and PCV13 in 2014.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Source: ESR

Lung cancer

- Leading cause of cancer death in NZ
- Most but not all are current or ex-smokers
- Screening?
  - Screening chest Xrays don't work
  - Annual low dose CT scans have been shown in NLST study to reduce lung cancer mortality, but questions remain
    - Cost and cost effectiveness
    - Applicability to non-trial population
    - Real life engagement

Lung cancer pathway

- HRC Auckland/Rotorua audit 2008
  - Delays in diagnosis were common
  - Delays more likely in those with early stage disease

- Chest Xray was a very important part of the work up
  - Abnormal in 90%, and played a key role in referral to secondary care
  - Only 65% had undergone a chest Xray at presentation to secondary care (compared to over 90% internationally)
  - (Denominator not clear)

Summary

- Preventing lung disease is very difficult, and would require major improvements in socio-economic deprivation
- Tobacco control is very important, as is smoke cessation
- Asthma treatments work well, but effective treatment of asthma patients is difficult due to poor adherence
- COPD is a systemic disease with important comorbidities
- Bronchiectasis is relatively common in NZ, and there are new treatments available
- Chest Xray plays an important role in early lung cancer diagnosis