CHEMOTHERAPY ADVERSE EVENTS IN A LARGE ADMINISTRATIVE DATASET

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Background

- Chemotherapy can be life extending for people with cancer
- But… it also causes side effects (adverse events)
- These side effects can:
  - Impact on patients physical wellbeing
  - Impact on patients quality of life (QoL)
  - Be expensive to manage

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 in chemotherapy economic evaluations
  - Clinical trials are the primary data source of side effect probabilities
  - Resource use is often estimated with expert opinion
- Clinical trials and expert opinion do not necessarily reflect clinical practice

Aims

- Explore in 'real life' clinical practice:
  - the incidence of chemotherapy side effects
  - the factors which influence the incidence of chemotherapy side effects
  - the resource use associated with chemotherapy side effects

- Outcome: To better inform models of chemotherapy cost effectiveness

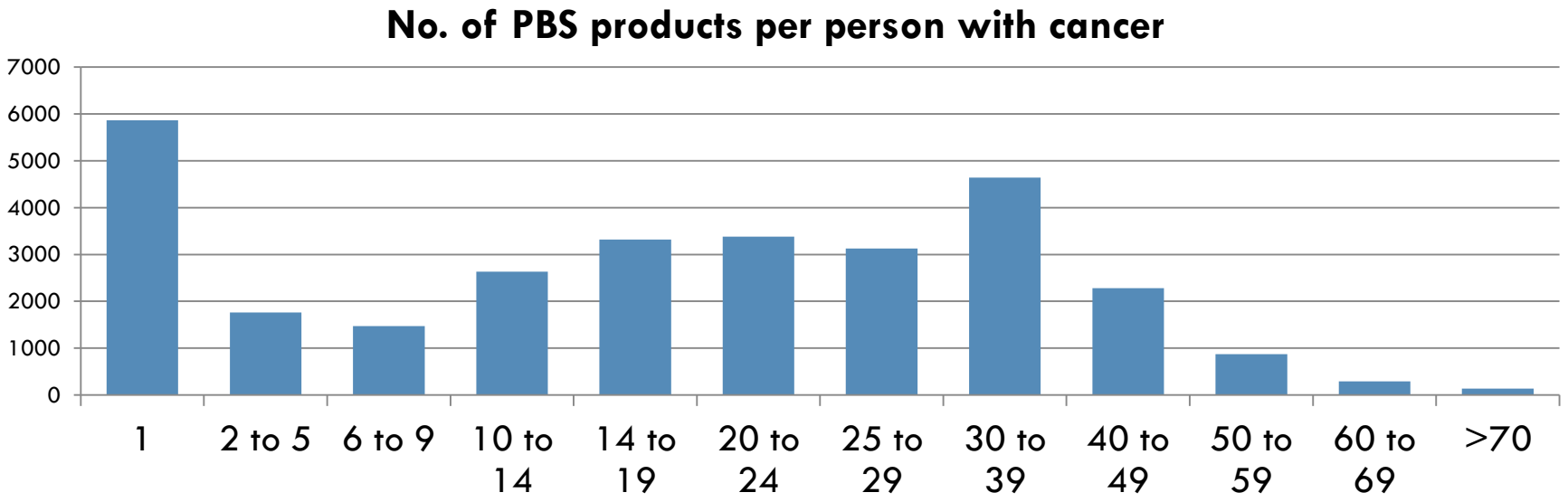
Data

- Extract of DVA clients residing in NSW for all or part of 1994 – 2007 from the DVA client database

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



Demographics of those with cancer and chemotherapy

Demographic		Chemo cohort
Proportion Males		72%
Mean Age (median) 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

Chemotherapy

Drug	Frequency	% of chemo	Used to treat…
Fluorouracil	2198	18.20	Breast, colorectal
Goserelin acetate	1909	15.80	Prostate, breast
Leuprorelin acetate	1307	10.82	Prostate
Bicalutamide	1005	8.32	Prostate, breast
Tamoxifen citrate	776	6.42	Breast
Capecitabine	327	2.71	Breast, colorectal
Rituximab	321	2.66	Lymphoma
Cyclophosphamide	305	2.53	Breast, leukemia
Anastrazole	280	2.32	Breast
Gemcitabine	276	2.28	Breast, lung, bladder, pancreas

Methods - assumptions

- 3 common side effects examined:
  - Diarrhoea
  - Anaemia
  - Nausea and vomiting
- 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

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

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%
By person	Diarrhoea	7,978	396	5%
	Anaemia	8,158	330	4%
	Nausea & vomiting	9,173	1,535	17%

Regression analysis

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

Variable	Levels
Gender	M/F
Age	<70 70 - 79 >79
RxRisk (comorbidities)	Quartiles (0-7, 8-9, 10-12, 13-26)
Chemo	Consolidated to 8 levels based on ATC code
Cancer	Consolidated to 7 levels based on ICD classification

Generalised estimating equations

- Allow the correlation of outcomes within an individual to be estimated and taken into account in the regression coefficients and their standard errors
- The regression coefficients obtained from GEE are correctly interpreted in a population averaged manner
- Specifications of my GEE models
  - Repeated subject variable — PPN
  - Distribution — Binomial
  - Link function — Logit
  - Correlation structure — Exchangeable

Summary of results – influence of variables on odds of side effect

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

- Females 1.4 times more likely to experience N&V
- The youngest age group has 40% lower odds of N&V and 80% lower odds of anemia
- Moving from highest to lowest RxRisk reduces odds of diarrhea 43% and anemia 50%

Summary of results – influence of variables on odds of side effect

Variable	Diarrhoea	Nausea & vomiting	Anaemia
Breast cancer	ND	ND	ND
Colorectal cancer	Increase**	ND	ND
Genital cancer	ND	ND	ND
Lung cancer	Decrease*	Increase***	ND
Non-solid tumours	Decrease***	ND	ND
Other	ND	ND	ND

- Compared to urinary cancer:
  - Colorectal cancer 2.4 times more likely to have diarrhoea
  - Lung cancer 2.5 times more likely to have N&V

Summary of results – influence of variables on odds of side effect

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

- Compared to immunosuppresants:
  - LHRH agonists lower all SE odds by 70 - 75%
  - Anti-androgens lower all SE odds by 54 - 74%
  - Antineoplastics have 3 times the odds of N&V

Preliminary results: Cost and side effects

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

Variable	Cost
Gender (female)	Decrease***
Age (being younger)	ND
RxRisk (fewer co-morbidities)	Decrease*
Breast	Decrease***
Colorectal	ND
Genital	Increase*
Lung	ND
Non-solid tumour	Increase***
Other	ND
More doses of chemo	Increase***
Any side effect	**Increase*** **

- Each additional dose of chemotherapy increases total cost by $461
- Experiencing an adverse event increases overall cost by $1506

Conclusions

- This large administrative dataset provides an opportunity to examine 'real life' incidence of chemotherapy side effects in older people
- Side effects are more common in individuals who are older or who have more co-morbidities
- Some side effects may be influenced by the type of cancer and chemotherapy an individual has
- Experiencing a side effect appears to significantly increase overall healthcare costs, however further analysis is required

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