



University
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Analysis of adverse events and quality of life data for an economic evaluation of adjuvant chemotherapy in colorectal cancer

Can we stop collecting QoL data?

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Assessment

On behalf of the SCOT study team

The SCOT study is supported by a trial grant from the MRC. Cancer Research UK supports the Glasgow Clinical Trials (Beatson West of Scotland Cancer Care) via a programme grant.

- **SCOT trial**
 - Phase III RCT, multi-centre (7 years)
 - Colorectal cancer patients (stage III)
 - 3 versus 6 months adjuvant chemotherapy
 - 3 year disease free survival (DFS)
 - Economic analysis: cost-effectiveness
 - resource use, adverse events, toxicity, quality of life (QoL)
- **Can we reduce toxicity, reduce cost & retain 3yr DFS?**
- **QoL & toxicity data collection**
 - Sample required less than overall trial sample
 - Burdensome for patients & professionals

When can we stop collecting QoL data from new recruits?

- **Interim Analysis**
 - Can we stop collecting qol data from new recruits?
 - Is the sample to date large enough to detect whether the AEs and severity of AEs impact on quality of life?
- **Background**
- **Methods**
- **Results**
- **Conclusions**

Method

- **Interim dataset Jan 2008-Dec 2010**
- **N=1292 participants with data on EQ-5D**
 - Baseline, each cycle, 9, 12, 18, 24 months, annually thereafter
 - Adverse Events (AEs)
 - Toxicity grade
 - QoL (EQ-5D)
- **Cleaned data, merged datasets**
- **STATA 10.0 (StataCorp, TX, USA)**

- **EQ-5D – QoL**
- **Adverse events**
 - 18 most common AEs also had greatest proportion \geq grade 3
- **Grades 0-5**
 - 0 = Reference case (no AE)
 - 5 = Death
- **New categorical grade variable**
 - 0= no AE, 1= grade 1 & 2, 2= grade 3 & 4
- **Univariate & multivariate analysis**

Results (1) – Adverse Events

Do adverse events impact on QoL?

Univariate

Regress each AE against QoL individually

All 18 AEs have a negative impact on QoL with a p-value of 4% or less

Multivariate

Regress all AEs against QoL simultaneously

AEs were highly correlated with one another

Inconclusive results

Adverse Event Impact on QoL

	Adverse Event	No AE (n)	< Grade 3 (n)	>=Grade 3 (n)	Impact on QoL	p-value
1	Alopecia	2082	246	8	-0.0168	0.039
2	Anaemia	2082	757	3	-0.0168	0.039
3	Anorexia	2083	315	22	-0.017	0.036
4	Constipation	2084	512	11	-0.017	0.037
5	Dairrhoea	2081	1190	94	-0.0168	0.042
6	Fatigue	2081	1826	60	-0.0166	0.042
7	Hand & Foot Syndrome	2082	383	21	-0.0168	0.039
8	Mucositis clinical	2082	181	60	-0.0168	0.039
9	Mucositis functional	2082	506	18	-0.0168	0.039
10	Nausea	2081	1117	29	-0.0168	0.039
11	Neuropathy Sensory	2081	2220	33	-0.0166	0.042
12	Neutropenia	2081	305	85	-0.0166	0.042
13	Photophobia	2083	43	20	-0.017	0.036
14	Rash	2082	161	15	-0.0168	0.039
15	Taste Alteration	2082	723	20	-0.0168	0.039
16	Thrombocytopenia	2083	324	8	-0.017	0.036
17	Vomiting	2081	257	22	-0.016	0.042
18	Watery Eye	2083	241	20	-0.017	0.036

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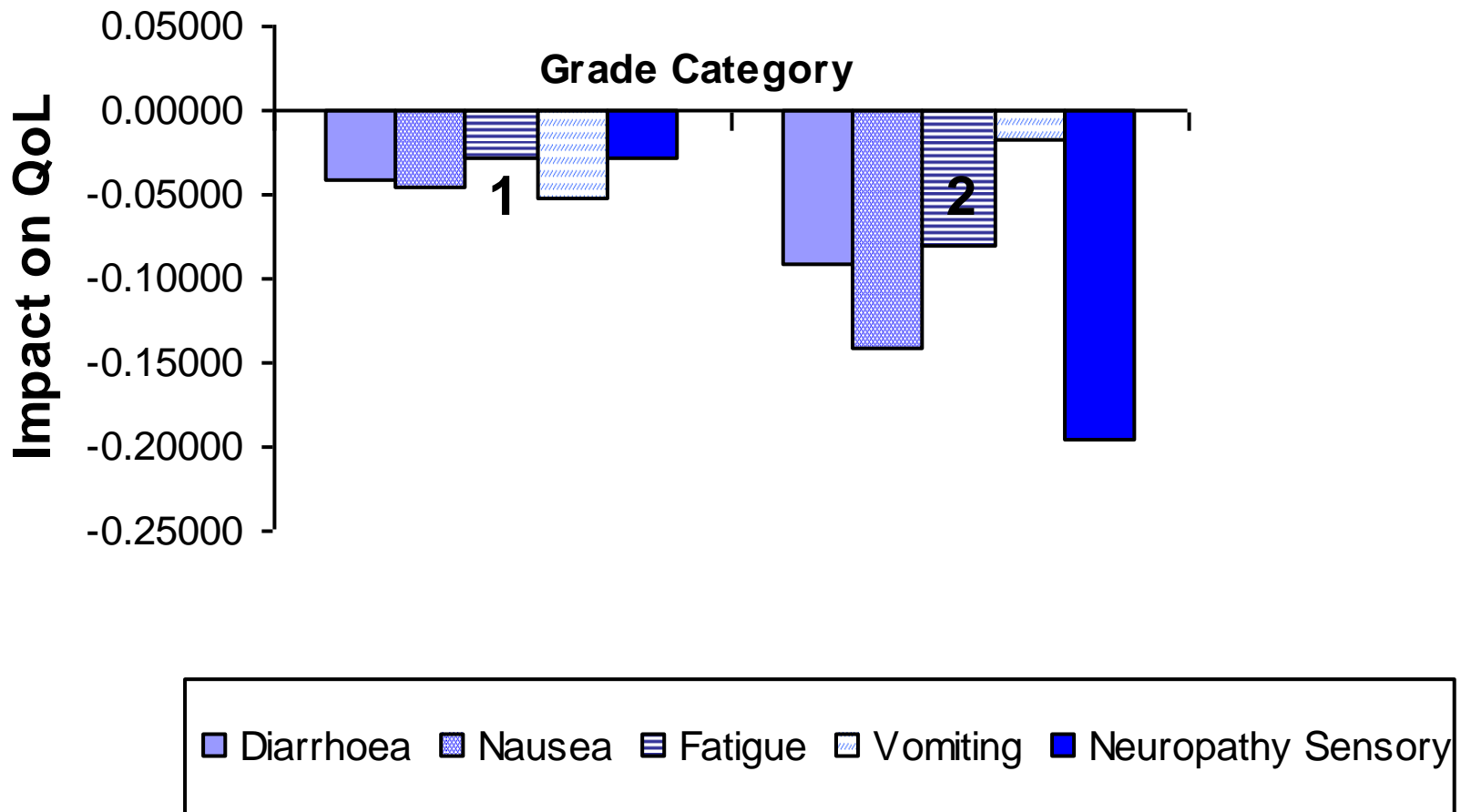
Inconclusive results

Results (2): Univariate AE Grade

0 No AE	1 Grade 1 & 2	2 Grade 3 & 4	3 Grade 5
Baseline	Significantly reduce QoL 12 AEs significantly reduced QoL	Variable results Few observations of grade 3 or 4	Dead No QoL
	Impact on QoL (p-value)	Impact on QoL (p-value)	
Diarrhoea	-0.04 (0.001)	-0.09 (0.010)	
Nausea	-0.046 (0.000)	-0.141 (0.067)	
Fatigue	-0.028 (0.007)	-0.08 (0.190)	
Vomiting	-0.052 (0.020)	-0.017 (0.800)	
Neuropathy	-0.029 (0.029)	-0.197 (0.031)	

In general an increasing grade has a negative impact on QoL

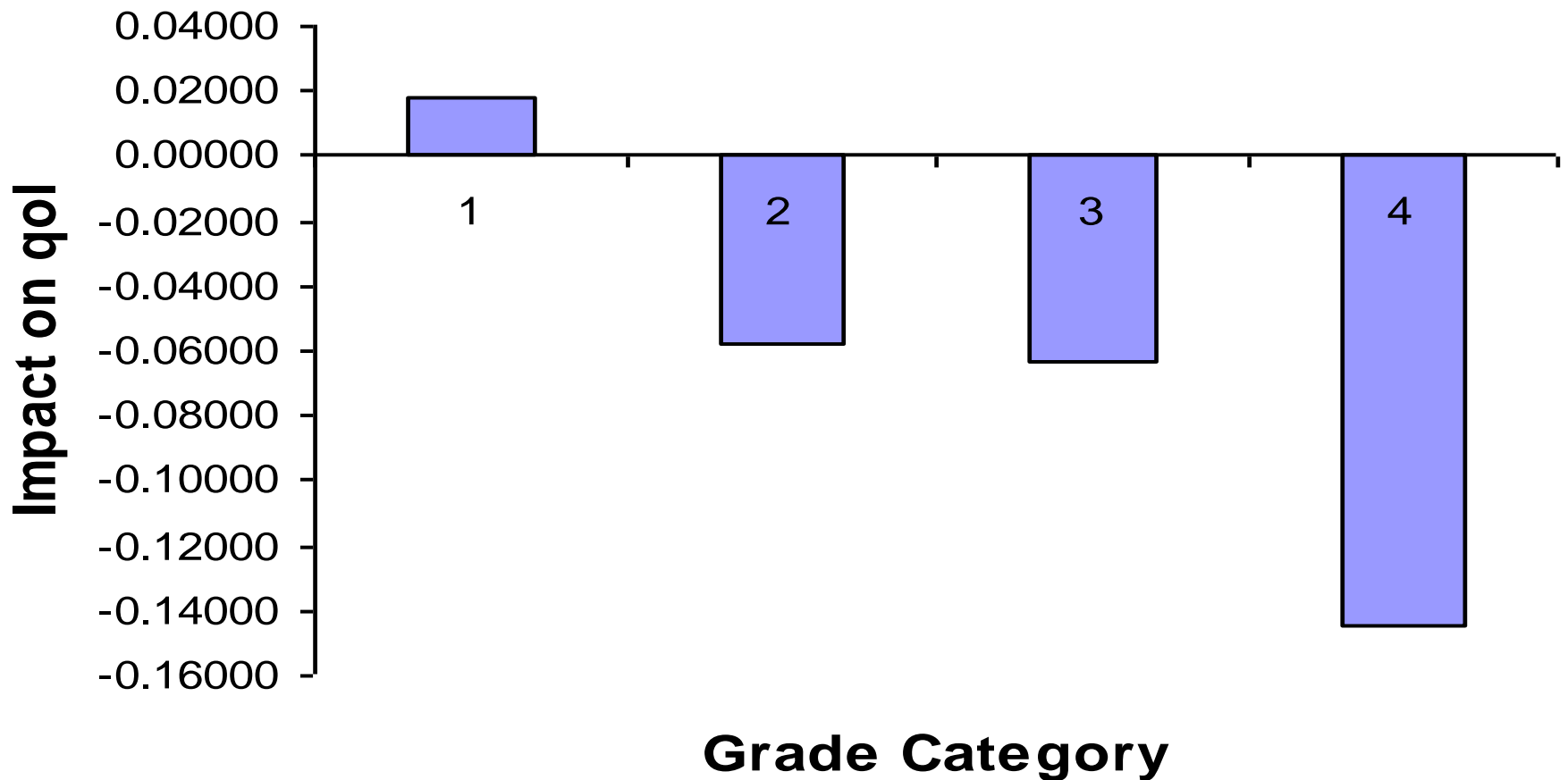
Adverse Event Grade Categories



- **Many variables are dropped**
- **None show a significant impact on QoL**
- **Some coefficients were positive, but...**
 - All have a –ive lower 95% CI
- **Multivariate analysis still inconclusive**

A final check

Overall Grade categories



Conclusion

Do AE and AE grades impact on QOL?

Univariate AE V QoL: all 18 AEs ↓ QoL (4% sig)
Increasing AE grade ↓ QoL
Increasing overall grade ↓ QoL

Multivariate AEs highly correlated
AEs do not occur independently
Multi-collinearity = inconclusive

In Absence of Multivariate = rely on univariate

We have sufficient evidence.....stop collecting!