Prostate cancer: Use case examples incorporating genetic testing, molecular diagnostics, and patient reported outcomes and patient generated wearable data from early diagnosis to advanced disease

Adam P Dicker, MD, PhD, FASTRO

Disclosures:

Dr. Dicker is an employee of Thomas Jefferson University

- Additional support from:
  - National Cancer Institute
  - Prostate Cancer Research Program (Dept. of Defense)
  - NRG Oncology
  - Prostate Cancer Foundation

  - He is an unpaid advisor to:
    - Google LaunchPad Accelerator, Self Care Catalyst

Acknowledgments:

- Heather Jim, PhD
- Nitin Ohri, MD
- Percy Ivy, MD
- Christine Tran, MS
- Stephen Blattner, MD
- Mark Tykocinski, MD

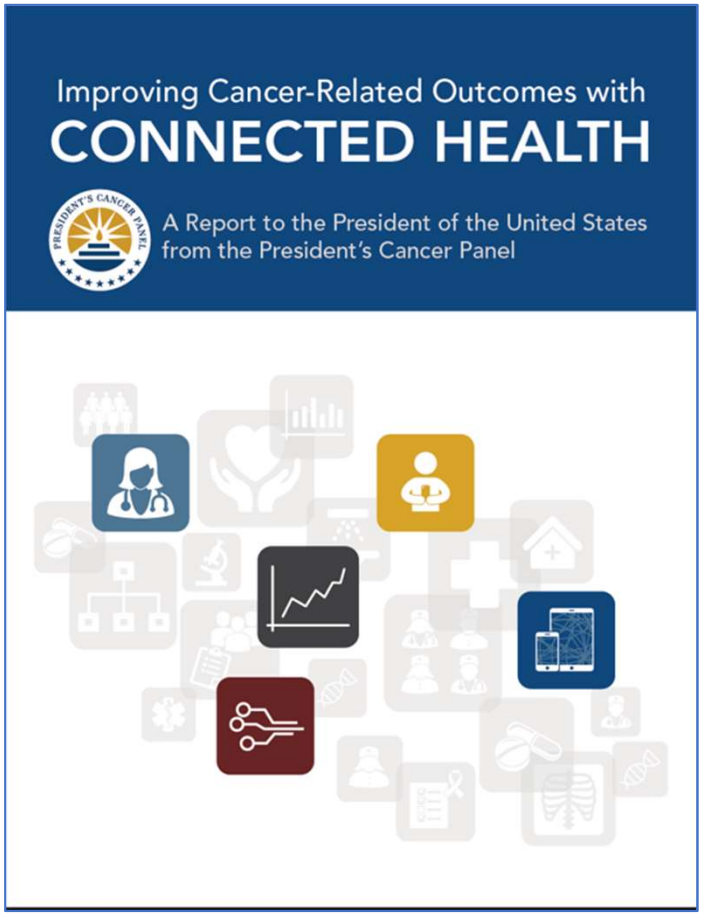
Four Questions:

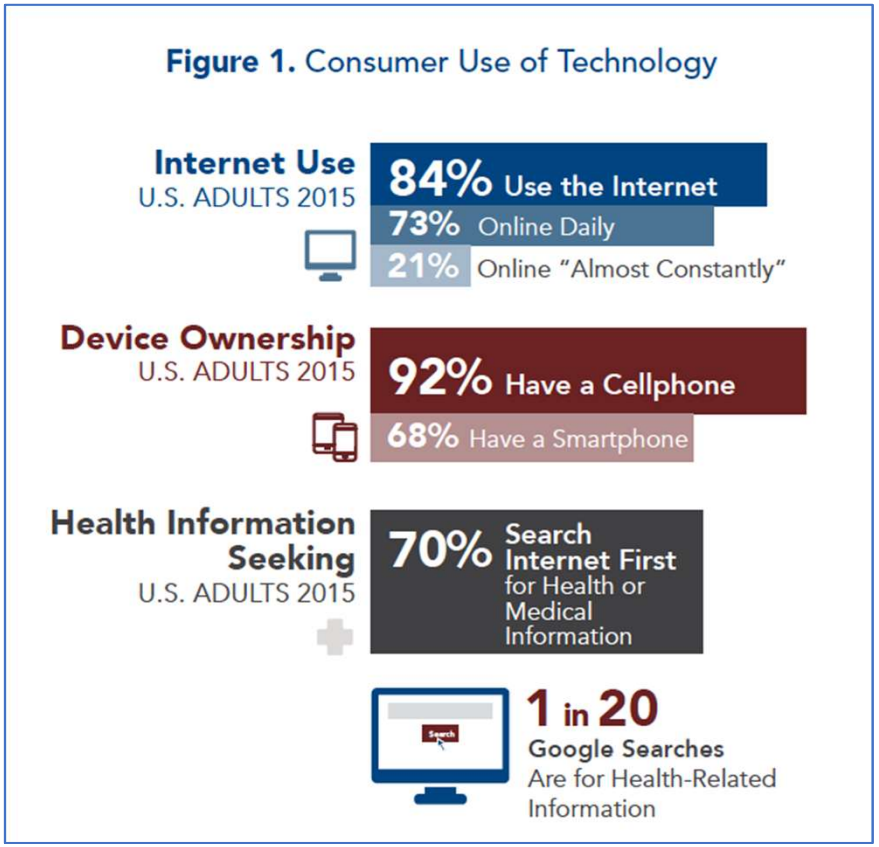
Sidney Kimmel Cancer Center
at Thomas Jefferson University
NCI-designated

- What are the use of molecular diagnosis for genetic counseling and therapeutic decision making for prostate cancer?
- How can ePROs & Apps improve adherence?

  example: mitigation of drug toxicity
- How can we nurture and develop this space?

  Sidney Kimmel Medical College & Cancer Center, Thomas Jefferson University, Phila, PA





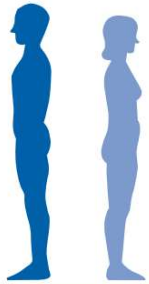
A web-based version of this report is available at: https://PresCancerPanel.cancer.gov/report/connectedhealth

Prostate Cancer Can Be Inherited

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2018 Estimates

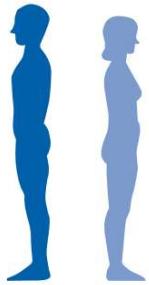
Estimated New Cases

Male			Female		
Prostate	164,690	19%	Breast	266,120	30%
Lung & bronchus	121,680	14%	Lung & bronchus	112,350	13%
Colon & rectum	75,610	9%	Colon & rectum	64,640	7%
Urinary bladder	62,380	7%	Uterine corpus	63,230	7%
Melanoma of the skin	55,150	6%	Thyroid	40,900	5%
Kidney & renal pelvis	42,680	5%	Melanoma of the skin	36,120	4%
Non-Hodgkin lymphoma	41,730	5%	Non-Hodgkin lymphoma	32,950	4%
Oral cavity & pharynx	37,160	4%	Pancreas	26,240	3%
Leukemia	35,030	4%	Leukemia	25,270	3%
Liver & intrahepatic bile duct	30,610	4%	Kidney & renal pelvis	22,660	3%
All sites	**856,370**	**100%**	**All sites**	**878,980**	**100%**



Estimated Deaths

Male			Female		
Lung & bronchus	83,550	26%	Lung & bronchus	70,500	25%
Prostate	29,430	9%	Breast	40,920	14%
Colon & rectum	27,390	8%	Colon & rectum	23,240	8%
Pancreas	23,020	7%	Pancreas	21,310	7%
Liver & intrahepatic bile duct	20,540	6%	Ovary	14,070	5%
Leukemia	14,270	4%	Uterine corpus	11,350	4%
Esophagus	12,850	4%	Leukemia	10,100	4%
Urinary bladder	12,520	4%	Liver & intrahepatic bile duct	9,660	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,400	3%
Kidney & renal pelvis	10,010	3%	Brain & other nervous system	7,340	3%
All sites	**323,630**	**100%**	**All sites**	**286,010**	**100%**



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Ranking is based on modeled projections and may differ from the most recent observed data.

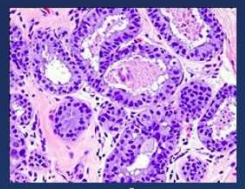
Approximately 5-15% of prostate cancer can be due to inherited genetic mutations in high-to-moderately penetrant genes

American Cancer Society. Cancer Facts and Figures 2018

"Genetic" Testing

Genomic Testing
- Performed in tissues
- Molecular signatures

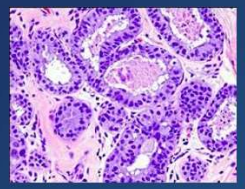
(Decipher, Prolaris, OncotypeDX, ConfirmMDX)



Inform decision-making treatment, and management

Tumor Sequencing
- Performed in tissues
- Tumor-specific mutations

(Foundation Medicine, Caris)



Inform targeted treatment

~15% inherited

Inherited Cancer Testing
- Mutations are inherited
- Substantially higher lifetime cancer risk

(Invitae, Myriad, Ambry, GeneDX, Color)

Blood or saliva

-Inform cancer screening and prevention
-Genetic testing in blood relatives
-Informing treatment and clinical trials

Germline Insights from Metastatic Prostate Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

C.C. Pritchard, J. Mateo, M.F. Walsh, N. De Sarkar, W. Abida, H. Beltran, A. Garofalo, R. Gulati, S. Carreira, R. Eeles, O. Elemento, M.A. Rubin, D. Robinson, R. Lonigro, M. Hussain, A. Chinnaiyan, J. Vinson, J. Filipenko, L. Garraway, M.-E. Taplin, S. AlDubayan, G.C. Han, M. Beightol, C. Morrissey, B. Nghiem, H.H. Cheng, B. Montgomery, T. Walsh, S. Casadei, M. Berger, L. Zhang, A. Zehir, J. Vijai, H.I. Scher, C. Sawyers, N. Schultz, P.W. Kantoff, D. Solit, M. Robson, E.M. Van Allen, K. Offit, J. de Bono, and P.S. Nelson

~12% of men with mCRPC have germline mutations:
BRCA2, ATM, CHEK2, BRCA1
RAD51D, PALB2

ABSTRACT

BACKGROUND
Inherited mutations in DNA-repair genes such as *BRCA2* are associated with increased risks of lethal prostate cancer. Although the prevalence of germline mutations in DNA-repair genes among men with localized prostate cancer who are unselected for family predisposition is insufficient to warrant routine testing, the frequency of such mutations in patients with metastatic prostate cancer has not been established.

METHODS
We recruited 692 men with documented metastatic prostate cancer who were unselected for family history of cancer or age at diagnosis. We isolated germline DNA and used multiplex sequencing assays to assess mutations in 20 DNA-repair genes associated with autosomal dominant cancer-predisposition syndromes.

RESULTS
A total of 84 germline DNA-repair gene mutations that were presumed to be deleterious were identified in 82 men (11.8%); mutations were found in 16 genes, including *BRCA2* (37 men [5.3%]), *ATM* (11 [1.6%]), *CHEK2* (10 [1.9% of 534 men with data]), *BRCA1* (6 [0.9%]), *RAD51D* (3 [0.4%]), and *PALB2* (3 [0.4%]). Mutation frequencies did not differ according to whether a family history of prostate cancer was present or according to age at diagnosis. Overall, the frequency of germline mutations in DNA-repair genes among men with metastatic prostate cancer significantly exceeded the prevalence of 4.6% among 499 men with localized prostate cancer ($P<0.001$), including men with high-risk disease, and the prevalence of 2.7% in the Exome Aggregation Consortium, which includes 53,105 persons without a known cancer diagnosis ($P<0.001$).

CONCLUSIONS
In our multicenter study, the incidence of germline mutations in genes mediating DNA-repair processes among men with metastatic prostate cancer was 11.8%, which was significantly higher than the incidence among men with localized prostate cancer. The frequencies of germline mutations in DNA-repair genes among men with metastatic disease did not differ significantly according to age at diagnosis or family history of prostate cancer. (Funded by Stand Up To Cancer and others.)

Role of Genetic Testing for Inherited Prostate Cancer Risk: Philadelphia Prostate Cancer Consensus Conference 2017

Sidney Kimmel Cancer Center at Jefferson
NCI – designated

Sidney Kimmel Cancer Center, Thomas Jefferson University

and

The Foundation for Breast and Prostate Health

Philadelphia, Pennsylvania

March 3 & 4, 2017

FOUNDATION FOR Breast & Prostate Health

Co-Chairs:

Leonard G. Gomella, MD

Veda N. Giri, MD

Karen E. Knudsen, PhD

-www.phillyprostate.com
-Giri et al. JCO 2017

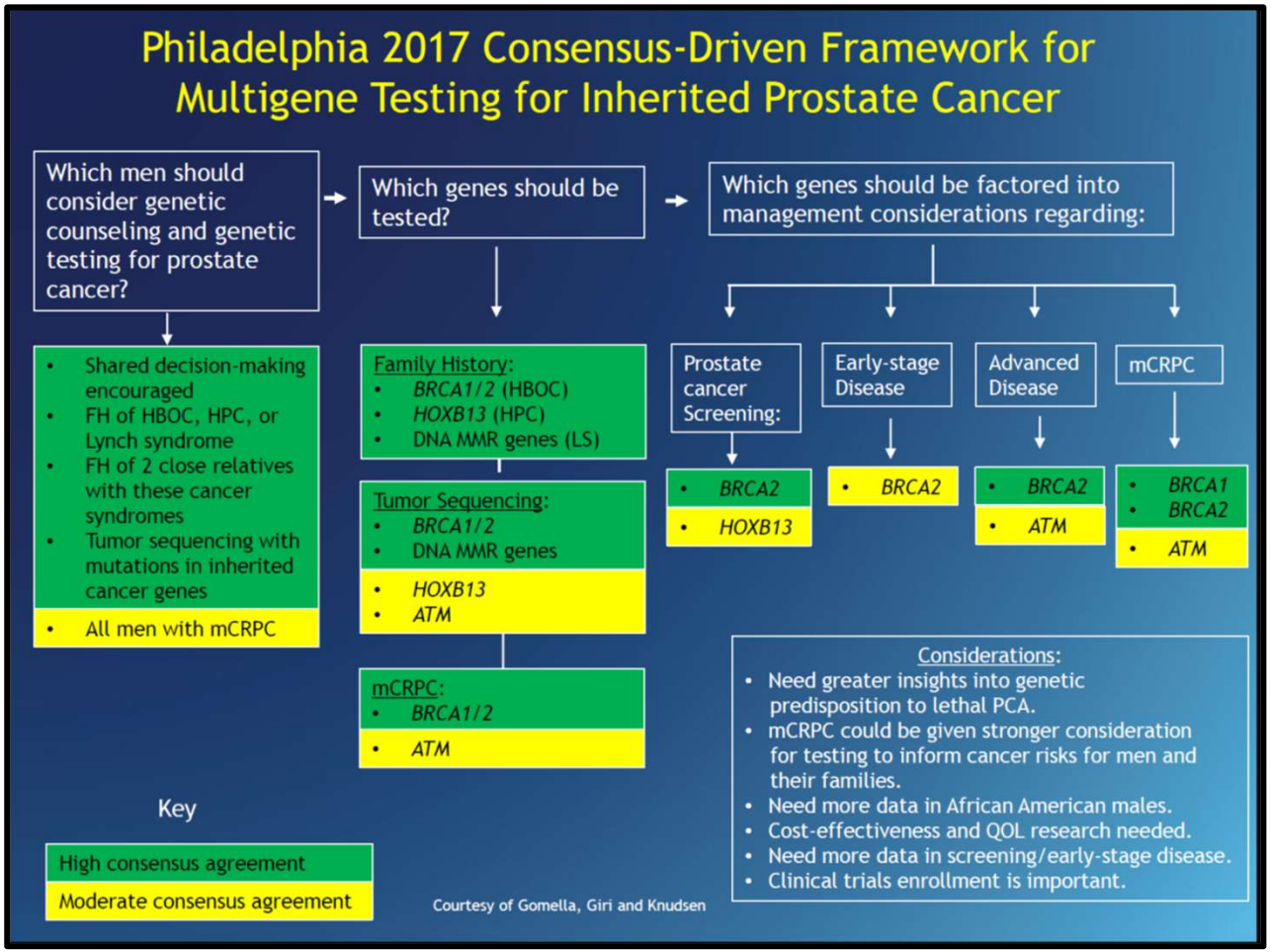
JOURNAL OF CLINICAL ONCOLOGY SPECIAL ARTICLE

Role of Genetic Testing for Inherited Prostate Cancer Risk: Philadelphia Prostate Cancer Consensus Conference 2017

Veda N. Giri, Karen E. Knudsen, William K. Kelly, Wassim Abida, Gerald L. Andriole, Chris H. Bangma, Justin E. Bekelman, Mitchell C. Benson, Amie Blanco, Arthur Burnett, William J. Catalona, Kathleen A. Cooney, Matthew Cooperberg, David E. Crawford, Robert B. Den, Adam P. Dicker, Scott Eggener, Neil Fleshner, Matthew L. Freedman, Freddie C. Hamdy, Jean Hoffman-Censits, Mark D. Hurwitz, Colette Hyatt, William B. Isaacs, Christopher J. Kane, Philip Kantoff, R. Jeffrey Karnes, Lawrence I. Karsh, Eric A. Klein, Daniel W. Lin, Kevin R. Loughlin, Grace Lu-Yao, S. Bruce Malkowicz, Mark J. Mann, James R. Mark, Peter A. McCue, Martin M. Miner, Todd Morgan, Judd W. Moul, Ronald E. Myers, Sarah M. Nielsen, Elias Obeid, Christian P. Pavlovich, Stephen C. Peiper, David F. Penson, Daniel Petrylak, Curtis A. Pettaway, Robert Pilarski, Peter A. Pinto, Wendy Poage, Ganesh V. Raj, Timothy R. Rebbeck, Mark E. Robson, Matt T. Rosenberg, Howard Sandler, Oliver Sartor, Edward Schaeffer, Gordon F. Schwartz, Mark S. Shahin, Neal D. Shore, Brian Shuch, Howard R. Soule, Scott A. Tomlins, Edouard J. Trabulsi, Robert Uzzo, Donald J. Vander Griend, Patrick C. Walsh, Carol J. Weil, Richard Wender, and Leonard G. Gomella

Representation: Urology (National and International), Medical Oncology, Radiation Oncology, Clinical Cancer Genetics, Genetic Counseling, Health Policy, Bioethics, Population Science, Molecular Epidemiology, Pathology, Breast/GI/Gyn Oncology, Genetic Basic Science Research, Patient Advocates, Patient Stakeholders, NCCN, NCI, ACS

Giri, et al J Clin Oncol. 2017 Dec 13 [Epub ahead of print].


Philadelphia 2017 Consensus-Driven Framework for Multigene Testing for Inherited Prostate Cancer
Which men should consider genetic counseling and genetic testing for prostate cancer?
Which genes should be tested?
Which genes should be factored into management considerations regarding:
Shared decision-making encouraged
FH of HBOC, HPC, or Lynch syndrome
FH of 2 close relatives with these cancer syndromes
Tumor sequencing with mutations in inherited cancer genes
All men with mCRPC
Family History:
BRCA1/2 (HBOC)
HOXB13 (HPC)
DNA MMR genes (LS)
Tumor Sequencing:
BRCA1/2
DNA MMR genes
HOXB13
ATM
mCRPC:
BRCA1/2
ATM
Prostate cancer Screening:
BRCA2
HOXB13
Early-stage Disease
BRCA2
Advanced Disease
BRCA2
ATM
mCRPC
BRCA1
BRCA2
ATM
Considerations:
Need greater insights into genetic predisposition to lethal PCA.
mCRPC could be given stronger consideration for testing to inform cancer risks for men and their families.
Need more data in African American males.
Cost-effectiveness and QOL research needed.
Need more data in screening/early-stage disease.
Clinical trials enrollment is important.
Key
High consensus agreement
Moderate consensus agreement
Courtesy of Gomella, Giri and Knudsen

Current NCCN Guidelines

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2019
BRCA-Related Breast and/or Ovarian Cancer Syndrome

NCCN Guidelines Index
Table of Contents
Discussion

BRCA1/2 TESTING CRITERIA[a,b]

Meeting one or more of these criteria warrants further personalized risk assessment, genetic counseling, and often genetic testing and management.

Testing of an individual without a cancer diagnosis should only be considered when an appropriate affected family member is unavailable for testing.

- **Individual from a family with a known *BRCA1/2* pathogenic/likely pathogenic variant, including such variants found on research testing[b]**
- **Personal history of breast cancer[c] + one or more of the following:**
  - **Diagnosed ≤45 y**
  - **Diagnosed 46-50 y with:**
    - **An additional breast cancer primary at any age[d]**
    - **≥1 close blood relative[e] with breast cancer at any age**
    - **≥1 close blood relative[e] with high-grade (Gleason score ≥7) prostate cancer**
    - **An unknown or limited family history[a]**
  - **Diagnosed ≤60 y with:**
    - **Triple-negative breast cancer**
  - **Diagnosed at any age with:**
    - **≥1 close blood relative[e] with:**
      - **– breast cancer diagnosed ≤50 y; or**
      - **– ovarian carcinoma;[f] or**
      - **– male breast cancer; or**
      - **– metastatic prostate cancer;[g] or**
      - **– pancreatic cancer**
    - **≥2 additional diagnoses[d] of breast cancer at any age in patient and/or in close blood relatives**
  - **Ashkenazi Jewish ancestry[h]**
- **Personal history of ovarian carcinoma[f]**
- **Personal history of male breast cancer**
- **Personal history of pancreatic cancer[i]**
- **Personal history of metastatic prostate cancer[g]**
- **Personal history of high-grade prostate cancer (Gleason score ≥7) at any age with**
  - **≥1 close blood relatives[e] with ovarian carcinoma, pancreatic cancer, or metastatic prostate cancer[g] at any age or breast cancer <50 y; or**
  - **≥2 close blood relatives[e] with breast, or prostate cancer (any grade) at any age; or**
  - **Ashkenazi Jewish ancestry[h]**
- ***BRCA1/2* pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis**

Regardless of family history, some individuals with an *BRCA*-related cancer may benefit from genetic testing to determine eligibility for targeted treatment[j]

- **An individual who does not meet the other criteria but with ≥1 first- or second-degree blood[e] relative[k] meeting any of the above criteria. The significant limitations of interpreting test results for an unaffected individual should be discussed.**

If *BRCA* testing criteria met → **See Follow-up (BRCA-2)**

If *BRCA* testing criteria not met, consider testing for other hereditary syndromes → **If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines**

[a] For further details regarding the nuances of genetic counseling and testing, see BR/OV-A.

[b] Irrespective of degree of relatedness.

[c] For the purposes of these guidelines, invasive and ductal carcinoma in situ breast cancers should be included.

[d] Two breast cancer primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors diagnosed either synchronously or asynchronously.

[e] Close blood relatives include first-, second-, and third-degree relatives on same side of family. (See BR/OV-B)

[f] Includes fallopian tube and primary peritoneal cancers. *BRCA*-related ovarian cancers are associated with epithelial, non-mucinous histology. Lynch syndrome can be associated with both non-mucinous and mucinous epithelial tumors. Be attentive for clinical evidence of Lynch syndrome (see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal). Specific types of non-epithelial ovarian cancers and tumors can also be associated with other rare syndromes. Examples include an association between sex-cord tumors with annular tubules and Peutz-Jeghers syndrome or Sertoli-Leydig tumors and DICER1-related disorders.

[g] Metastatic prostate cancer is biopsy-proven and/or with radiographic evidence and includes distant metastasis and regional bed or nodes. It is not a biochemical recurrence.

[h] Testing for Ashkenazi Jewish founder-specific pathogenic/likely pathogenic variant(s), should be performed first. Comprehensive genetic testing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or if other *BRCA*-related criteria are met. Founder pathogenic/likely pathogenic variants exist in other populations.

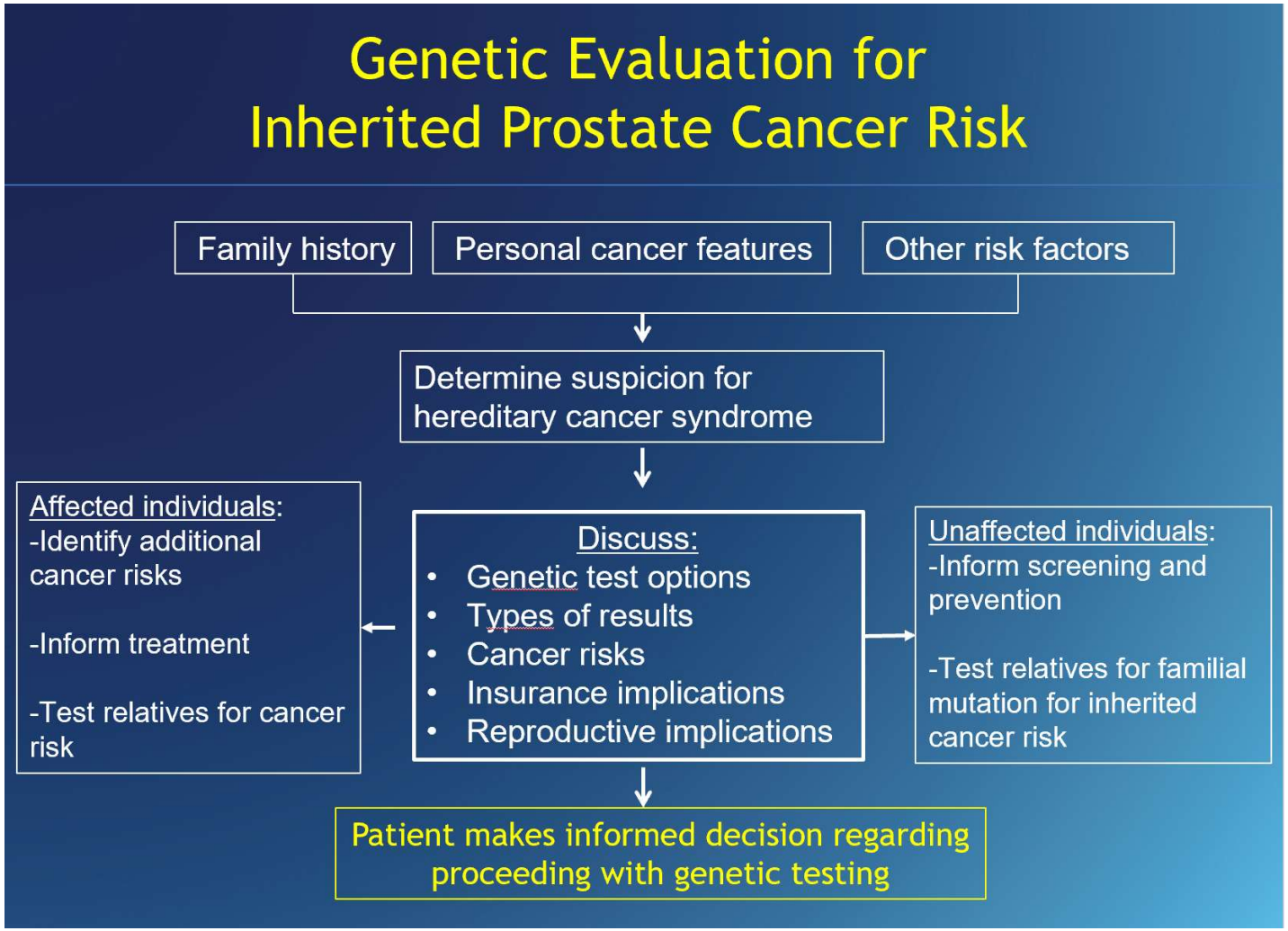
[i] Approximately 2%–5% of unselected cases of pancreatic adenocarcinoma will have a *BRCA1/2* pathogenic/likely pathogenic variant. However, the disease is highly lethal and the option to test the affected relative may not be available in the future. Thus, there may be significant benefit to family members in testing these patients near the time of diagnosis. In addition, increasing evidence suggests that identification of a *BRCA1/2* pathogenic/likely pathogenic variant may direct use of targeted therapies for patients with pancreatic cancer (See NCCN Guidelines for Pancreatic Adenocarcinoma). (Holter S, Borgida A, Dodd A, et al. J Clin Oncol 2015;33:3124-3129. Shindo K, Yu J, Suenaga M, et al. J Clin Oncol 2017;35:3382-3390.)

[j] Eg, PARP inhibitors for ovarian cancer and metastatic HER2-negative breast cancer; platinum therapy for prostate cancer. See the relevant NCCN treatment guidelines (eg, NCCN Guidelines for Breast Cancer; NCCN Guidelines for Prostate Cancer) for further details.

[k] This may be extended to an affected third-degree relative if related through two male relatives (eg, paternal grandfather's mother or sister).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Genetic Evaluation for Inherited Prostate Cancer Risk



Gene Panel Options for Prostate Cancer Genetic Testing

- **Invitae "Prostate Cancer Panel" (up to 15 genes)**
  - *ATM BRCA1 BRCA2 CHEK2 EPCAM HOXB13 MLH1 MSH2 MSH6 NBN PMS2 TP53; ADD ON FANCA, PALB2, RAD51D*
  - *HOXB13*: Analysis is limited to the NM_006361.5:c.251G>A, p.Gly84Glu variant.
  - Ability to customize testing

- **Ambry Genetics "ProstateNext" (14 gene)**
  - *ATM, BRCA1, BRCA2, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, RAD51D, TP53*
  - Some ability to customize testing

- **GeneDx "Prostate Cancer Panel" (12 gene)**
  - *ATM, BRCA1, BRCA2, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, NBN, PMS2, TP53*

- **Myriad- No prostate panel but "myRisk" 28 gene screen for:**
  Breast,Ovarian,Colorectal,Endometrial,Melanoma,Pancreatic,Gastric,Prostate,Others
  - *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, GREM1, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, POLD1, POLE, RAD51C, RAD51D, SMAD4, STK11, TP53*
  - *HOXB13* not included

- **Color Genomics- No prostate panel but "Hereditary Cancer Panel" 30 gene screen for:**
  Breast,Ovarian,Colorectal,Endometrial,Melanoma,Pancreatic,Gastric,Prostate,Others
  - *APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, GREM1, MITF, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, POLD1, POLE, RAD51C, RAD51D, SMAD4, STK11, TP53*
    - *PMS2*: Excludes exons 11-14
    - *HOXB13* not included

Courtesy: L. Gomella, MD

Olaparib combined with abiraterone in patients with metastatic castration-resistant prostate cancer: A randomized Phase II trial

Noel Clarke,[1] Pawel Wiechno,[2] Boris Alekseev,[3] Nuria Sala,[4] Robert Jones,[5] Ivo Kocak,[6] Vincenzo Emanuele Chiuri,[7] Jacek Jassem,[8] Aude Fléchon,[9] Charles Redfern,[10] Carsten Goessl,[11] Joseph Burgents,[11] Robert Kozarski,[12] Darren Hodgson,[13] Fred Saad[14]

[1]The Christie and Salford Royal Hospitals, Manchester, UK; [2]Maria Skłodowska-Curie Memorial Cancer Center, Warsaw, Poland; [3]Moscow Hertzen Cancer Research Institute, Moscow, Russia; [4]Catalan Institute of Oncology, Hospital Josep Trueta, Girona, Spain; [5]Velindre Cancer Centre and Cardiff University, Cardiff, UK; [6]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [7]Ospedale Vito Fazzi, Lecce, Italy; [8]Medical University of Gdańsk, Gdańsk, Poland; [9]Centre Léon Bérard, Lyon, France; [10]Sharp HealthCare, San Diego, CA, USA; [11]AstraZeneca, Gaithersburg, MD, USA; [12]AstraZeneca, Cambridge, UK; [13]AstraZeneca, Macclesfield, UK; [14]Centre Hospitalier de l'Université de Montréal, Montreal, Canada

ClinicalTrials.gov identifier: NCT01972217. This study was sponsored by AstraZeneca

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Rahul Aggarwal

Trial design

- mCRPC
- Prior treatment with docetaxel for mCRPC
- ≤2 prior lines of chemotherapy
- No prior 2nd-generation antihormonal agents
- Candidate for abiraterone treatment

Olaparib tablets 300 mg bid + abiraterone* 1000 mg od

Randomized 1:1 Double-blind

Placebo + abiraterone* 1000 mg od

Treatment until disease progression

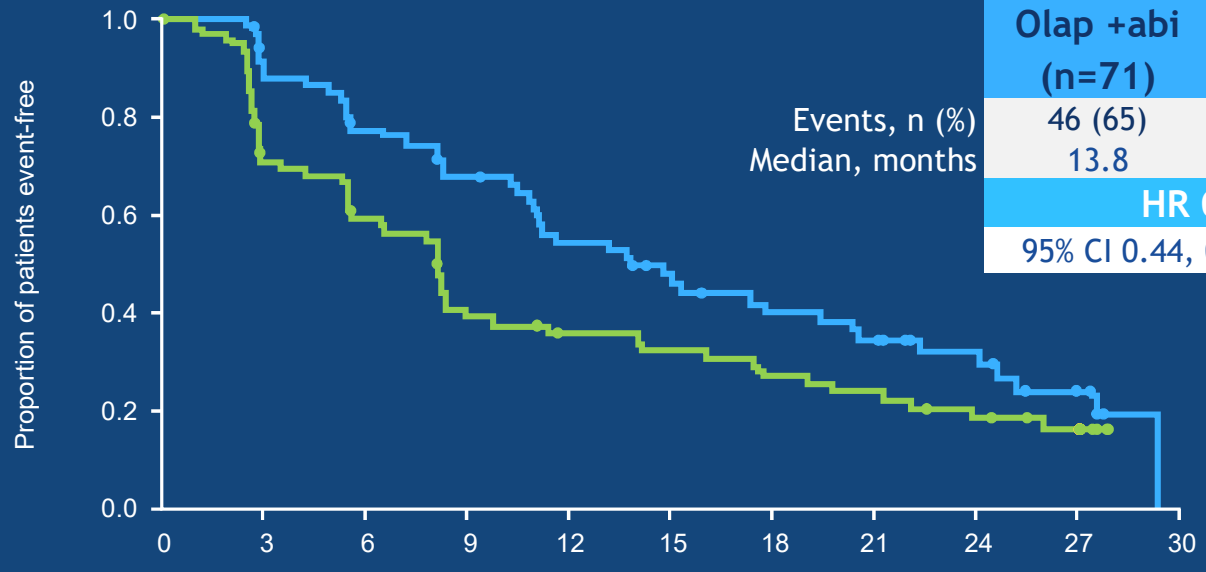
Primary endpoint:

- Radiologic progression-free survival (RECIST 1.1; PCWG2)

- rPFS by HRRm status
- Time to second progression (PFS2)
- Overall survival (OS)
- Objective response rate (ORR)
- Times to first and second subsequent therapies (TFST/TSST)
- CTC-conversion rate
- Health-related quality of life (HRQoL)
- Safety and tolerability

*Prednisone/prednisolone (5 mg) was administered alongside abiraterone as indicated. bid, twice daily; CTC, circulating tumor cell; HRRm, homologous recombination repair gene mutation; mCRPC, metastatic castration-resistant prostate cancer; od, once daily; PCWG, Prostate Cancer Working Group; RECIST, Response Evaluation Criteria in Solid Tumors; rPFS, radiologic progression-free survival

Primary endpoint: Investigator-assessed Radiographic progression free survival



	Olap +abi (n=71)	Abi (n=71)
Events, n (%)	46 (65)	54 (76)
Median, months	13.8	8.2
HR 0.65		
95% CI 0.44, 0.97; *P*=0.034		

N at risk											
Olaparib + abiraterone arm	71	58	50	42	33	26	21	18	13	8	0
Abiraterone arm	71	48	39	25	21	19	16	14	10	7	0

CI, confidence interval; HR, hazard ratio

Clarke N, et al. ASCO 2018 Abstract #5003

Radiographic progression free survival by DNA repair mutation status

Positive Mutation

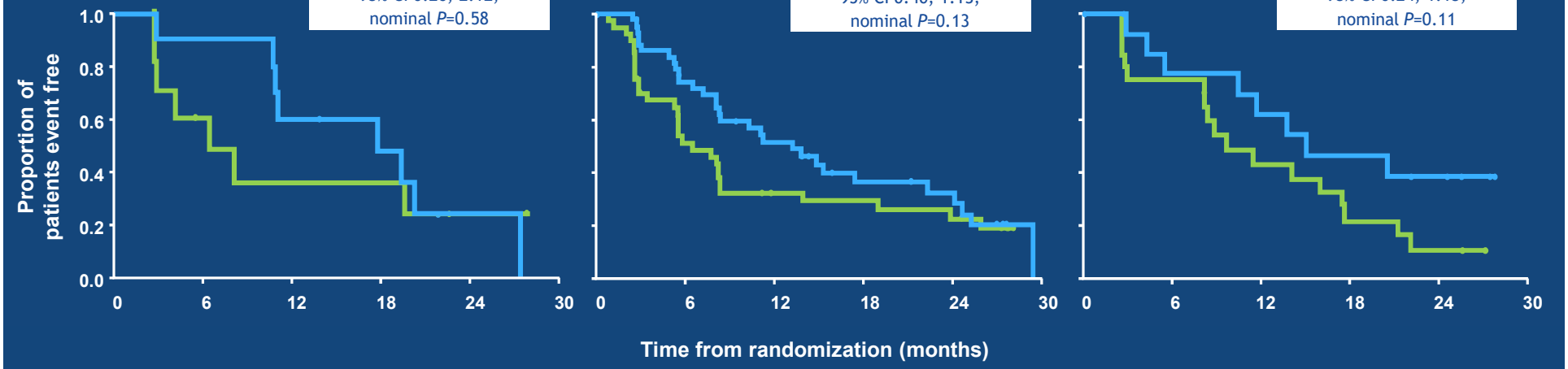
	Olap + abi (n=11)	Abi (n=10)
Events, n (%)	8 (73)	7 (70)
KM median, months	17.8	6.5
HR 0.74		
95% CI 0.26, 2.12; nominal *P*=0.58		

Wild type, plasma/ germline only

	Olap + abi (n=45)	Abi (n=41)
Events, n (%)	30 (67)	30 (73)
KM median, months	13.1	6.4
HR 0.67		
95% CI 0.40, 1.13; nominal *P*=0.13		

Wild type, tissue evaluable

	Olap + abi (n=15)	Abi (n=20)
Events, n (%)	8 (53)	17 (85)
KM median, months	15.0	9.7
HR 0.52		
95% CI 0.24, 1.15; nominal *P*=0.11		



Safety summary

	Olaparib + abiraterone (n=71)	Abiraterone (n=71)
Median duration of olaparib/placebo, days	309	253
Median duration of abiraterone, days	338	253
Any adverse event, n (%)	66 (93)	57 (80)
Grade ≥3 adverse event, n (%)	38 (54)	20 (28)
Serious adverse event, n (%)	24 (34)	13 (18)
Fatal adverse event, n (%)	4 (6)	1 (1)
Adverse event leading to dose interruption, n (%)	24 (34)	9 (13)
Adverse event leading to dose reduction, n (%)	13 (18)	0
Adverse event leading to treatment discontinuation, n (%)	21 (30)	7 (10)

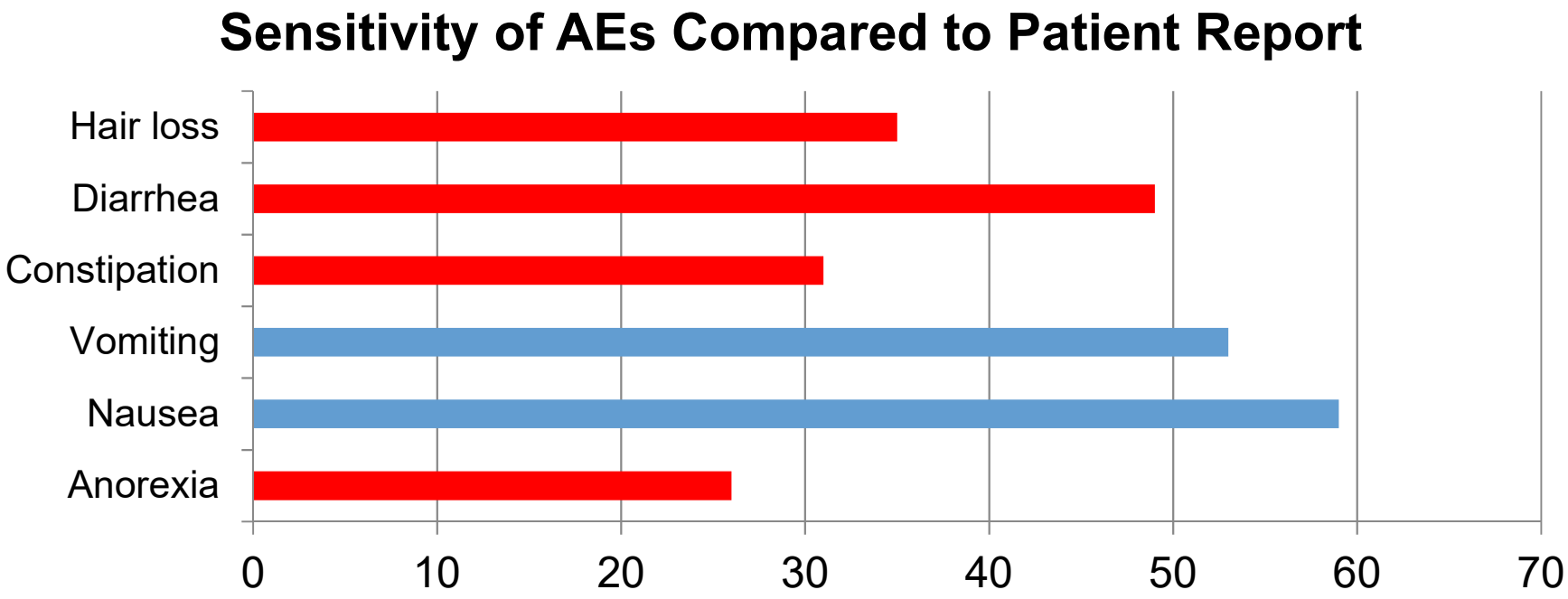
Clarke N, et al. ASCO 2018 Abstract #5003

Patient-Reported Outcomes (PROs)

"Any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."

Kluetz et al., *Clin Cancer Res* 2016; 22:1553-8.

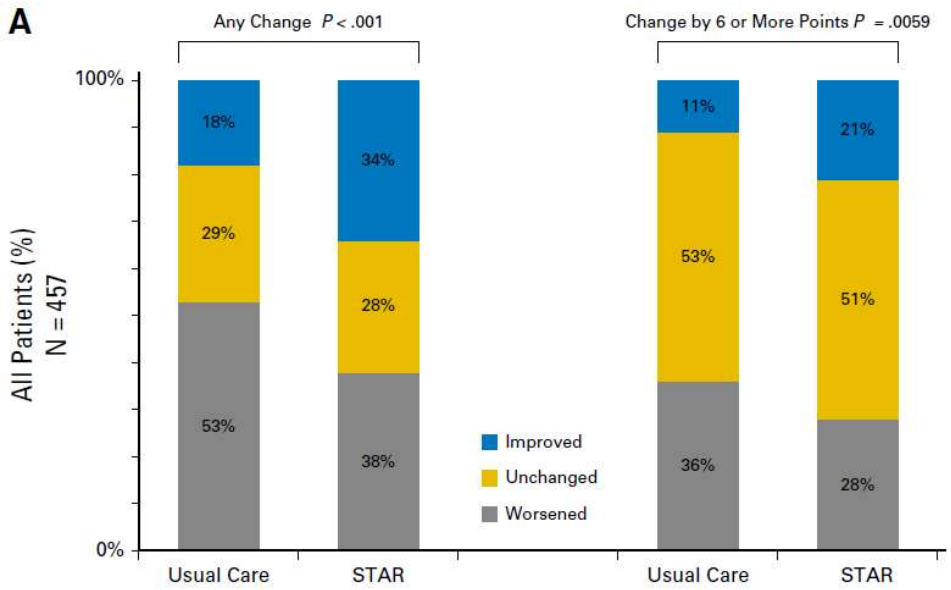
Adverse Events Don’t Accurately Capture Toxicity



Di Maio et al., *JCO* 2015; 33: 910-5.

PROs Can Improve Outcomes

- High relevance for managing toxicity in combination trials
- Clinic-based monitoring of 12 common symptoms using the PRO-CTCAE in 766 patients
- Treated with chemotherapy for metastatic breast, GU, Gyn, or lung cancer
- Triggered email alerts to nurses with severe or significantly worsening symptoms



Basch et al., *JCO* 2016; 34: 557-565-34.

PROs Can Improve Outcomes

- ER visits at one year (34% vs. 41%) (p=.02)
- Median months on chemotherapy (8.2 vs. 6.3) (p=.002)
- Quality-adjusted one year survival (75% vs. 69%) (p=.05)
- More pronounced benefits for computer-inexperienced patients

Basch et al., *JCO* 2016; 34: 557-565-34.

Technology APPlications:
Use of digital health technology to enable drug development

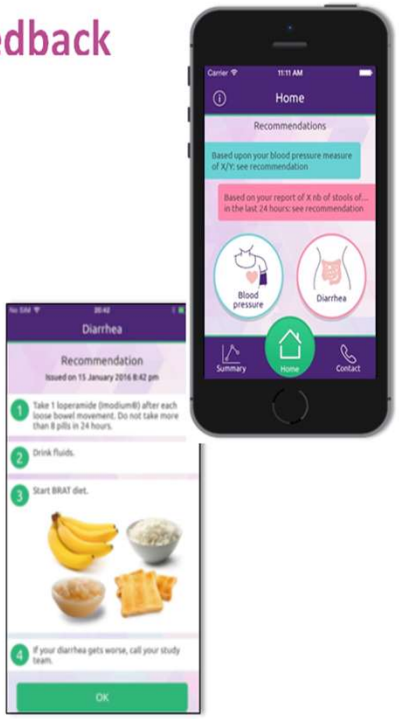
A pilot study to evaluate the feasibility, usability, and perceived satisfaction with eCO (eCediranib-Olaparib), a mobile application for side effect monitoring and reporting, in women with recurrent ovarian cancer.

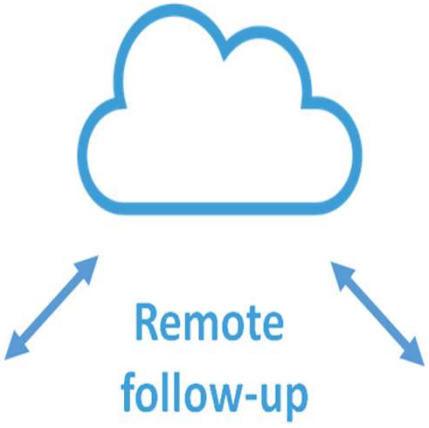
NRG-004 and 005 and other NCI-sponsored studies using risk based monitoring

Percy Ivy, MD

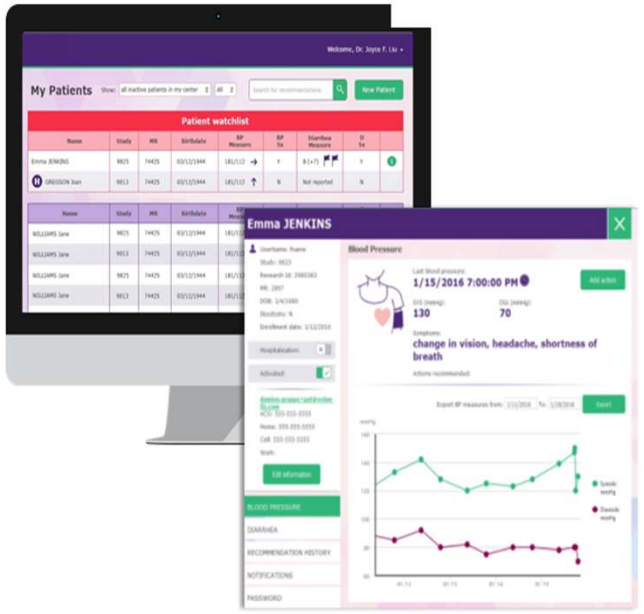
Web Portal View of Patient Data

Personalized and immediate feedback



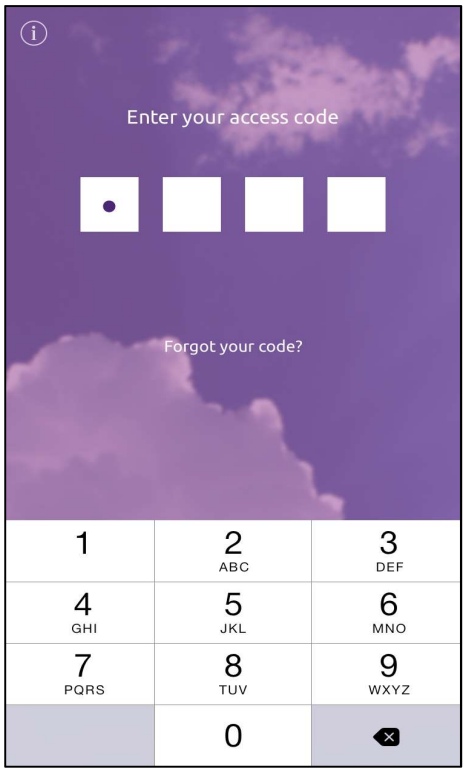


Data Reports and Trends



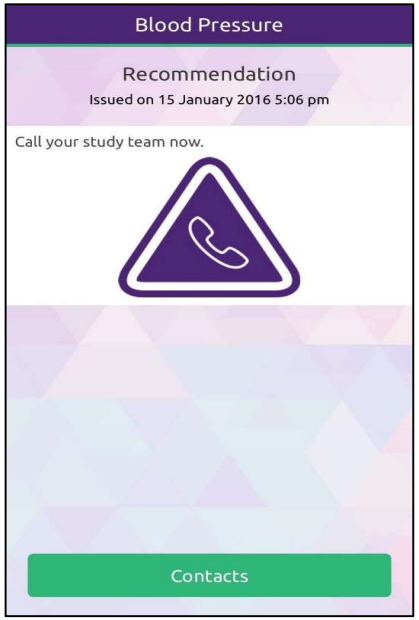
VOLUNTIS

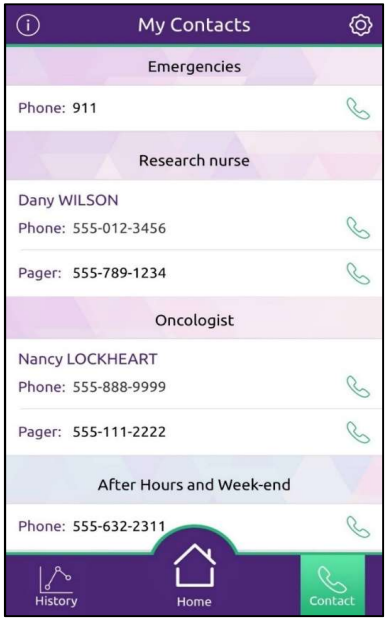
Secure Access for Patients



- Data is stored on a secure server and not on patient phone
- Access is prescription only using
- Access code entry adds additional layer of security for patients

Real Time Collaboration When Needed

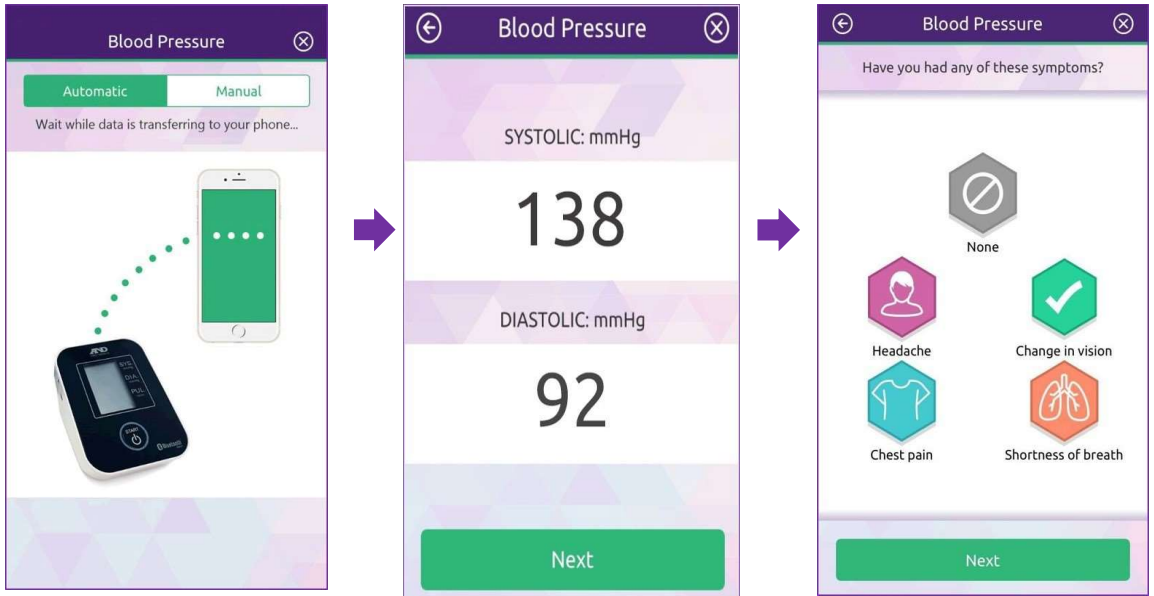




NATIONAL CANCER INSTITUTE

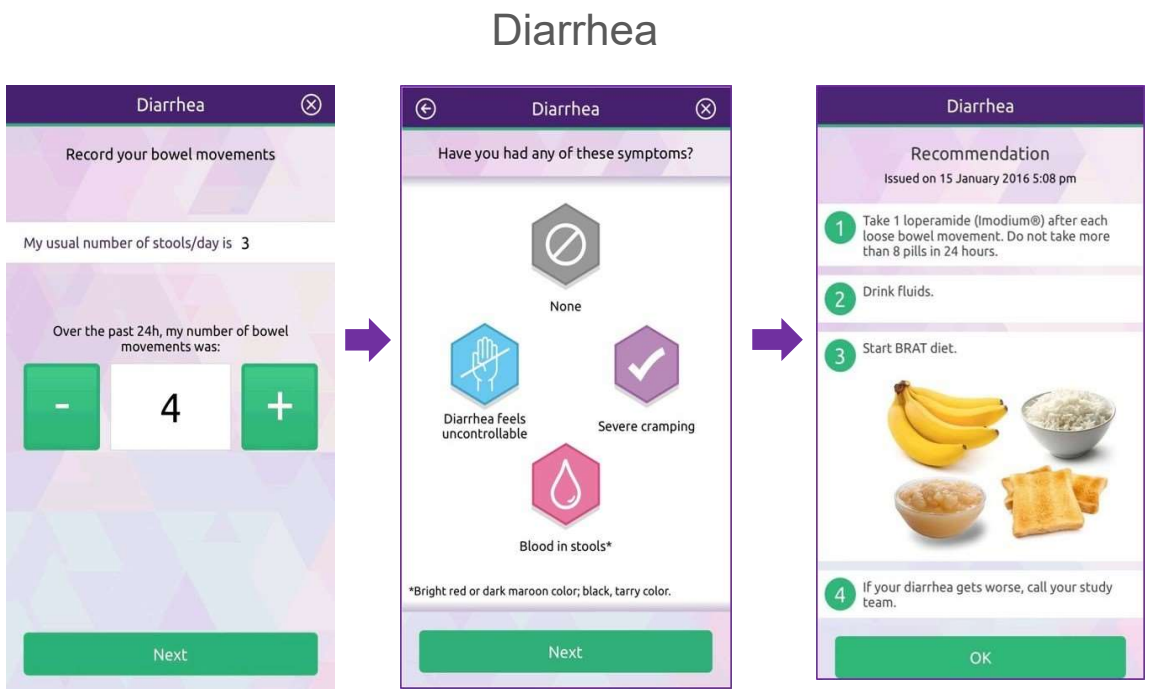
Real Time Data Entry and Assessment

Blood Pressure



NATIONAL CANCER INSTITUTE

Real Time Data Entry and Assessment



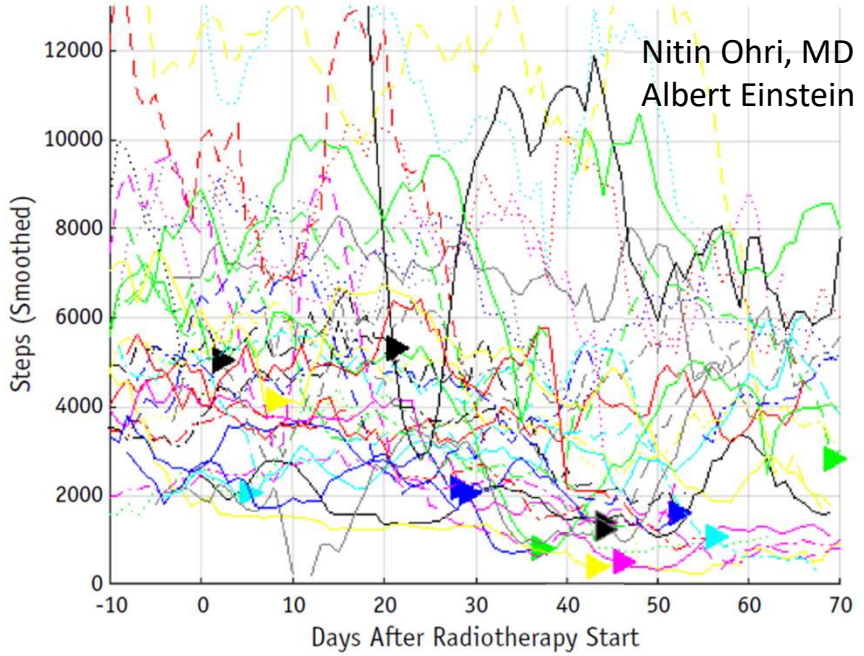
Liu J, Lee J, Strock E, Phillips R, Mari K, Killam B, Bonnam M, Milenkova T, Kohn E, Ivy, P.
Technology APPlications: Use of digital health technology to enable drug development. Journal of Clinical Oncology Informatics

Continuous Activity Monitoring During Concurrent Chemoradiotherapy

Nitin Ohri, MD,* Rafi Kabarriti, MD,* William R. Bodner, MD,*
Keyur J. Mehta, MD,* Viswanathan Shankar, DrPH,†
Balazs Halmos, MD,‡ Missak Haigentz, Jr, MD,‡ Bruce Rapkin, PhD,†
Chandan Guha, MBBS, PhD,* Shalom Kalnicki, MD,*
and Madhur Garg, MD*

Nitin Ohri, MD
Albert Einstein

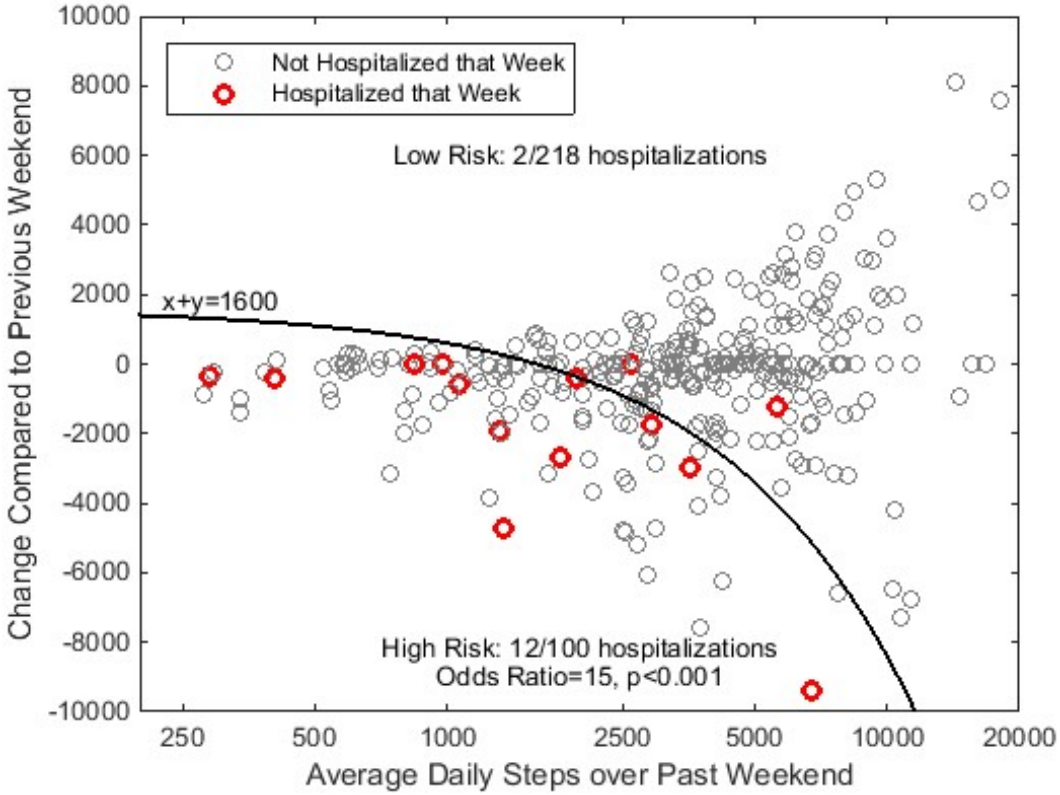
- Key findings:
  - Step counts were obtained for 94% of days during patients' treatment courses.
  - 14/38 subjects were hospitalized due to acute toxicities (triangles).
  - 38% reduction in the risk of hospitalization for every 1,000 steps taken each day (HR=0.62, p<0.001)



Int J Radiation Oncol Biol Phys, Vol. 97, No. 5, pp. 1061–1065, 2017

“Activity Score” Predicts Hospitalizations

Nitin Ohri, MD
Albert Einstein



Digital Literacy - Urban Cancer Population: Who Are We Leaving Out?

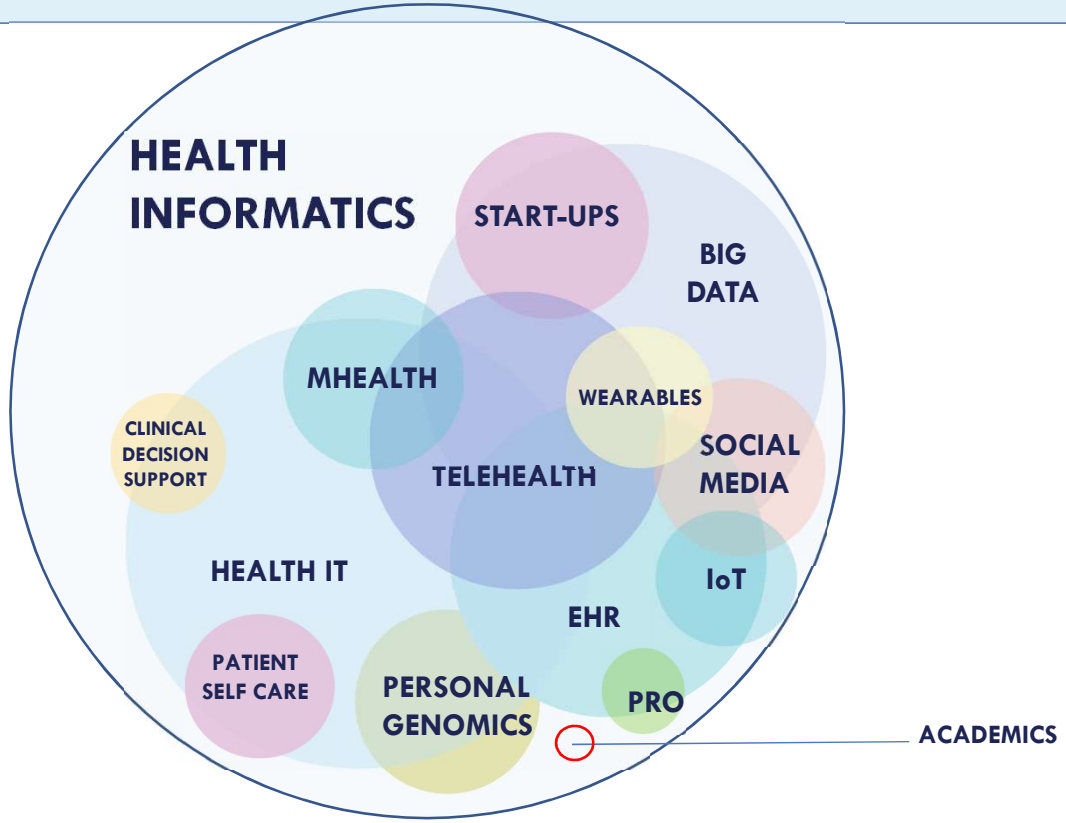
Patients with less than a high school diploma are 12X less likely to have access to the Internet than those with an advanced degree.

Factors that influence whether patients will use the internet to learn about their cancer are race (African American) and education (HS diploma or less)

Factors that influence whether patients will use the internet to learn about their cancer are race (African American) and education (HS diploma or less)

51% of our patients use MyChart on a regular basis. However, patients who were white or with an advanced degree were 2X likely to report using MyChart than patients of a minority race or those with less than a high school diploma.

THE DIGITAL HEALTH LANDSCAPE



PROBLEM

SOLUTION


DESIGN
HEALTHCARE
TECHNOLOGY
A NEW CROSS-TRAINED INDIVIDUAL

JeffMD Digital Health & Data Science

Robert Bloom

Cassra Clarke

Justin Dang

Lillian Flashner

Jeffrey Lu

Sara Long

Marissa Ruggiero

Abhishek Surampudy

Brendan Gleason

Taylor Jones

George Titomihelakis

Christine Wamsley

Ji-Hui (Gavyn) Ooi

Sabrina Lefcochilos-Fogelquist

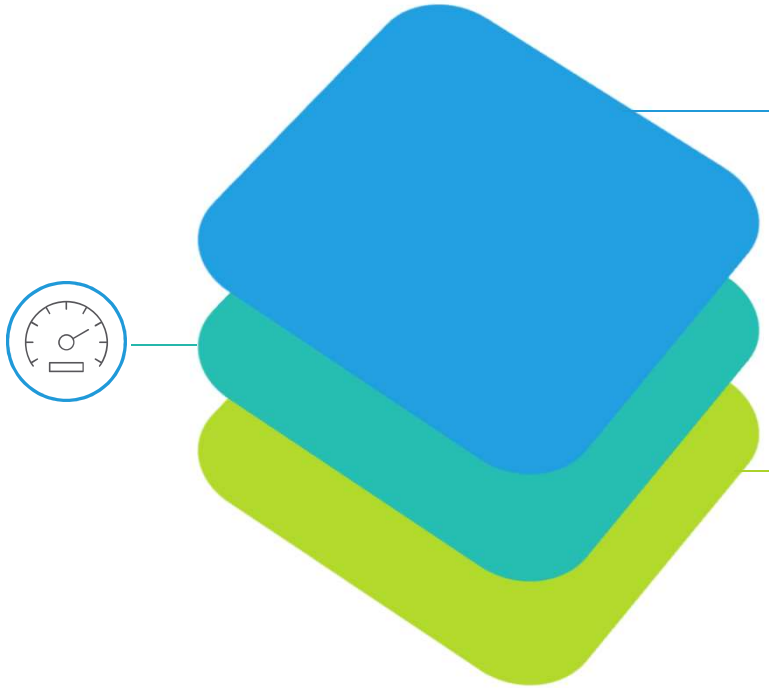
Chaim Miller

Victoria Nguyen

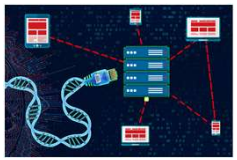
ExMDHMS Digital Health
Sample/Proposed Foundational Courses

Course Clusters – all Masters' Level	Anticipated Participants: Healthcare Learners	Anticipated Participants: Tech Learners	Anticipated Participants: Design Learners
Healthcare system overview: Evolution, Organization, Delivery, Culture, Finance, Architecture, Design, Innovation History, HSS		X	X
Introduction to Design Thinking and Innovation: Fundamentals of functional design and materials	X		
Comparative technology architecture	X		X
Fundamentals of clinical and basic research: Design, interpretation, funding, operations and management		X	X
Fundamentals of biologic and physiologic monitoring		X	X
Fundamentals of population science and population health		X	X
Healthcare safety and quality management: Systems, measurement, reporting, improvement science		X	X
Principles of user experience	X	X	X
Fundamentals of health information technology and clinical informatics: Health tech, data and systems, interoperability, information exchange	X	X	X
Seminars in cross disciplinary teams: Function, leadership, effectiveness	X	X	X
Clinical and econometric outcomes analysis	X	X	X
Organization of the biotechnology industry and markets	X	X	X
Introduction to business and legal issues for entrepreneurs: IP law and practices, contracts, funding sources, business structures	X	X	X
Fundamentals of digital and mobile design methods	X		
Leadership: Seminar Organizational Integration of Innovation	X	X	X

A tiered approach for a comprehensive, personalized, molecular, patient centered perspective



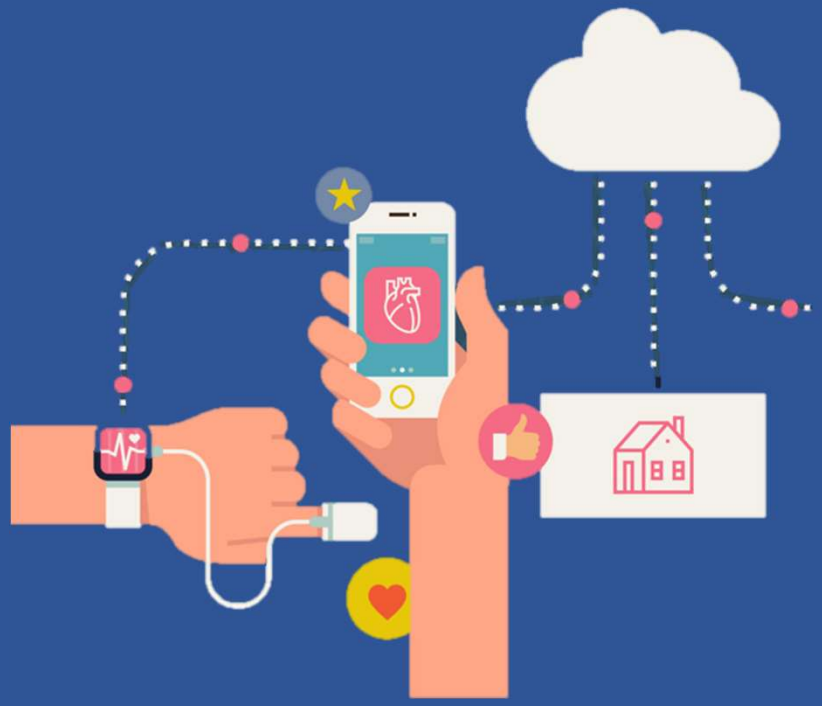
Translational molecular profile



Imaging Data
-Functional
-Spatial

Patient Reported Outcomes + Wearable data
-PRO-CTCAE
-Remote collection
-Weekly
-Shared with patient

Thank you!



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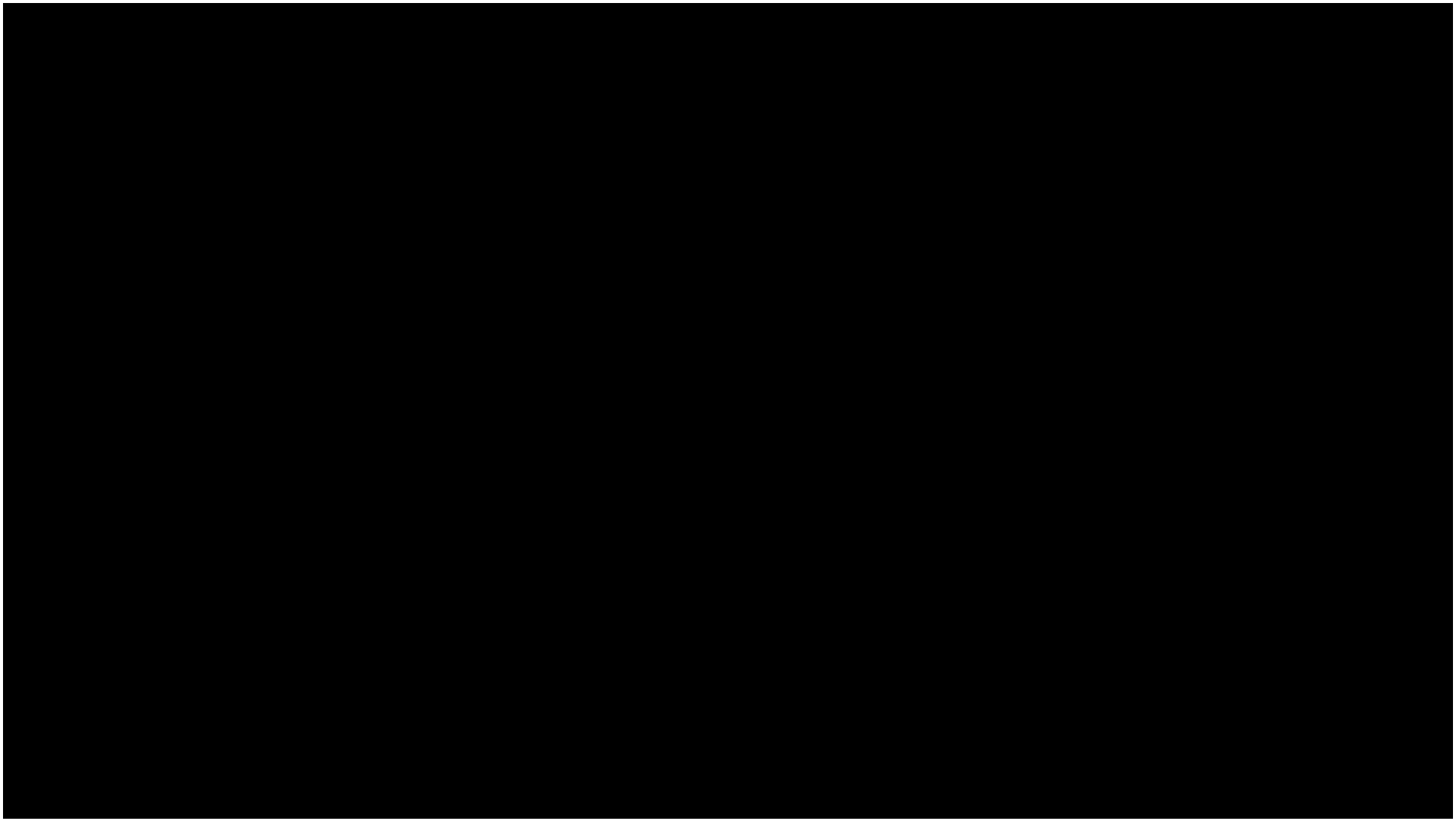


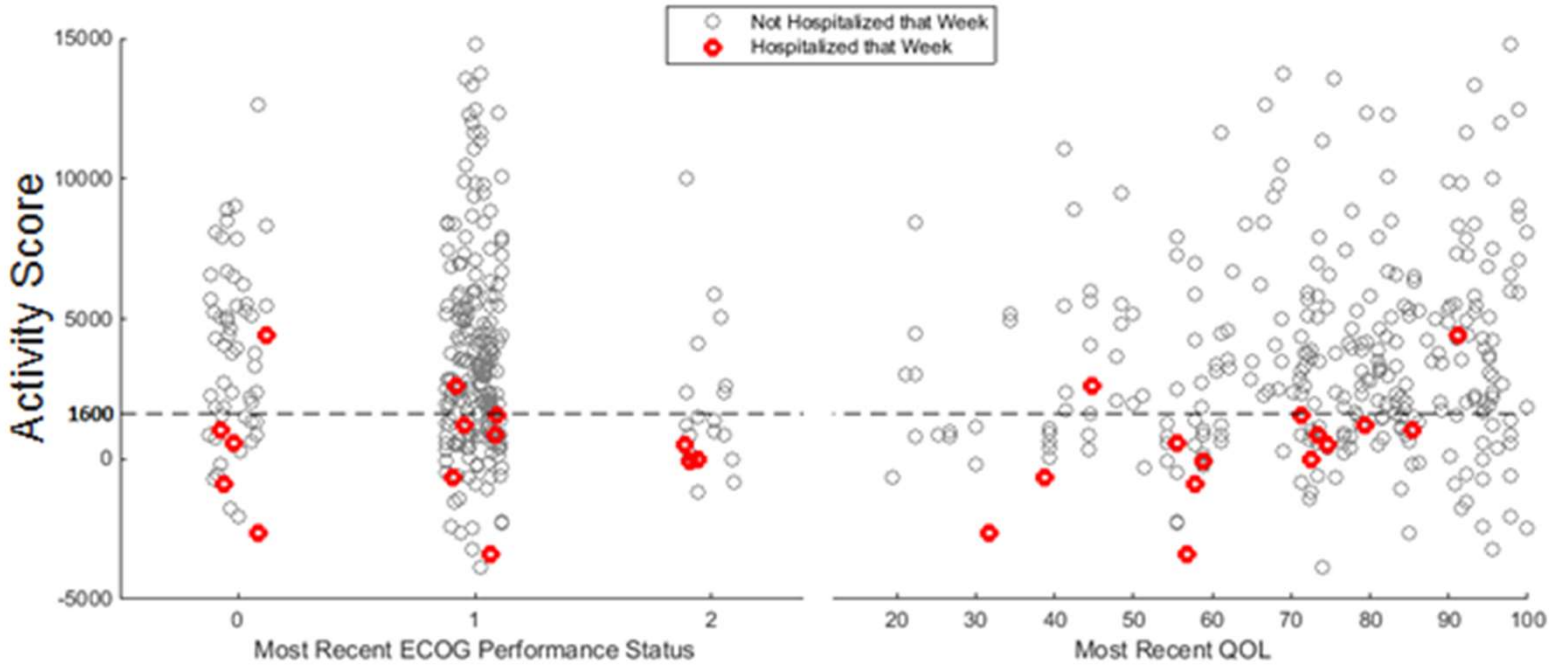
Hypothesis:

- A combination of electronic patient reported outcomes and remote monitoring will improve the lives of patients

ePROs +

Sidney Kimmel Cancer Center
at Thomas Jefferson University
NCI-designated

Predicting Hospitalization: Activity Score v. PS and QoL



Recent step counts are better predictors of hospitalization risk than physician-rated performance status (left, where 4 patients with PS=0 were hospitalized) and patient reported QOL (average score on EORTC QLC-C30, right).

Nitin Ohri, MD

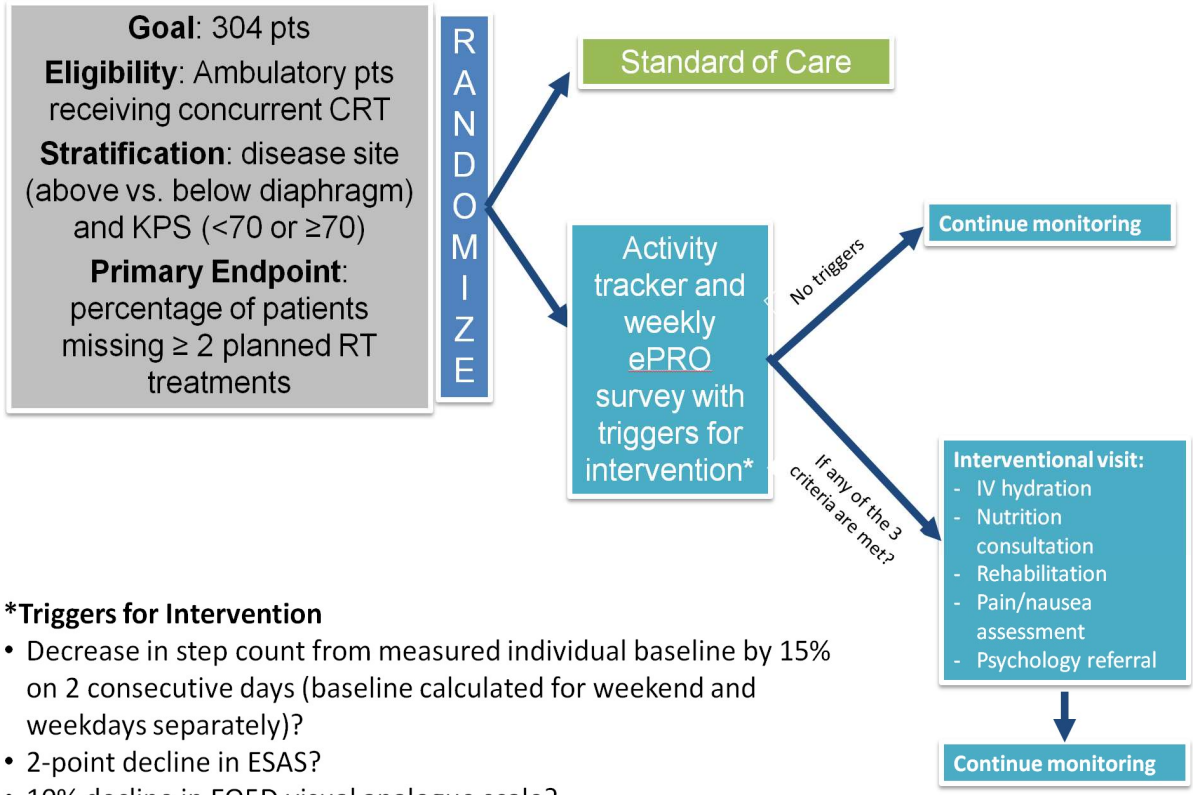
PRO-RAM: The investigation of remote electronic Patient-Reported Outcomes in combination with Remote Activity Monitoring to reduce missed treatments in patients receiving concomitant chemoradiotherapy

Noelle Williams

- Aim 1: To investigate compliance rates with the activity trackers (% wearing / syncing the device over total prescribed time) and ePRO completion.
- Aim 2: To explore correlations between validated ePROs (Edmonton Symptom Assessment Tool and EQ-5D-5L) and activity tracker data and to characterize types and costs of interventions initiated by our care team that were triggered by declining step data and/or ePRO scores.
- Aim 3: To prospectively demonstrate that an early targeted intervention system (triage visit with subsequent outpatient supportive care measures) as triggered by remote ePRO scores and activity tracker data for patients receiving chemoradiotherapy (CRT) will reduce the rates of patients missing ≥ 2 RT treatment visits when compared to the usual model of care.

Sidney Kimmel Cancer Center
at Thomas Jefferson University
NCI-designated

Randomized phase II study investigating remote activity monitoring with remote electronic patient-reported outcomes to reduce missed treatments in patients receiving concomitant chemoradiotherapy



***Triggers for Intervention**

- Decrease in step count from measured individual baseline by 15% on 2 consecutive days (baseline calculated for weekend and weekdays separately)?
- 2-point decline in ESAS?
- 10% decline in EQ5D visual analogue scale?

Sidney Kimmel Cancer Center
at Thomas Jefferson University
NCI-designated

Utilizing Digital Health to Collect Electronic Patient-Reported Outcomes in Prostate Cancer: A Prospective Feasibility and Acceptability Study

Clinical Trial Apps

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Strength
THROUGH INSIGHT

About
THE SURVEY

The **Strength Through Insight** app allows patients and their caregivers to build a partnership for communication throughout their cancer treatment. The survey uses standard questions which can be answered digitally via an app at a set schedule. The survey allows easier and immediate sharing of a patient's perspective on their life, treatment, and illness to enable shared decision making. The Strength Through Insight study aims to assess the feasibility of collecting survey data from patients using digital technologies and hand held devices.

Which HRQoL Tool?

Recommended Patient-Reported Core Set of Symptoms to Measure in Prostate Cancer Treatment Trials

Ronald C. Chen, Peter Chang, Richard J. Vetter, Himansu Lukka, William A. Stokes, Martin G. Sanda, Deborah Watkins-Bruner, Bryce B. Reeve, Howard M. Sandler

Manuscript received May 24, 2013; revised April 3, 2014; accepted April 11, 2014.

Correspondence to: Ronald C. Chen, MD, MPH, Department of Radiation Oncology, University of North Carolina at Chapel Hill, 101 Manning Dr, CB #7512, Chapel Hill, NC 27516 (e-mail: ronald_chen@med.unc.edu).

The National Cancer Institute (NCI) Symptom Management and Health-Related Quality of Life Steering Committee convened four working groups to recommend core sets of patient-reported outcomes to be routinely incorporated in clinical trials. The Prostate Cancer Working Group included physicians, researchers, and a patient advocate. The group's process included 1) a systematic literature review to determine the prevalence and severity of symptoms, 2) a multistakeholder meeting sponsored by the NCI to review the evidence and build consensus, and 3) a postmeeting expert panel synthesis of findings to finalize recommendations. Five domains were recommended for localized prostate cancer: urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms. Four domains were recommended for advanced prostate cancer: pain, fatigue, mental well-being, and physical well-being. Additional domains for consideration include decisional regret, satisfaction with care, and anxiety related to prostate cancer. These recommendations have been endorsed by the NCI for implementation.

Localized Prostate Cancer:

Epic-26 HRQoL Domains

- Urinary
- Bowel
- Sexual
- Vitality/Hormonal

Advanced Prostate Cancer:

Epic-CP HRQoL Domains

- Urinary
- Bowel
- Sexual
- Vitality/Hormonal

FAPSI-8 HRQoL Domains

- Pain
- Fatigue/Lack of energy
- Weight loss
- Worry
- Urinary Difficulties

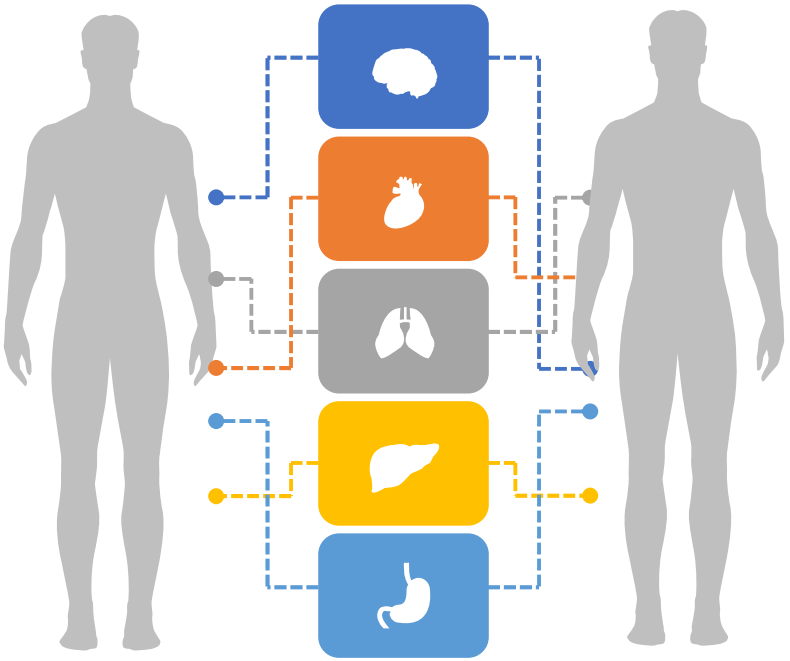
Chen, R. C., Chang, P., Vetter, R. J., Lukka, H., Stokes, W. A., Sanda, M. G., ... & Sandler, H. M. (2014). Recommended patient-reported core set of symptoms to measure in prostate cancer treatment trials. *Journal of the National Cancer Institute*, *106*(7), dju132.

Measurement

Localized Prostate Cancer:

Epic-26 HRQoL Domains

- Urinary
- Bowel
- Sexual
- Vitality/Hormonal



Advanced Prostate Cancer:

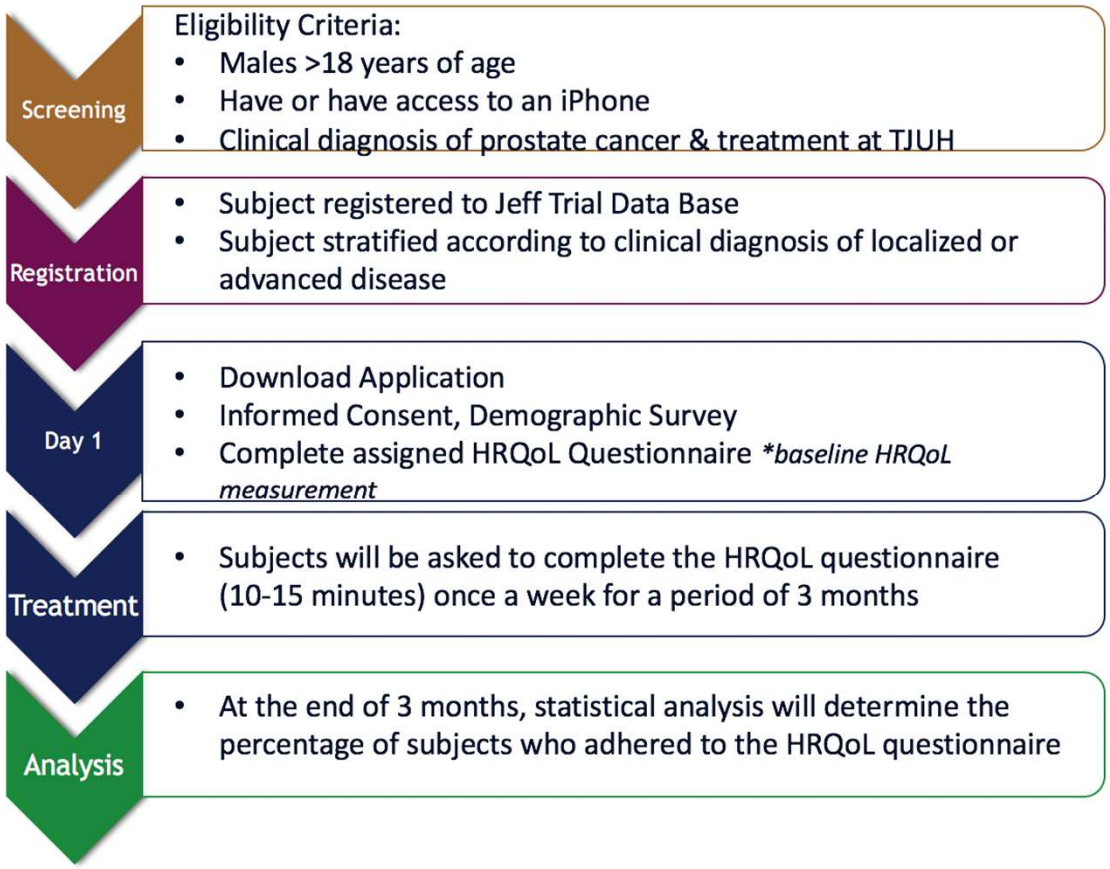
Epic-CP HRQoL Domains

- Urinary
- Bowel
- Sexual
- Vitality/Hormonal

FAPSI-8 HRQoL Domains

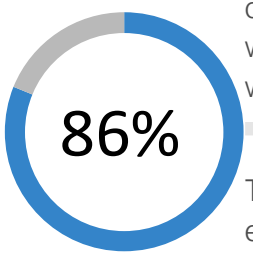
- Pain
- Fatigue/Lack of energy
- Weight loss
- Worry
- Urinary Difficulties

Study Design



Statistical Analysis: The primary measure of this feasibility study will be a dichotomous measure of satisfactory completion defined as 60% of weekly questionnaires over a 3 month period.

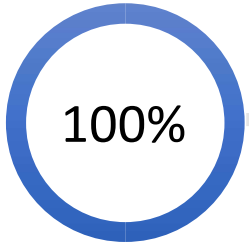
Quantitative Evaluation: Feasibility (Assessment of Satisfactory Completion)



86.2% (25/29) of participants reached satisfactory questionnaire completion defined as completion of 60% of weekly questions over 12 weeks

The lower bound of the exact one-sided 95% confidence interval was 71.2% exceeding the 70% feasibility threshold.

3 participants reported technical issues (app randomly closing/needing to restart app) as the main reason for missing questions.



All participants were able to complete informed consent through the smartphone app.

Patterns of missing data showed a decline in responses after week six.

Journals focused on Digital Health (partial list)

Article | 19 February 2018 | OPEN

Delivering digital cognitive behavioral therapy for insomnia at scale: does using a wearable device to estimate sleep influence therapy?

Annemarie I. Luik, Pedro Farias Machado & Colin A. Espie

Article | 12 February 2018 | OPEN

Frequent discussion of insomnia and weight gain with glucocorticoid therapy: an analysis of Twitter posts

Rikesh Patel, Maksim Belousov [...] William G. Dixon

Article | 25 January 2018 | OPEN

Highly flexible, wearable, and disposable cardiac biosensors for remote and ambulatory monitoring

Stephen P. Lee, Grace Ha [...] Roozbeh Ghaffari

Perspective | 25 January 2018 | OPEN

Mobile and pervasive computing technologies and the future of Alzheimer's clinical trials

P. Murali Doraiswamy, Vaibhav A. Narayan & Husseini K. Manji

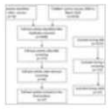
Perspective | 15 January 2018 | OPEN

Population measurement for health systems

Bruce R. Schatz

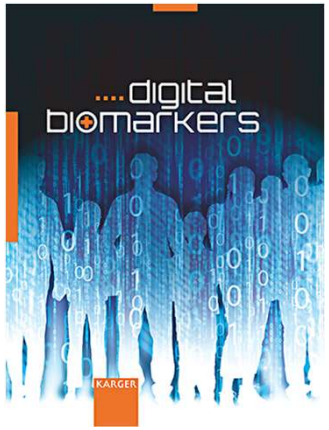
Review Article | 15 January 2018 | OPEN

Impact of remote patient monitoring on clinical outcomes: an updated meta-analysis of randomized controlled trials



Benjamin Noah, Michelle S. Keller [...] Brennan M. R. Spiegel

All Articles »



JCO™ | CLINICAL CANCER INFORMATICS

An American Society of Clinical Oncology® journal

npj | Digital Medicine

JMIR Publications

The Leading eHealth Publisher

Journal of Medical Internet Research

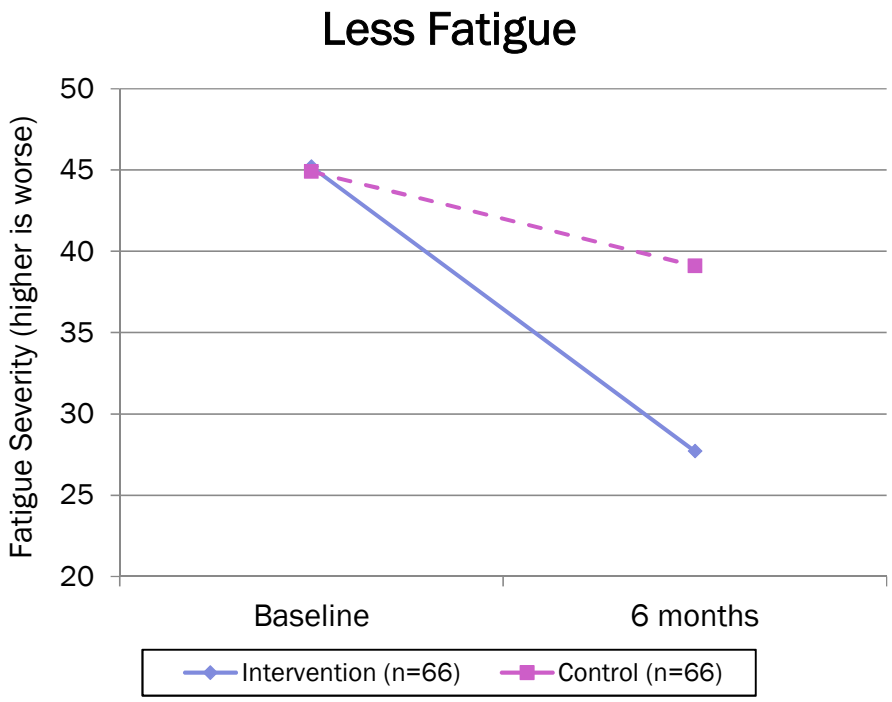
energize

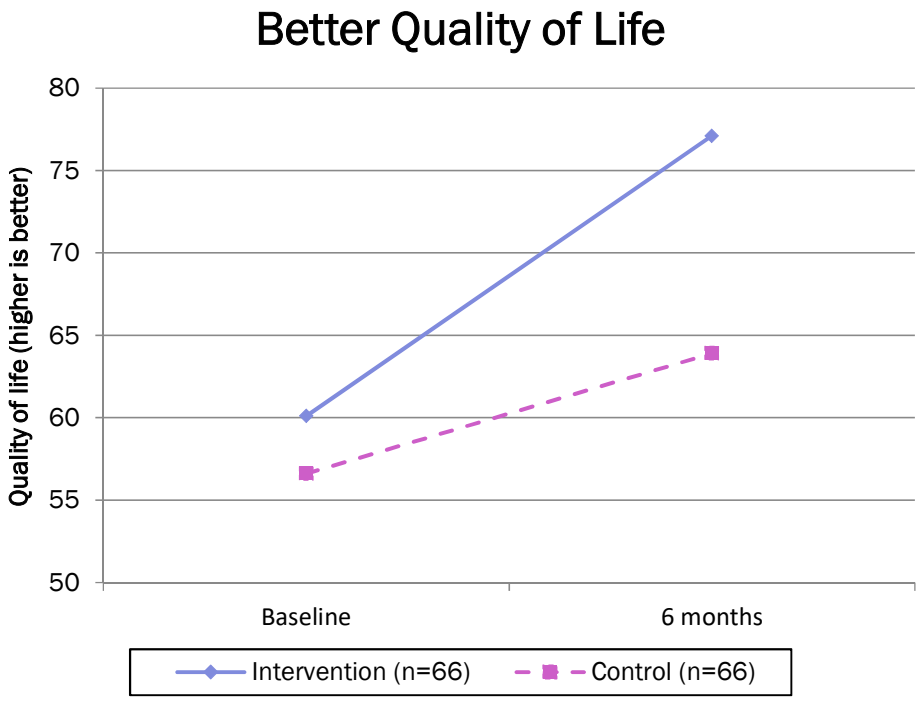
Do What Matters

Heather Jim, PhD, Associate Member
Department of Health Outcomes and Behavior

MOFFITT CANCER CENTER

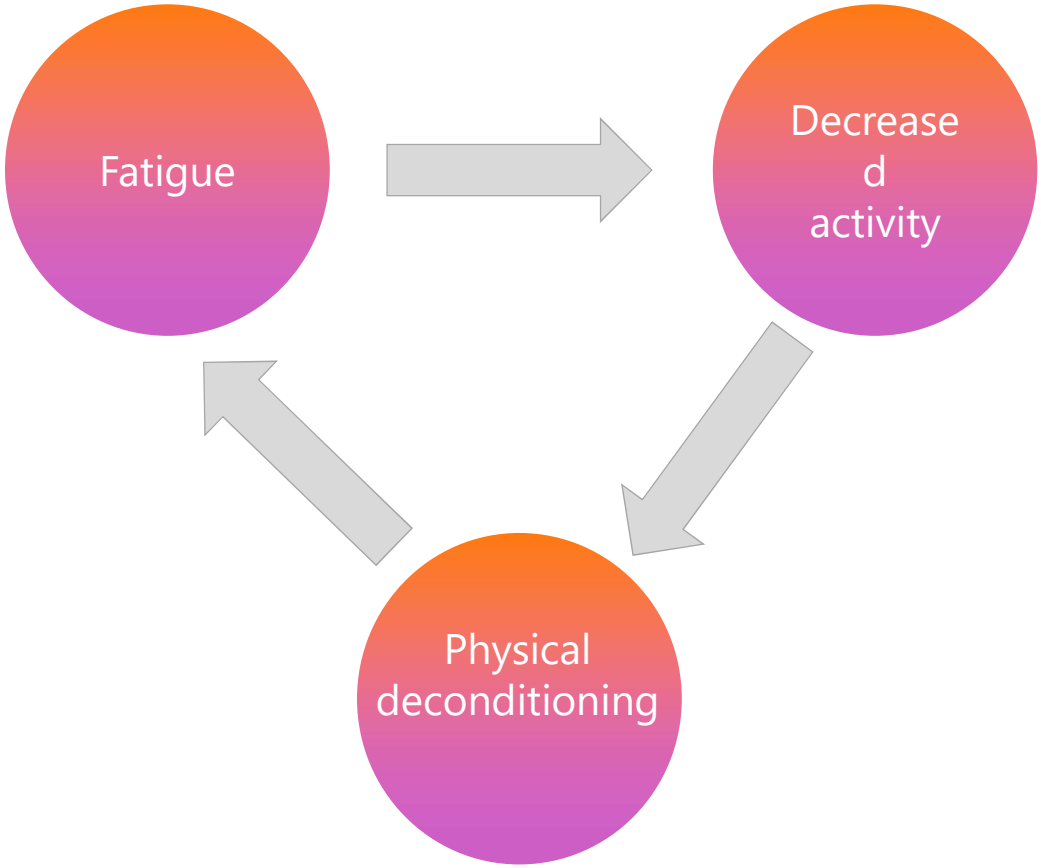
Efficacy in Randomized Trials





MOFFITT CANCER CENTER

Cancer-Related Fatigue



MOFFITT CANCER CENTER

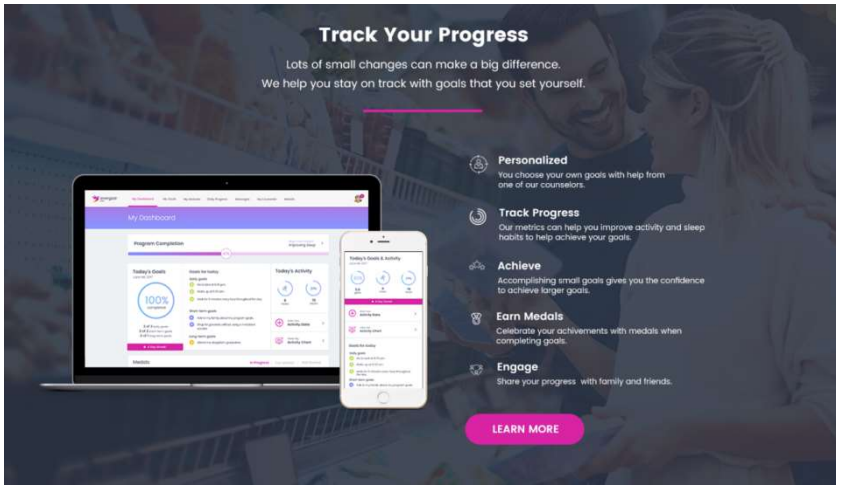
Energize Modules

Activity pacing

Sleep hygiene

Thinking differently about fatigue

Plus optional modules

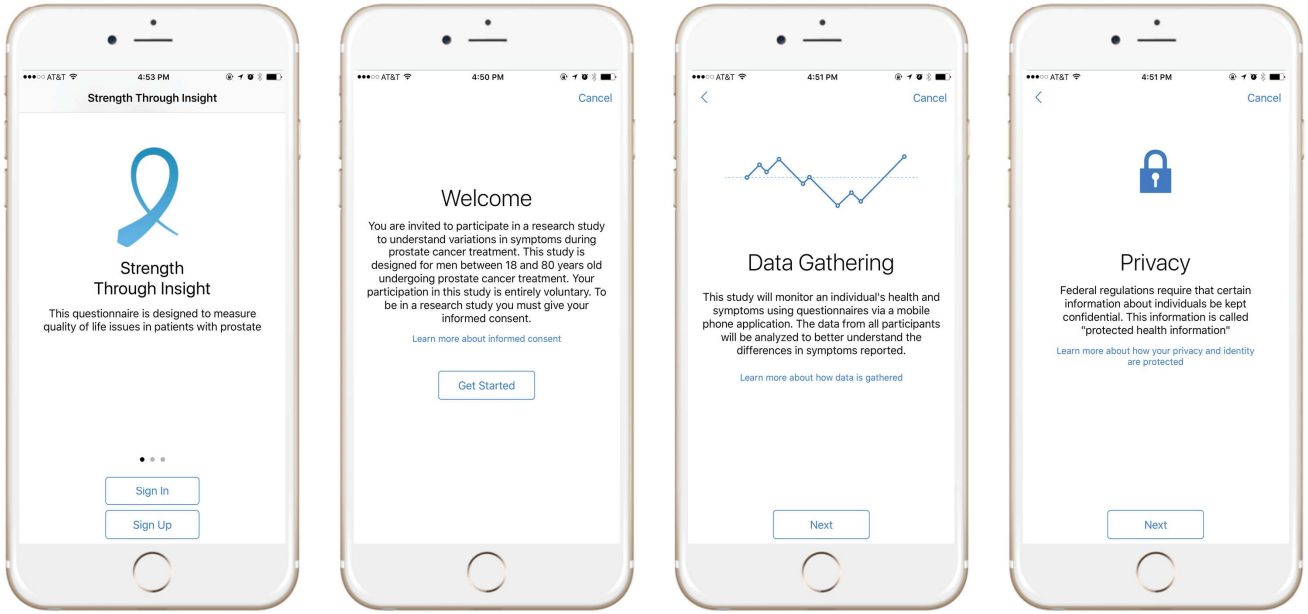


Why Research Kit

- Open source platform.
- Ready to use components for collecting research data. For e.g. questionnaires, iPhone camera, electronic consent process template.
- Ability to promote app in Apple Store and entire Apple ecosystem
- Ability to reach and attract many participants for clinical trials faster compared to traditional cumbersome participant recruiting methods. More participants mean more data points.
- Help create awareness among communities about certain diseases and conditions.
- Use of advanced sensors to collect more precise and real time data for researchers to leverage.

ResearchKit | Jefferson HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

THE APP



ResearchKit

Jefferson
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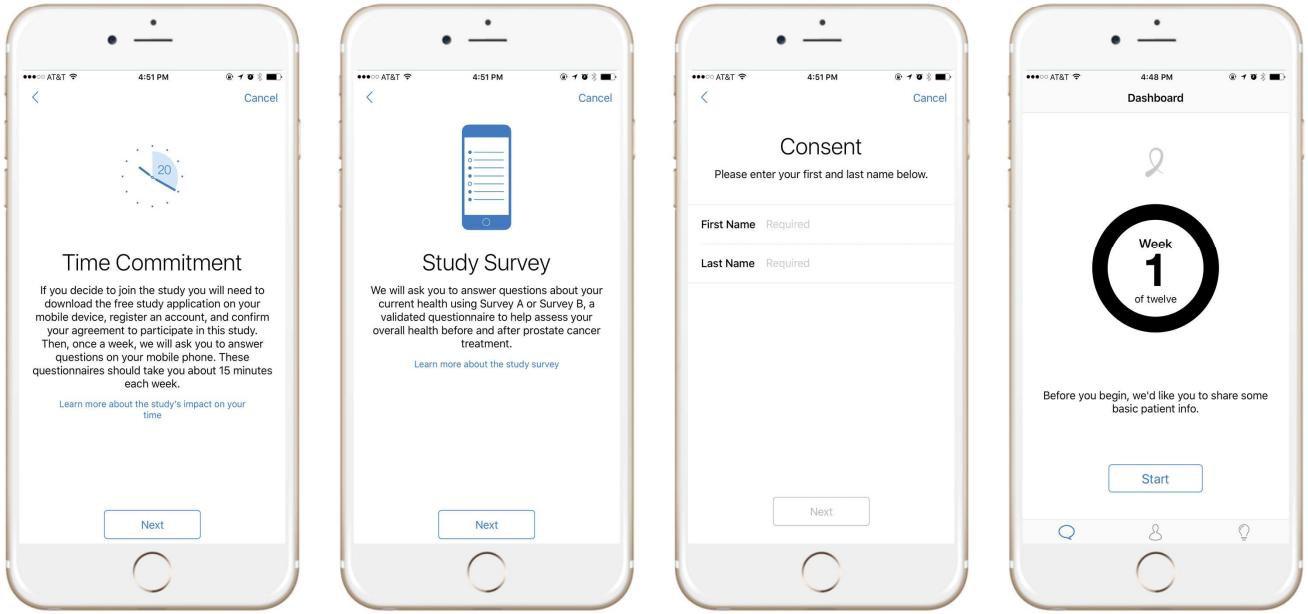
THE APP



ResearchKit

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Sociodemographic and clinical characteristics of the sample	
Characteristics	**No. of Patients (n=29)**
Age (range)	
Race: n (%) Caucasian	
Martial status: n(%) married	
Education: n (%) college grad	
Annual household income: n (%) $40,000 or more	
Diagnosis: n (%)	
Localized Prostate Cancer	X
Advanced Prostate Cancer	X
Digital Health Literacy Level: n (%) High	27

Theme 1

The value of emotional-support and wellness in cancer treatment

"I'd rather an app pay attention to how I'm doing emotionally. Weeks go by and I still end up sleeping the day or weekend away because I'm depressed and tired. I avoided seeing anyone and used symptoms I didn't even have as an excuse."

Theme 2

The rise of online patient communities and networks

"I go on there because I'm interested and want to know more and those are the people I want to talk to. They make me feel like I can take my life back and move on."

Theme 3

Concerns over privacy

"It's hard to trust. We don't have the same type of security on the internet than we do in the real-world. Especially with companies, I don't believe they have my best interest in mind. I don't see my opinion changing."

Theme 4

Personalization for patient engagement

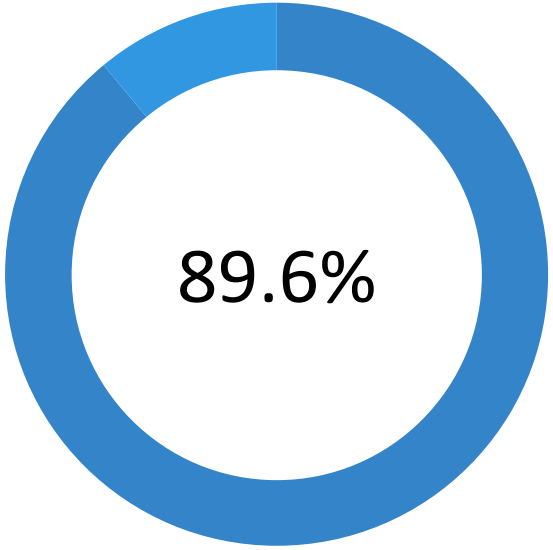
“Without some kind of data analysis, I feel like I’m just the product giving you information, not the consumer.”

Results

A total of 30 patients consented to the study; 1 patient failed to complete any of the questionnaires and was left out of the analysis of the intervention. Out of the remaining 29 participants, , 25 86.2% (one-sided95% CI lower bound 71.2% completed at least 60% of weekly questions over the 12-week period exceeding our pre-specified threshold of 70%. Most participants self-identified with having a high digital literacy level (defined as the ability to use, understand, evaluate, and analyze information from multiple formats from a variety of digital sources) and only a few participants identified with having a low digital literacy level, (defined as only having the ability to gather information on the web).

Thank you!

Quantitative Evaluation: Feasibility (Assessment of Satisfactory Completion)



Notifications

Optional push notification reminder was used by 89.6% of participants (26/29), all of which were participants identified to have localized disease.

- *Of those who opted-in to receive push notifications, most participants reported notifications to fill out weekly surveys as an effective tool as a passive reminder to monitor their health.*