The case for routine symptom monitoring and quality of life assessment in advanced cancer care

David Cella, PhD

Robert H. Lurie Comprehensive Cancer Center
Northwestern University
Chicago, IL USA

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

Con il patrocinio di
UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

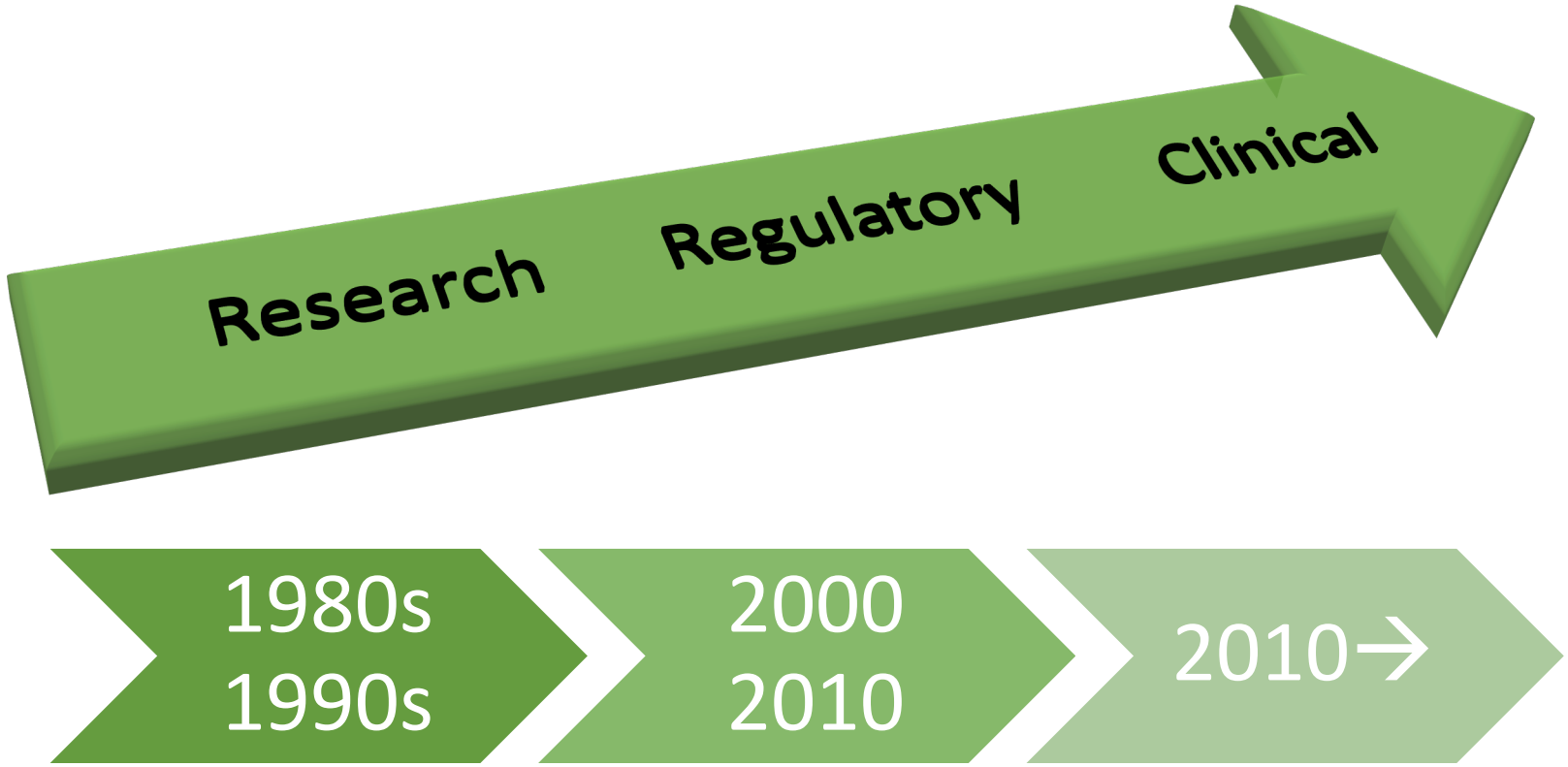
LE CURE PALLIATIVE PRECOCI IN
EMATO-ONCOLOGIA:
la nuova risposta ai bisogni di pazienti e caregivers

19 maggio 2023 **Roma**, Hotel Donna Camilla Savelli

Disclosures of Name Surname

Company name	Research support	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Astellas Pharma.		X				
Black Diamond Therapeutics		X				
Bristol Myers Squibb	X	X				
Day One Biopharmaceuticals		X				
Fulcrum Therapeutics		X				
Human Health		X				
IPSEN PHARMA SAS	X	X				
Merck	X	X				
Novartis		X				
Semonix		X				
Vinehealth		X				

Snapshot History of QoL Measurement



Palliative Care and Quality of Life Research Have Traveled this Path Together

Regarding Symptom Monitoring and Management…

Today I will discuss:


Why?
Why ?
Why ?
Why ?

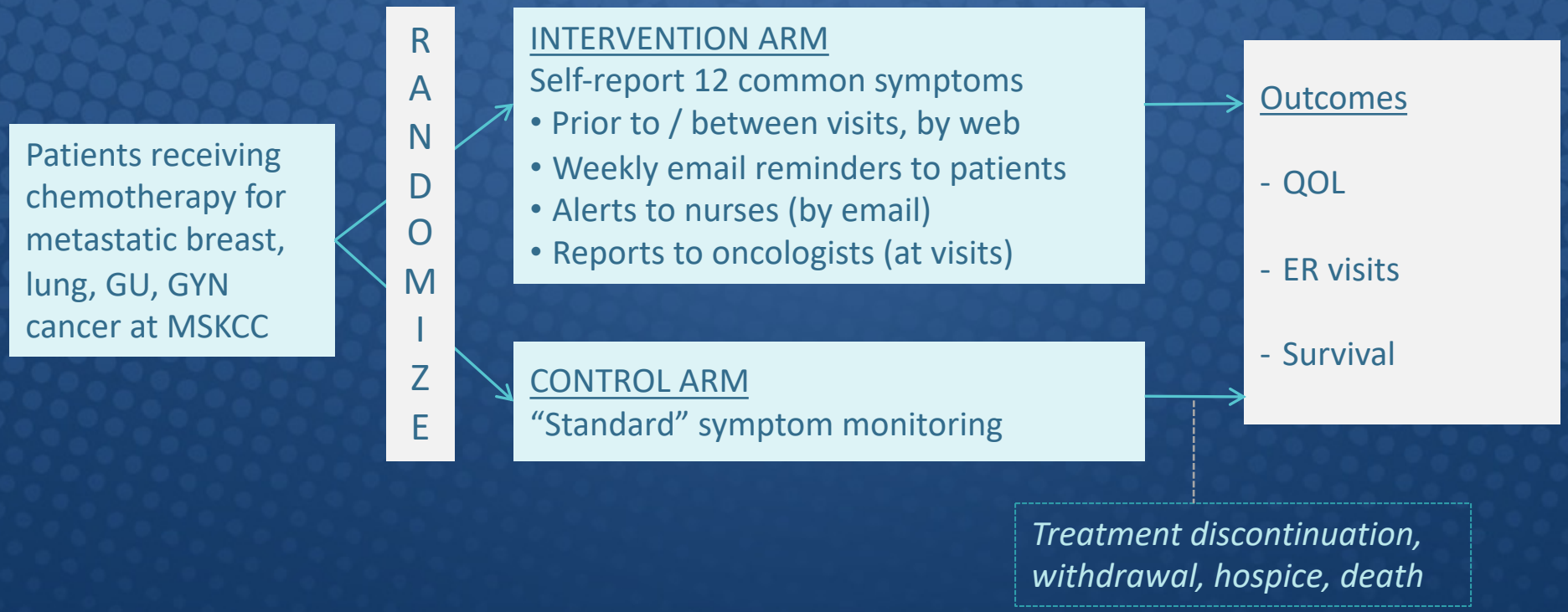
Symptoms are Common in Cancer

- Interfere with physical function and daily activities
- Interfere with treatment planning
- Lead to avoidable ER/hospital visits, readmissions

Symptom management is a cornerstone of quality care

- Do we adequately detect and manage symptoms?

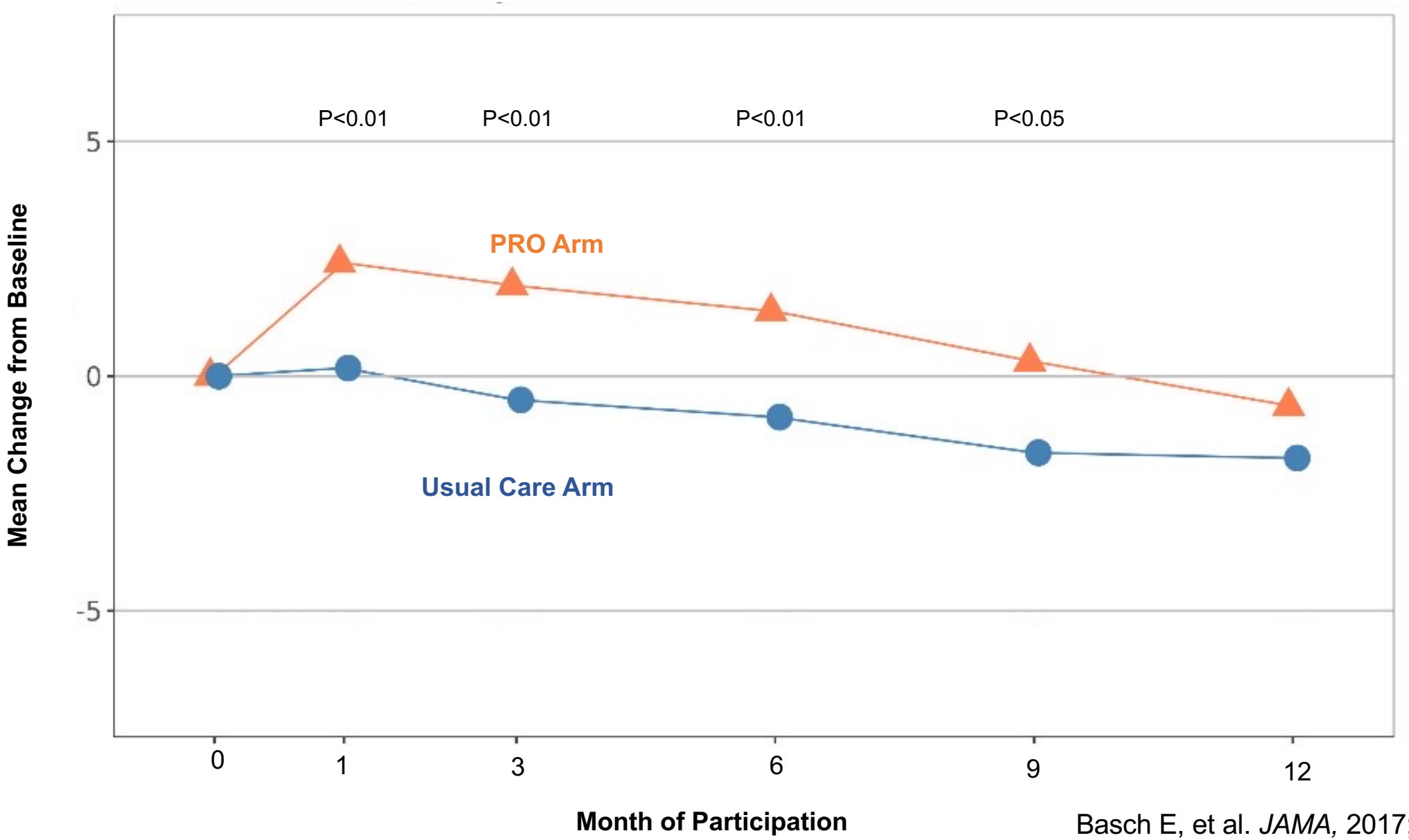
MSKCC "STAR" Study: Impact on Clinical Outcomes



766 patient participants; median follow up 7 years

Basch E, et al. *JAMA*, 2017;318(2):197-198

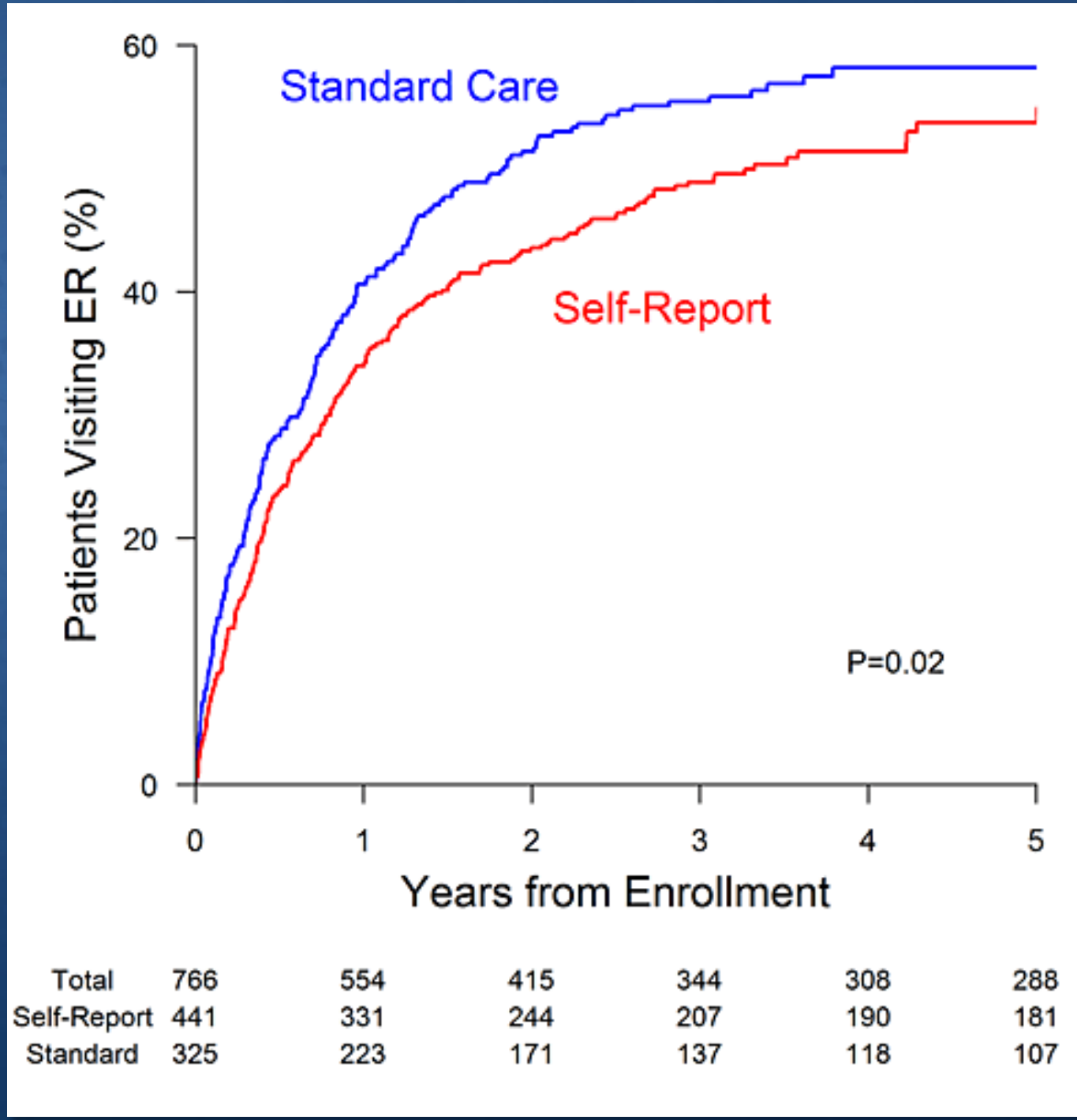
Results: Effects on Health-Related Quality of Life



Basch E, et al. *JAMA,* 2017;318(2):197-198

Emergency Room Visits

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



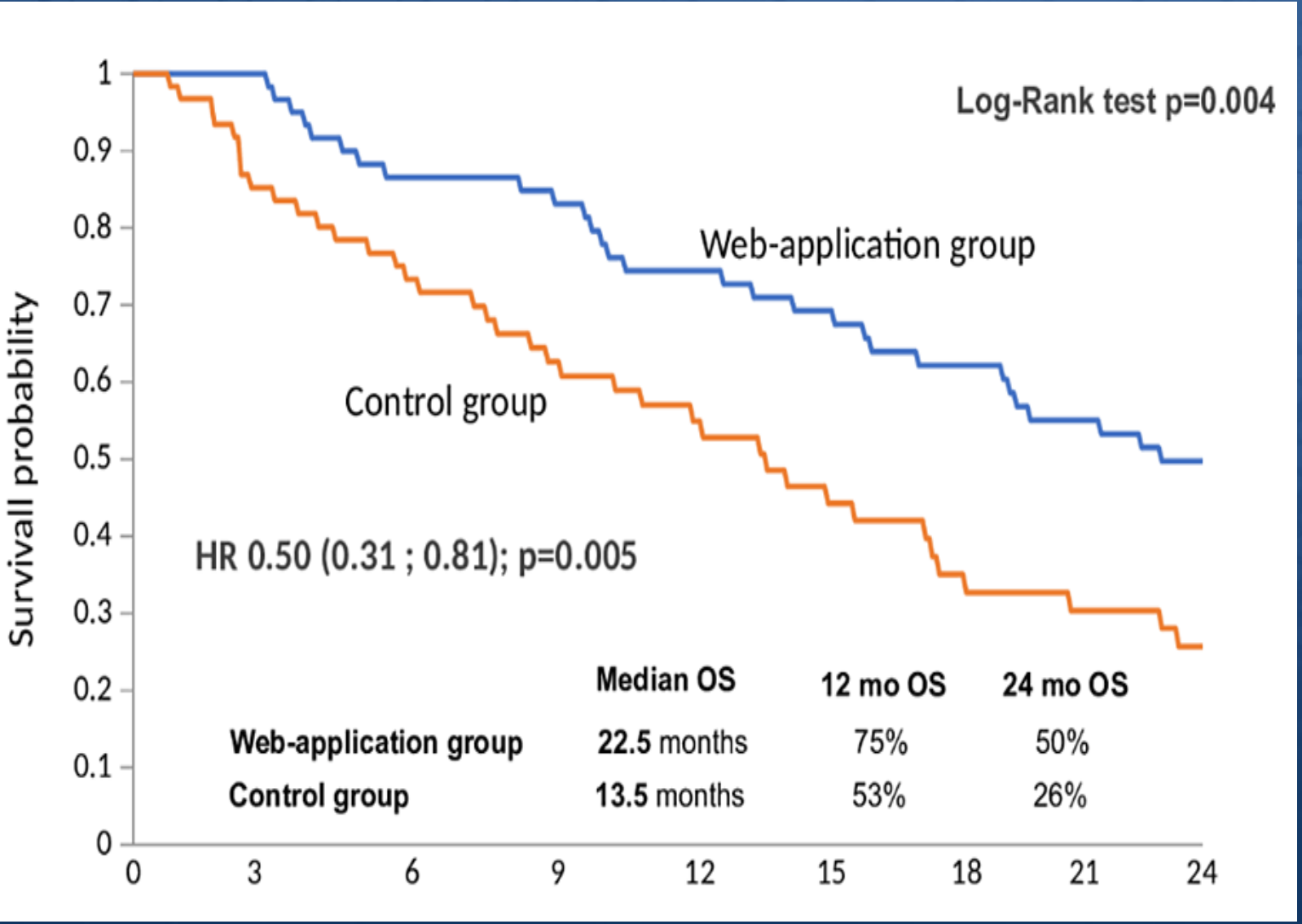
Basch E, et al. *JAMA,* 2017;318(2):197-198

MSKCC STAR RCT: Metastatic Solid Tumors

- 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*)
- Significant in multivariable analysis:
  Adjusted hazard ratio 0.832 (*95% CI; 0.696, 0.995*)
- 5-year absolute survival benefit of 8%

Basch E, et al. *JAMA,* 2017;318(2):197-198

French Lung Cancer RCT



- N=121 @ 5 centers in France
- Weekly PRO monitoring

Results:

- Overall survival: 22.5 vs 13.5 months (P=0.03)
- Optimal treatment 72.4% vs 32.5% (P<0.001)

Denis et al: JAMA, 2019

Canadian Population-Based Study (N>128,000)

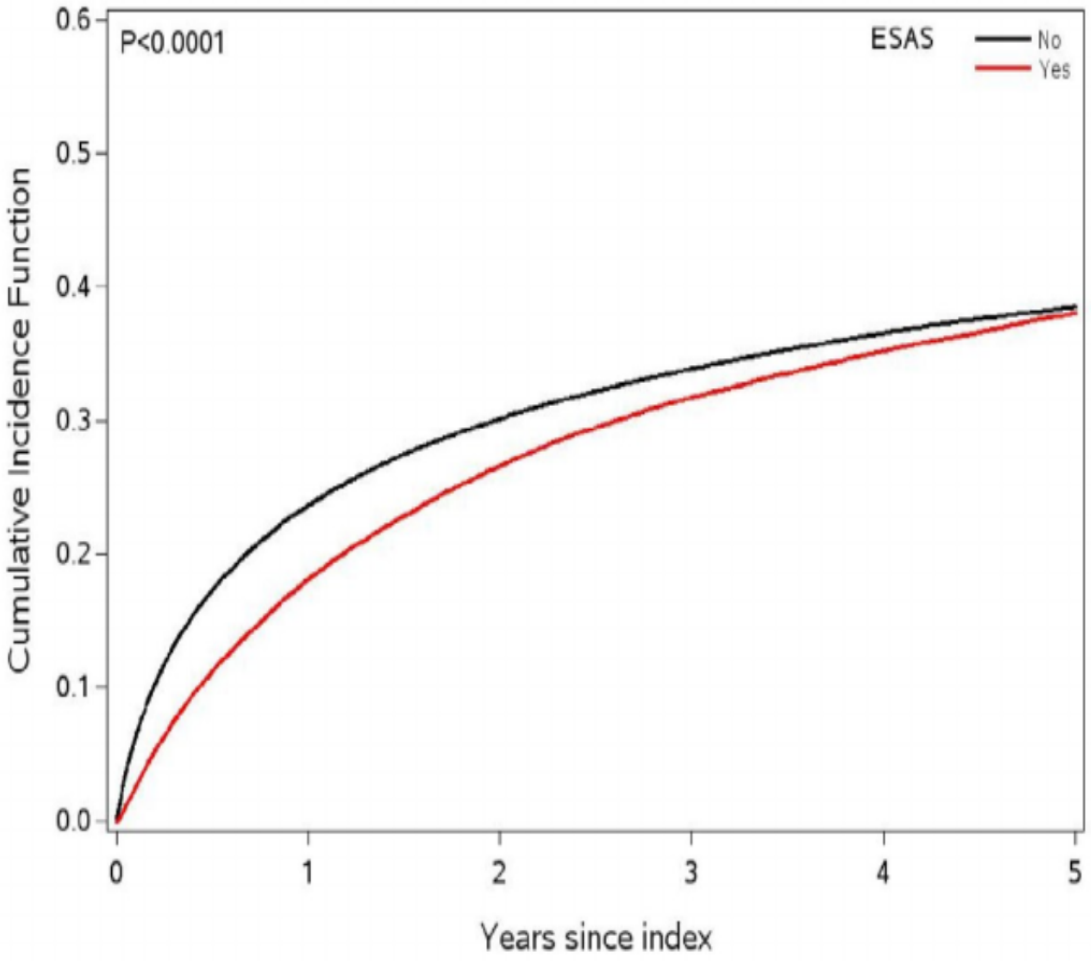


FIGURE 2 Cumulative incidence function of death for patients exposed and unexposed to ESAS

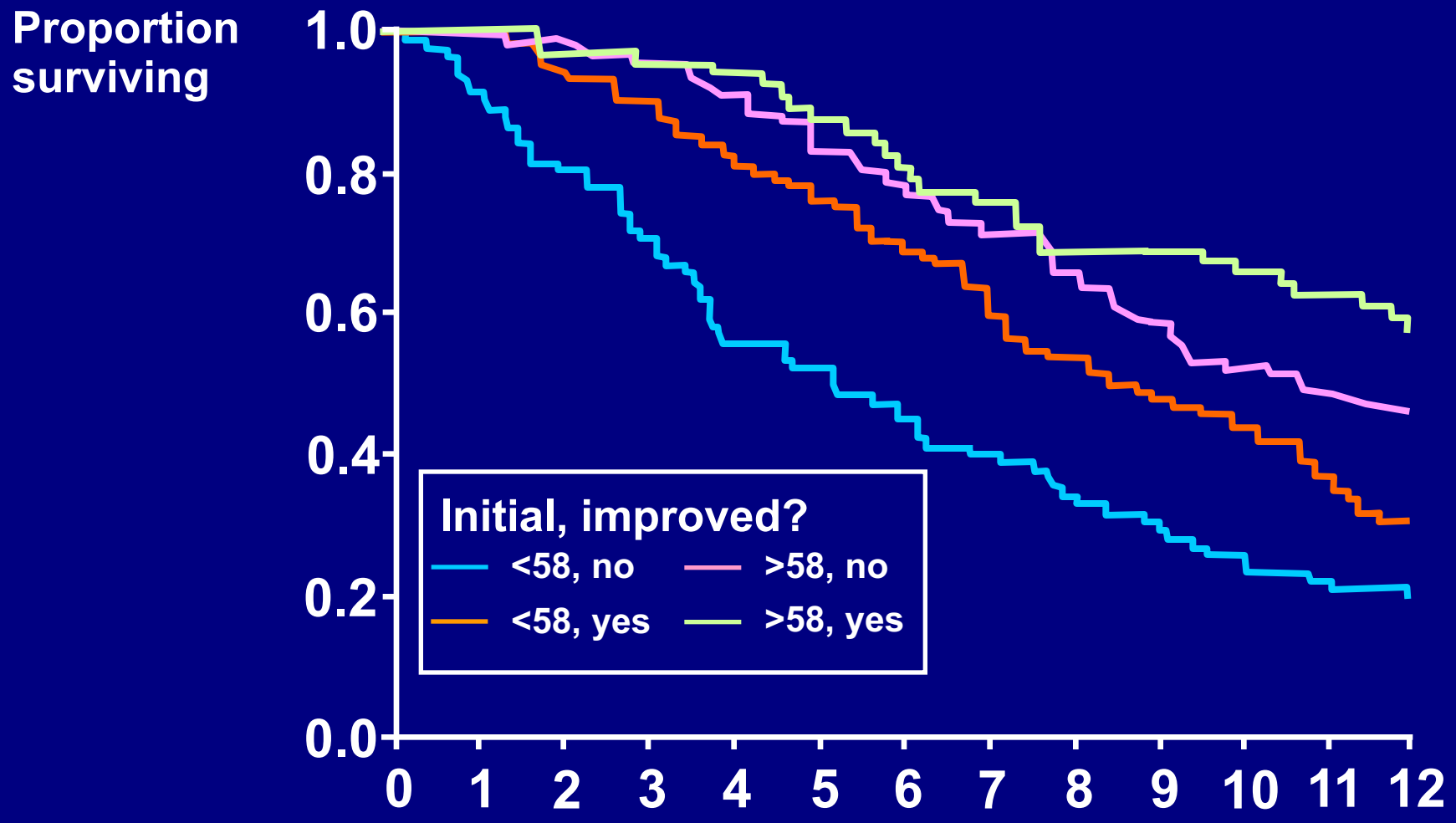
- PROs in clinics across Ontario

Results:

- 1 year survival: 82% vs 76% (P=0.0001)
- 8% decrease emergency visits
- 14% decrease hospitalizations

Barbera: Cancer Med, 2020; Barbera: JCO Clin Pract, 2020

E5592: Lung cancer survival by baseline and 6-week change in FACT-L TOI (n=352)*



*Pts with missing QoL excluded

Eton et al, J Clin Onc, 2003, 21(8): 1536-1543

VOLUME 27 · NUMBER 34 · DECEMBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Quality of Life Supersedes the Classic Prognosticators for Long-Term Survival in Locally Advanced Non–Small-Cell Lung Cancer: An Analysis of RTOG 9801

Benjamin Movsas, Jennifer Moughan, Linda Sarna, Corey Langer, Maria Werner-Wasik, Nicos Nicolaou, Ritsuko Komaki, Mitchell Machtay, Todd Wasserman, and Deborah Watkins Bruner

Conclusion

In this analysis, baseline global QOL score replaced known prognostic factors as the sole predictor of long-term OS for patients with locally advanced NSCLC.

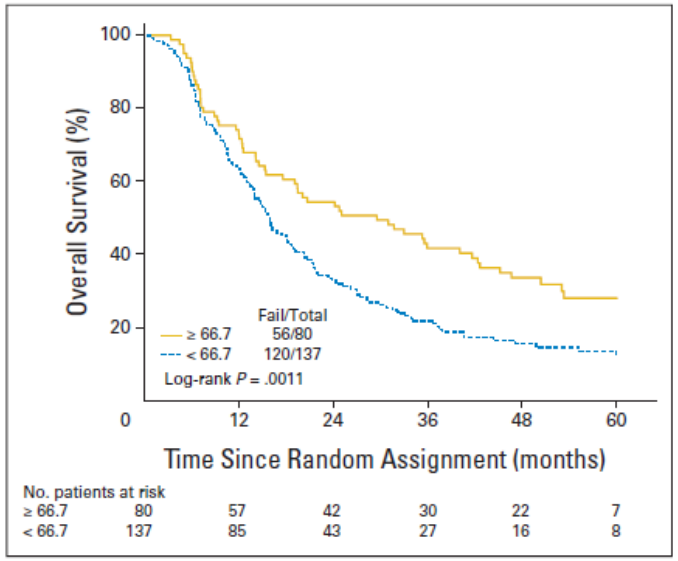
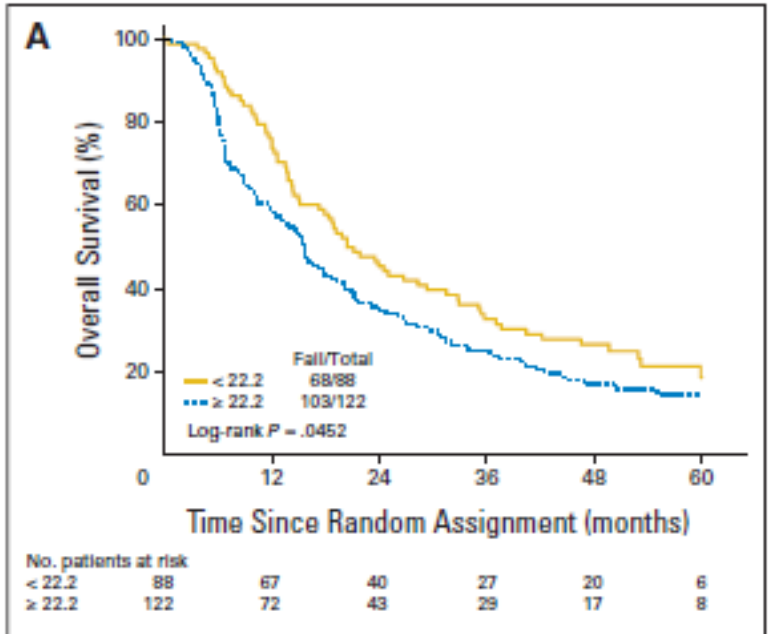


Fig 1. Overall survival rates based on the baseline European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 global quality-of-life (QOL) score (5-year overall survival of 27% *v* 11% for global QOL scores above and below the median level, respectively).



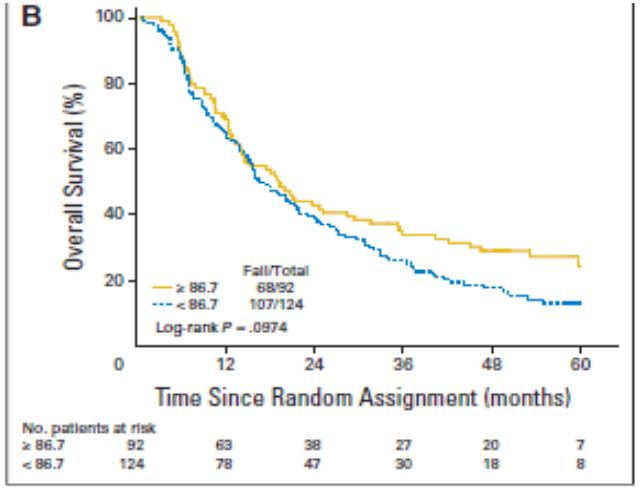


Fig 2. (A) Overall survival (OS) rates based on the baseline European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Lung Cancer 13 (EORTC QLQ LC-13) dyspnea score (5-year OS of 15% *v* 19% for EORTC QLQ LC-13 dyspnea scores above and below the median level, respectively). (B) OS rates based on the baseline EORTC QLQ-C30 physical functioning score (5-year OS of 23% *v* 12% for EORTC QLQ-C30 physical functioning scores above and below the median level, respectively).

Quality of life supersedes the classic prognosticators for long-term survival in locally advanced non-small-cell lung cancer: an analysis of RTOG 9801.
Movsas B, Moughan J, Sarna L, Langer C, Werner-Wasik M, Nicolaou N, Komaki R, Machtay M, Wasserman T, Bruner DW.
J Clin Oncol. 2009 Dec 1;27(34):5816-22. doi: 10.1200/JCO.2009.23.7420. Epub 2009 Oct 26.
PMID: 19858383

Self-reported Fatigue independently predict Overall Survival in Higher-Risk Patients with MDS

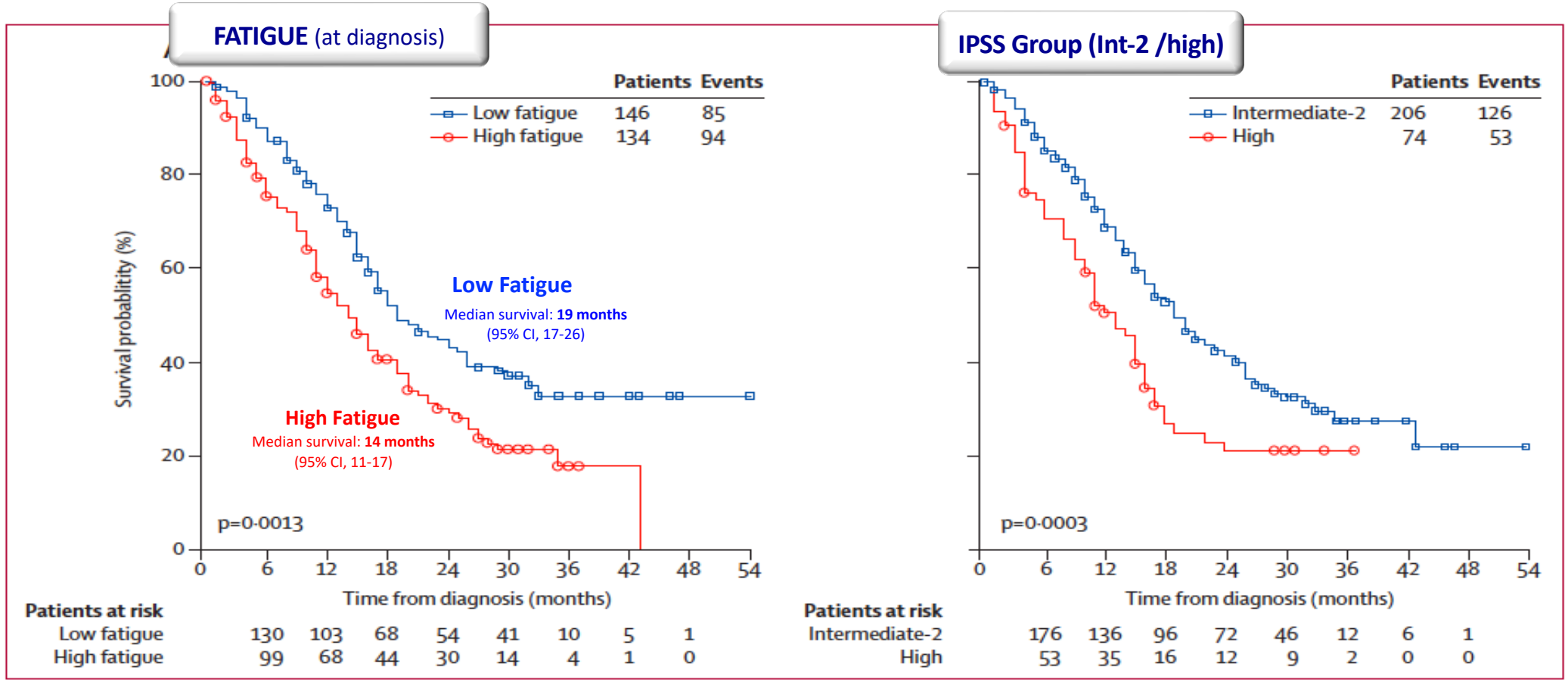


***Figure 1*: Overall survival by baseline patient's self-reported fatigue severity and IPSS risk group**
Low fatigue denotes patients reporting a baseline EORTC QLQ-C30 fatigue score lower than median value (34 points). High fatigue denotes patients reporting a baseline EORTC QLQ-C30 fatigue score equal or higher than the median value. EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer, quality of life questionnaire-core 30. IPSS=International Prognostic Scoring System.

Efficace et al, Lancet Oncology 2015 Nov;16(15):1506-14

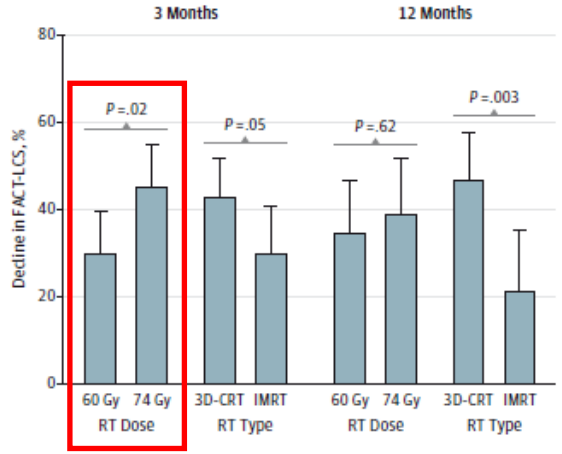
Original Investigation

Quality of Life Analysis of a Radiation Dose–Escalation Study of Patients With Non–Small-Cell Lung Cancer
A Secondary Analysis of the Radiation Therapy Oncology Group 0617 Randomized Clinical Trial

Benjamin Movsas, MD; Chen Hu, PhD; Jeffrey Sloan, PhD, HSR; Jeffrey Bradley, MD; Ritsuko Komaki, MD; Gregory Masters, MD; Vivek Kavadi, MD; Samir Narayan, MD; Jeff Michalski, MD; Douglas W. Johnson, MD; Christopher Koprowski, MD; Walter J. Curran Jr, MD; Yolanda I. Garces, MD; Rakesh Gaur, MD; Raymond B. Wynn, MD; John Schallenkamp, MD; Daphna Y. Gelblum, MD; Robert M. MacRae, MD; Rebecca Paulus, BS; Hak Choy, MD

Conclusions and Relevance—Despite few differences in provider-reported toxicity between arms, QOL analysis demonstrated a clinically meaningful decline in QOL on the 74Gy arm at 3 months, confirming the primary QOL hypothesis. Baseline QOL was an independent prognostic factor for survival.

Figure 2. Decline in Patient-Reported Quality of Life by Type and Dose of RT



FACT-LCS indicates Functional Assessment of Cancer Therapy–Lung Cancer Subscale; IMRT, intensity-modulated RT; RT, radiation therapy; 3D-CRT, 3-dimensional conformal RT.

Table 3. Multivariate Cox Model of Overall Survival[a]

Covariate	Comparison	Standard-Dose Dead/Total[b]	High-Dose Dead/Total[c]	HR (95 CI)	*P* Value[d]
Radiation level	High dose vs standard dose (RL)	97/155	106/147	1.42 (1.07-1.87)	.01
Cetuximab assignment	No cetuximab vs cetuximab (RL)	90/133	133/169	0.90 (0.68-1.19)	.44
PTV	Continuous	203/302		1.001 (1.000-1.001)	.04
Heart V5	Continuous	203/302		1.007 (1.002-1.012)	.01
FACT-TOI[e]	Continuous	203/302		0.901 (0.813-0.998)	.046

Abbreviations: FACT, Functional Assessment of Cancer Therapy; heart V5, volume of heart receiving 5 Gy or more radiation; HR, hazard ratio; PTV, planning target volume; RL, reference level; TOI, Trial Outcome Index.

[a] Underlying multivariate model developed in the primary end point analysis.[1]

[b] For standard-dose group or cetuximab group.

[c] For high-dose group or no cetuximab group.

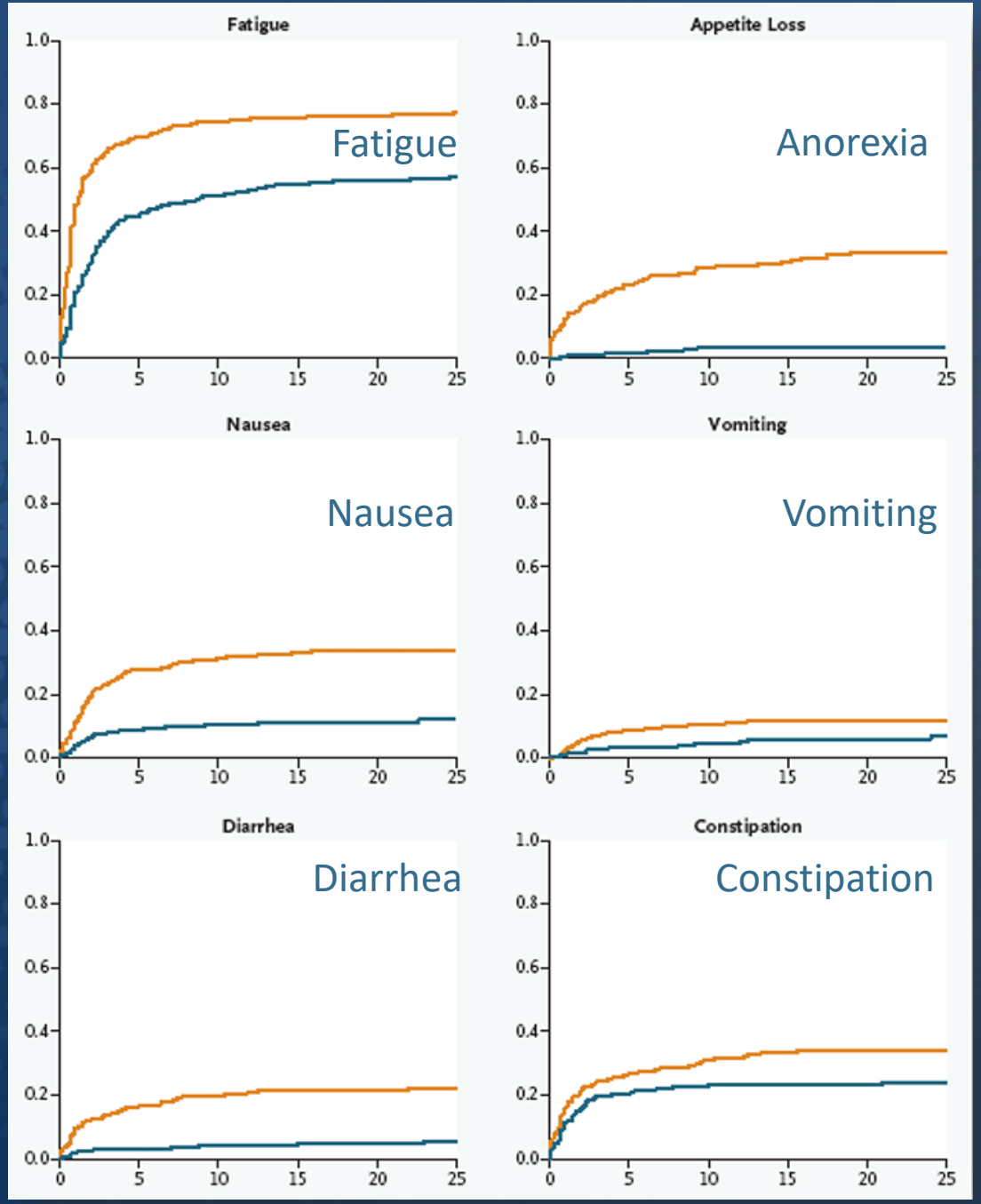
[d] Two-sided *P* value.

[e] Baseline FACT-TOI, every 10 points.

Movsas B, Hu C, Sloan J, Bradley J, Komaki R, Masters G, Kavadi V, Narayan S, Michalski J, Johnson DW, Koprowski C, Curran WJ Jr, Garces YI, Gaur R, Wynn RB, Schallenkamp J, Gelblum DY, MacRae RM, Paulus R, Choy H. Quality of Life Analysis of a Radiation Dose-Escalation Study of Patients With Non-Small-Cell Lung Cancer: A Secondary Analysis of the Radiation Therapy Oncology Group 0617 Randomized Clinical Trial. **JAMA Oncol**. 2016 Mar;2(3):359-67. doi: 10.1001/jamaoncol.2015.3969. PMID: 26606200

Clinician vs Patient-Reported Symptoms

Clinicians miss a substantial number of our patients' symptoms – what are the potential consequences, and opportunities for improvement?



Patient-reported

Clinician-reported

Basch: NEJM, 2010

Between-Arm Comparison: CTCAE and PRO-CTCAE: mPC Trial

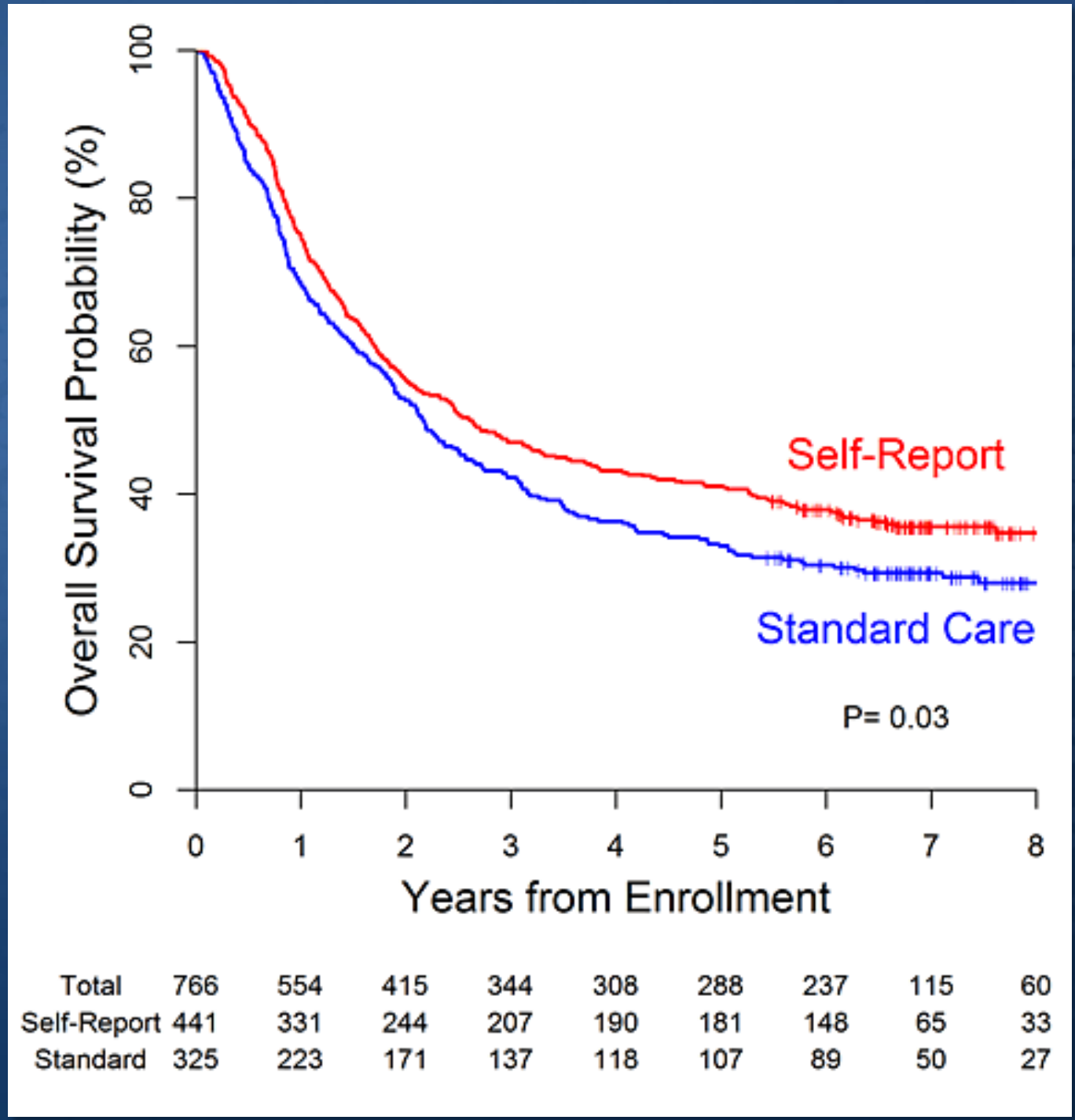
of significant between-arm AE differences:

- By investigator report (CTCAE): 0
- By patient report (PRO-CTCAE): 4

SYMPTOM	INVESTIGATOR-REPORTED *CTCAE Max Grade 3+*			PATIENT-REPORTED *PRO-CTCAE Max 3+*		
	Cabo	**Mito**	***P***	**Cabo**	**Mito**	***P***
Constipation	3.3%	1.8%	1.00	26%	13%	0.04
Decrease appetite	1.7%	5.3%	0.36	38%	15%	0.008
Diarrhea	8.3%	1.8%	0.21	44%	11%	<0.001
Fatigue	18.0%	8.8%	0.18	36%	26%	0.30
Nausea				38%	15%	0.008
Short of breath	--	5.3%	0.11	14%	13%	1.00
Vomiting	1.7%	7.0%	0.20	12%	7%	0.52

Dueck et al, JAMA Oncol 2020

Back to the Landmark Trial: Why?



Basch E, et al. *JAMA,* 2017;318(2):197-198

Mechanisms of Action

1. Proactive monitoring prompts clinicians to intervene early, before symptoms worsen and cause serious downstream complications
   - *Nurses acted on >75% of PRO alerts*
2. Symptom control enables patients to stay more functional, which is known to be associated with better survival
   - *Better physical functioning in PRO arm (P=.01)*
3. Symptom monitoring enables control of chemotherapy side effects, enabling more intensive and longer duration of cancer treatment
   - *Longer time on chemotherapy in PRO arm (8 months vs. 6 months)*

Basch: JAMA, 2017

Why should standard cancer care include patient reported outcomes?

- Patient reported QOL is **predictive** of survival and a **better** predictor of survival than traditional indicators[1]

- Physician reported QOL is **different** and is not predictive of survival[2]

- Real-time patient reported QOL monitoring may **improve survival and quality of life**[3]

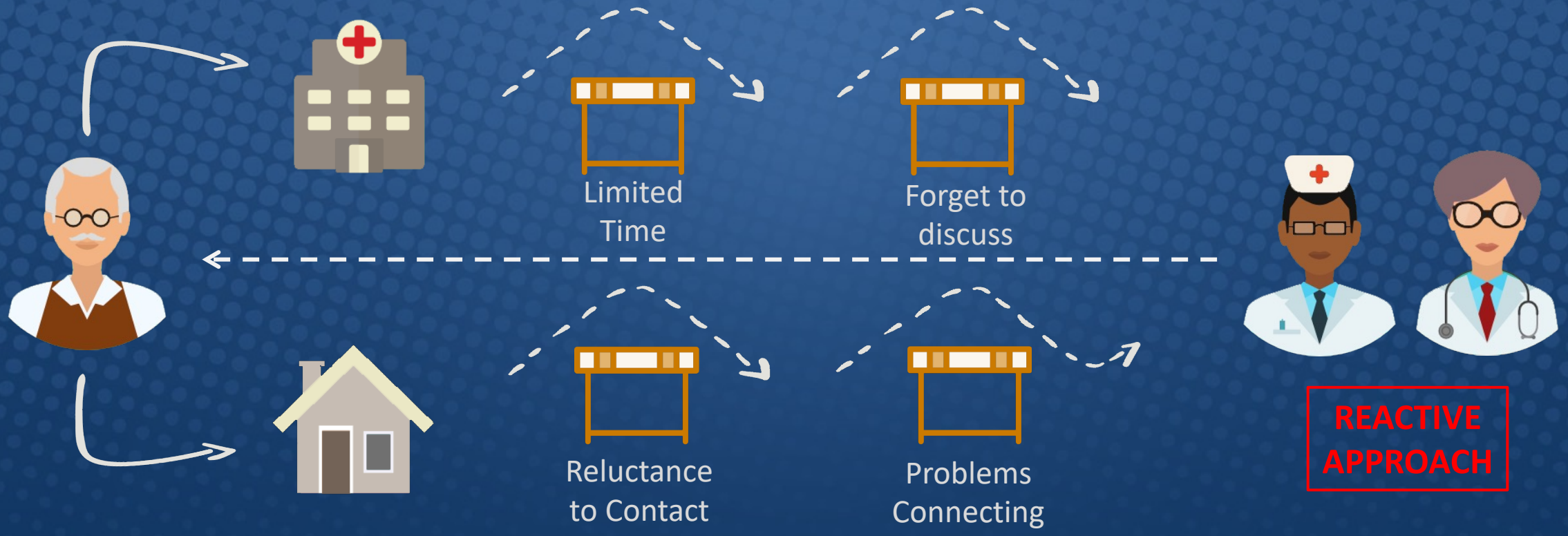
1. Quality of life supersedes the classic prognosticators for long-term survival in locally advanced non-small-cell lung cancer: an analysis of RTOG 9801. Movsas B, Moughan J, Sarna L, Langer C, Werner-Wasik M, Nicolaou N, Komaki R, Machtay M, Wasserman T, Bruner DW. **J Clin Oncol**. 2009 Dec 1;27(34):5816-22. doi: 10.1200/JCO.2009.23.7420. Epub 2009 Oct 26. PMID: 19858383

2. Movsas B, Hu C, Sloan J, Bradley J, Komaki R, Masters G, Kavadi V, Narayan S, Michalski J, Johnson DW, Koprowski C, Curran WJ Jr, Garces YI, Gaur R, Wynn RB, Schallenkamp J, Gelblum DY, MacRae RM, Paulus R, Choy H. Quality of Life Analysis of a Radiation Dose-Escalation Study of Patients With Non-Small-Cell Lung Cancer: A Secondary Analysis of the Radiation Therapy Oncology Group 0617 Randomized Clinical Trial. **JAMA Oncol**. 2016 Mar;2(3):359-67. doi: 10.1001/jamaoncol.2015.3969. PMID: 26606200

3. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, Schrag D. **JAMA.** 2017 Jul 11;318(2):197-198. doi: 10.1001/jama.2017.7156. No abstract available. PMID: 28586821


HOW?

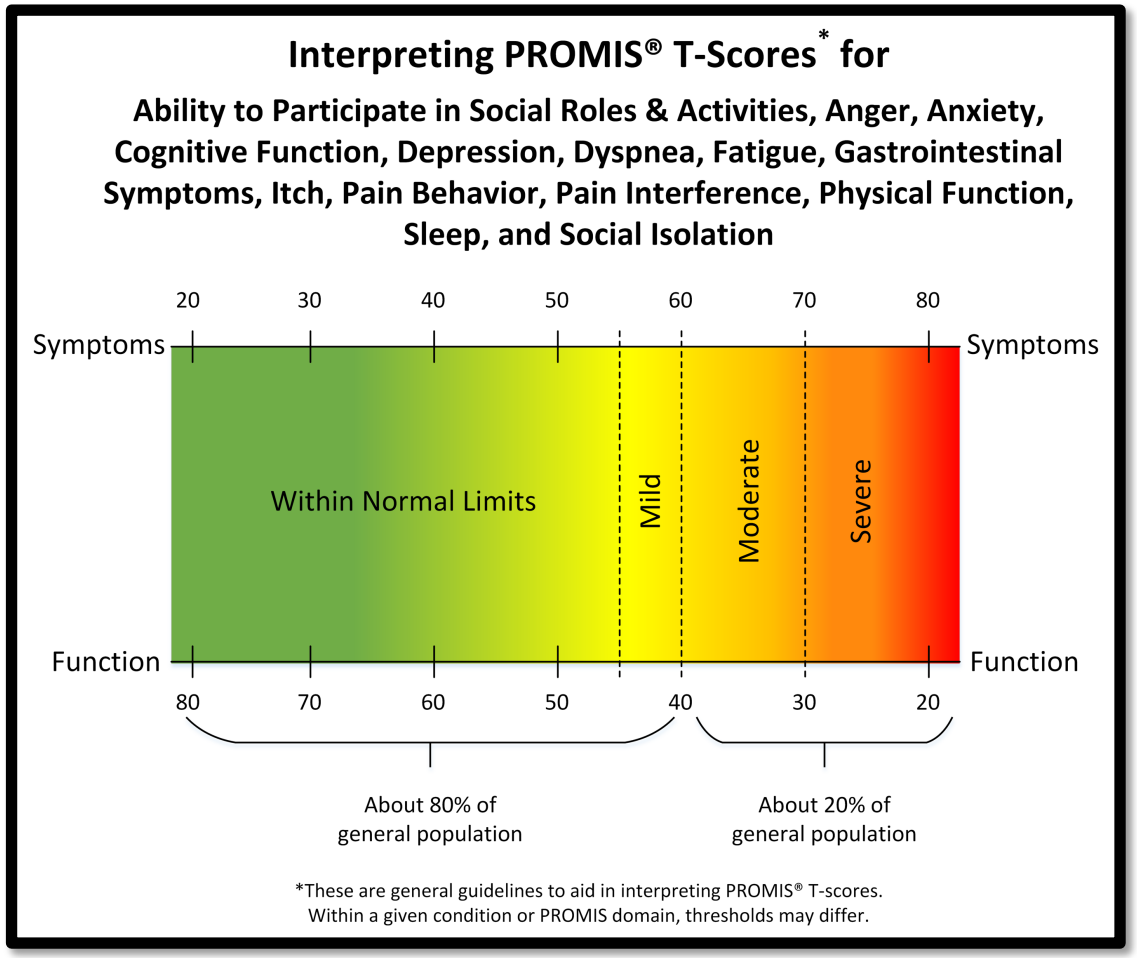
Standard Approach to Symptom Monitoring



Model for Systematic Symptom Monitoring Using Electronic Patient-Reported Outcomes

Henry Ford Cancer Patient Reported QOL
REVIEW of the Instrument

- Quality of Life domains assessed:
  - **Fatigue**
  - **Pain interference**
  - **Physical function**
  - **Depression**
- NIH PROMIS CAT instrument:
  - Patient-Reported Outcomes Measurement Information Systems Computer Adaptive Test
  - Completion times range from **2-4 minutes**
- **All outpatient cancer visits**

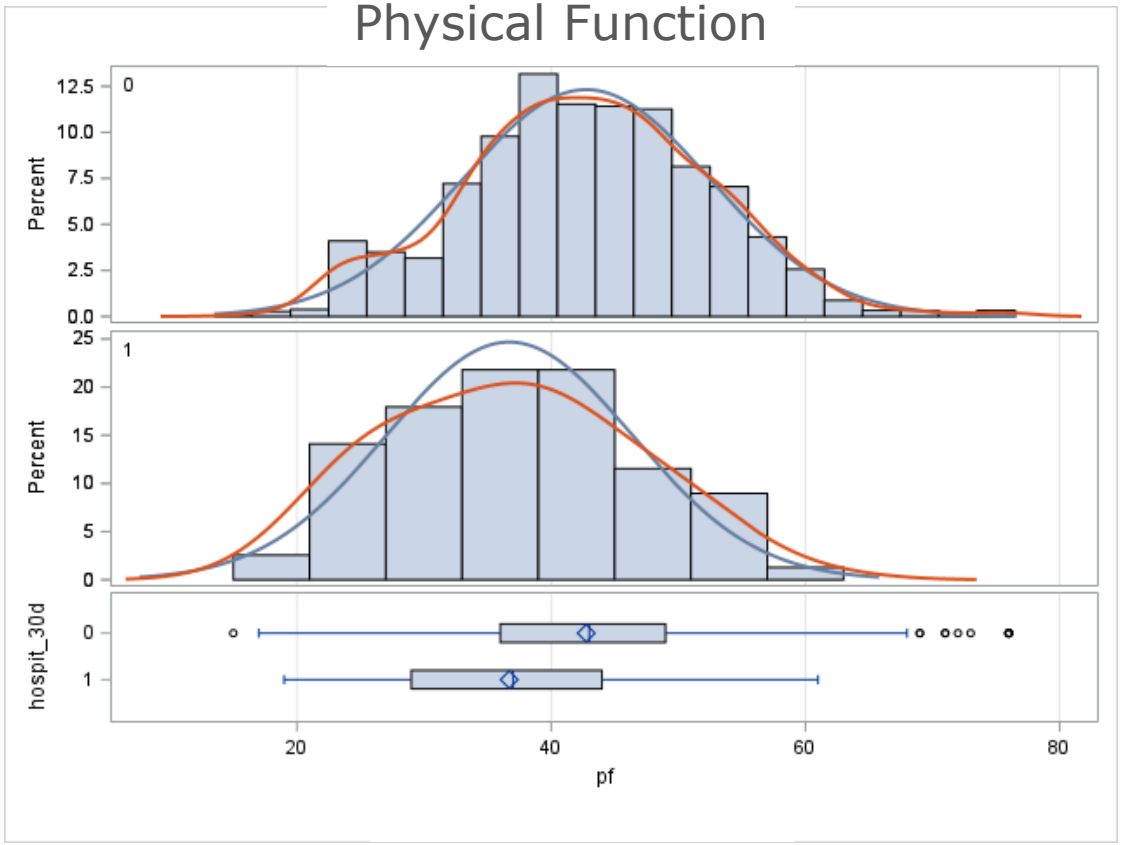


https://commonfund.nih.gov/promis/index

PRO QOL predicts hospital admissions
Physical function is most predictive

- After controlling for age, sex, and comorbidity, pain, fatigue, and physical function predicted hospitalizations in the next 30 days. Depression did not.
- When all 4 PRO scores were included as predictors along with age, sex, and comorbidity, significant predictors were:
  - younger age
  - male sex
  - greater comorbidity
  - poorer physical function:

OR=0.97, 95% CI (0.94, 0.99) , p<.01



*Through **HFH-MSU Pilot Grant**: analysis performed by **MSU partner – Alla Sikorskii** with **HAP** claims data*

For ED/urgent care, key predictor is **pain** over the other PROs

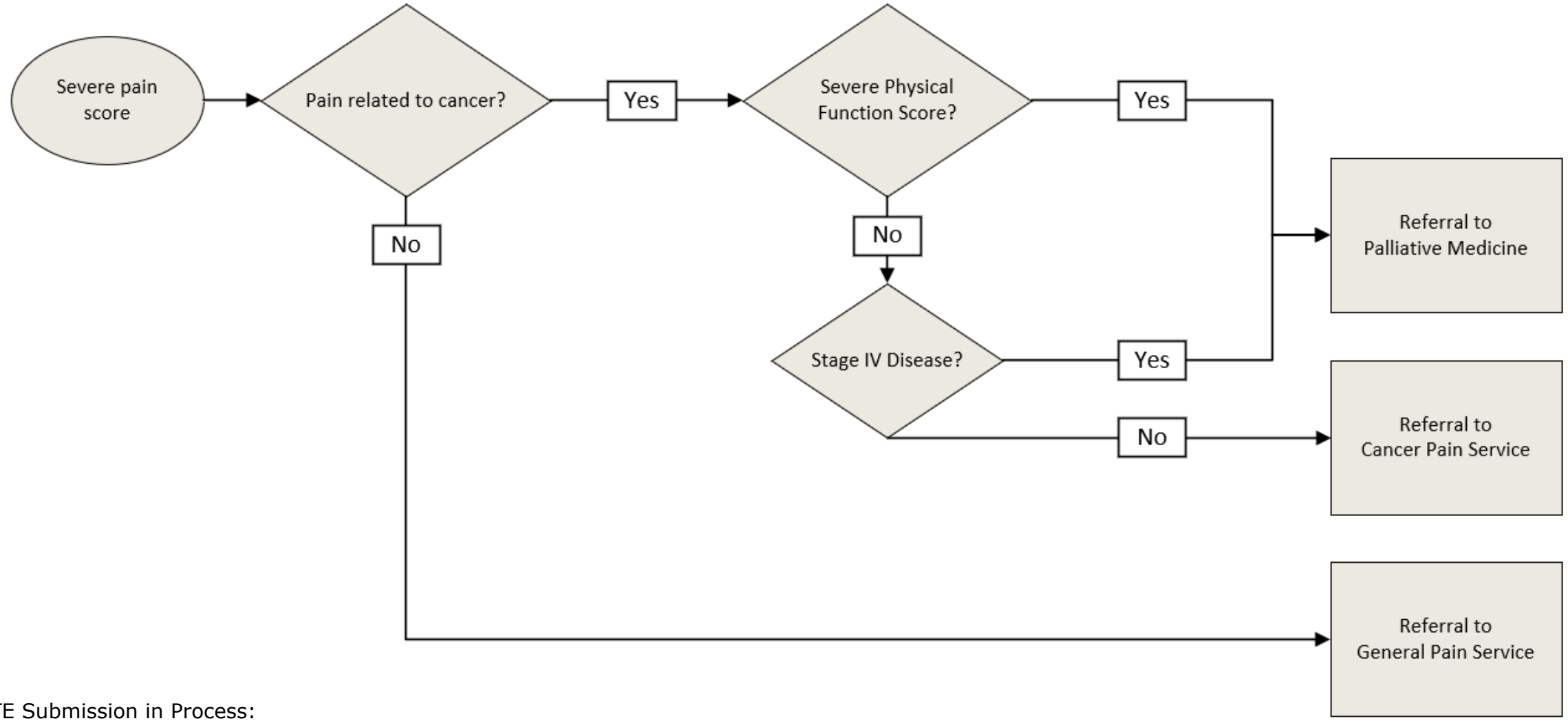
	ED/urgent care visit in the next 14 days			ED/urgent care visit in the next 30 days		
PRO	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Pain interference	1.06	(1.03, 1.09)	<.01	1.04	(1.01, 1.07)	<.01
Physical function	0.97	(0.94, 0.99)	.04	0.97	(0.95, 0.99)	.04
Fatigue	1.02	(0.99, 1.05)	.22		(0.99, 1.05)	.06
Depression	1.01	(0.98, 1.04)	.72	1.01	(0.99, 1.03)	.28

Table 2. The effect of per unit increase in PROs on ED/urgent care visits in the next 14 and 30 days, adjusted for age at first PRO assessment, sex, comorbidity, advanced cancer, median household income and high school education in the Census tract.

Note: Controlling for site of cancer does not change these results in an appreciable way.

*Through **HFH-MSU Pilot Grant**: analysis performed by **MSU partner – Alla Sikorskii** with **HAP** claims data*

Henry Ford (Detroit): Guideline for Patients with **Severe Pain**



LTE Submission in Process:
Utilizing a System-Wide Patient-Reported Outcomes Initiative to Guide Referrals to Pain Management and Palliative Medicine to Improve Patient Experience

HFH Partners: Sarah Money, Fadi Jirjees, Kristen Chasteen
MSU Partner: Alla Sikorskii

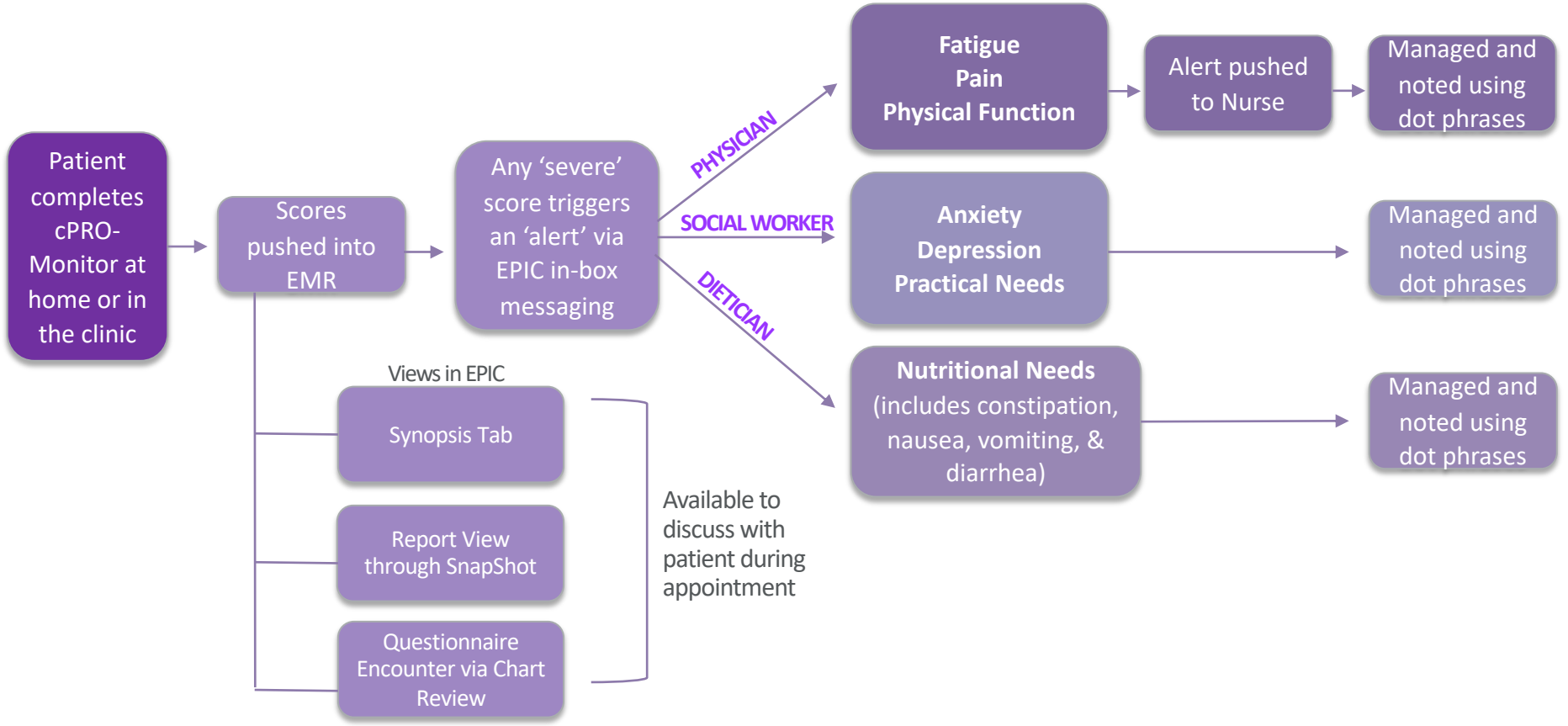
IMPACT
Improving the Management of symPtoms during And following Cancer Treatment

Consortium Overview

- Supported by the National Cancer Institute with funding provided through the Cancer Moonshot[SM]
- Three Research Centers symptom management interventions integrated in the electronic health record (EHR) to trigger guideline-concordant clinical response
- Outcomes are quality of life and healthcare utilization
- Implementation science approaches examine feasibility, acceptability, scalability and sustainability
- Pooled consortium-wide data will evaluate intervention effects across symptoms, the cancer continuum, and in underserved populations

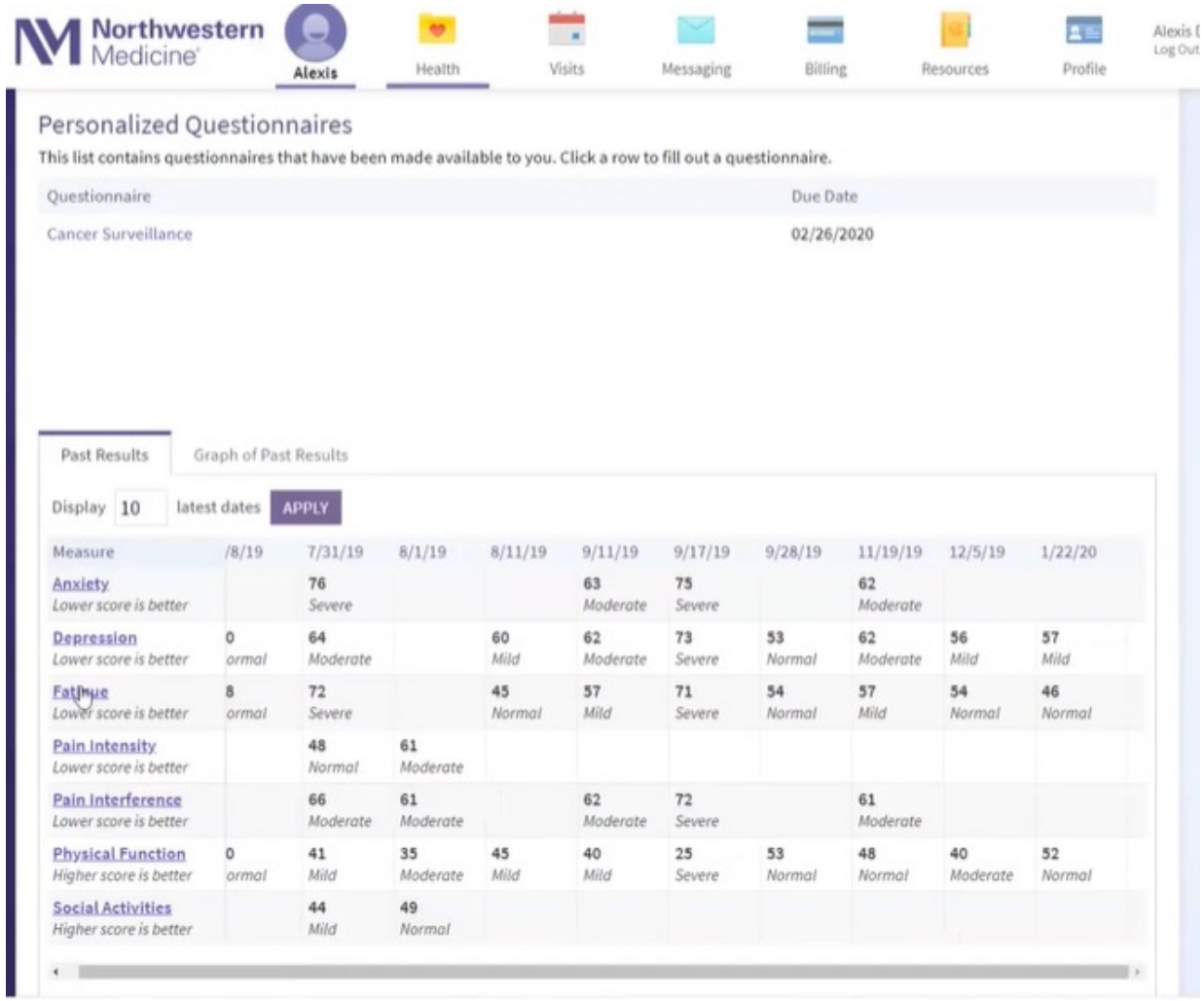
For more information about IMPACT visit https://impactconsortium.org

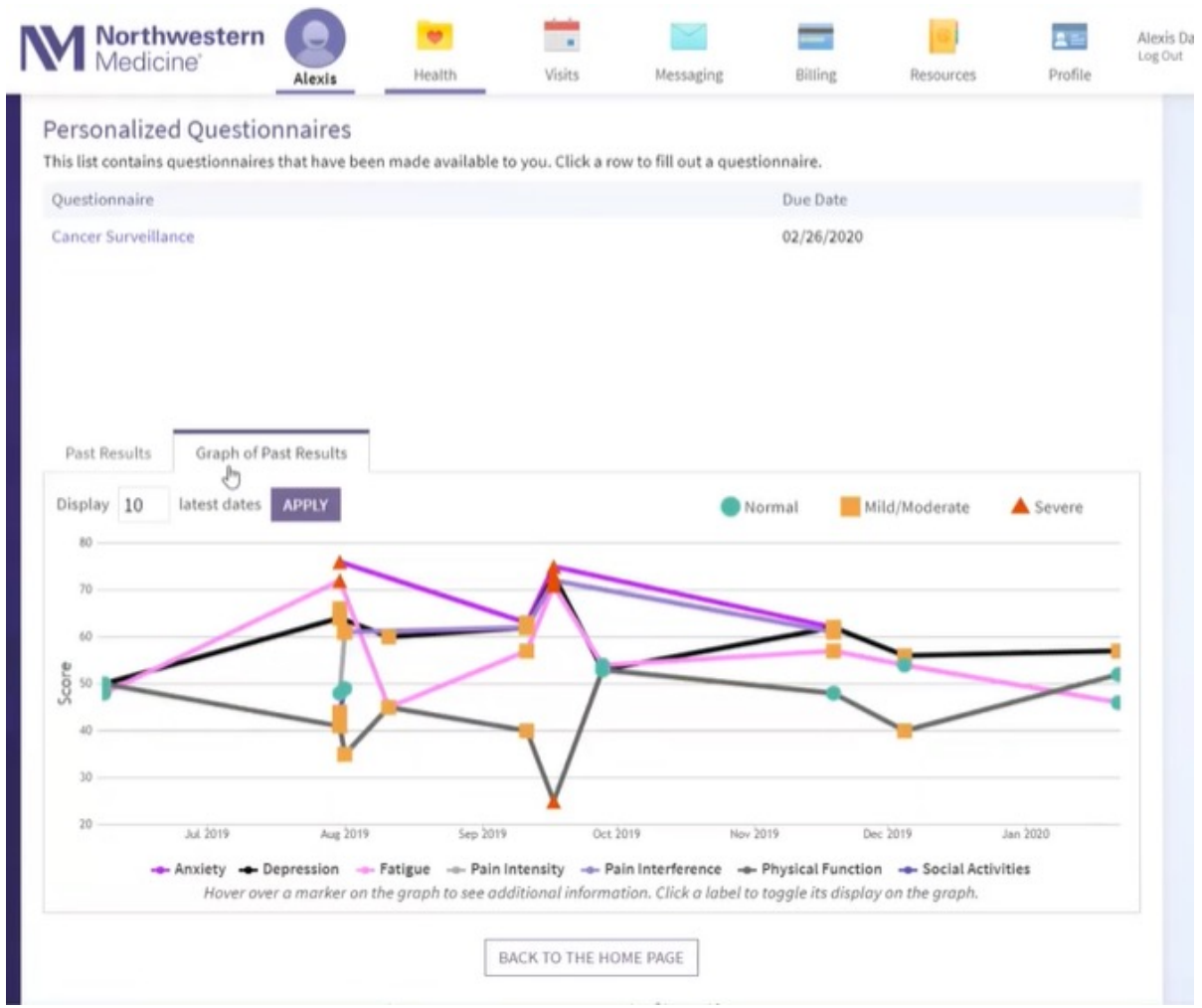
Sample Alert Response Workflow



Northwestern Medicine®

My Chart Display of NMPRO Results





Threats to successful implementation of PROs

- Clinician resistance
  - Champion necessary but not sufficient
- Institutional support
- Work flow reality (support staff)
- Technology often not sufficiently flexible
- System culture and values
- Patient disposition and culture

What you need to succeed

- Mechanism to collect PROs in clinical routine
- Benefits of PRO assessment (shared "value proposition")
- Score interpretation/thresholds
- Integration of PROs into the clinical record
  - *Review of systems*
  - *Smart phrases*
  - *Clinical action triggers (PROs guide communication and care*);
- Solid implementation plan
  - Identify barriers and facilitators
  - Integrate with clinical workflow
  - Manage technical details
- Change culture
  - HCP attitudes
  - Reframe as patient-centricity patient *engagement*
  - *Motivating examples*
    - *Peer storytelling: Why I do it; what it taught me; how I gave better care as a result*

IMPACT
Improving the Management of symPtoms during And following Cancer Treatment

Consortium Members

Research Triangle Institute Coordinating Center **Principal Investigator:** Barbara Kroner Grant No. U24CA232980	Northwestern University IMPACT (NU IMPACT) Research Center **Principal Investigator:** David Cella Grant No. UM1CA233035	Symptom Management Implementation of Patient Reported Outcomes in Oncology (SIMPRO) Research Center **Principal Investigators:** Michael Hassett, Ray Osarogiagbon, Deborah Schrag, Sandra Wong Grant No. UM1CA233080	Enhanced, Electronic Health Record-Facilitated Cancer Symptom Control (E2C2) Research Center **Principal Investigator:** Andrea Cheville Grant No. UM1CA233033	National Cancer Institute Division of Cancer Control and Population Sciences Healthcare Delivery Research Program **Program Director:** Lynn Adams
Mary-Anne Ardini Lisa DiMartino Karla Hemming Liliana Preiss Joshua Richardson Ben Tyndall Bryan Weiner	Michael Bass Ava Coughlin Ann Marie Flores Sofia Garcia Martha Garcia Sheetal Kircher Nicola Lancki Quan Mai Mary Lillian O'Connor Frank Penedo Denise Scholtens Philip Silberman Justin D. Smith Kippy Webster Betina Yanez	Paige Ahrens Fiona Barrett Ethan Basch Meg Begnoche Jessica Bian Kimberly Caron Christine Cronin Samira Dias Don Dizon Nick Faris Hannah Hazard Jennifer Mallow Nadine McCleary Loretta Pearson Tiana Poirier James Reich Scot Remick Jaci Simpson Laura Tasker Angela Tramontano Hajime Uno	Jessica Austin Linda Chlan Joan Griffin Jeph Herrin Kurt Kroenke Veronica Lam Sarah Minter Deirdre Pachman Jewel Podratz Parvez Rahman Jennifer Ridgeway Kathryn Ruddy Karen Schaepe Nathan Tesch Cindy Tofthagen	**Science Officers:** Ashley Wilder Smith Sandra Mitchell Roxanne Jensen **Scientific Advisor:** Wynne Norton **Patient representatives** Christine Hodgdon Kimberly Richardson

We gratefully acknowledge our study participants and patient representatives

Conclusions

Patient self-reporting improves symptom monitoring and both clinical and quality of life outcomes

- Expands our understanding of patient experience
- Engages patients

System change to implement routine symptom management is quite challenging