CHERE
CENTRE FOR HEALTH ECONOMICS RESEARCH AND EVALUATION

UNIVERSITY OF TECHNOLOGY SYDNEY

CHEMOTHERAPY ADVERSE EVENTS IN A LARGE AUSTRLIAN ADMINISTRATIVE DATASET

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Chemotherapy

- Chemotherapy drugs can be life extending for people with cancer. But…
  - They contribute a small amount to survival
  - They are increasingly expensive
  - They cause side effects, which:
    - Impact on physical well-being and quality of life
    - Potentially effect cancer survival
    - Can be expensive to manage




Background – Economic evaluation

- In Australia, new drugs are listed for public subsidy on the basis of economic evaluation
- Literature review examined how side effects are incorporated into economic evaluations of chemotherapy
  - Costs and outcomes of side effects are not included in any systematic way
  - Clinical trials are the primary source of probabilities
  - Resource use is often estimated with expert opinion or based on best practice
- These data sources may not reflect clinical practice
- If side effects aren't accounted for (accurately) then outcomes of economic evaluations may be biased

Aims & Objectives

- Overall aim: To better inform models of chemotherapy cost effectiveness

- Objectives: Explore in clinical practice:
  1. the incidence of chemotherapy side effects
  2. the factors which influence the incidence of chemotherapy side effects
  3. the resource use associated with chemotherapy side effects

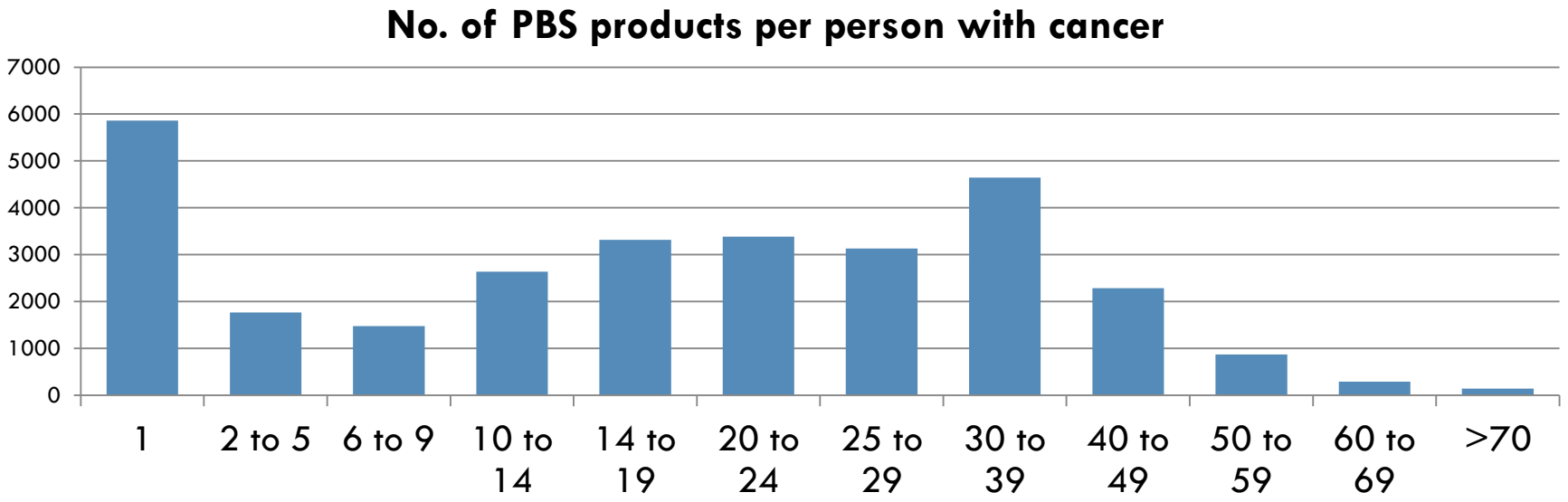
Data – data linkage

- Extract from DVA client database – individuals residing in NSW 1994 – 2007
- Linked by CHeReL to NSW population data

Registry	Start Date	End Date
NSW Cancer Registry	Jan 1994	Dec 2009
Repatriation PBS	01 July 2004	31 Jan 2010
Repatriation MBS	01 Jan 2000	31 Jan 2010
Admitted Patient Data Collection	01 July 2000	30 June 2009
Emergency Department Data	01 Jan 2005	31 Dec 2009
Resource utilisation period	**01 Jan 2005**	**30 June 2009**

Sample

- Individual Gold Card Holders 129,307
  - Individuals with a cancer diagnosis 29,480
  - Individuals who received chemotherapy 12,030
  - Total doses of chemotherapy 111,059



Sample demographics

Demographic		Chemo cohort
Proportion Males		72%
Mean (median) Age in years		81 (83)
Age range		46 - 106
Age group	<70 yrs	14%
	70-80 yrs	23%
	>80 yrs	63%
Mean Rx Risk score (weighted comorbidities)		8.83
RxRisk score range		0 - 26

Cancer

Cancer site	N	% of cancer
Prostate	3124	39.17
Breast	1059	13.28
Melanoma of skin	881	11.05
Colon	491	6.16
Lung	354	4.44
Non-Hodgkin's lymphoma	349	4.38
Rectum, rectosigmoid, anus	279	3.5
Bladder	186	2.33
Ill-def & unspec site	136	1.71
Head & neck	591	0.65

Cancer spread	% of spread
Localised	39.27
In-situ	4.5
Regional	12.98
Distant	7.25
Unknown	36.01

Methods – overview of assumptions

- 4 common side effects examined:
  - Diarrhoea
  - Anaemia
  - Nausea and vomiting (N&V)
  - Neutropenia
- Drugs, medical resources and hospitalisations associated with treating these side effects were specified based on best practice guidelines
- Treatment of a side effect was considered related to chemotherapy when it occurred on or within three days after a dose of chemotherapy

Methods - overview

- Aim 1: The **incidence** of each side effect was calculated
- Aim 2: **Multiple regression** analysis using **generalised estimating equations** identified factors which influence the incidence of each side effect
- Aim 3: **Multiple linear regression** identified whether those who experienced an adverse event had higher chemotherapy costs

Aim 1: Methods & outcome measure

- No direct data on whether someone experiences a side effect, so require a proxy
- Standard treatments are used for side effects, so these can be 'related' to chemotherapy by time
- In interpretation, need to consider:
  - individuals may have these treatments for other reasons
  - individuals may have side effects and not receive these treatments
- For each dose of chemotherapy dispensed, a search was done of any side effect treatments which were given to the same individual within 3 days

Aim 1 Results: Incidence of side effects

	Side effects	No. with chemotherapy	No. with side effect	% with side effect
By doses	Diarrhoea	89,594	879	1%
	Anaemia	84,872	638	<1%
	Nausea & vomiting	84,378	5,415	6%
	Neutropenia	84,495	601	<1%
By person	Diarrhoea	7,978	396	5%
	Anaemia	8,158	330	4%
	Nausea & vomiting	9,173	1,535	17%
	Neutropenia	8,069	242	3%

Aim 2: Methods

- Multiple regression used to identify factors which influence the incidence of each side effect
- Binary outcome, so logistic model required
- Correlated data noted
  - Can restructure data to remove correlation, using a summary measure (eg: ever had a side effect), or
  - Can use technique designed for correlated data, such as Generalised Estimating Equations (GEE)

$$side\ effect \sim \alpha + gender + age + RxRisk + chemo + cancer + \varepsilon$$

Aim 2: Summary of results (1/3)

Variable	Diarrhoea	Nausea & vomiting	Anaemia	Neutropenia
Gender (female)	ND	Increase***	ND	ND
Age (younger)	Increase***	Increase***	ND	ND
RxRisk (fewer co-morbidities)	Decrease*	Decrease*	Decrease***	Decrease**

* <0.05, **<0.01, ***<0.001

- Females are1.6 times more likely to experience N&V
- Every additional year of age decreases odds of diarrhea by 4% and decreases odds of N&V by 3%
- Moving from highest to lowest RxRisk reduces odds of a side effect by 25% (N&V) to 60% (neutropenia)

Aim 2: Summary of results (2/3)

Variable	Diarrhoea	N&V	Anaemia	Neutropenia
Breast cancer	ND	Decrease*	ND	Increase***
Colorectal cancer	ND	ND	ND	Increase***
Genital cancer	ND	ND	ND	Increase***
Lung cancer	Decrease*	ND	ND	Increase***
Non-solid tumours	Decrease*	Decrease***	ND	Increase***
Other	ND	ND	ND	Increase***

* <0.05, **<0.01, ***<0.001

- Compared to urinary cancer:
  - Diarrhoea odds were 70% lower in lung and 60% lower in non-solid cancers
  - N&V odds were reduced by nearly half in breast cancer and by over 60% in non-solid tumours
  - The increase of odds of neutropenia was highest for non-solid tumours (50-fold) and lung cancers (20-fold)

Aim 2: Summary of results (3/3)

Variable	Diarrhoea	N&V	Anaemia	Neutropenia
Antineoplastic	Decrease***	Increase***	ND	Increase*
Progestogens	ND	Increase*	ND	ND
LHRH agnoists	Decrease***	Increase***	Decrease**	Increase***
Anti-estrogens	Decrease*	Increase***	ND	Increase***
Anti-androgens	Decrease**	Increase***	Decrease***	Increase*
Aromatase inhibitors	Decrease*	ND	Decrease*	ND
Immunostimulants	ND	ND	ND	Increase***

* <0.05, **<0.01, ***<0.001

- Compared to immunosuppresants:
  - Antineoplastics lower odds of diarrhea by over 70%
  - Anti-androgens increased odds of N&V by 13-fold
  - AIs decrease odds of anemia by 84%
  - Immunostimulants increased odds of neutropenia by 700-fold

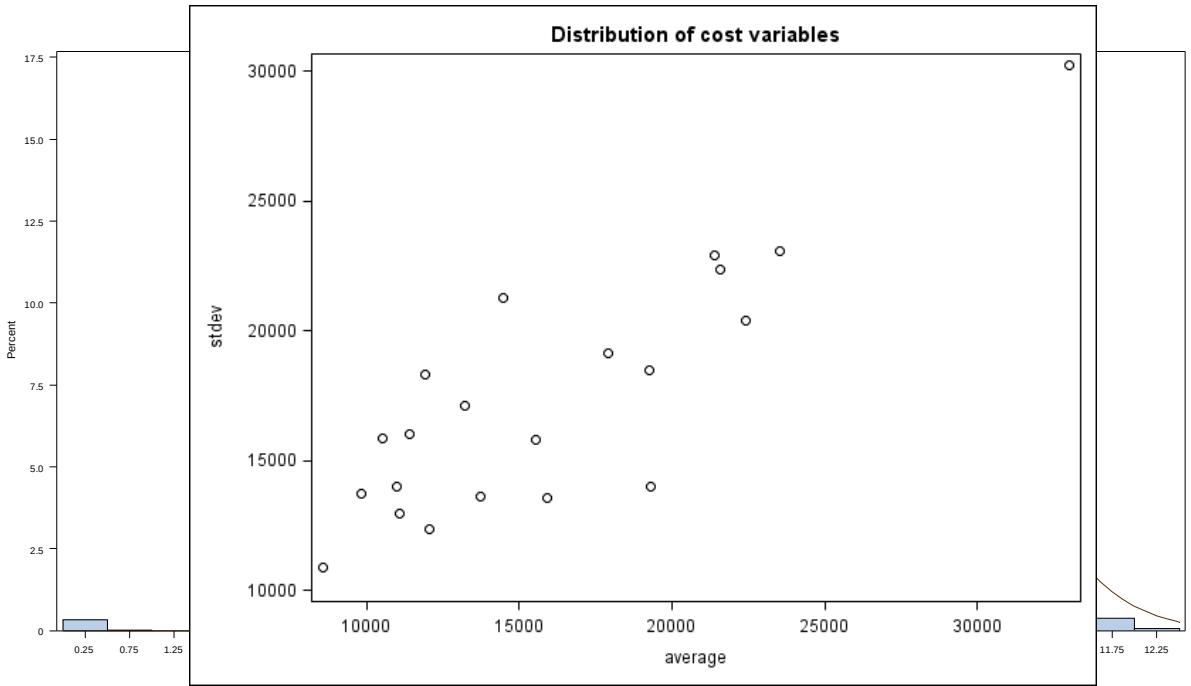
Aim 3 methods: Cost and side effects

$$Total\ cost \sim \alpha + gender + age + RxRisk + cancer + doses + any\ se + \varepsilon$$

Variable	Levels
Total cost	Total health care expenditure (medical services, hospitalisation &/or pharmaceuticals) during the 6-month period following the first dose of a new chemotherapy regimen from 1st Jan 2005
Gender	Male / Female
Age	<70 years 70 – 79 years >79 years
RxRisk	Quartiles (0-7, 8-9, 10-12, 13-26)
Doses	Total number of doses of chemotherapy (continuous)
Cancer	Consolidated to 7 levels based on ICD classification
Any side effect	Diarrhoea OR Anaemia OR N&V OR Neutropenia

Aim 3: Results
Data distribution

- Data highly skewed
- Log-transformed data approaches normal
- Mean vs standard deviation for raw costs shows an approximate constant coefficient of variation



Aim 3 Results: Generalised linear model

Parameter	Category	Exp (Estimate)	Exp (Wald 95% Confidence Limits)	
Intercept		14237.01	10515.44	19273.76
anydia	1	0.89	0.79	1.00
anynausea	1	**1.61**	1.51	1.72
anyanemia	1	**1.33**	1.18	1.51
anyneut	1	**1.54**	1.34	1.76
Scale		2.95	2.85	3.06

Conclusions

- This large administrative dataset provides an opportunity to examine 'real life' incidence of chemotherapy side effects in older people
- Being treated for a likely side effect is more common in individuals who are older or who have more co-morbidities
- Being treated for a likely side effect may be influenced by the type of cancer and chemotherapy an individual has
- Being treated for a likely side effect significantly increases overall healthcare costs

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