The Leeds Teaching Hospitals NHS
NHS Trust

Patient Reported Outcome Measures (PROMS) in oncology practice.

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PCOR Patient Centered Outcomes Research

pog Patient Reported Outcomes Group

UNIVERSITY OF LEEDS

eRAPID

NHS National Institute for Health Research

St James's Institute of Oncology

United Kingdom West Yorkshire Leeds

EORTC Quality of Life

Leeds Cancer Centre

ISOQOL
International Society for Quality of Life Research

Outline

- HRQOL and PROs in clinical trials
- New PRO concepts in cancer clinical trials
  - Tolerability of cancer treatments
  - NCI PRO-CTCAE items
  - EORTC Item Library
- PROs in routine oncology practice
  - Review of available evidence
  - Work in Leeds

Outline

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Why are we interested in measurement of quality of life and patient-reported outcomes

- Changing pattern of diseases in the 20th century
  - Predominance of chronic diseases as long-term condition
  - Maintaining functioning and well-being
- Increased interest in measurement of health, functioning and well-being
- We cure a larger proportion of cancers “Cancer survivorship”
- Many advanced cancers are becoming a “Chronic disease” “Incurable but treatable cancer”
- New targeted treatments provide longer-term disease control in advanced cancers
- “Tolerability” of long-term treatments

CONSORT PRO extension

Reporting of Patient-Reported Outcomes in Randomized Trials

The CONSORT PRO Extension

Melanie Calvert, PhD
Jane Blazeby, MD
Douglas G. Altman, DSc
Dennis A. Revicki, PhD
David Moher, PhD
Michael D. Brundage, MD
for the CONSORT PRO Group

The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs); however, it lacks guidance on the reporting of patient-reported outcomes (PROs), which are often inadequately reported in trials, thus limiting the value of these data. In this article, we describe the development of the CONSORT PRO extension based on the methodological framework for guideline development proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network. Five CONSORT PRO checklist items are recom-

		Results	
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	The number of PRO outcome data at baseline and at subsequent time points should be made transparent
	13b	For each group, losses and exclusions after randomization, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Including baseline PRO data when collected
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Required for PRO results
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, the estimated effect size, and its precision (such as 95% confidence interval)	For multidimensional PRO results from each domain and time point
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	

Example of HRQOL in a large trial

THE LANCET Oncology

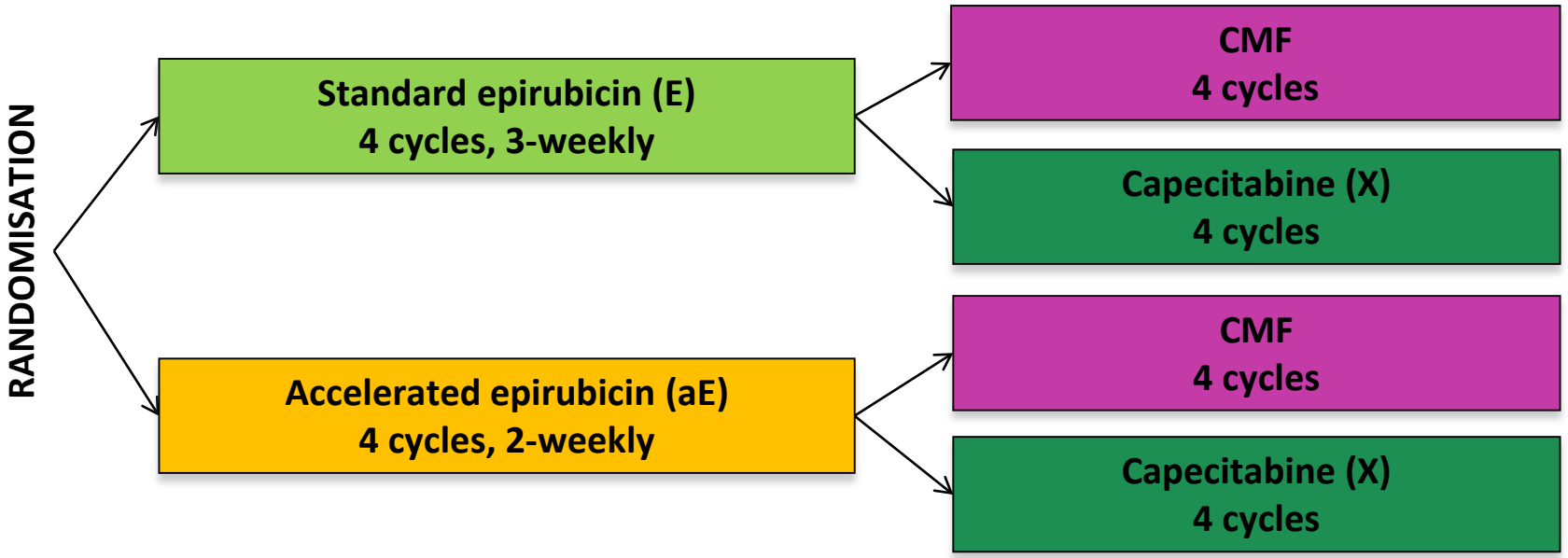
TACT 2 TRIAL OF ACCELERATED CHEMOTHERAPY

Accelerated versus standard epirubicin followed by cyclophosphamide, methotrexate, and fluorouracil or capecitabine as adjuvant therapy for breast cancer in the randomised UK TACT2 trial (CRUK/05/19): a multicentre, phase 3, open-label, randomised, controlled trial

David Cameron, James P Morden, Peter Canney, Galina Velikova, Robert Coleman, John Bartlett, Rajiv Agrawal, Jane Banerji, Gianfilippo Bertelli, David Bloomfield, A Murray Brunt, Helena Earl, Paul Ellis, Claire Gaunt, Alexa Gillman, Nicholas Hearfield, Robert Laing, Nicholas Murray, Niki Couper, Robert C Stein, Mark Verrill, Andrew Wardley, Peter Barrett-Lee, Judith M Bliss, on behalf of the TACT2 Investigators

Background

Moderate risk early breast cancer patients NOT requiring taxane chemotherapy



TACT2, a phase III trial with 2 x 2 factorial design

Two hypotheses: 1. Accelerating Anthracycline chemotherapy offers greater efficacy
2. Capecitabine gives similar efficacy but better toxicity profile to CMF

Primary Outcome- Overall Survival

HRQOL and specific symptoms measured at baseline, end of E, end of CMF/X, 12 and 24 months

Materials and Methods

Main study

4391 patients randomised Dec 05 – Dec 08

HRQOL substudy

1179 pts (of 1493 approached, 79%) completed at least one QL questionnaire

HRQOL questionnaires collected at:

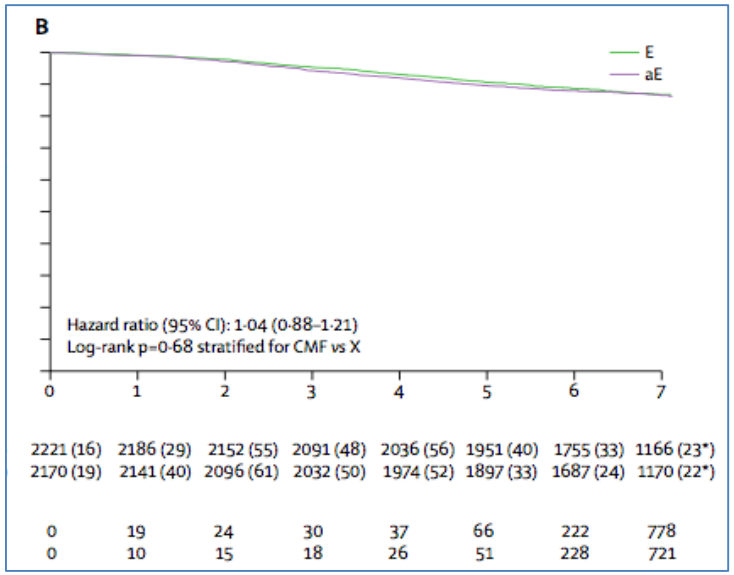
- Baseline
- End of E/aE (phase 1)
- End of CMF/X (phase 2)
- 12 months
- 24 months

Instruments used: EORTC QLQ-C30, EORTC QLQ-BR23, HADS, Fatigue Symptoms Inventory (FSI), TACT2 Toxicity questionnaire

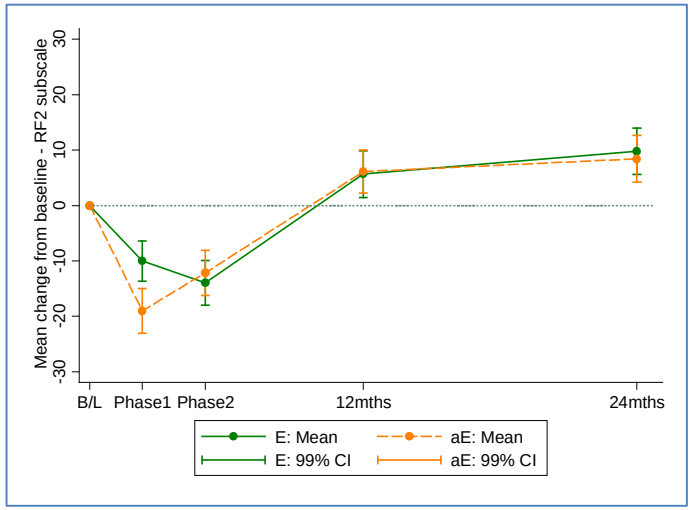
- Changes from baseline to each time point were compared between groups using ANCOVA, adjusting for baseline scores
- Generalised estimating equations (GEE) models were used to analyse data longitudinally across all time points
- Results considered statistically significant if $p<0.01$ to make some allowance for multiple testing

Hypothesis A - E vs aE

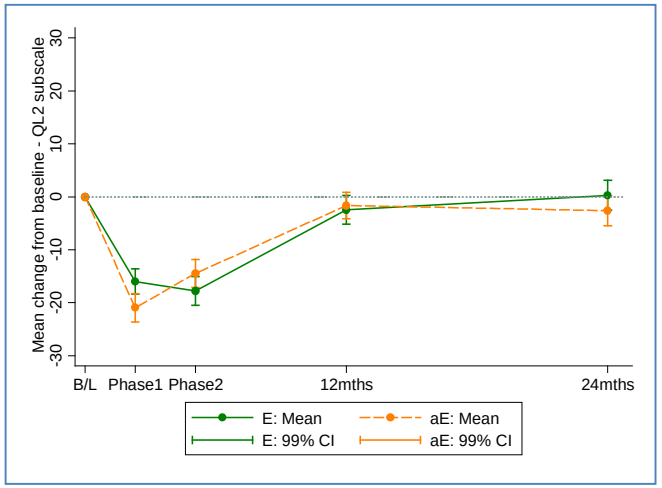
Overall survival



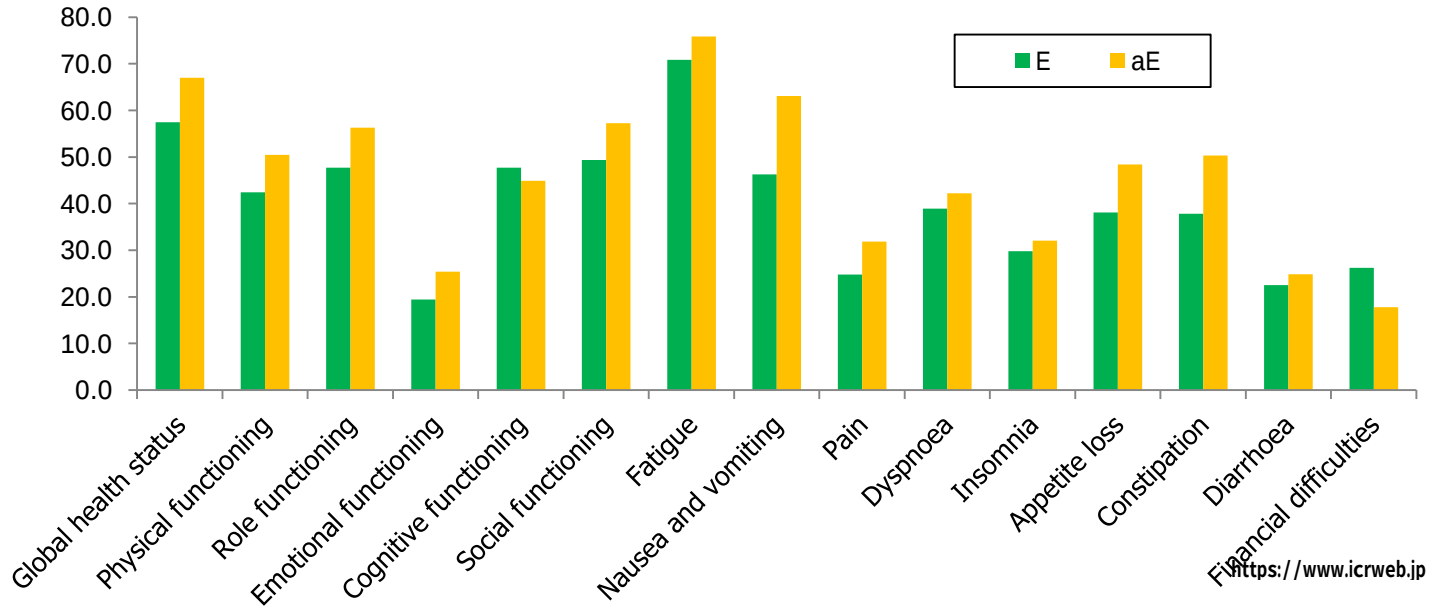
EORTC QLQ-C30 Role functioning



Global QOL



Responder analysis
Proportion of patients with ≥10 point deterioration by the end of phase 1 treatment

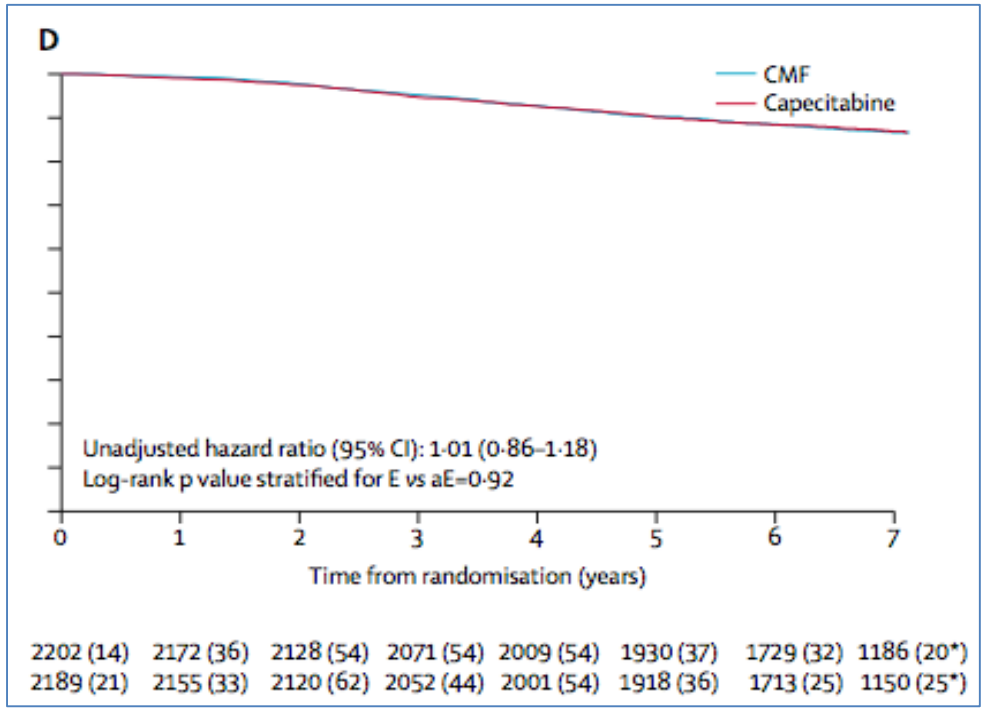


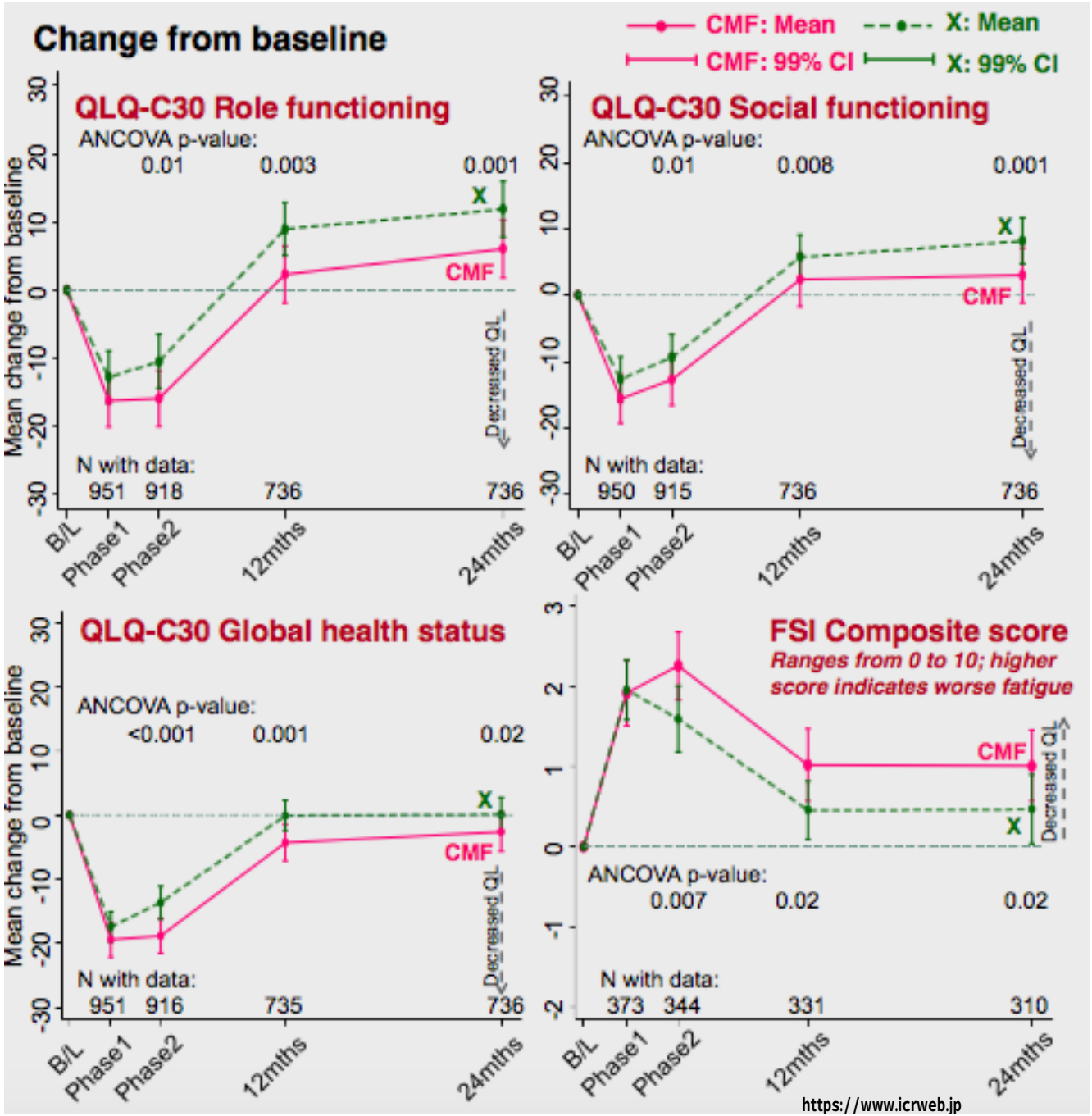
Conclusions aE vs E

- Accelerating anthracycline chemotherapy did not offer greater efficacy (identical Overall survival)
- Contrary to previous data and clinical expectations aE was more toxic during the treatment
- Patient-reported worse symptoms, functioning and HRQOL with aE compared with E but the difference did not persist in the long term
- aE can not be recommended as an alternative to standard 3-weekly E for adjuvant treatment of moderate risk early breast cancer

CMF vs X

Overall survival





CMF vs X during and after treatment

Longitudinal modelling

Subscale	p-value	Subscale	p-value
QLQ-C30		**QLQ-BR23**	
Global health status	<0.001	Body image	0.008
Physical functioning	0.004	Sexual functioning	0.16
Role functioning	<0.001	Sexual enjoyment	0.04
Emotional functioning	0.67	Future perspective	0.17
Cognitive functioning	0.006	Systemic side-effects	<0.001
Social functioning	<0.001	Breast symptoms	0.63
Fatigue	<0.001	Arm symptoms	0.12
Nausea and vomiting	0.004*	Hair loss	0.10
Pain	0.71		
Dyspnoea	<0.001	**HADS total score**	0.03
Insomnia	<0.001		
Appetite loss	<0.001	**Wu Fatigue score**	0.59
Constipation	<0.001*		
Diarrhoea	0.15	**FSI Composite score**	0.03
Financial difficulties	0.03		

All subscales which are statistically significantly ($p<0.01$) favour **X** over **CMF**

**Significant interaction observed between E/aE and CMF/X treatment*

Conclusions-2 CMF vs X

- CMF had identical efficacy to X when following Anthracycline chemotherapy (similar Overall Survival)
- The hypothesis that CMF is more toxic than X was confirmed
- Patients reported significantly more serious side-effects which influenced their functioning and HRQL
- The differences persisted at 12 and 24 months
- X can be safely used as adjuvant treatment for moderate risk early breast cancer following Anthracyclines
- This is important information for clinicians and patients to support decisions on adjuvant treatments
- Recent trial recommended Capecitabine (X) as treatment for residual disease after neo-adjuvant chemotherapy.

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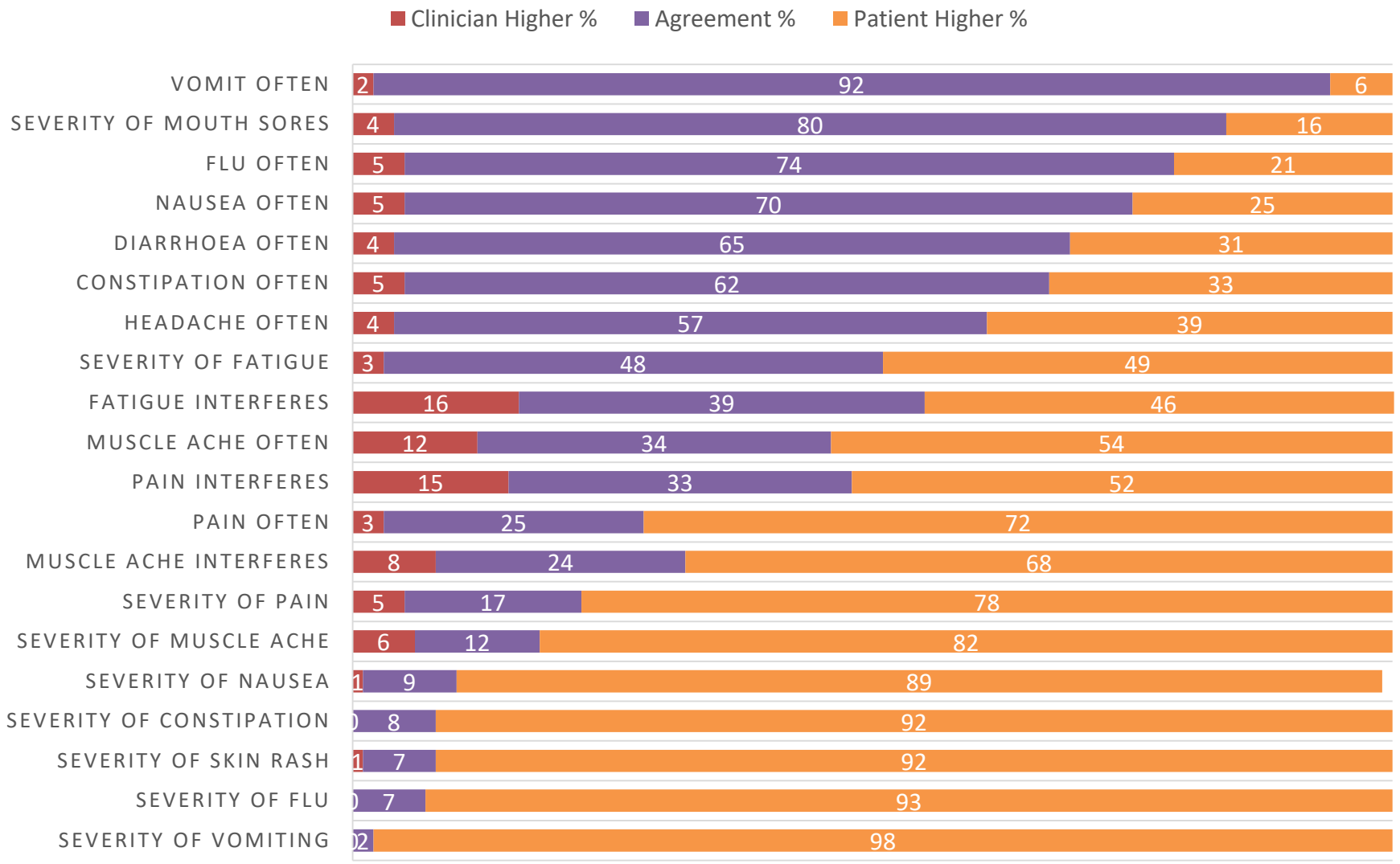
Patient vs Clinician reporting- NCI PRO-CTCAE



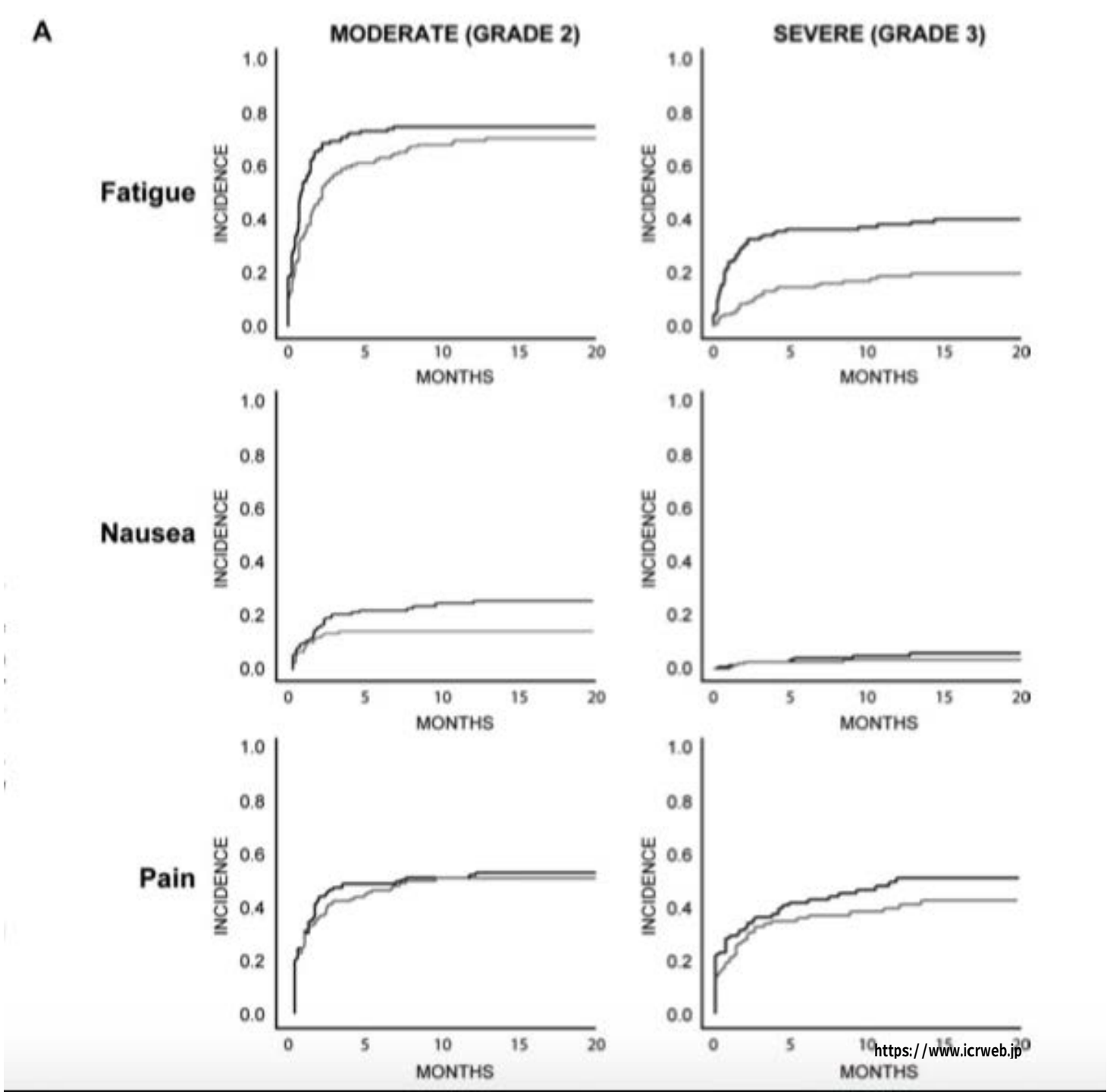
ARTICLE

Adverse Symptom Event Reporting by Patients vs Clinicians: Relationships With Clinical Outcomes

Ethan Basch, Xiaoyu Jia, Glenn Heller, Allison Barz, Laura Sit, Michael Fruscione, Mark Appawu, Alexia Iasonos, Thomas Atkinson, Shari Goldfarb, Ann Culkin, Mark G. Kris, Deborah Schrag

Background In cancer treatment trials, the standard source of adverse symptom data is clinician reporting by use of items from the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE). Patient self-reporting has been proposed as an additional data source, but the implications of such a shift are not understood.

Cumulative incidence of symptom reporting by patients vs clinicians



Potential beneficiaries of patient-reporting of adverse symptoms in cancer treatment trials

Stakeholder	Potential benefits
Clinical trial participants	Earlier detection of toxic effects through improved communication with clinical staff
Investigators and/or sponsors	More complete adverse event data during drug development
FDA reviewers	Additional toxicity data to balance safety with efficacy during regulatory review
Clinicians	Improved information about prior patients' experiences with treatments, for use when counselling future patients or assessing adverse reactions
Future patients	Access to information about prior patients' experiences with particular treatments, to inform therapy decisions

Cancer treatment safety and tolerability

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journal homepage: www.elsevier.com/locate/jval

Policy Perspective

Informing the Tolerability of Cancer Treatments Using Patient-Reported Outcome Measures: Summary of an FDA and Critical Path Institute Workshop

Paul G. Kluetz, MD[1,], Bindu Kanapuru, MD[2], Steven Lemery, MD[2], Laura Lee Johnson, PhD[2], Mallorie H. Fiero, PhD[2], Karen Arscott, DO[3], Yolanda Barbachano, PhD[4], Ethan Basch, MD[5], Michelle Campbell, PhD[2], Joseph C. Cappelleri, PhD[6], David Cella, PhD[7], Charles Cleeland, PhD[8], Corneel Coens, MSc[9], Selena Daniels, PharmD[2], Crystal S. Denlinger, MD[10], Dianne L. Fairclough, PhD[11],*

Safety Tolerability and Patient experiences

Safety
- Clinician Reported Symptoms (CTCAE)
- Other Adverse Events

Informs

Tolerability
- Dose Modifications
- Treatment Discontinuation

Informs

Patient Experience
- Patient-Reported Symptoms (PRO-CTCAE or EORTC Item Library)
- Burden of treatment

NCI PRO-CTCAE program

CTCAE vs. PRO-CTCAE™ Item Structures

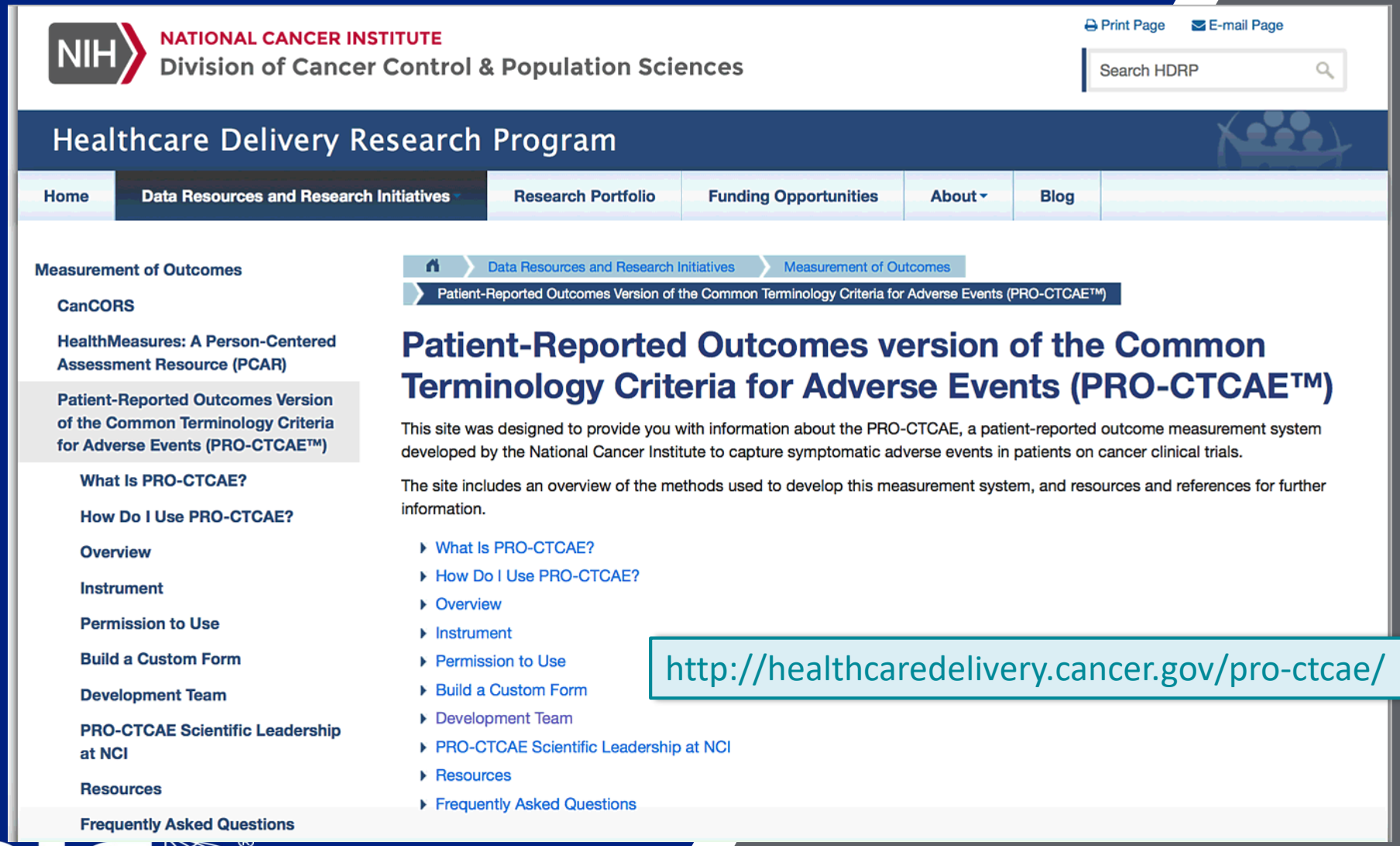
CTCAE					
Adverse Event	**Grade**				
	1	**2**	**3**	**4**	**5**
Mucositis oral	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain; not interfering with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated	-

PRO-CTCAE™
Please think back over the past 7 days:
What was the severity of your MOUTH OR THROAT SORES at their WORST? None / Mild / Moderate / Severe / Very severe
How much did MOUTH OR THROAT SORES interfere with your usual or daily activities? Not at all / A little bit / Somewhat / Quite a bit / Very much

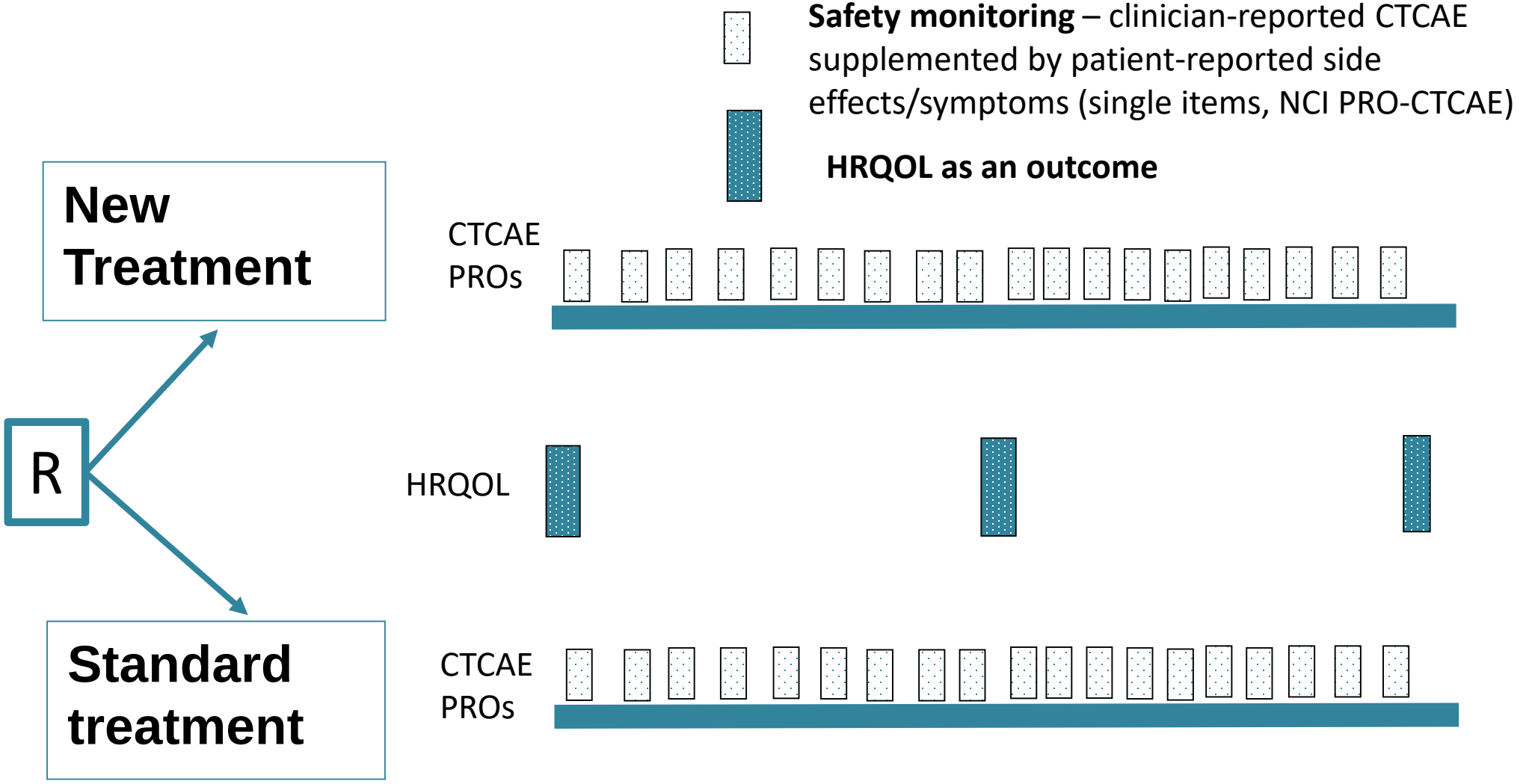
PRO-CTCAE™ Measurement System

1. Item Library	2. Software
• 78 symptomatic adverse events drawn from CTCAE • Items evaluate frequency, severity, interference, amount, presence of these symptoms	• Creates customized surveys; manages survey administration • Patient interface: choice of web or IVR • Conditional branching (skip patterns) • Write-ins with automatic mapping to standardized terminology • Automated alerts

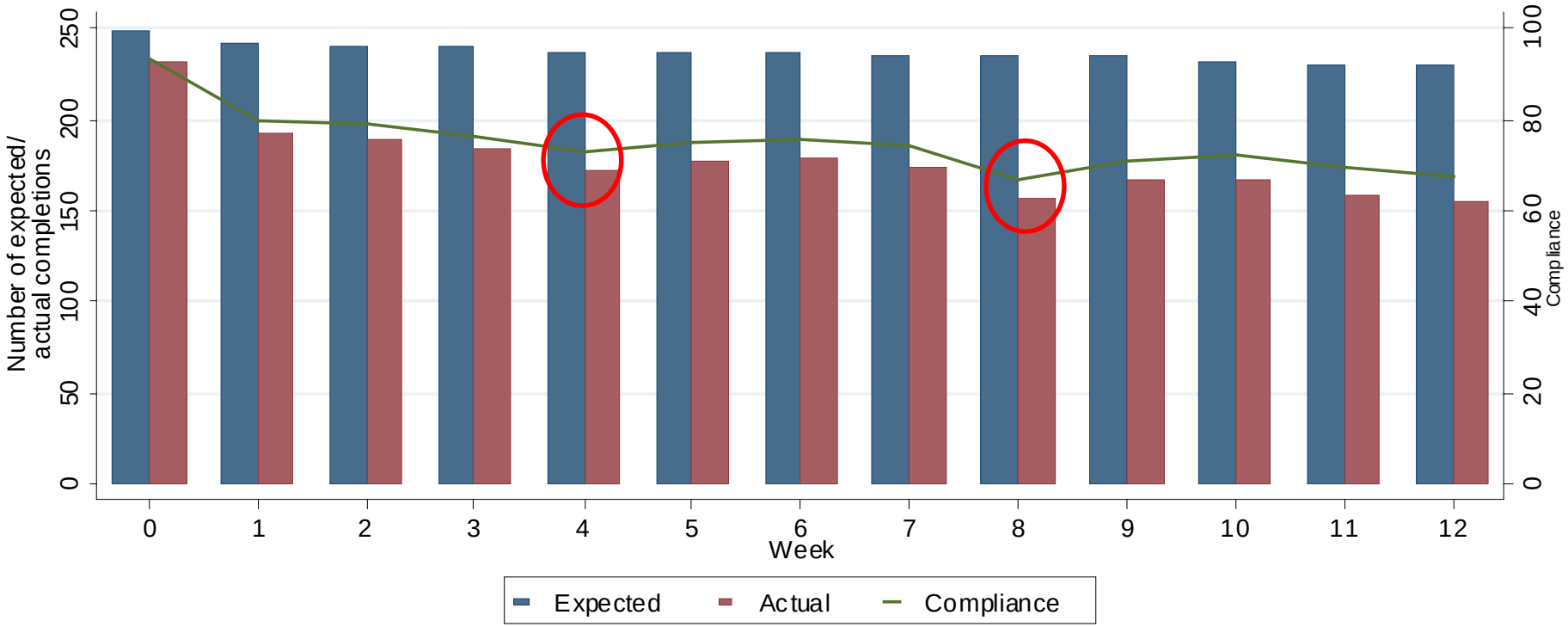
For more information visit: http://healthcaredelivery.cancer.gov/pro-ctcae/



Example of a clinical trial with both PROs and HRQOL

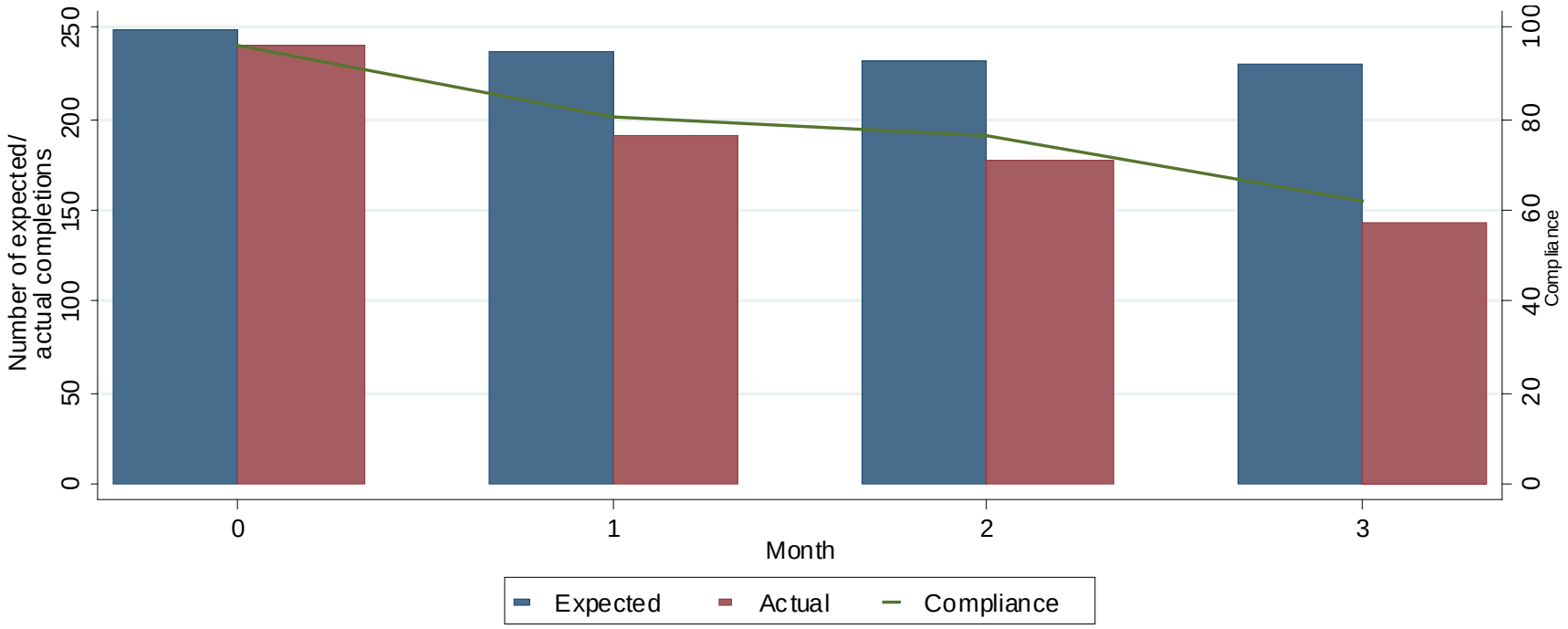


Compliance – weekly PRO-CTCAE



- 93% at baseline to 67% in week 12
- Weeks 4 and 8 show a decrease compared to previous or following weeks

Compliance – monthly EORTC



- 96% at baseline to 62% at month 3 (12 weeks)
- At monthly points EORTC availability may have affected weekly PRO-CTCAE completions as not all participants completed both

Ongoing work

Original Investigation

FREE

August 2017

Feasibility Assessment of Patient Reporting of Symptomatic Adverse Events in Multicenter Cancer Clinical Trials

Ethan Basch, MD, MSc[1,2]; Amylou C. Dueck, PhD[3]; Lauren J. Rogak, MA[2]; et al

» Author Affiliations | Article Information

JAMA Oncol. 2017;3(8):1043-1050. doi:10.1001/jamaoncol.2016.6749

- 285 patients enrolled in 9 US multicentre cancer treatment trials
- 93.9% of expected times symptomatic adverse events were self-reported by patients

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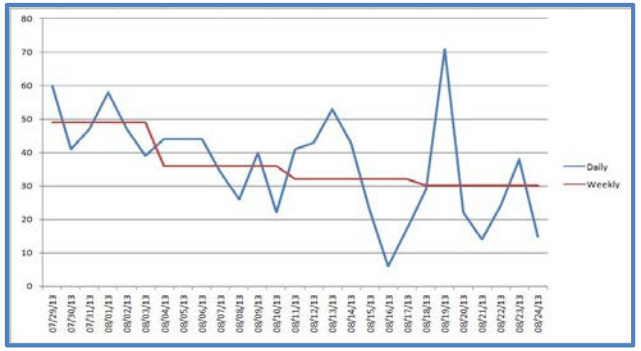
Patient Reported Outcomes (PROs) to support patient care in daily oncology practice



Clinical method - Medical interview

- Gathering of subjective information
- Diagnostic aim
- Not designed to monitor change or
- assess outcomes

Patient Reported Outcomes Measures

- Quantitative information on symptom
- Track changes over time

Benefits

- Detect and monitor physical and emotional problems
- Impact on patient-doctor communication
- Facilitate patient involvement in decision making

Measuring Quality of Life in Routine Oncology Practice Improves Communication and Patient Well-Being: A Randomized Controlled Trial

Galina Velikova, Laura Booth, Adam B. Smith, Paul M. Brown, Pamela Lynch, Julia M. Brown, and Peter J. Selby

From the Cancer Research UK Clinical Centre–Leeds, Cancer Medicine Research Unit, St James's University Hospital; and Northern and Yorkshire Clinical Trials and Research Unit, Leeds, United Kingdom.

Submitted June 18, 2003; accepted December 5, 2003.

Supported by grants from Cancer Research UK (formerly Imperial Cancer

ABSTRACT

Purpose

To examine the effects on process of care and patient well-being, of the regular collection and use of health-related quality-of-life (HRQL) data in oncology practice.

Patients and Methods

In a prospective study with repeated measures involving 28 oncologists, 286 cancer patients were randomly assigned to either the intervention group (regular completion of European Organization for Research and Treatment of Cancer–Core Quality of Life Questionnaire version 3.0, and Hospital Anxiety

Study design

Patients receiving chemotherapy for breast, GYN, GI, testicular lung cancer at St James's Hospital, Leeds

RANDOMIZE

INTERVENTION ARM- 50%
Self-report on TS computers
- Prior to consultations
- EORTC QLQ-C30
- HADS
- **Feedback - Printed reports to oncologists (at visits)**

ATTENTION-CONTROL ARM-25%
Self-report on TS computers
- Prior to consultations
- EORTC QLQ-C30
- HADS
- **No Feedback to oncologists**

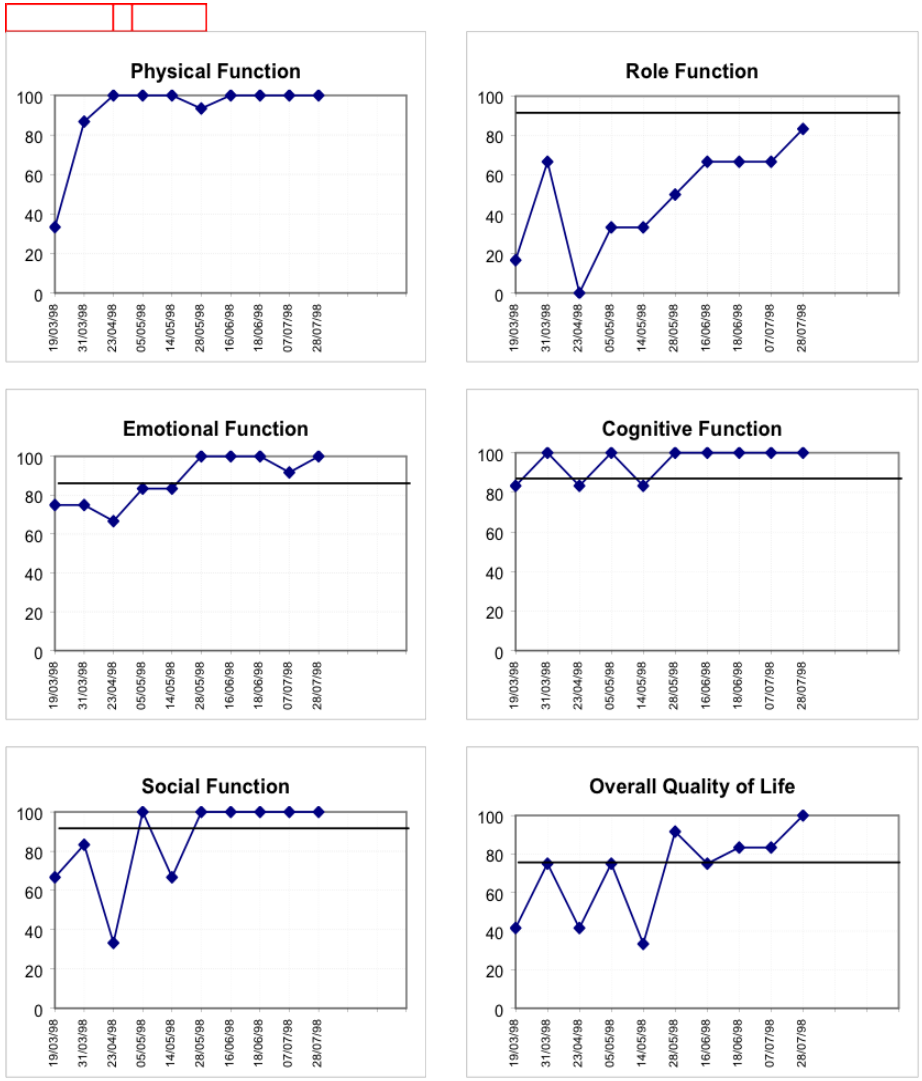
CONTROL ARM -25%
"Standard" symptom monitoring

Outcomes

- **Process outcomes**: Doctor-Patient Communication (2000 audio-recorded consultations)
- **Patient outcomes**
- QOL (FACT-G) and symptom control
- Continuity Co-ordination of care
- Satisfaction with care
- **Measured at**
- Baseline
- After 3 visits
- 4 and 6 months

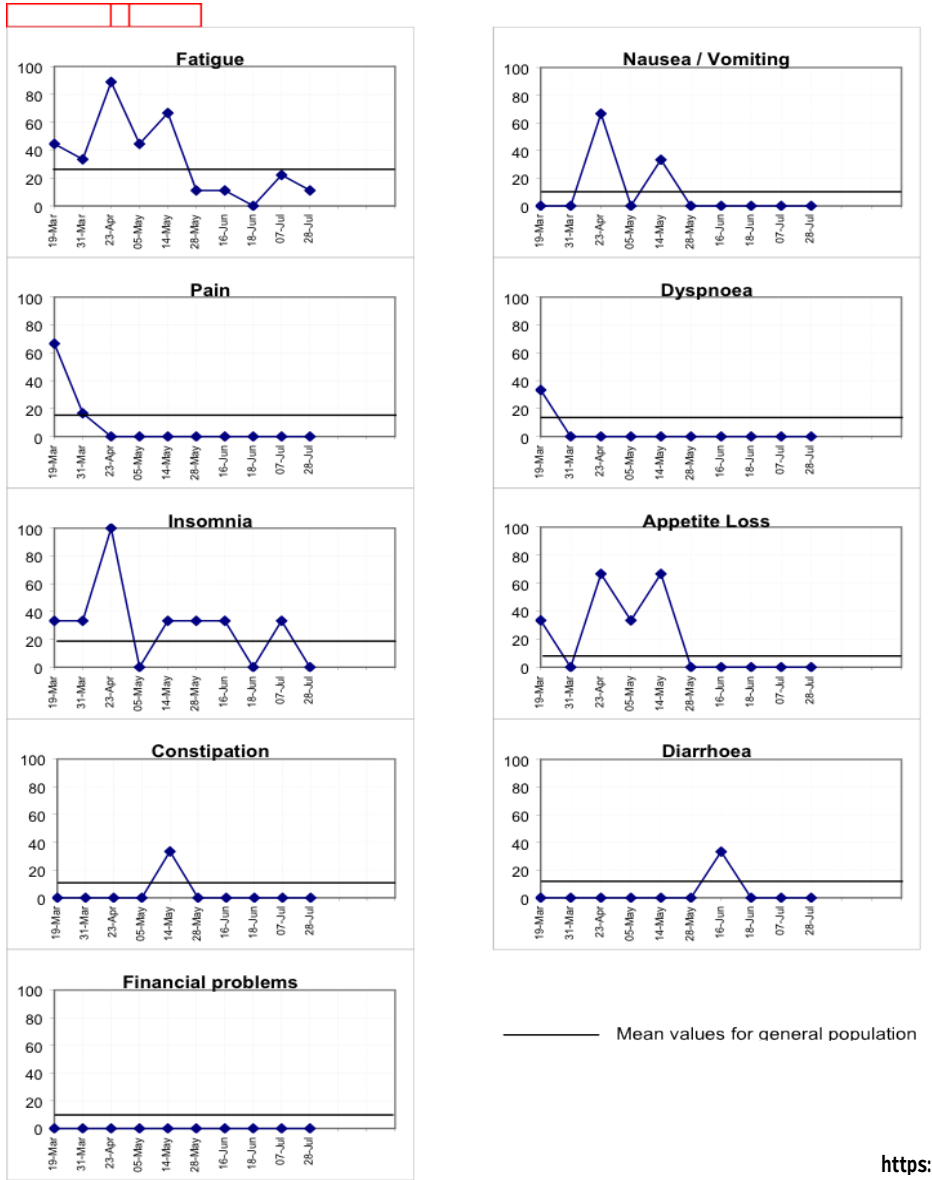
EORTC QLQ-C30
Functional Scales

Higher score means better function
Lower score means less symptoms



Mean values for general population

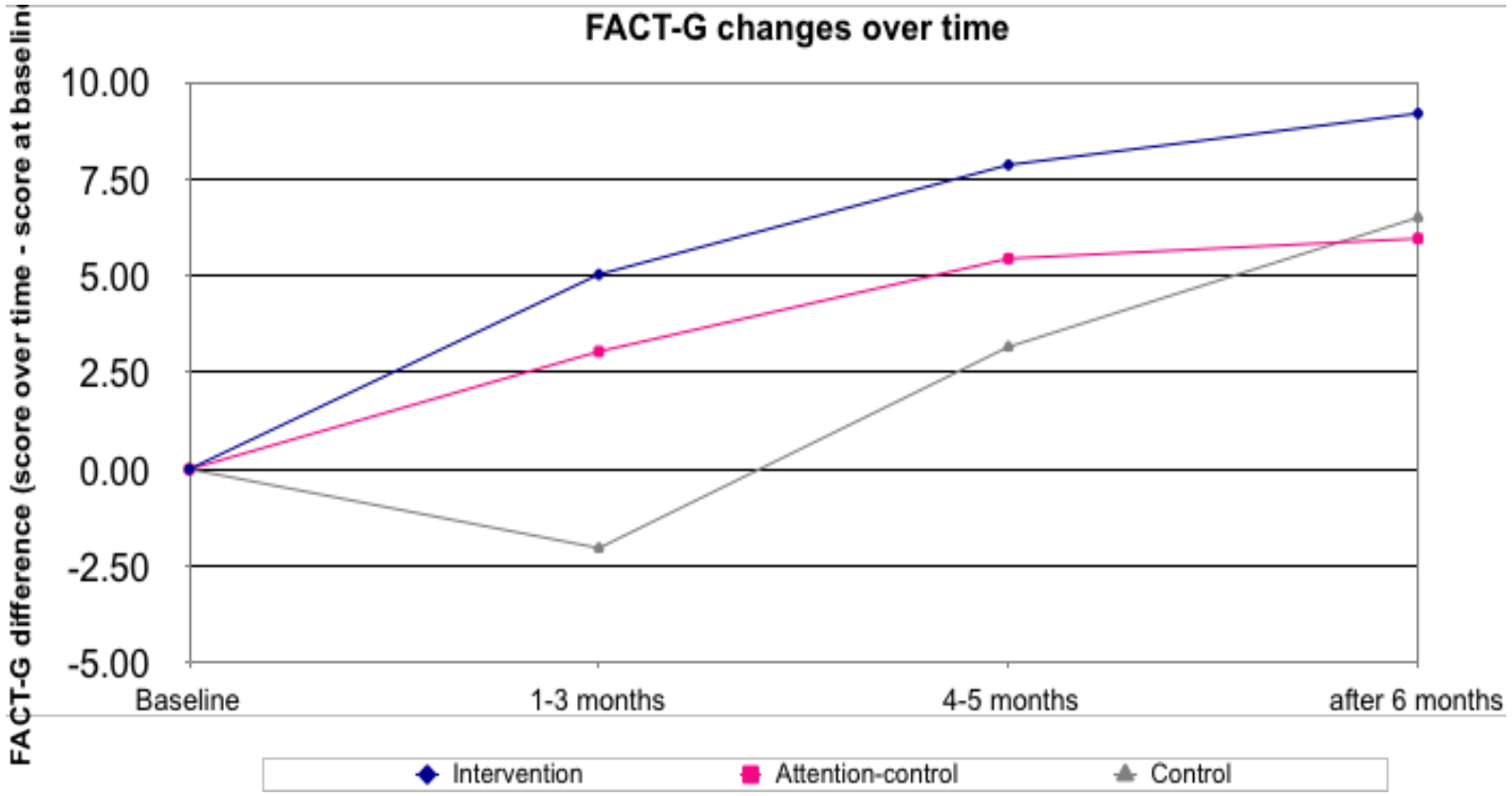
EORTC QLQ-C30
Symptom Scales



Mean values for general population

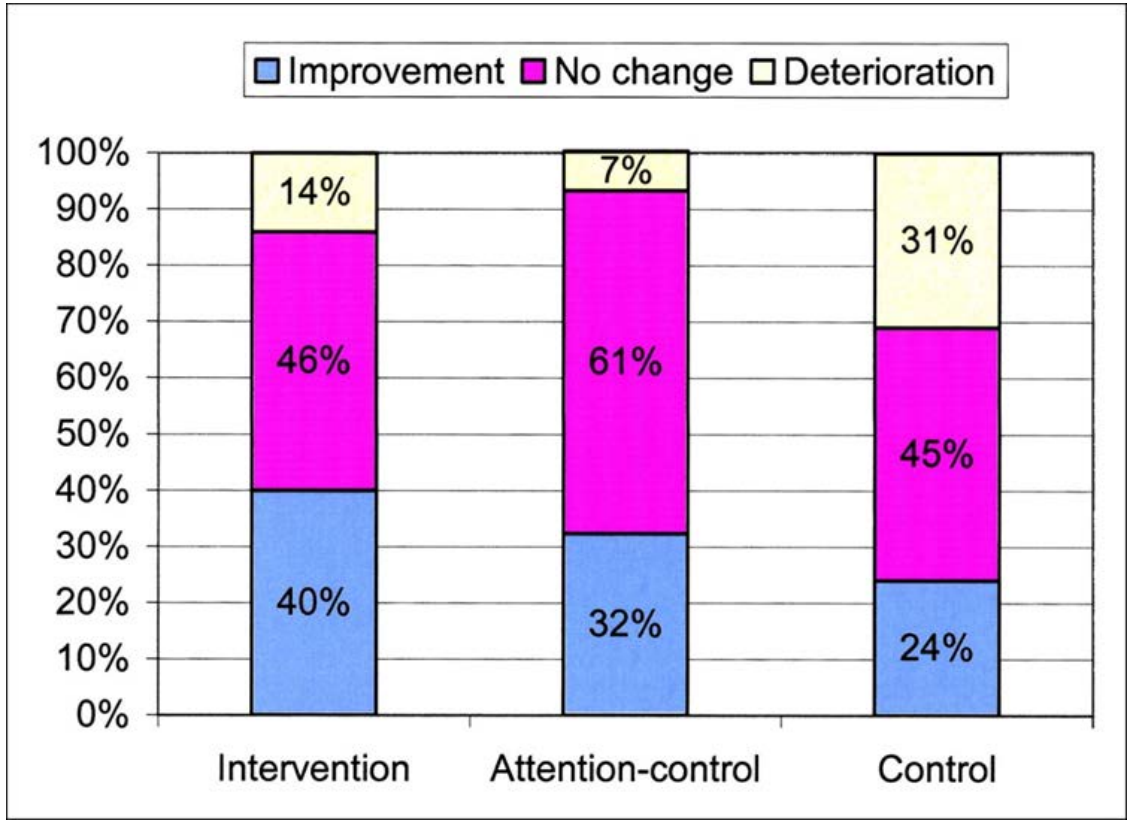
Results - Improved patient well-being

Improvement in FACT-G scores over time



Improves Patient well-being

Proportions of patients with clinically significant change in FACT-G



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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial

Ethan Basch, Allison M. Deal, Mark G. Kris, Howard I. Scher, Clifford A. Hudis, Paul Sabbatini, Lauren Rogak, Antonia V. Bennett, Amylou C. Dueck, Thomas M. Atkinson, Joanne F. Chou, Dorothy Dulko, Laura Sit, Allison Barz, Paul Novotny, Michael Fruscione, Jeff A. Sloan, and Deborah Schrag

See accompanying editorial on page 527

Ethan Basch, Mark G. Kris, Howard I. Scher, Clifford A. Hudis, Paul Sabbatini, Lauren Rogak, Thomas M. Atkinson, Joanne F. Chou, Dorothy Dulko, Laura Sit, Michael Fruscione, and Deborah Schrag, Memorial Sloan Kettering Cancer Center,

ABSTRACT

Purpose

There is growing interest to enhance symptom monitoring during routine cancer care using patient-reported outcomes, but evidence of impact on clinical outcomes is limited.

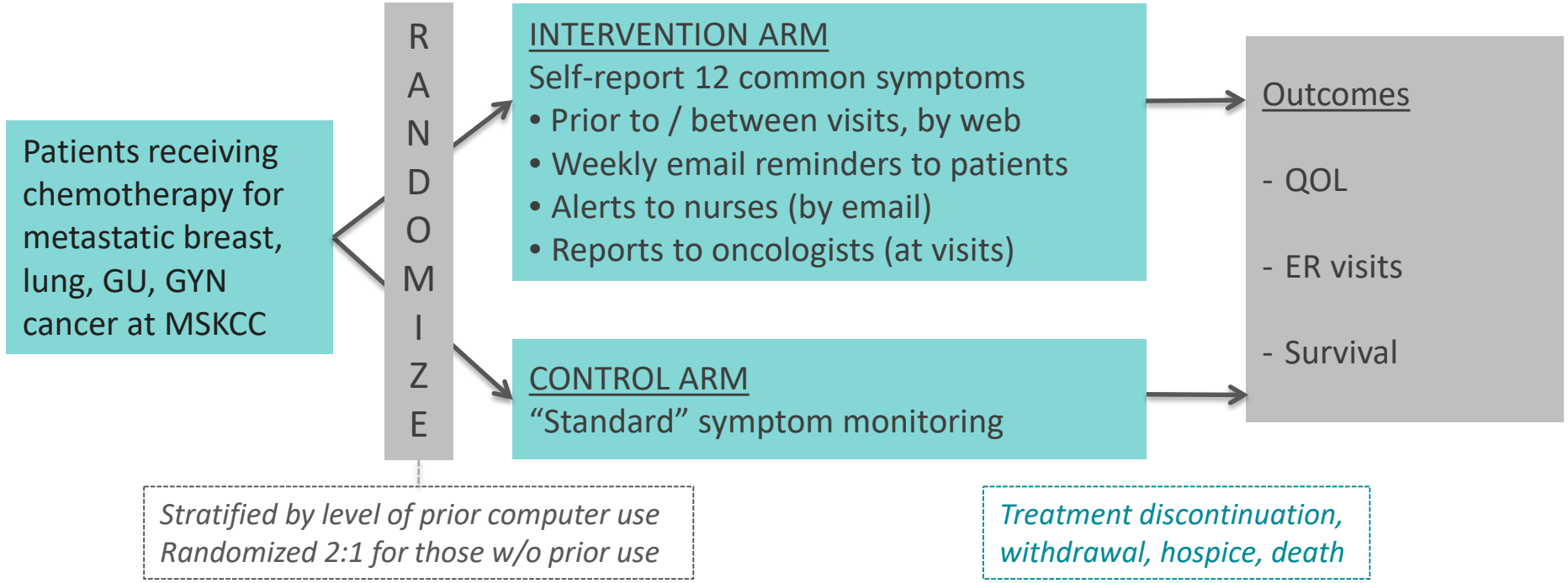
Basch et al. J Clin Oncol 2016

NCRI National Cancer Research Institute

"STAR" Study

JAMA The Journal of the American Medical Association

ASCO American Society of Clinical Oncology



Basch: JAMA, 2017

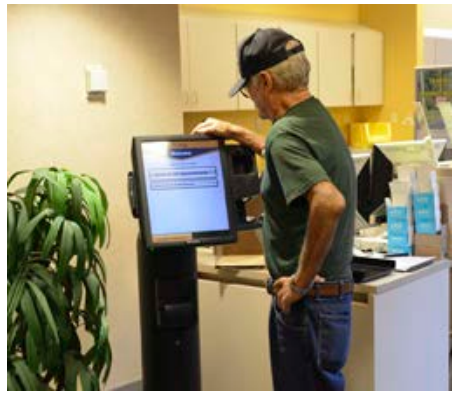
Slides curtesy to Ethan Basch

NCRI
National Cancer
Research Institute

Patient Self-Reporting Interface

U.S. National Cancer Institute CTCAE Scale – Example: Pain

○ None	I have not had pain.
● Grade 1 (Mild)	I have had mild pain, but it does not interfere with my normal functioning.
○ Grade 2 (Moderate)	I have had moderate pain, and my pain or my use of pain medications interferes with my normal functioning. But I am still able to carry out my normal daily activities.
○ Grade 3 (Severe)	I have had severe pain, and my pain or my use of pain medications severely interferes with my normal daily activities.
○ Grade 4 (Disabling)	My pain has been disabling.

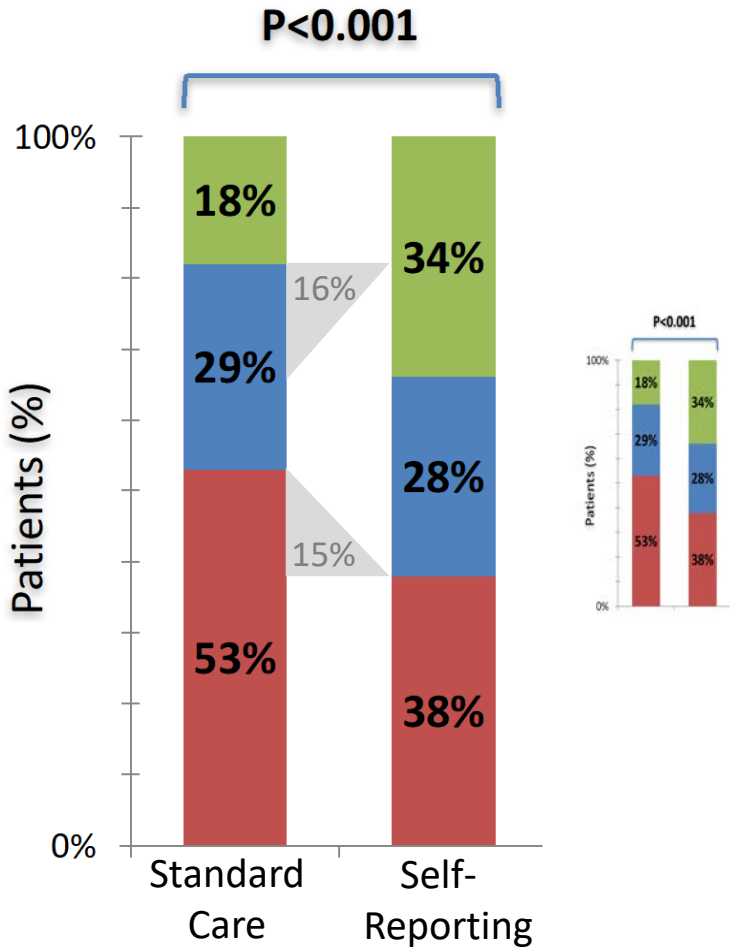


NCRI
National Cancer
Research Institute

Quality of Life- EQ5D

- Assessed at 6 months, compared to baseline
- Compared to standard care, 31% more patients in the self-reporting arm experienced QOL benefits *(P<0.001)*

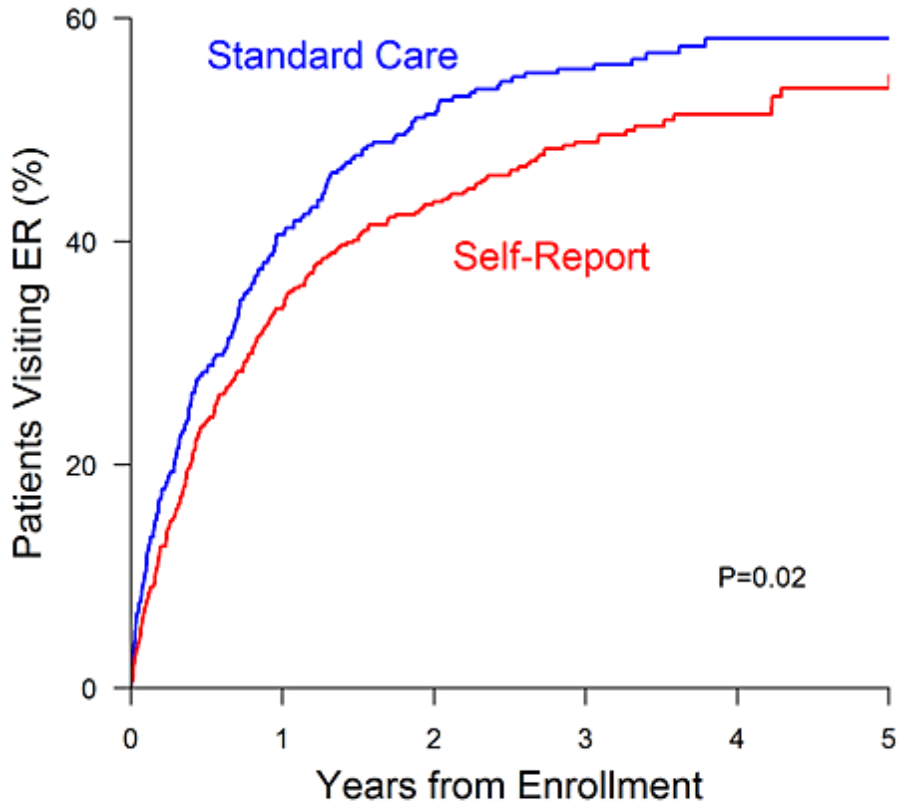
Basch: J Clin Oncol 2016;34:557-565



NCRI
National Cancer
Research Institute

Proportion of Patients Visiting Emergency Room

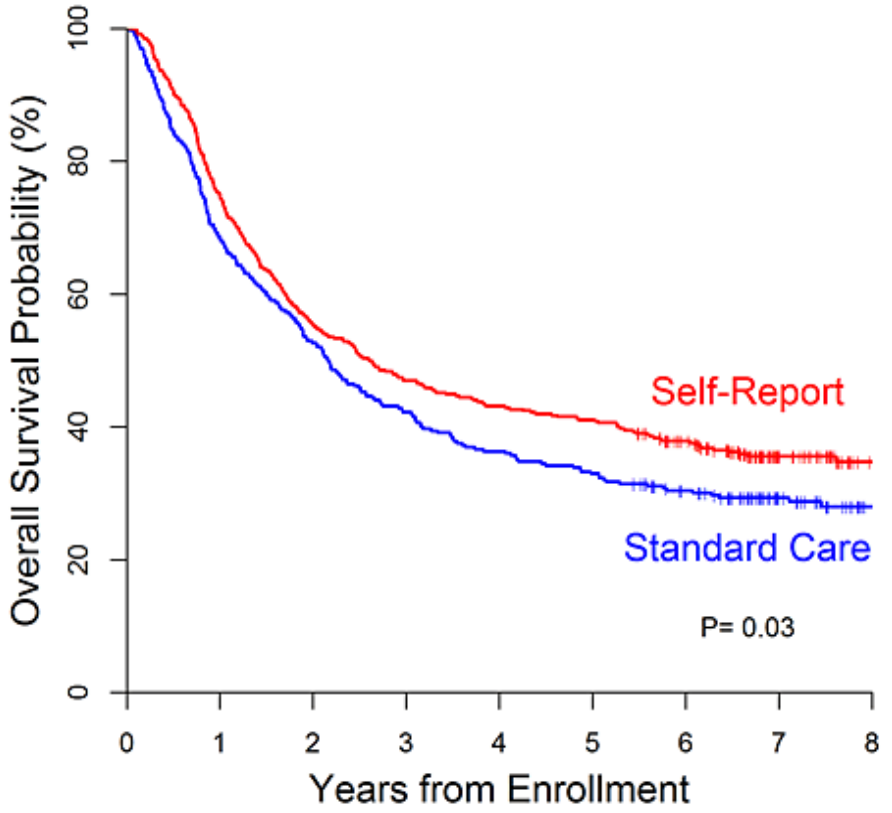
- Compared to standard care, 7% fewer patients in the self-reporting arm visited the ER, with durable effects throughout the study *(P=0.02)*



Total	766	554	415	344	308	288
Self-Report	441	331	244	207	190	181
Standard	325	223	171	137	118	107

Overall Survival

- Compared to standard care, median survival was 5 months longer among patients in the self-reporting arm (31.2 vs. 26.0 months) (*P=0.03*)
- Remained significant in multivariable analysis: Adjusted hazard ratio 0.832 (*95% CI; 0.696, 0.995*)



Total	766	554	415	344	308	288	237	115	60
Self-Report	441	331	244	207	190	181	148	65	33
Standard	325	223	171	137	118	107	89	50	27

Randomized Trial Comparing a Web-Mediated Follow-Up via Patient-Reported Outcomes (PRO) vs. Routine Surveillance in Lung Cancer Patients: Final Results

Abstract #6500

Fabrice DENIS MD, PhD

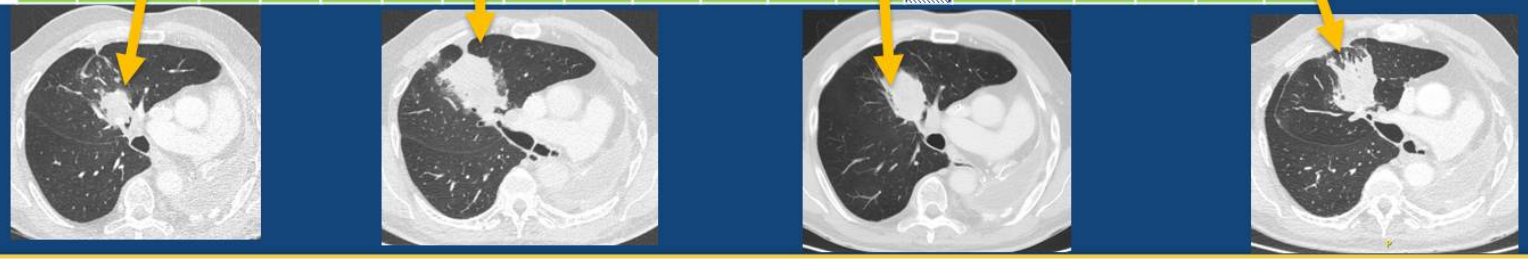
Jean Bernard Cancer Institute, Le Mans, FRANCE

f.denis@cjb72.org

Tumor Response Assessment Improvement

>1-year immunotherapy duration... and ongoing

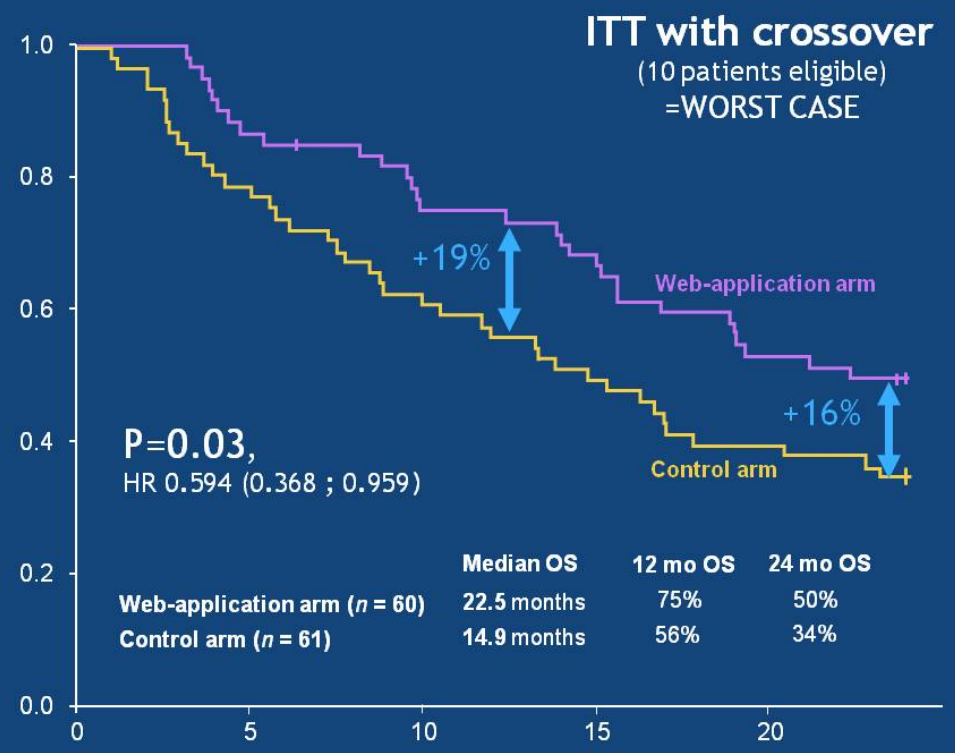
JJ/MM	04/04	10/04	18/04	24/04	09/05	16/05	22/05	29/05	06/06	12/06	27/06	04/07	10/07	24/07		19/02	26/02	05/03	11/03	19/03	02/04
aa	17	17	17	17	17	17	17	17	17	17	17	17	17	17		18	18	18	18	18	18
Weight	93.3	93	93.3	93	93	93	93	92.5	92.3	92.3	91.3	91.3	92.5	92.3		91	91	91	91	90.5	90.5
Weight variation	-0.3	0.3	0	0.5	1	0.5	0.5	1	1.2	1	2	2	0.8	0.7		0	0	0	0	0.5	0.5
Appetite loss	1	2	2	2	2	2	2	1	1	2	2	2	2	2		1	1	1	1	1	1
Weakness	1	2	1	1	2	3	2	1	1	1	1	1	1	1		1	1	1	2	1	1
Pain	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0
Cough	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
Breathlessness	1	1	2	2	2	2	0	1	1	1	1	1	1	1		0	0	0	0	0	0
Depression	3	0	0	0	0	0	0	0	0	0	0	0	0			2	2	2	2	2	2
Fiever	0	0	0	0	0	0	0	0	0	0	0	0	0			0	0	0	0	0	0
Face swelling	0	0		0	0	0	0	0	0	0	0	1	0	0		0	0	0	0	0	0
Lump under skin	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0
Voice changing	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0
Blood in sputum	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0

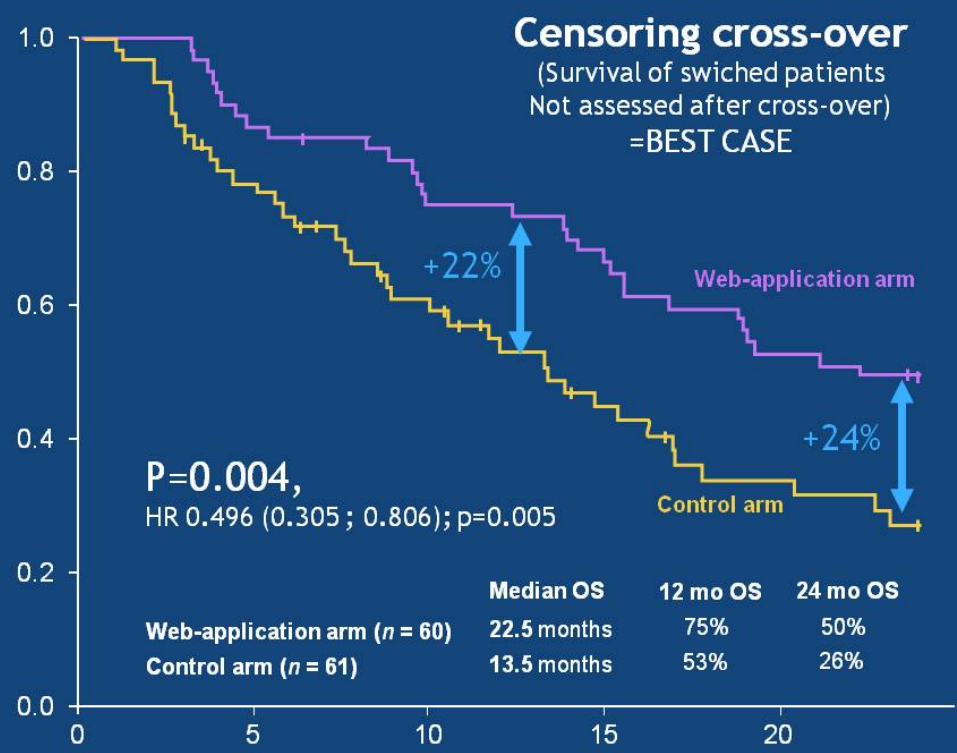


4/2017
Nivolumab initiated

6/2018
Nivolumab ongoing

Final OS analysis (2-Yrs follow-up)





PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Fabrice DENIS MD,PhD

Conclusions

Integration of patient-reported symptoms into cancer care is associated with clinical benefits

This approach should be considered for inclusion in standard symptom management to improve and measure quality of care

Future efforts should focus on strategies for integrating self-reporting into clinical workflow and electronic health records

Click here to complete eRAPID symptom report

- LOG OUT
- Home
- Managing Treatment Symptoms and Side Effects +
- Keeping Healthy During Cancer Treatment +
- Coping With Cancer and Your Treament +

HOME

Welcome to the home page of the University of Leeds and Leeds Teaching Hospitals, eRAPID research project funded by a National Institute for Health Research (NIHR) Programme Grant (RP-PG-0611-20008).

eRAPID stands for "Electronic patient self-Reporting of Adverse-events: Patient Information and aDvice".

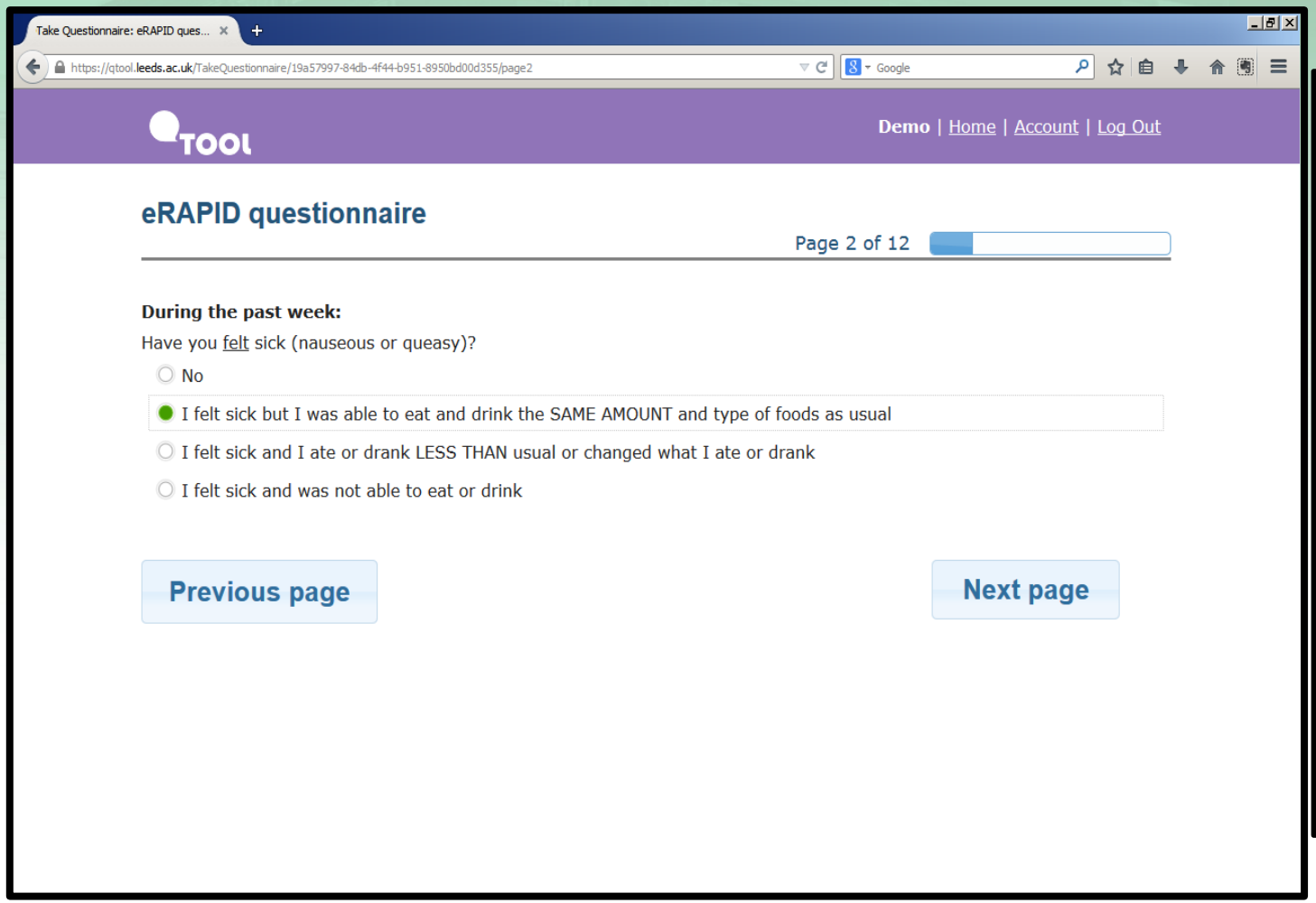
The aim is to develop an integrated web-system for patients to report symptoms and side effects during and after cancer treatment. Data that is reported by patients using the web-system (called QTool) will be documented in individual patient electronic health records. Where patients report mild side effects they will receive advice on how to manage them and to seek timely medical advice.

If you have any queries regarding the content of this website, please contact **The Patient Reported Outcomes Group (POG)** on **(0113) 20 68968.**

Please visit our Patient Reported Outcomes website www.pogweb.org to view our other studies. Our research primarily involves developing and evaluating web based systems for cancer patients to report information about their health and wellbeing.

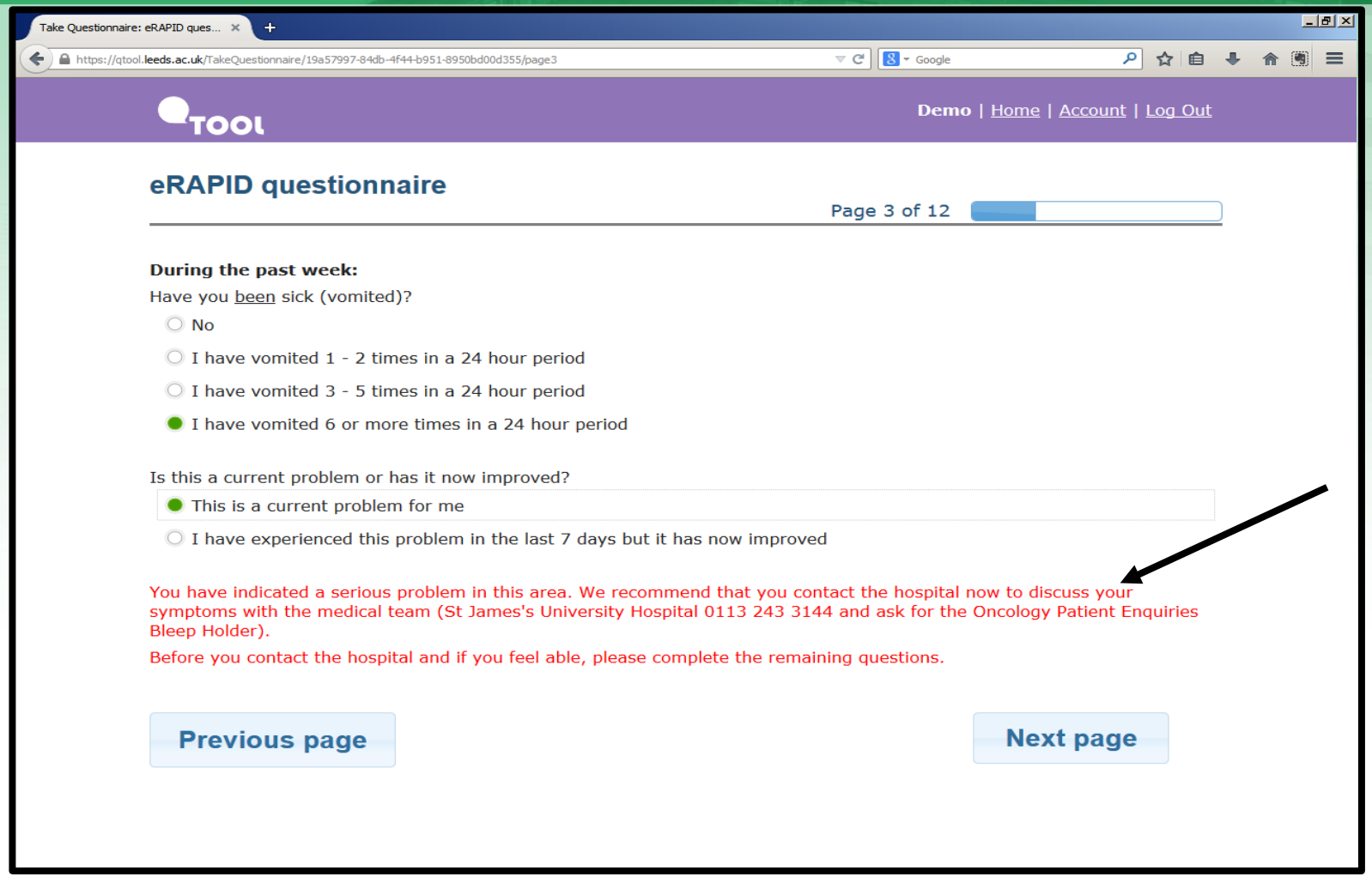



Patient symptom report- QTool



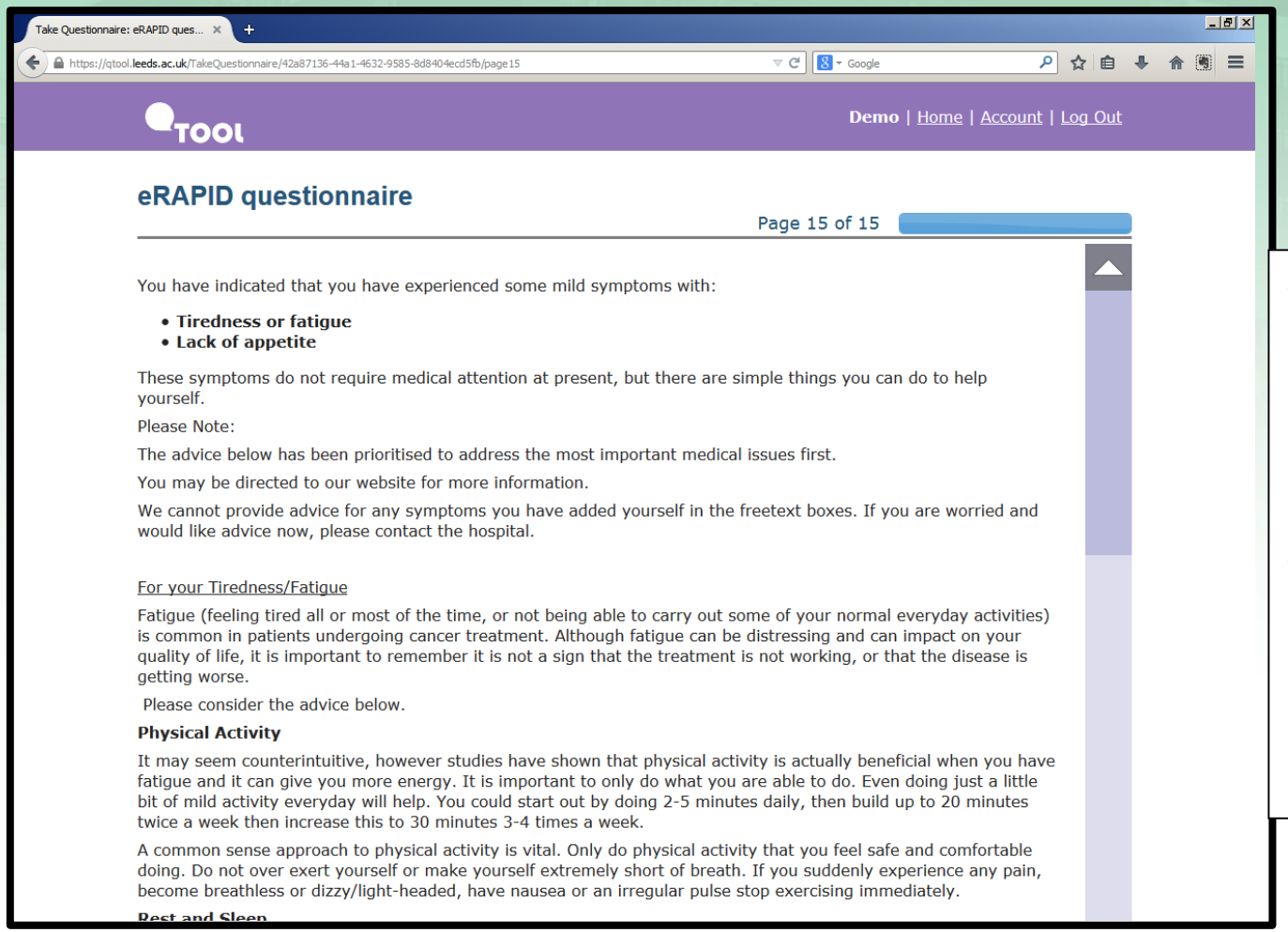
- Patients log in using a unique username and password
- Answer 12-15 symptom questions
- Nausea, vomiting, bowels, pain, fatigue, etc
- Varies between tumour groups
- Based on CTCAE criteria
- Option to add additional symptoms at the end

Patient symptom report- QTool



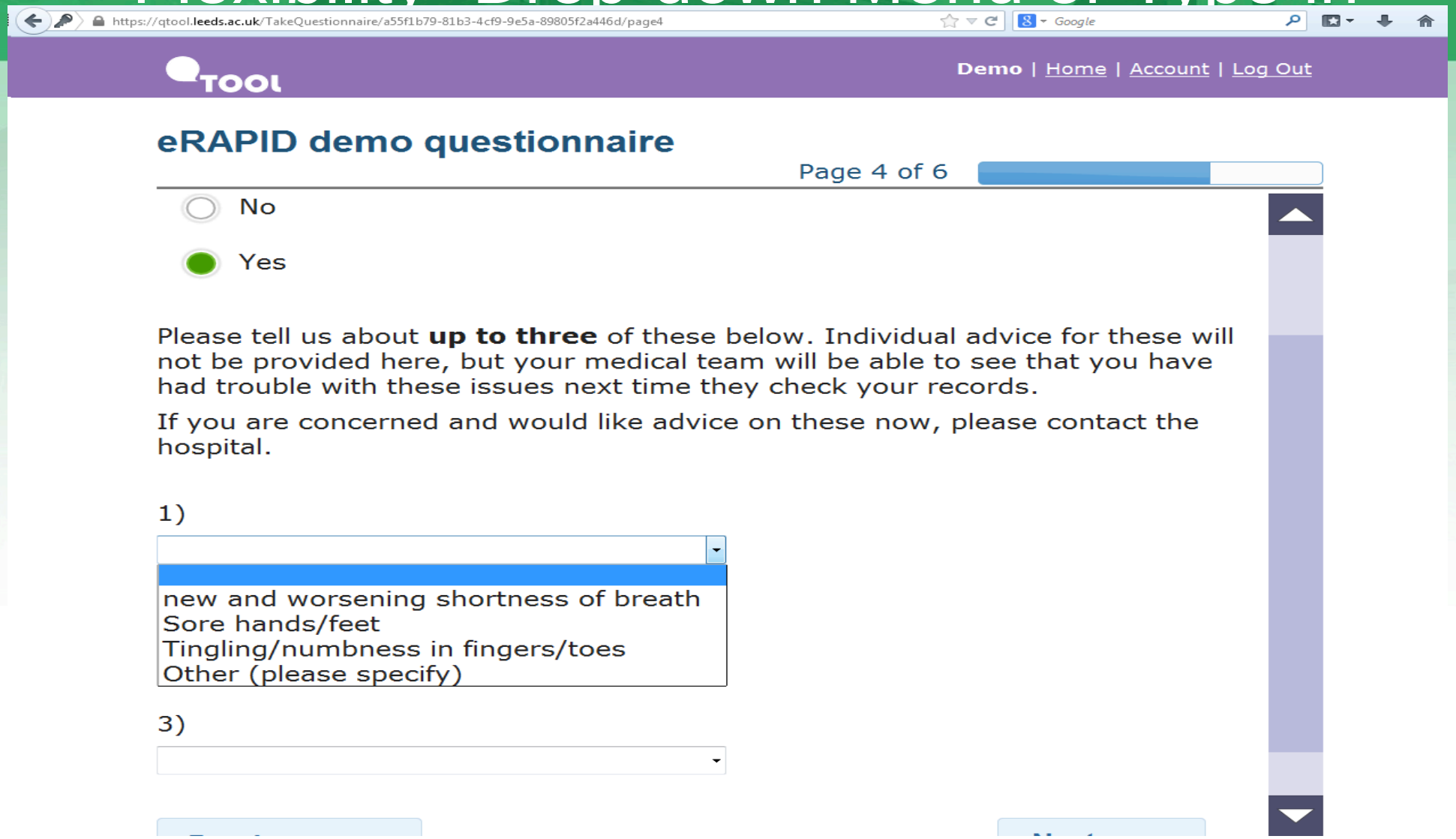
If the patient reports a symptom that needs immediate medical attention, they are immediately advised to contact the oncology bleep holder.

Advice for self-management- QTool



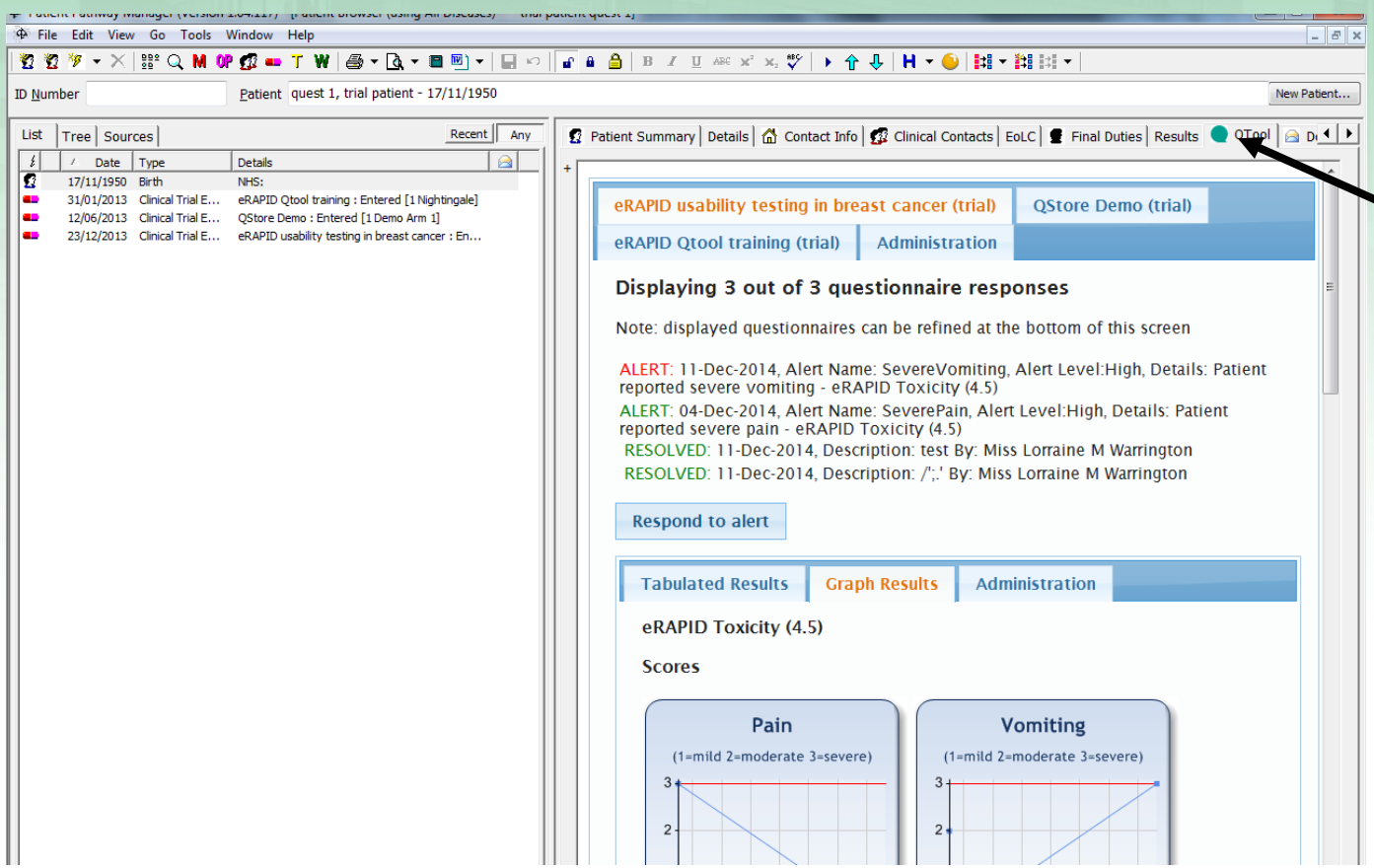
- For less serious symptoms advice for helping patients self-manage these issues is provided.
- Information on all symptoms and side effects is also available on the eRAPID website.

Flexibility- Drop-down Menu or Type in



Patient symptom reports in EHR

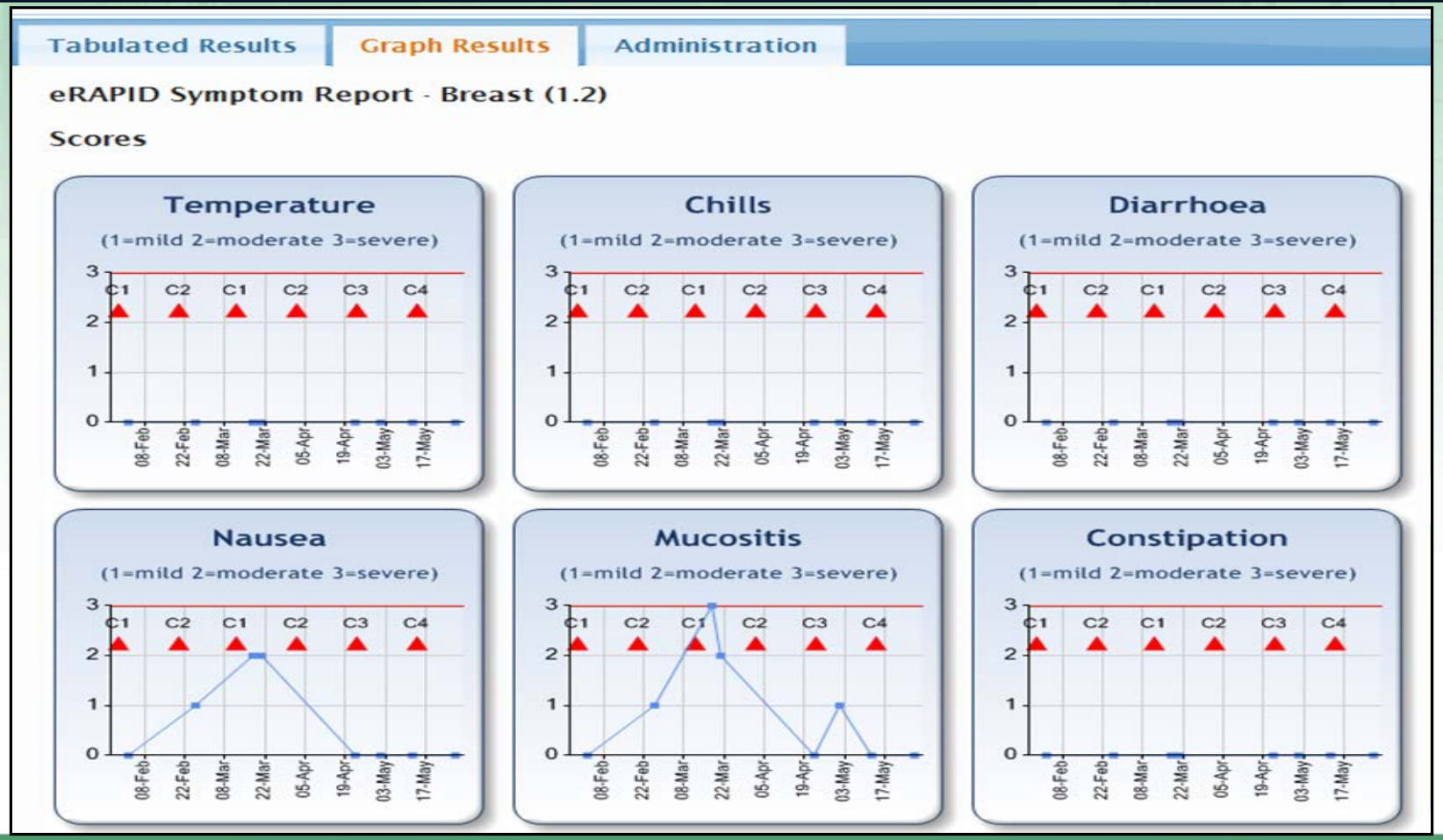
Patient reported data is immediately transferred from QTool to PPM



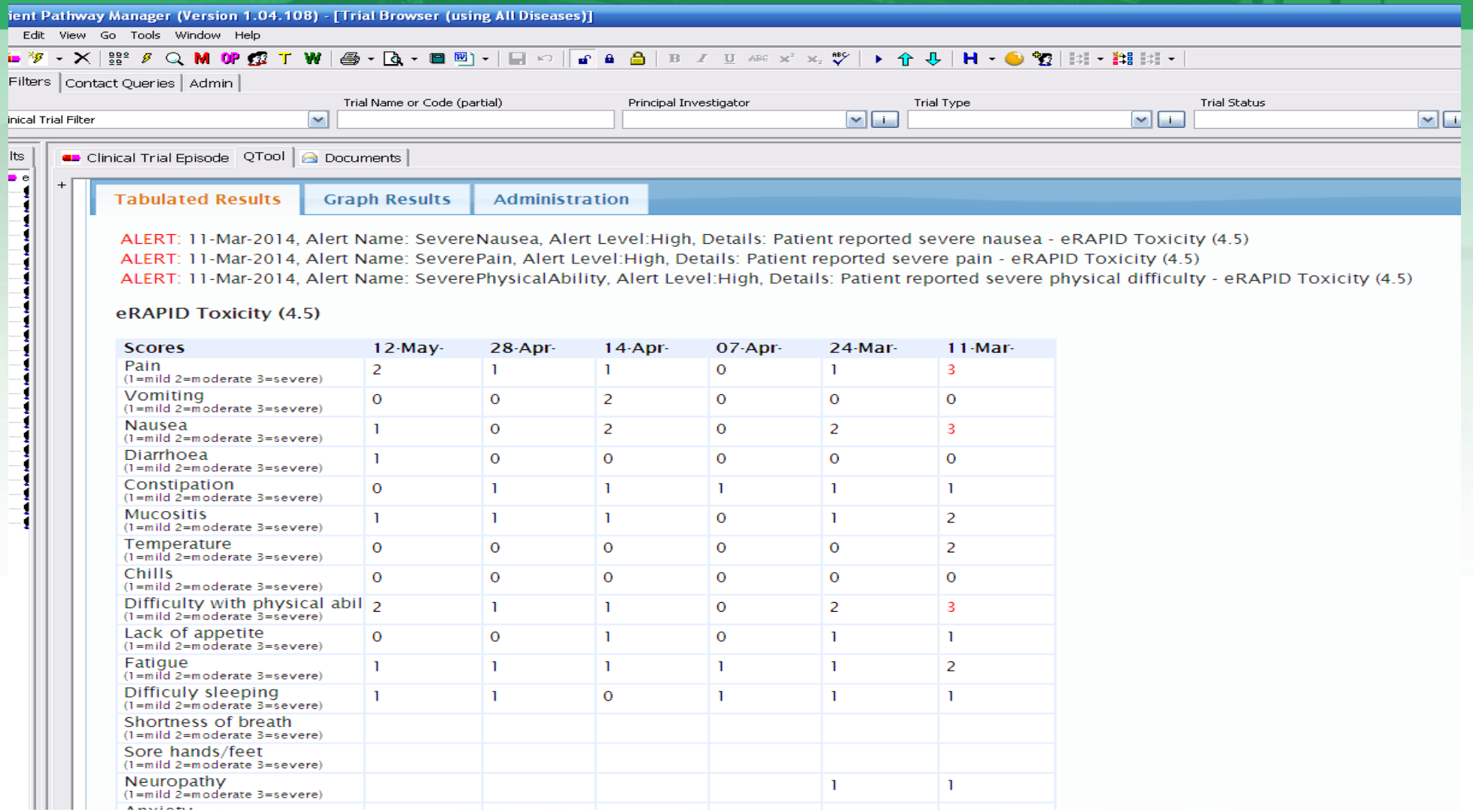
QTool tab in PPM

Clinician view EHR- graphs

Patient reported data is immediately transferred to EHR



Clinician View in EHR - Table



Scores	12-May-	28-Apr-	14-Apr-	07-Apr-	24-Mar-	11-Mar-
Pain (1=mild 2=moderate 3=severe)	2	1	1	0	1	3
Vomiting (1=mild 2=moderate 3=severe)	0	0	2	0	0	0
Nausea (1=mild 2=moderate 3=severe)	1	0	2	0	2	3
Diarrhoea (1=mild 2=moderate 3=severe)	1	0	0	0	0	0
Constipation (1=mild 2=moderate 3=severe)	0	1	1	1	1	1
Mucositis (1=mild 2=moderate 3=severe)	1	1	1	0	1	2
Temperature (1=mild 2=moderate 3=severe)	0	0	0	0	0	2
Chills (1=mild 2=moderate 3=severe)	0	0	0	0	0	0
Difficulty with physical abil (1=mild 2=moderate 3=severe)	2	1	1	0	2	3
Lack of appetite (1=mild 2=moderate 3=severe)	0	0	1	0	1	1
Fatigue (1=mild 2=moderate 3=severe)	1	1	1	1	1	2
Difficuly sleeping (1=mild 2=moderate 3=severe)	1	1	0	1	1	1
Shortness of breath (1=mild 2=moderate 3=severe)						
Sore hands/feet (1=mild 2=moderate 3=severe)						
Neuropathy (1=mild 2=moderate 3=severe)					1	1

View of free text entered by patients

(1=mild 2=moderate 3=severe 4=very severe)						
Anxiety (1=mild 2=moderate 3=severe)						

Question	21-Nov-2016 (Latest)	13-Nov-2016	11-Nov-2016	05-Nov-2016	03-Nov-2016	29-Oct-2016
Site of pain	Bladder		Knees	Knees		
Other symptom		Blood in urine	Nose bleeds	Blood in urine		Blood in urine
Severity (1=mild 2=moderate 3=severe 4=very severe)		1	1	1		1
Other symptom		Nosebleeds				Nosebleeds
Severity (1=mild 2=moderate 3=severe 4=very severe)		2				1
Other symptom						

Note

- Results displayed were correct as of 24-Nov-2016 13:33
- All results shown are patient reported unless indicated otherwise
- QTool is checked for new completed questionnaires every 5 minutes
- A cross is displayed on a graph to denote an unanswered question

Refine results

Show results from a range of questionnaire responses | Show results from a single questionnaire response

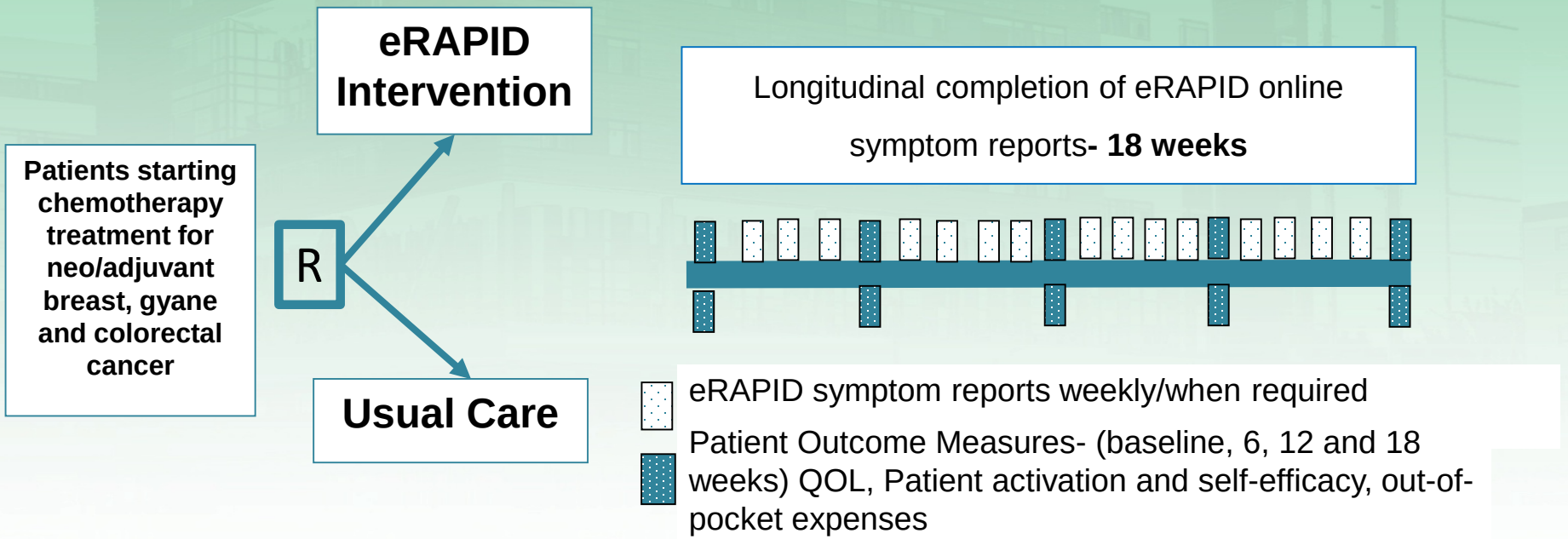
AEs items severity grades and alert thresholds

Pain	**Have you had pain or discomfort anywhere on your body?**	No	Standard	Standard	Standard
		I had mild pain or discomfort	1	1	1
		I had moderate pain or discomfort and I was not able to do some of the things I normally do (e.g. household chores, shopping)	2	2	2
		I had severe pain or discomfort and I was not able to care for myself (e.g. getting out of bed, bathing, dressing)	3	3	3
Nausea	**Have you felt sick (nauseous or queasy)?**	No	Standard	Standard	Standard
		I felt sick but I was able to eat and drink **the same amount** and type of foods as usual	1	1	1
		I felt sick and I ate or drank **less than usual** or changed what I ate or drank	2	2	2
		I felt sick and was **not able** to eat or drink	3	3	3
Sleep	**Have you had difficulty sleeping? OR What was the severity of your difficulty sleeping?**	No	Standard	Dropdown	Standard
		I occasionally have difficulty falling asleep, staying asleep or I wake too early	1	1	1
		I often have difficulty falling asleep, staying asleep or I wake too early	1	1	1
		I always have difficulty falling asleep, staying asleep or I wake too early	2	2	2
Neuropathy	**Have you had tingling or numbness in your fingers or toes? OR What was the severity of the tingling or numbness in your fingers or toes?**	No	Dropdown	Standard	Standard
		I had a bit of tingling or numbness (perhaps when handling cold or hot objects)	1	1	1
		I had tingling or numbness and I was not able to do some of the things I normally do (e.g. buttoning up or using cutlery)	1	1	1
		I had tingling or numbness and I was not able to carry out daily activities (e.g. I had difficulty walking, dropped things or stepped on things by accident)	2	2	2

Clinical algorithms- Overview

Algorithm	Summary	Immediate advice message in QTool
A1	One or more Level 3 problem, current - contact the hospital now	You have indicated a serious problem in this area. We recommend that you contact the hospital now to discuss your symptoms with the medical team (St James's University Hospital 0113 243 3144 and ask for the Oncology Patient Enquiries Bleep Holder).
A2	Level 3 problem(s) which improved, contact the team when convenient	You have reported that you have been experiencing some serious problems which have now improved. If you have not already been in contact with your medical team, we recommend that you contact them to discuss your symptoms when convenient, or mention them at your next clinic appointment (if in the next 1-2 weeks). If you have already been in touch with your medical team regarding your symptoms, please follow the advice they have given you.
B	Three or more Level 2 medically important problems; contact the team when convenient	If your symptoms are new or have changed recently, please either contact the hospital when convenient to discuss your symptoms with the medical team or mention them at your next clinic appointment (if in the next 1-2 weeks).
C	Mild symptoms, do not require medical attention at present, self-management advice	Follow self management advice
D	No problems reported	No advice

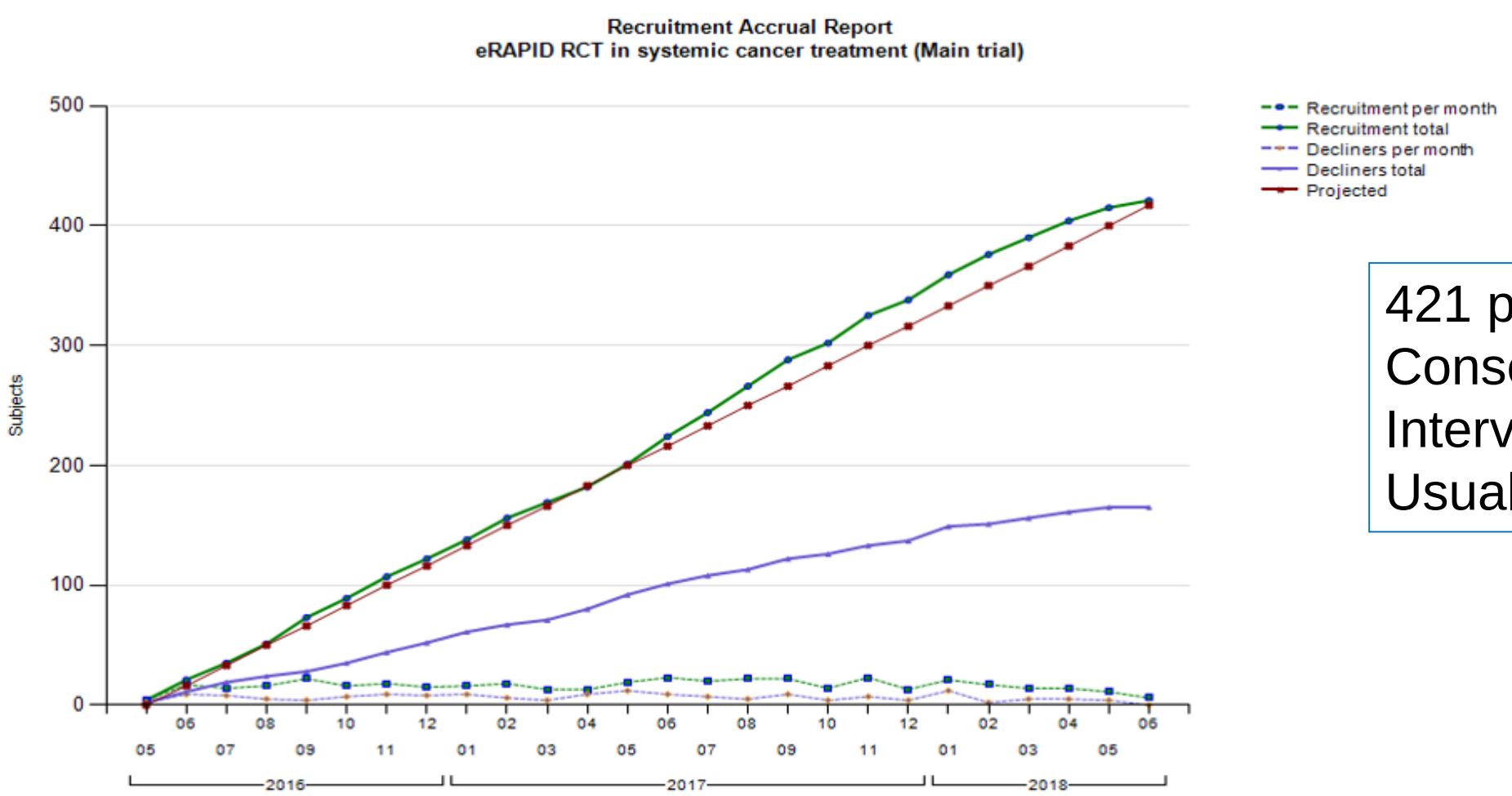
eRAPID Systemic RCT diagram



Endpoints and analysis

- Recruitment, attrition, missing data
- Quality of life (FACT-G), EORTC QLQ-C30
- Clinical process measures- number of hospital contacts, alerts and hospital admissions, clinician records of symptoms, changes to treatment
- Use of resources- hospital and community contacts, medications and treatment related expenses
- End of study interviews with participants and clinical staff

Recruitment graph– Main trial (18/05/2016 – 11/06/2018)



421 patients consented
Consent rate 72%
Intervention N = 212
Usual care N=209

Pilot Study- Activation of clinical algorithms

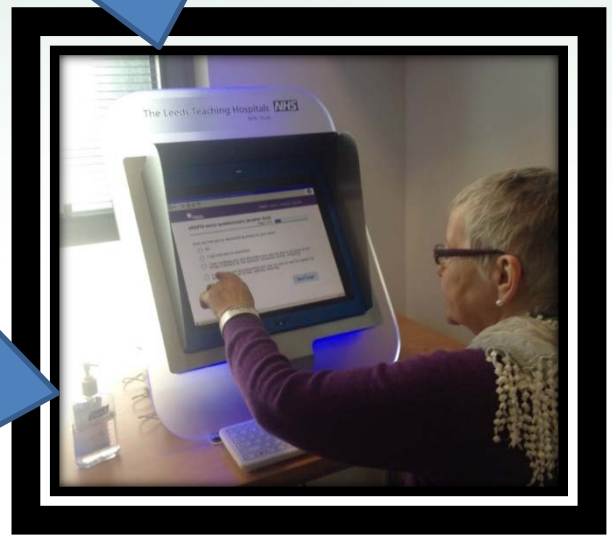
Algorithm	Breast	Ovarian	Colorectal
Total Online completions	382	73	85
Alert -contact the hospital immediately	2%	0	0
Serious symptoms improved, contact when convenient	10%	10%	5%
3 or more moderate symptoms, contact when convenient	17%	22%	4%
Mild symptoms, self-management advice	69%	67%	91%
No problems	1%	1%	1%

Feedback from patients and staff

…puts your mind at ease as you can have a lot of questions or problems regarding your illness and with one click they can be answered …No waiting till your next appointment.

Informative as patient completed through cycle so I was able to see progress

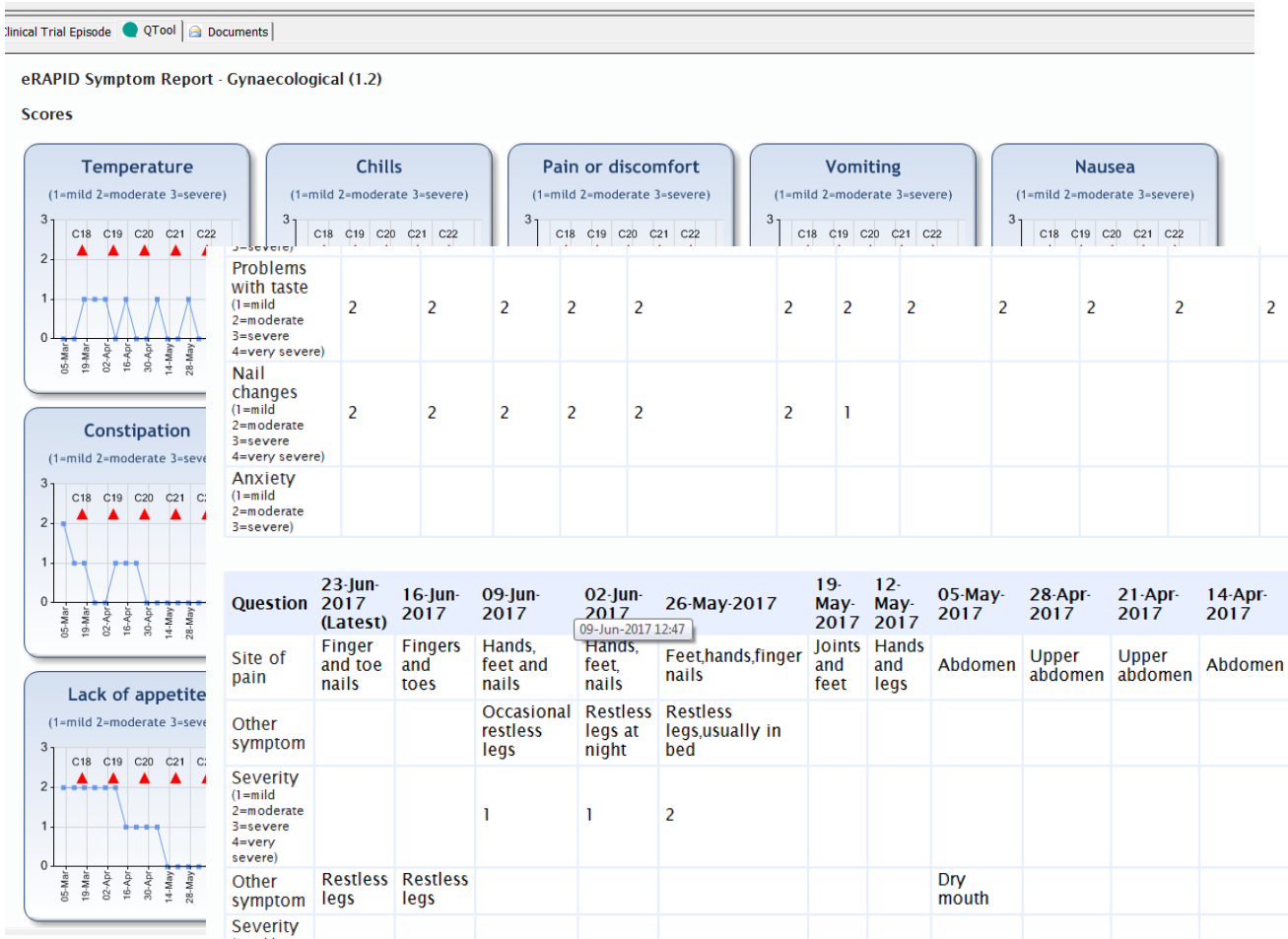
It's like a life line when you feel isolated when you're at home and feeling poorly



Very valuable, good graphical values, very easy to interpret

Case study-ovarian cancer, patient-reported CTCAE items

- 75 year old lady
- 2011 - Stage 3c/4 high grade serous ovarian adenocarcinoma. No pathogenic gBRCA mutation
- Chemotherapy with interval debulking surgery
- 2012-2017 - 7 lines of systemic treatment incl. bevacizumab, Tamoxifen, Carbo, paclitaxel, Caelyx.
- **Feb - Jun 17: Low-dose weekly paclitaxel/carboplatin x 6. Lymph nodes, peritoneal disease, ascites**
- **Partial response on CT and CA125 - normalised**



Problems with taste (1=mild 2=moderate 3=severe 4=very severe)	2	2	2	2	2	2	2	2	2	2	2	2
Nail changes (1=mild 2=moderate 3=severe 4=very severe)	2	2	2	2	2	2	1					
Anxiety (1=mild 2=moderate 3=severe)												

Question	23-Jun-2017 (Latest)	16-Jun-2017	09-Jun-2017	02-Jun-2017	26-May-2017	19-May-2017	12-May-2017	05-May-2017	28-Apr-2017	21-Apr-2017	14-Apr-2017
Site of pain	Finger and toe nails	Fingers and toes	Hands, feet and nails	Hands, feet, nails	Feet,hands,finger nails	Joints and feet	Hands and legs	Abdomen	Upper abdomen	Upper abdomen	Abdomen
Other symptom			Occasional restless legs	Restless legs at night	Restless legs,usually in bed						
Severity (1=mild 2=moderate 3=severe 4=very severe)			1	1	2						
Other symptom	Restless legs	Restless legs						Dry mouth			
Severity (1=mild 2=moderate 3=severe 4=very	1	1						2			

09-Jun-2017 12:47

Brief Conclusions

- **HRQOL and PROs in clinical trials**
  - Provide important additional information
- **New PRO concepts in cancer clinical trials**
  - Tolerability of cancer treatments is important
  - Tools for tolerability assessment
    - NCI PRO-CTCAE items
    - EORTC Item Library
- **PROs in routine oncology practice**
  - Benefits for patient care

Available resources

Available Resources

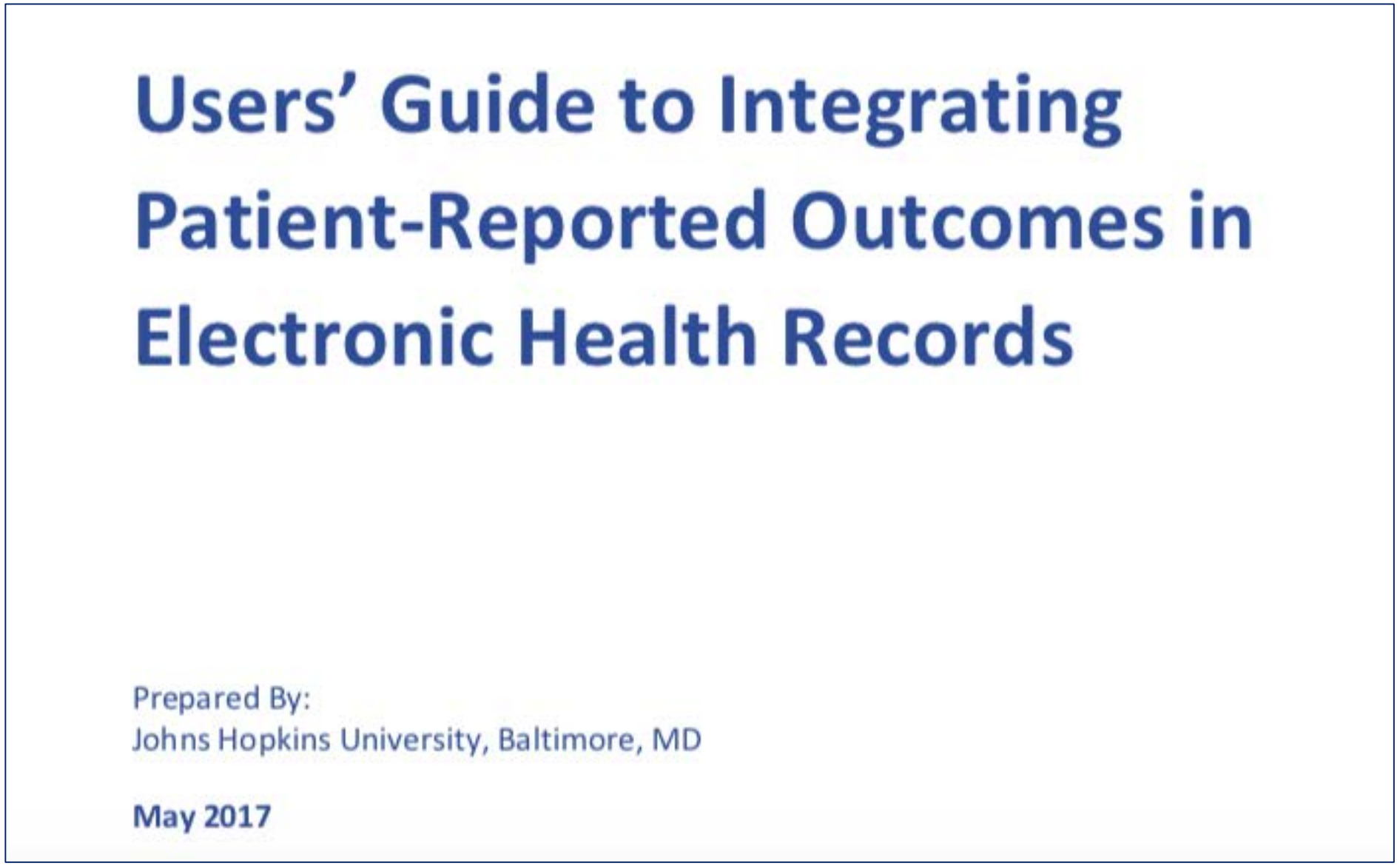
International Society for Quality of Life Research

User's Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice (2015)

http://www.isoqol.org/UserFiles/2015UsersGuide-Version2.pdf

User's Guide to Integrating Patient-Reported Outcomes in Electronic Health Records (2017)

https://www.pcori.org/sites/default/files/PCORI-JHU-Users-Guide-To-Integrating-Patient-Reported-Outcomes-in-Electronic-Health-Records.pdf



https://www.pcori.org/sites/default/files/PCORI-JHU-Users-Guide-To-Integrating-Patient-Reported-Outcomes-in-Electronic-Health-Records.pdf

Available Resources

EORTC guidelines

European Journal of Cancer 68 (2016) 73–81

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

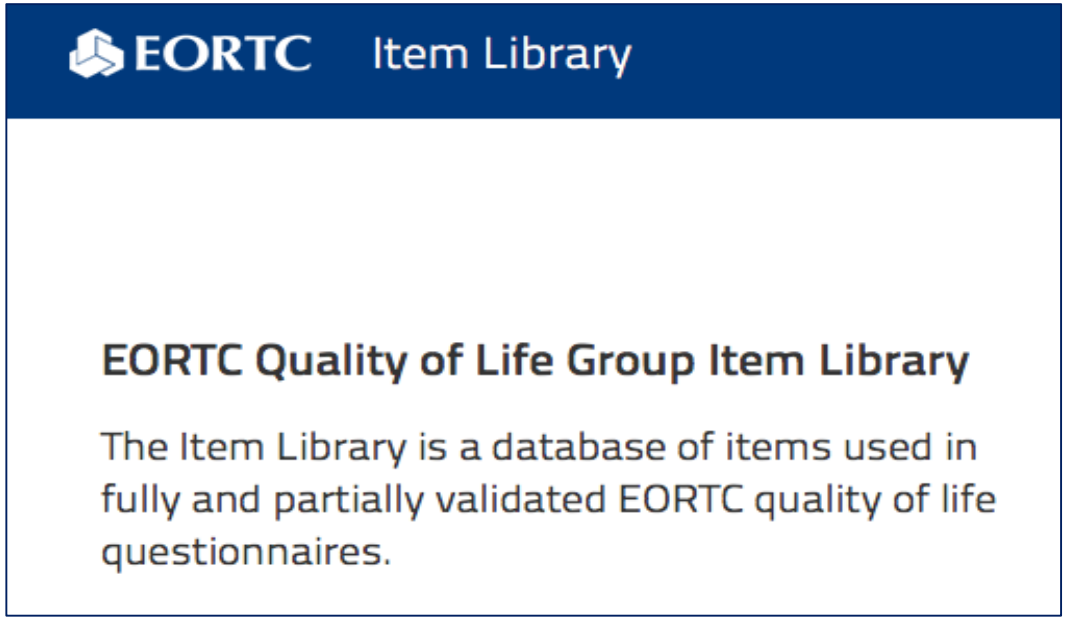
ELSEVIER

Review

The use of EORTC measures in daily clinical practice—A synopsis of a newly developed manual

Lisa M. Wintner [a,*], Monika Sztankay [a], Neil Aaronson [b], Andrew Bottomley [c], Johannes M. Giesinger [a], Mogens Groenvold [d], Morten Aa Petersen [d], Lonneke van de Poll-Franse [e], Galina Velikova [f], Irma Verdonck-de Leeuw [g], Bernhard Holzner [a] on behalf of the EORTC Quality of Life Group

http://groups.eortc.be/qol/manuals



EORTC Item Library

EORTC Quality of Life Group Item Library

The Item Library is a database of items used in fully and partially validated EORTC quality of life questionnaires.

EORTC Quality of Life Home Instrument Development EORTC CAT

CHES platform

Electronic data collection infrastructure for EORTC Quality of Life Group projects

PRO instrument development platform

EORTC CAT measures

PRO monitoring in daily oncological practice

NCI PRO-CTCAE

Patient-Reported Outcomes version of the
Common Terminology Criteria for Adverse Events

http://appliedresearch.cancer.gov/pro-ctcae

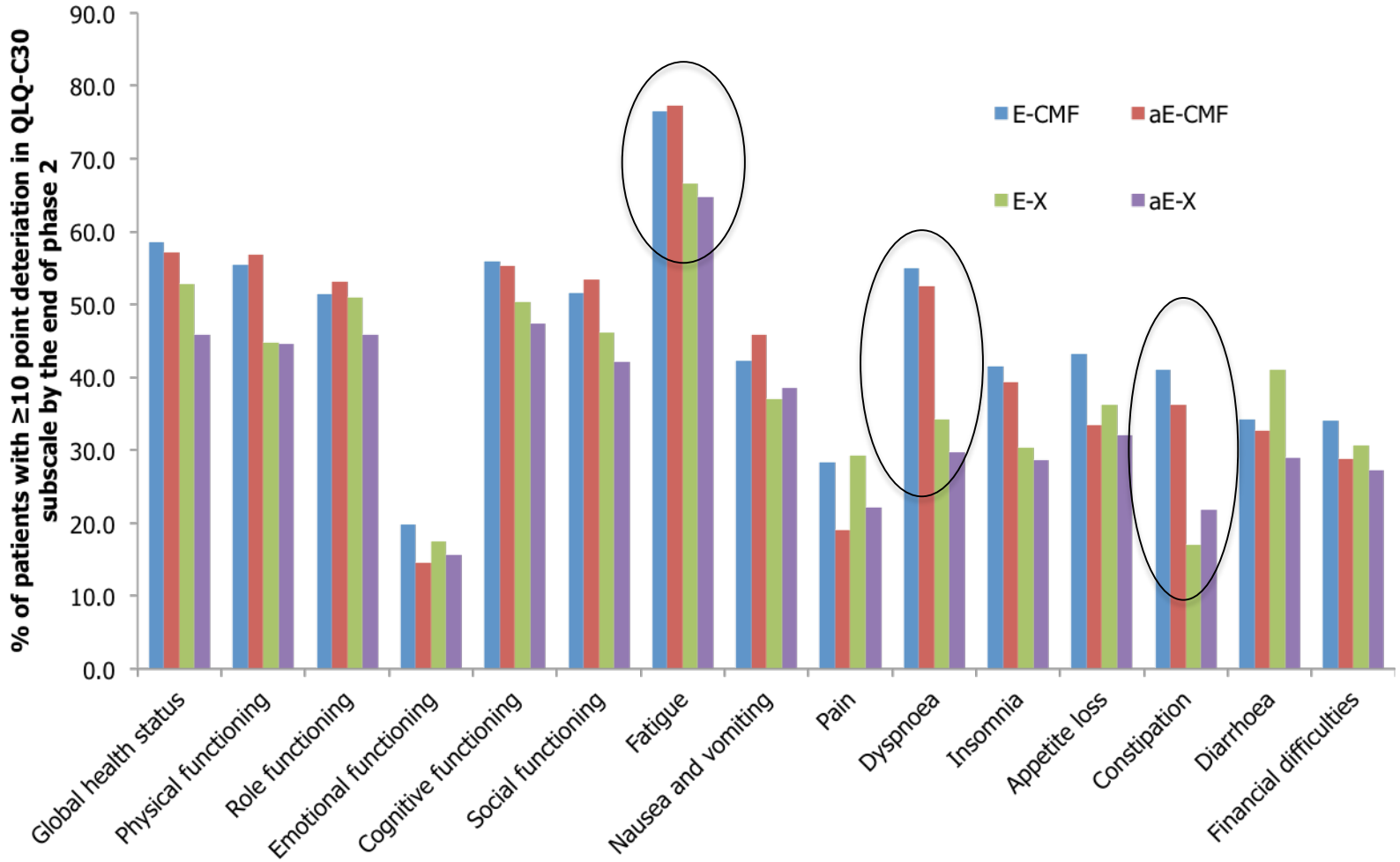
Reserve slides

Longitudinal modelling

Subscale	p-value	Subscale	p-value
QLQ-C30		**QLQ-BR23**	
Global health status	0.96	Body image	0.45
Physical functioning	0.79	Sexual functioning	0.62
Role functioning	0.97	Sexual enjoyment	0.06
Emotional functioning	0.92	Future perspective	0.07
Cognitive functioning	0.66	Systemic side-effects	0.08
Social functioning	0.33	Breast symptoms	0.98
Fatigue	0.98	Arm symptoms	0.81
Nausea and vomiting	0.02*	Hair loss	0.33
Pain	0.77		
Dyspnoea	0.69	**HADS total score**	0.90
Insomnia	0.34		
Appetite loss	0.12	**Wu Fatigue score**	0.25
Constipation	0.61*		
Diarrhoea	0.44	**FSI Composite score**	0.26
Financial difficulties	0.02		

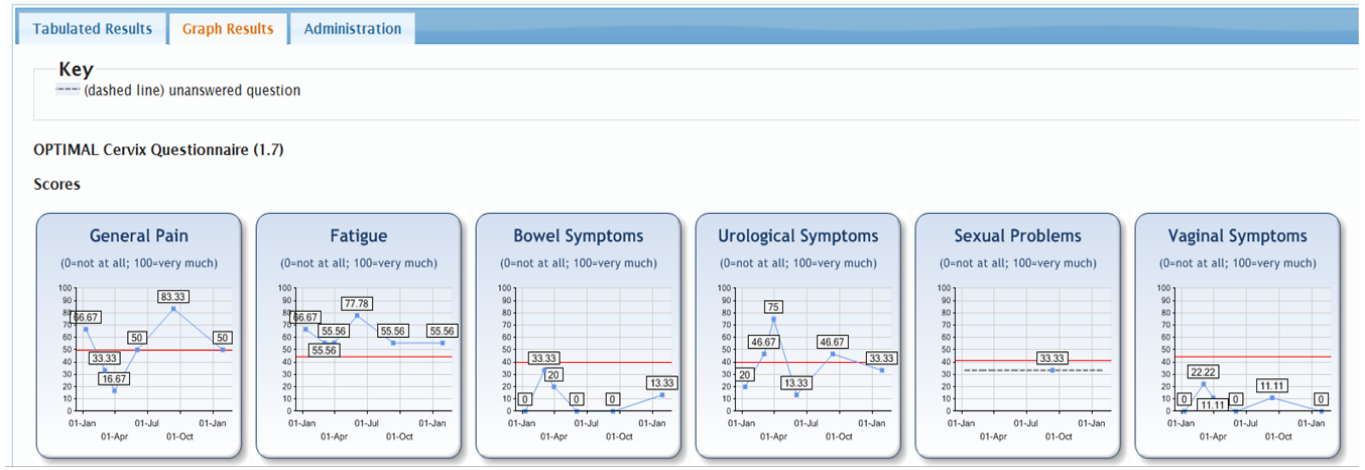
“Responder analysis”

Proportion of patients with ≥10 point deterioration by the end of phase 2, by treatment arm



Case study-Cx cancer chemoradiotherapy, QLQ-C30 and Cx module

- 31 year old lady, bleeding 27 weeks pregnancy
- Poorly differentiated SCC, MRI - 5x3x4cm tumour extending into the left parametrium
- Planned 48Gy in 28 fractions of radiotherapy with 5 cycles of weekly concurrent cisplatin chemotherapy
- Planned to proceed with intracavity brachytherapy 21Gy in 3 fractions
- Instead - external beam phase 2 boost to the residual tumour volume (18Gy in 10 fractions with two further concurrent cisplatin cycles)
- Potential for increased toxicity
- Complete remission on MRI and PET at 3 months
- 18 months follow-up – neuropathy, radiation cystitis and bowel toxicity
- EORTC QLQ-C30 and CX module



Scores	27-Jan-2016 (Latest)	11-Sep-2015	02-Jun-2015	30-Mar-2015	03-Mar-2015	09-Jan-2015
Urinary Frequency (0=not at all; 100=very much)	33.33	66.67	0	100	66.67	33.33
Urinary Urgency (0=not at all; 100=very much)	66.67	66.67	33.33	66.67	66.67	0
Urinary Incontinence (0=not at all; 100=very much)	66.67	66.67	33.33	33.33	33.33	33.33
Dysuria (0=not at all; 100=very much)	0	0	0	100	66.67	33.33
Bladder emptying difficulties (0=not at all; 100=very much)	0	33.33	0	Missing	0	0
Menopausal Symptoms (0=not at all; 100=very much)	33.33	0	100	66.67	33.33	0
Sexual Worry (0=not at all; 100=very much)	66.67	66.67	66.67	33.33	66.67	0
Sexual Activity (0=not at all; 100=very much)	0	33.33	0	0	0	0

NIHR eRAPID Multi-centre programme in systemic therapy, radiotherapy and surgery

The Leeds Teaching Hospitals NHS
NHS Trust

Dr Alexandra Gilbert
NIHR Clinical PhD student

Prof Jane Blazeby

Dr Susan Davidson
Jacki Routledge
Dr Ananya Chaudhuri

University Hospitals Bristol NHS
NHS Foundation Trust

The Christie NHS
NHS Foundation Trust

UNIVERSITY OF LEEDS

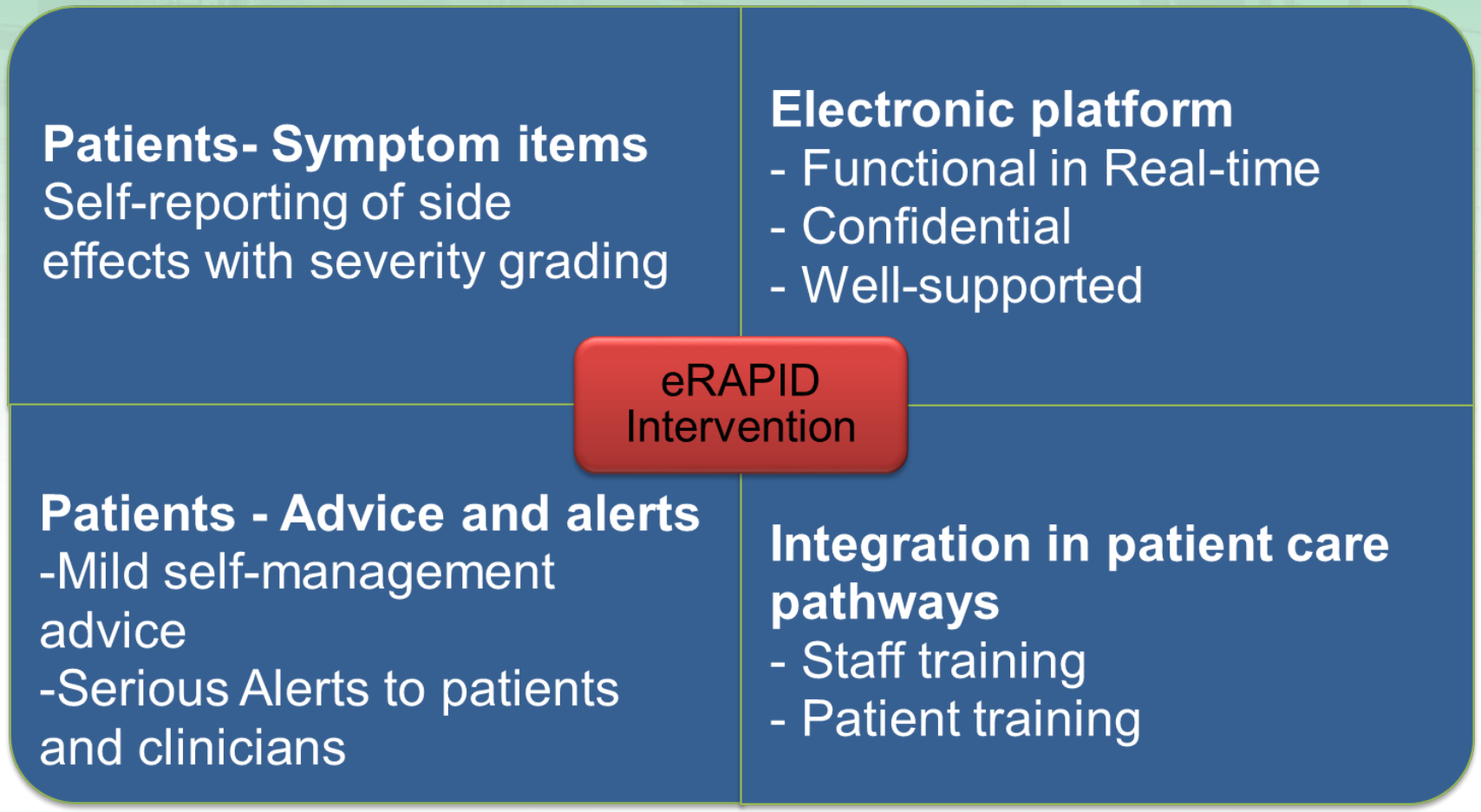
eRAPID

Electronic patient self-Reporting of Adverse-events: Patient Information and aDvice

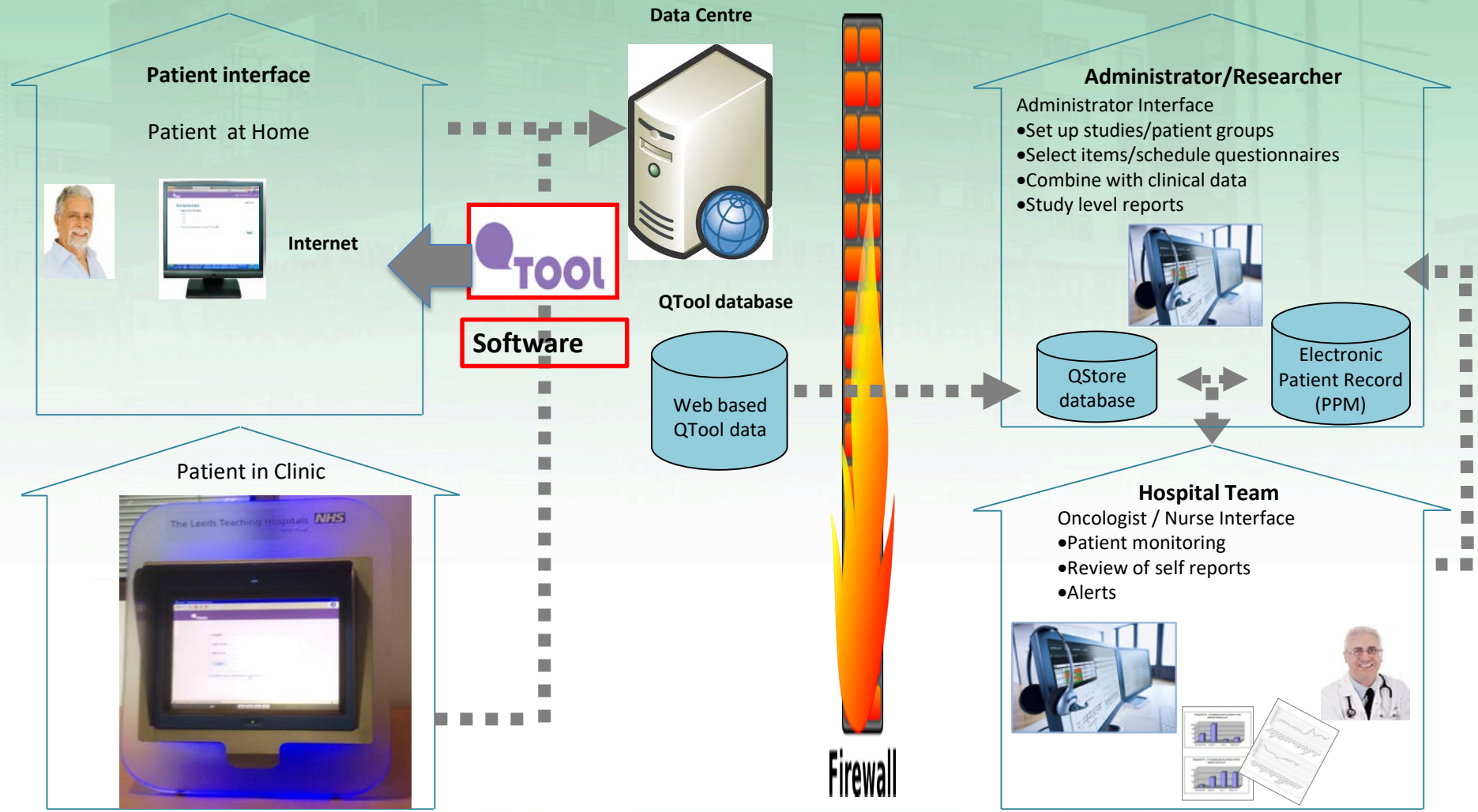
NHS National Institute for Health Research

eRAPID is a complex intervention

(NIHR programme grant)



Electronic platform – QTool EHR System



CTCAE-Patient self-reporting format

CTCAE Item	Patient self-report item
Mucositis oral **Definition:** A disorder characterized by inflammation of the oral mucosal. **Attributes:** Severity, Interference	**Have you had a sore mouth or tongue?**
	No
Grade 1. Asymptomatic or mild symptoms; intervention not indicated	My mouth was a bit sore
Grade 2. Moderate pain; not interfering with oral intake; modified diet indicated	My mouth was quite sore but I was still able to drink and eat soft foods
Grade 3. Severe pain; interfering with oral intake	My mouth was very sore and I was not able to eat or drink