Brighton and Sussex University Hospitals NHS Trust

NCIN national cancer intelligence network
Using information to improve quality & choice

Simplifying the measurement of co-morbidities and their influence on chemotherapy toxicity

Dr Rajesh Sinha BSc MBBS MRCP, Clinical Research Fellow in Medical Oncology

Dr Alistair Ring MA BM BCh MRCP MD, Senior Lecturer and Honorary Consultant in Medical Oncology

Sussex Cancer Network

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CIRU Brighton and Sussex Clinical Investigation and Research Unit

Co-Morbidity + Fitness

- Impact in the physicians' choice/decision of chemotherapy usage and regimen for an individual patient
- No-one agreed gold standard method of using and measuring co-morbidity and assessing fitness, and how this influences treatment

Methods

- August 2009 to August 2011
- REC-approved research project (Brighton East REC09/H1107/60)
- Approached all patients over ≥18 in Sussex Cancer Network who were to undergo a new course of chemotherapy in any setting
- 533 patients were invited to take part
- Demographics
- Cancer + chemotherapy data
- Consent for access to hospital notes (HN) and Primary Physician Summaries (PPS) and in a proportion of patients, HES (Hospital Episode Statistics) data
- Co-Morbidity
  - Charlson Co-Morbidity Index (CCI)
  - Adult Co-Morbidity Evaluation (ACE-27)
  - Coders
    - Physician (PHY)
    - Healthcare assistant (HCA)
- Self-complete a fitness screening test (G8 score) and questionnaires regarding their functional status (VES-13 and performance status)

Aims

Aims

- Co-Morbidity
  - To compare the co-morbidity index scoring between physician and healthcare assistant by two methods from two sources
  - To compare Charlson Co-Morbidity Index Scoring between hospital notes and Hospital Episode Statistics data
  - Does poor co-morbidity predict severe chemotherapy toxicity
- Functional Status/Fitness
  - Does G8/VES-13/WHO PS score predicts severe chemotherapy toxicity
  - Severe Chemotherapy Toxicity
    - Grade III/IV toxicity (CTCAE [Common Terminology Criteria for Adverse Events] Version 3.0 criteria)
    - Dose reduction
    - Unplanned hospitalization
    - Treatment discontinuation
    - Death within 30 days of treatment

Analysis

Comparing scorers + sources

- Two way contingency tables and measure agreement by Cohen's kappa were used
- Agreement would be regarded as
  - Good if kappa > 0.80
  - Substantial if 0.61 ≤ kappa ≤ 0.80
  - Moderate if 0.41 ≤ kappa ≤ 0.60
  - Fair if 0.21 ≤ kappa ≤ 0.4
  - Poor if kappa ≤ 0.20

Co-Morbidity score/Functional status and prediction of chemotherapy toxicity

- Chi-Squared test

CCI

- Each significant co-morbidity generates a score
- More serious the co-morbidity, higher the score
- Sum of the scores (0-37)
- However very broad medical groupings
- CCI Database – over 3150 separate entries

Co-morbidities	Present	Points
Myocardial infarction		1
Congestive cardiac failure		1
Peripheral vascular disease		1
Cerebrovascular disease (except hemiplegia)		1
Dementia		1
Chronic obstructive pulmonary disease		1
Connective tissue disease		1
Ulcers		1
Mild liver disease		1
Diabetes Mellitus (without end-organ damage)		1

Co-morbidities	Present	Points
Diabetes Mellitus (with end-organ damage)		2
Hemiplegia		2
Moderate / Severe chronic renal failure		2
Second malignancy (non metastatic)		2
Leukaemia		2
Lymphoma		2
Moderate / Severe liver disease		3
Second malignancy (metastatic)		6
AIDS		6
Total points (0-37)		….

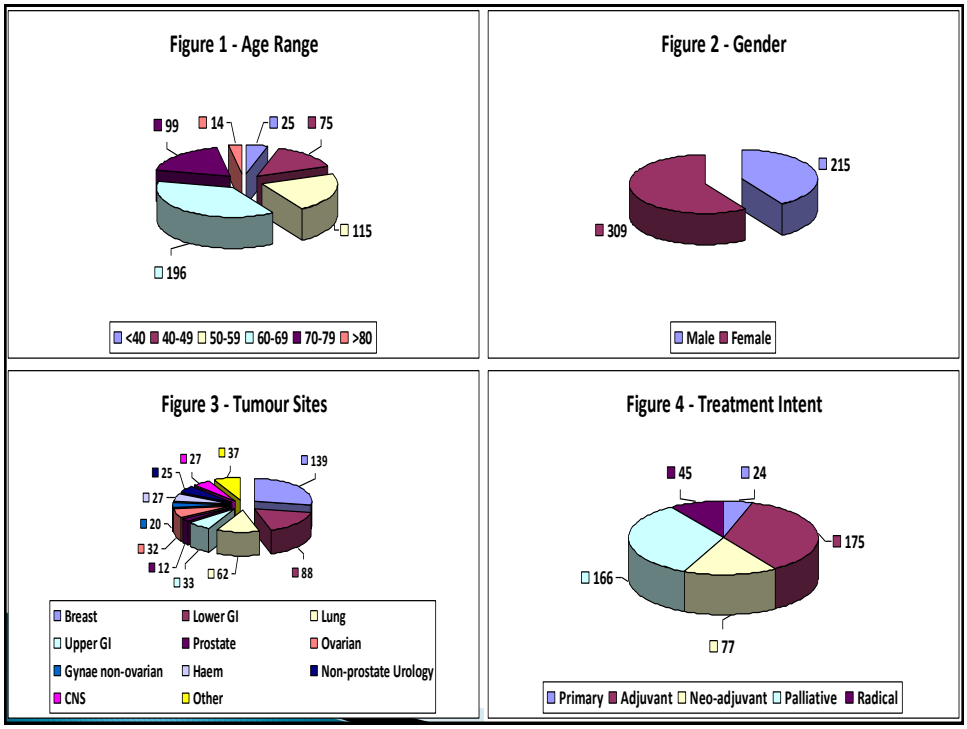
ACE-27

- Broad medical groupings
- Severity
- Highest score is what is recorded (0-3)
- Score a 2 in two separate systems, the score generated is 3
- No database

Cogent comorbid ailment	Grade 3 Severe Decompensation	Grade 2 Moderate Decompensation	Grade 1 Mild Decompensation
Cardiovascular System			
Myocardial Infarct	☐ MI ≤ 6 months	☐ MI > 6 months ago	☐ MI by ECG only, age undetermined
Angina / Coronary Artery Disease	☐ Unstable angina	☐ Chronic exertional angina ☐ Recent (≤ 6 months) Coronary Artery Bypass Graft (CABG) or Percutaneous Transluminal Coronary Angioplasty (PTCA) ☐ Recent (≤ 6 months) coronary stent	☐ ECG or stress test evidence or catheterization evidence of coronary disease without symptoms ☐ Angina pectoris not requiring hospitalization ☐ CABG or PTCA (>6 mos.) ☐ Coronary stent (>6 mos.)
Congestive Heart Failure (CHF)	☐ Hospitalized for CHF within past 6 months ☐ Ejection fraction < 20%	☐ Hospitalized for CHF >6 months prior ☐ CHF with dyspnea which limits activities	☐ CHF with dyspnea which has responded to treatment ☐ Exertional dyspnea ☐ Paroxysmal Nocturnal Dyspnea (PND)
Arrhythmias	☐ Ventricular arrhythmia ≤ 6 months	☐ Ventricular arrhythmia > 6 months ☐ Chronic atrial fibrillation or flutter ☐ Pacemaker	☐ Sick Sinus Syndrome ☐ Supraventricular tachycardia
Hypertension	☐ DBP≥130 mm Hg ☐ Severe malignant papilledema or other eye changes ☐ Encephalopathy	☐ DBP 115-129 mm Hg ☐ DBP 90-114 mm Hg while taking antihypertensive medications ☐ Secondary cardiovascular symptoms: vertigo, epistaxis, headaches	☐ DBP 90-114 mm Hg while not taking antihypertensive medications ☐ DBP <90 mm Hg while taking antihypertensive medications ☐ Hypertension, not otherwise specified
Venous Disease	☐ Recent PE (≤ 6 mos.) ☐ Use of venous filter for PE's	☐ DVT controlled with Coumadin or heparin ☐ Old PE > 6 months	☐ Old DVT no longer treated with Coumadin or Heparin
Peripheral Arterial Disease	☐ Bypass or amputation for gangrene or arterial insufficiency < 6 months ago ☐ Untreated thoracic or abdominal aneurysm (≥6 cm)	☐ Bypass or amputation for gangrene or arterial insufficiency > 6 months ago ☐ Chronic insufficiency	☐ Intermittent claudication ☐ Untreated thoracic or abdominal aneurysm (< 6 cm) ☐ s/p abdominal or thoracic aortic aneurysm repair
Respiratory System			
	☐ Marked pulmonary insufficiency ☐ Restrictive Lung Disease or COPD with dyspnea at rest despite treatment ☐ Chronic supplemental O_2 ☐ CO_2 retention (pCO_2 > 50 torr) ☐ Baseline pO_2 < 50 torr ☐ FEV1 (< 50%)	☐ Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnea which limits activities ☐ FEV1 (51%-65%)	☐ Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnea which has responded to treatment ☐ FEV1 (66%-80%)
Gastrointestinal System			
Hepatic	☐ Portal hypertension and/or esophageal bleeding ≤ 6 mos. (Encephalopathy, Ascites, Jaundice with Total Bilirubin > 2)	☐ Chronic hepatitis, cirrhosis, portal hypertension with moderate symptoms "compensated hepatic failure"	☐ Chronic hepatitis or cirrhosis without portal hypertension ☐ Acute hepatitis without cirrhosis ☐ Chronic liver disease manifested on biopsy or persistently elevated bilirubin (>3 mg/dl)
Stomach / Intestine	☐ Recent ulcers(≤ 6 months ago) requiring blood transfusion	☐ Ulcers requiring surgery or transfusion > 6 months ago	☐ Diagnosis of ulcers treated with meds ☐ Chronic malabsorption syndrome ☐ Inflammatory bowel disease (IBD) on meds or h/o with complications and/or surgery
Pancreas	☐ Acute or chronic pancreatitis with major complications (phlegmon, abscess, or pseudocyst)	☐ Uncomplicated acute pancreatitis ☐ Chronic pancreatitis with minor complications (malabsorption, impaired glucose tolerance, or GI bleeding)	☐ Chronic pancreatitis w/o complications

Cogent comorbid ailment	Grade 3 Severe Decompensation	Grade 2 Moderate Decompensation	Grade 1 Mild Decompensation
Renal System			
End-stage renal disease	☐ Creatinine > 3 mg% with multi-organ failure, shock, or sepsis ☐ Acute dialysis	☐ Chronic Renal Insufficiency with creatinine >3 mg% ☐ Chronic dialysis	☐ Chronic Renal Insufficiency with creatinine 2-3 mg%.
Endocrine System	**(Code the comorbid ailments with the (*) in both the Endocrine system and other organ systems if applicable)**		
Diabetes Mellitus	☐ Hospitalization ≤ 6 months for DKA ☐ Diabetes causing end-organ failure ☐ retinopathy ☐ neuropathy ☐ nephropathy* ☐ coronary disease* ☐ peripheral arterial disease*	☐ IDDM without complications ☐ Poorly controlled AODM with oral agents	☐ AODM controlled by oral agents only
Neurological System			
Stroke	☐ Acute stroke with significant neurologic deficit	☐ Old stroke with neurologic residual	☐ Stroke with no residual ☐ Past or recent TIA
Dementia	☐ Severe dementia requiring full support for activities of daily living	☐ Moderate dementia (not completely self-sufficient, needs supervising)	☐ Mild dementia (can take care of self)
Paralysis	☐ Paraplegia or hemiplegia requiring full support for activities of daily living	☐ Paraplegia or hemiplegia requiring wheelchair, able to do some self care	☐ Paraplegia or hemiplegia, ambulatory and providing most of self care
Neuromuscular	☐ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder and requiring full support for activities of daily living	☐ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder, but able to do some self care	☐ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder, but ambulatory and providing most of self care
Psychiatric			
	☐ Recent suicidal attempt ☐ Active schizophrenia	☐ Depression or bipolar disorder uncontrolled ☐ Schizophrenia controlled w/ meds	☐ Depression or bipolar disorder controlled w/ medication
Rheumatologic	**(Incl. Rheumatoid Arthritis, Systemic Lupus, Mixed Connective Tissue Disorder, Polymyositis, Rheumatic Polymyositis)**		
	☐ Connective Tissue Disorder with secondary end-organ failure (renal, cardiac, CNS)	☐ Connective Tissue Disorder on steroids or immunosuppressant medications	☐ Connective Tissue Disorder on NSAIDS or no treatment
Immunological System	**(AIDS should not be considered a comorbidity for Kaposi's Sarcoma or Non-Hodgkin's Lymphoma)**		
AIDS	☐ Fulminant AIDS w/KS, MAI, PCP (AIDS defining illness)	☐ HIV+ with h/o defining illness. CD4⁺ < 200/μL	☐ Asymptomatic HIV+ patient. ☐ HIV⁺ w/o h/o AIDS defining illness. CD4⁺ > 200/μL
Malignancy	**(Excluding Cutaneous Basal Cell Ca., Cutaneous SCCA, Carcinoma in-situ, and Intraepithelial Neoplasm)**		
Solid Tumor including melanoma	☐ Uncontrolled cancer ☐ Newly diagnosed but not yet treated ☐ Metastatic solid tumor	☐ Any controlled solid tumor without documented metastases, but initially diagnosed and treated within the last 5 years	☐ Any controlled solid tumor without documented metastases, but initially diagnosed and treated > 5 years ago
Leukemia and Myeloma	☐ Relapse ☐ Disease out of control	☐ 1st remission or new dx <1yr ☐ Chronic suppressive therapy	☐ H/o leukemia or myeloma with last Rx > 1 yr prior
Lymphoma	☐ Relapse	☐ 1st remission or new dx <1yr ☐ Chronic suppressive therapy	☐ H/o lymphoma w/ last Rx >1 yr prior
Substance Abuse	**(Must be accompanied by social, behavioral, or medical complications)**		
Alcohol	☐ Delirium tremens	☐ Active alcohol abuse with social, behavioral, or medical complications	☐ H/o alcohol abuse but not presently drinking
Illicit Drugs	☐ Acute Withdrawal Syndrome	☐ Active substance abuse with social, behavioral, or medical complications	☐ H/o substance abuse but not presently using
Body Weight			
Obesity		☐ Morbid (i.e., BMI ≥ 38)	

OVERALL COMORBIDITY SCORE (Circle one.)	0 None	1 Mild	2 Moderate	3 Severe	9 Unknown

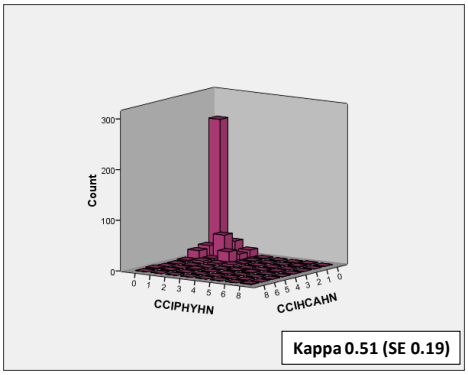


Co-Morbidity Scoring

- 533 patients approached
- 523/533 analysed - 10 excluded (consent/significant data missing)
- 465/523 (89%) sets of Hospital Notes (HN) and 323 (62%) Primary Physician Summaries (PPS)
- 320 (61%) HES records
- Gold standard
  - 459/465 HN able to score CCI + ACE-27
  - 309 CCIPHYHN scored 0 (67%)
  - 230 ACEPHYHN scored 0 (50%)
- For statistical significance, agreement was regarded as substantial if $0.61 \leq \text{kappa} \leq 0.80$ and good if kappa > 0.80.
- Compared scorers as well as sources

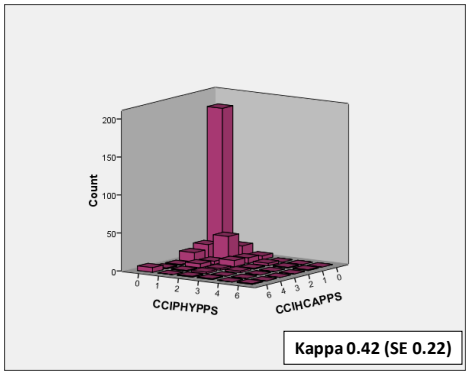
Agreement between PHY vs. HCA

Figure 5 – CCI comparison scores between PHY + HCA from HN



Kappa 0.51 (SE 0.19)

Figure 6 - CCI comparison scores between PHY + HCA from PPS



Kappa 0.42 (SE 0.22)

Cohen's Kappa agreement is regarded as

- Good if Kappa > 0.80
- Moderate if 0.41 < Kappa < 0.60
- Poor if Kappa < 0.20

Substantial if 0.61 < Kappa <0.80
Fair if 0.21 < Kappa < 0.4

Figure 7 - ACE comparison scores between PHY + HCA from HN

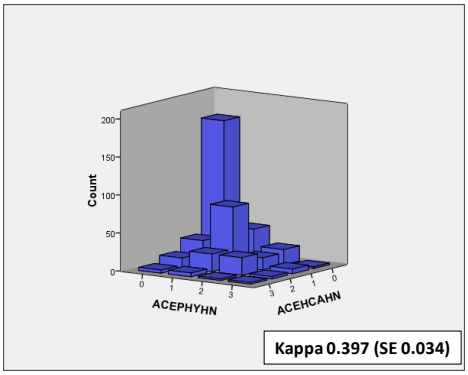
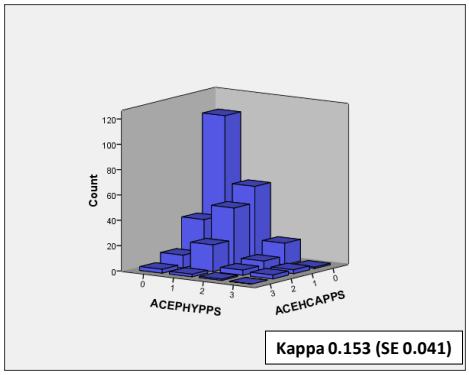


Figure 8 - ACE comparison scores between PHY + HCA from PPS



Cohen's Kappa agreement is regarded as

- Good if Kappa > 0.80
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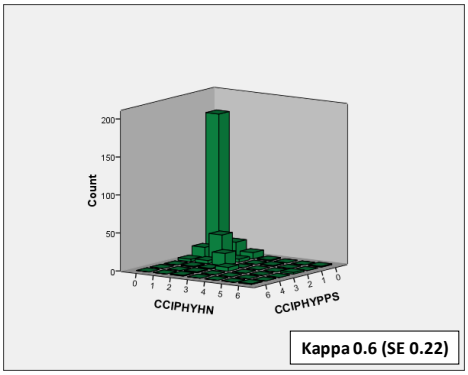
Substantial if 0.61 < Kappa <0.80
Fair if 0.21 < Kappa < 0.4

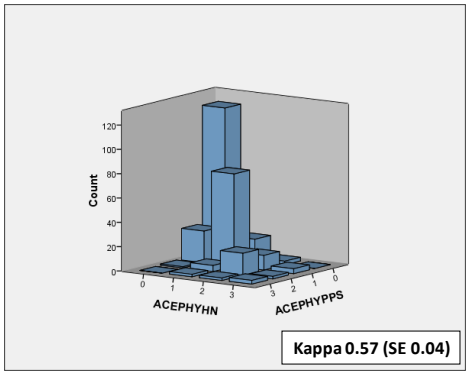
Agreement between Sources

Figure 9 – CCI comparison scores between HN + PPS by PHY



Kappa 0.6 (SE 0.22)

Figure 10 – ACE-27 comparison scores between HN + PPS by PHY



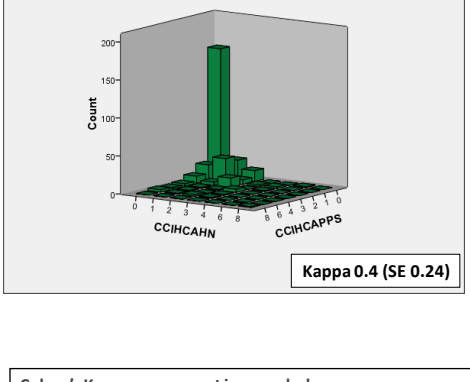
Kappa 0.57 (SE 0.04)

Cohen's Kappa agreement is regarded as

- Good if Kappa > 0.80
- Moderate if 0.41 < Kappa < 0.60
- Poor if Kappa < 0.20

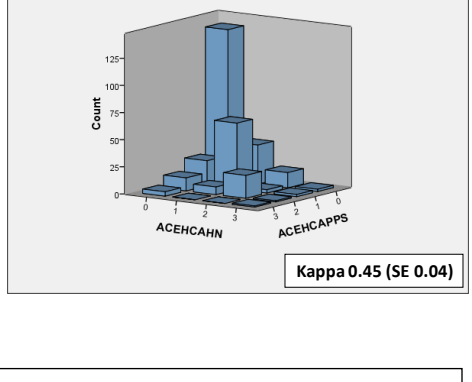
Substantial if 0.61 < Kappa <0.80
Fair if 0.21 < Kappa < 0.4

Figure 11 – CCI comparison scores between HN + PPS by HCA



Kappa 0.4 (SE 0.24)

Figure 12 – ACE-27 comparison scores between HN + PPS by HCA



Kappa 0.45 (SE 0.04)

Cohen's Kappa agreement is regarded as

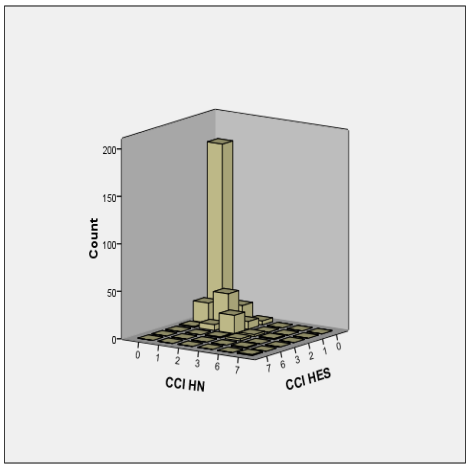
- Good if Kappa > 0.80
- Moderate if 0.41 < Kappa < 0.60
- Poor if Kappa < 0.20

Substantial if 0.61 < Kappa <0.80
Fair if 0.21 < Kappa < 0.4

HES Data Extraction

- Data sent for years 1997 – 2012 - sent as inpatient + outpatient data in Notepad form (25 folders)
- Largest folder had 953 separate episodes
- Identifiable data was only NHS Number/Episodes defined as in ICD-10 code
- Format into Excel + search each NHS Number in all Excel folders
- Copy + paste all ICD codes found with each NHS number
- Compare each ICD code with a possible linked CCI score in the HES/CCI database (over 1800 entries)
- Only record the episodes before the cancer event
- The above process for one NHS Number would take about 15 -20 minutes
- Northern and Yorkshire Cancer Registry and Information Service – James Thomas

Figure 11 – CCI comparison scores between HES + HN by PHY



Kappa 0.56 (SE 0.05)

Comparing Co-Morbidity

- Hospital Notes
  - Very good source availability but more time taken to score
- Primary Physician Summaries
  - Misinterpretation of the data sent + less in number compared to hospital notes
  - Appeared to be a reliable source
- Hospital Episode Statistics
  - Time taken to generate the scores was of immense proportions
  - Reasonable comparative source of scoring
- Health Care Assistant could provide a more economical and time saving process
  - Comparison between the two coders was not even substantial
- Co-morbidity scoring even by a physician has also subjective connotations and differing interpretations

Co-Morbidity + Toxicity

- 449/523 patients presence/absence of severe chemotherapy toxicity recorded (86%)
- 405/449 had presence/absence of severe chemotherapy toxicity recorded with co-morbidity scores (90%)
- Poor co-morbidity
  - CCI Score ≥2
  - ACE-27 Score ≥2

Table 1
Cross-tabulation CCI score (0-1 vs. ≥2) and severe chemotherapy toxicity

	Severe chemotherapy toxicity Yes	No	Total
CCI score			
O or 1	217	131	348
≥2	35	22	57
Total	252	153	405

$\chi 2$ =0.19, p =0.891

Table 2
Cross-tabulation ACE-27 score (0-1 vs.≥ 2) and severe chemotherapy toxicity

	Severe chemotherapy toxicity Yes	No	Total
ACE-27 score			
O or 1	210	128	338
≥2	41	26	67
Total	251	153	405

$\chi 2$ =0.30, p =0.863

Functional Status

- G8, VES-13 and PS scores
- Self assessment of functional status by patients is perceived to be the ideal method of obtaining the scores, as especially oncologists tend to use performance status as the gold standard
- Generated immediately or within a couple of minutes following a oncologist-patient consultation
- 448/449 had full data (presence/absence of severe chemotherapy toxicity and functional scores)

G8

- G8 score is a measure of functional status, nutrition and symptomology
- G8 scores of ≤14 has been shown to be predictive of failing a comprehensive geriatric assessment

Table 3

	Toxicity	Present {%}	Absent {%}	Total
G8 score	0-14	113 {66%}	56 {34%}	171
	>14	167 {60%}	110 {40%}	277
		282	166	448

$\chi 2$ =2.198, p =0.138

VES-13 (Vulnerable Elders Survey)

- Functional capacity
- Covers age, self-rated health, limitations in physical function and functional disabilities
- Score >3 is predictive of death and functional decline in older patients

Table 4

	Toxicity	Present {%}	Absent {%}	Total
VES-13 Score	>3	88 {73%}	33 {37%}	121
	≤3	194 {59%}	133 {41%}	327
		282	166	448

$\chi 2$ =6.799, p =0.009

Performance Status

- Universally accepted method of assessing fitness
- Subjective - "30 seconds"
- Performance Status "1-2"

Table 5

	Toxicity	Present {%}	Absent {%}	Total
PS Score	≥2	81 {69%}	36 {31%}	117
	0-1	201 {61%}	130 {39%}	331
		282	166	448

$\chi 2 = 2.681$, $p = 0.102$

Conclusions

- Role of co-morbidity in fitness assessment
- No one gold standard, widely accepted tool
  - Time taken to score
  - No one accepted source
  - No one accepted coder
- Co-morbidity scoring does not appear to predict significant chemotherapy toxicity
- Functional status to supersede performance status as a more objective way of predicting how well a patient may tolerate treatment?


NCIN
Joanna Stokoe
Joanne Curry
Jamie Pearce
James Thomas