

# Should we screen for precursor conditions

Irene Ghobrial, MD

Lavine Family Chair of Preventative Cancer Therapy

Professor of Medicine

Harvard Medical School

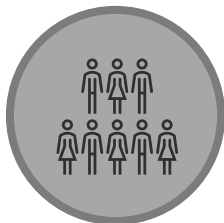
Dana Farber Cancer Institute

Boston, MA

## Conflict of Interest

- IMG is a consultant for Janssen, Pfizer, Sanofi, BMS, Takeda, GSK, Binding Site.

# Early detection and interception saves lives



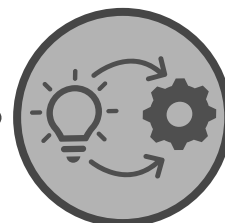
Pre-malignant conditions are very common and affect millions of people



Cancer centers and industry have been focusing largely on improving survival for late-stage cancers



Patients are diagnosed by chance when they have symptoms

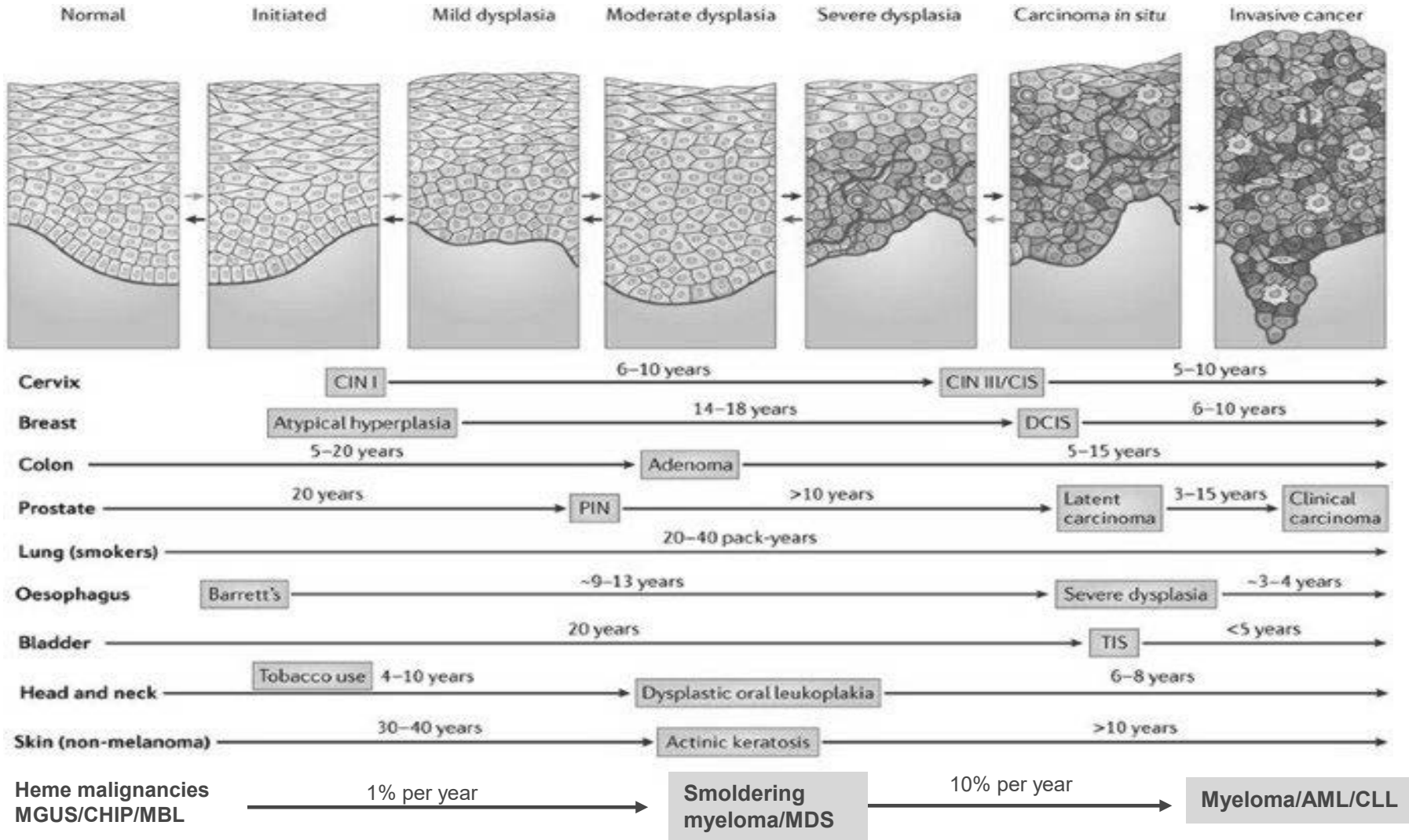


**Early detection** can disrupt cancer diagnosis, care delivery, and survival

**Early intervention** on premalignant precursors can prevent cancer altogether

*We can **change the cancer experience** if we can find it early at a curable stage.*

# The opportunity



nature > outlook > article

OUTLOOK | 18 November 2020

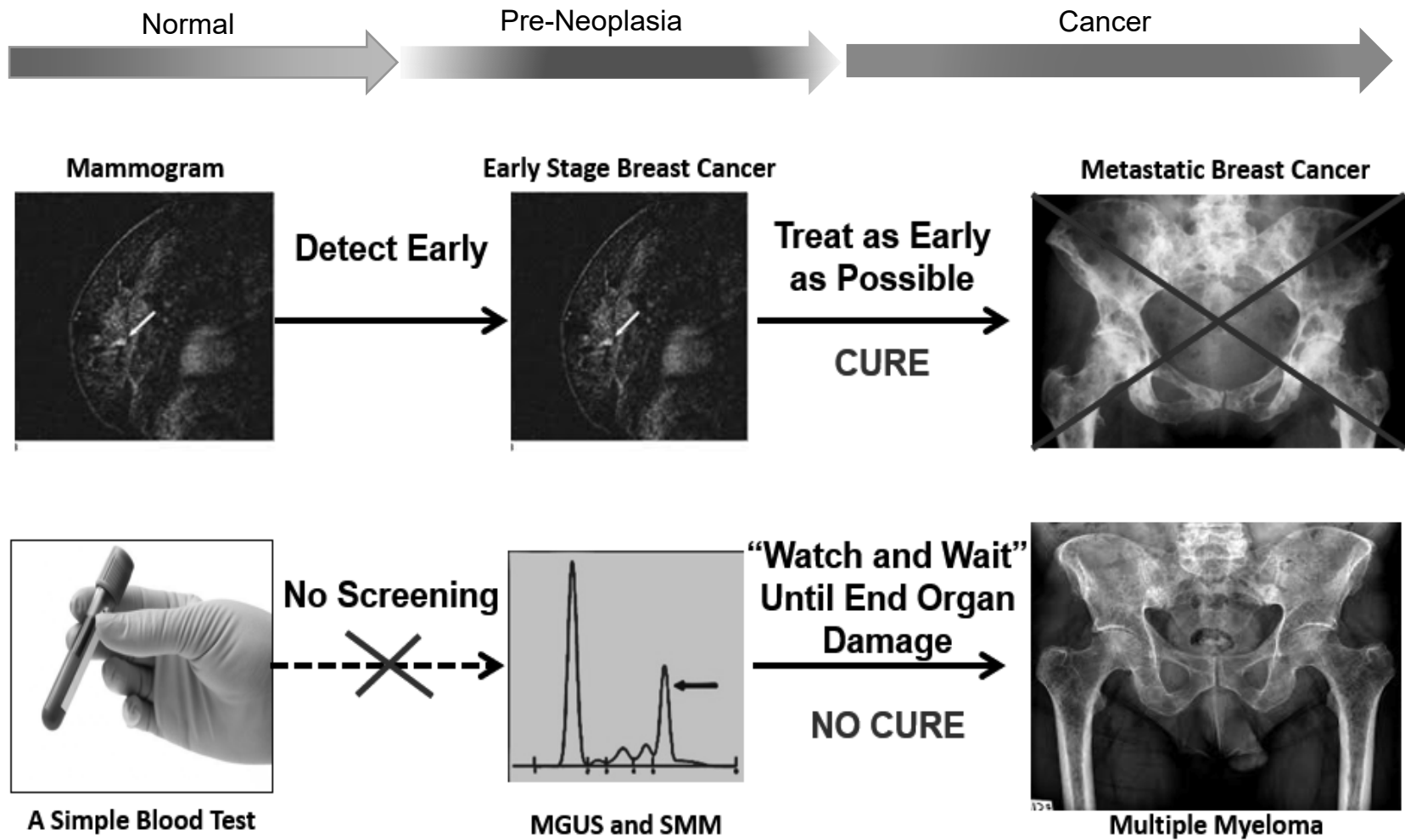
# The screening imperative for multiple myeloma

S. Vincent Rajkumar says there is enough evidence to begin testing, and treating, people at high risk of the disease much earlier.

S. Vincent Rajkumar 



# Cancer screening saves lives



# Early therapeutic interventions prolong survival in SMM

## Lenalidomide plus Dexamethasone for High-Risk Smoldering Multiple Myeloma

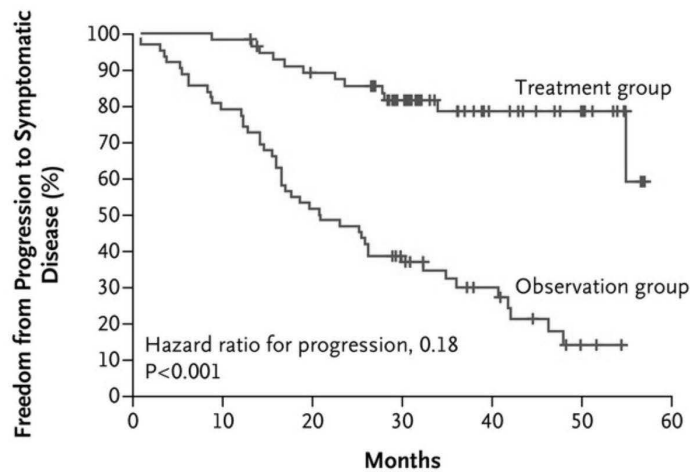
María-Victoria Mateos, M.D., Ph.D., Miguel-Teodoro Hernández, M.D., Pilar Giraldo, M.D., Javier de la Rubia, M.D., Felipe de Arriba, M.D., Ph.D., Lucía López Corral, M.D., Ph.D., Laura Rosiñol, M.D., Ph.D., Bruno Paiva, Ph.D., Luis Palomera, M.D., Ph.D., Joan Bargay, M.D., Albert Oriol, M.D., Felipe Prosper, M.D., Ph.D., Javier López, M.D., Ph.D., do Olavarría, M.D., Ph.D., Nuria Quintana, M.D., José-Luis García, M.D., Joan Bladé, M.D., Ph.D., Juan-José Lahuerta, M.D., Ph.D., and Jesús-F. San Miguel, M.D., Ph.D.

rapid communicator

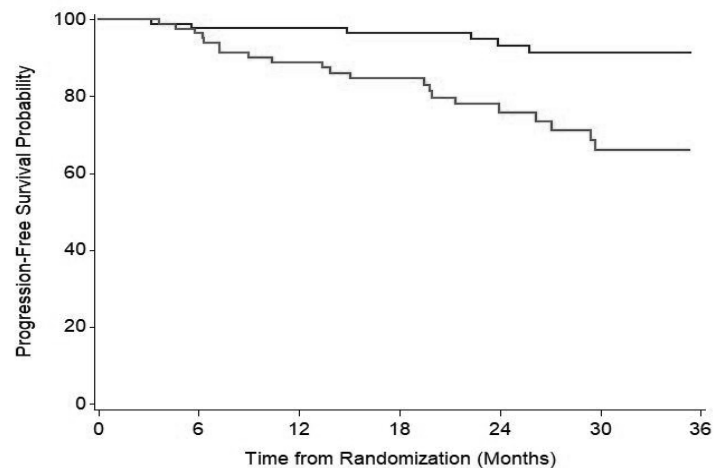
## Randomized Trial of Lenalidomide Versus Observation in Smoldering Multiple Myeloma

Sagar Lonial, MD<sup>1</sup>; Susanna Jacobus, MSc<sup>2</sup>; Rafael Fonseca, MD<sup>3</sup>; Matthias Weiss, MD<sup>4</sup>; Shaji Kumar, MD<sup>5</sup>; Robert Z. Orlowski, MD, PhD<sup>6</sup>; Jonathan L. Kaufman, MD<sup>1</sup>; Abdurraheem M. Yacoub, MD<sup>7</sup>; Francis K. Buadi, MD<sup>8</sup>; Timothy O'Brien, MD<sup>9</sup>; Jeffrey V. Matous, MD<sup>9</sup>; Daniel M. Anderson, MD<sup>10</sup>; Robert V. Emmons, MD<sup>11</sup>; Anuj Mahindra, MD<sup>12</sup>; Lynne I. Wagner, PhD<sup>13</sup>; Madhav V. Dhodapkar, MBBS<sup>1</sup>; and S. Vincent Rajkumar, MD<sup>9</sup>

A

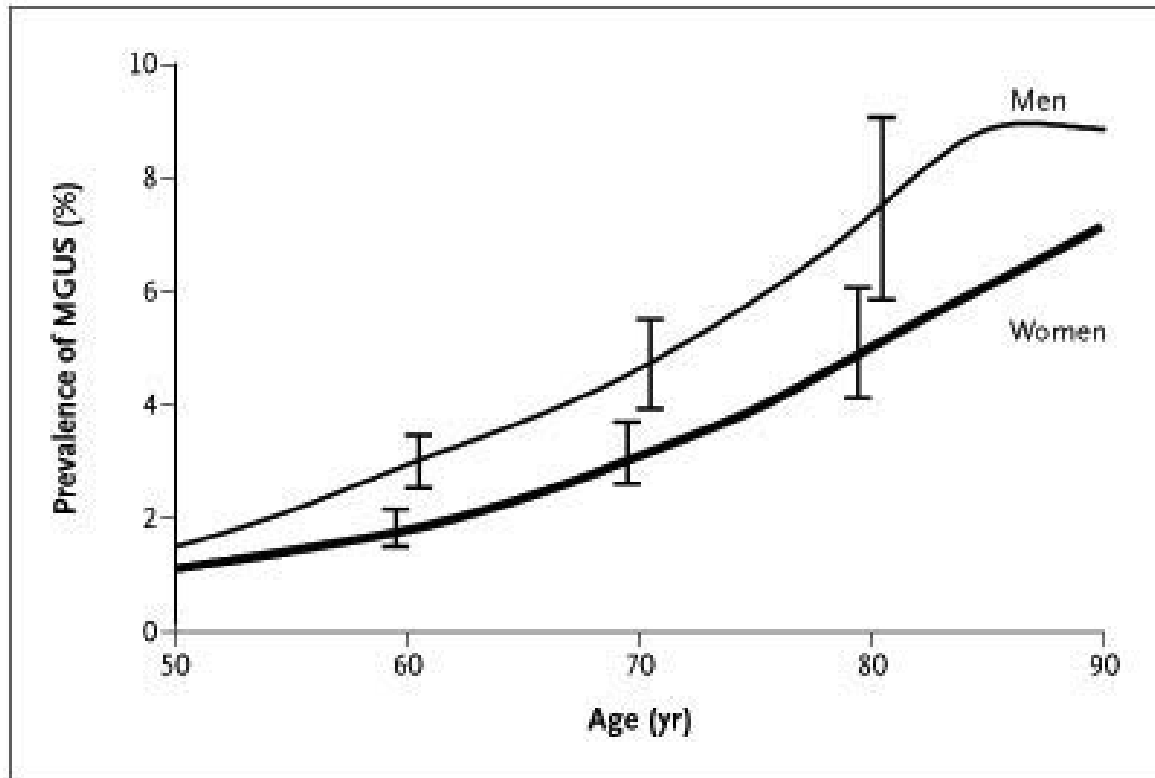


No. at Risk	0	10	20	30	40	50	60
Treatment group	57	57	48	38	20	14	0
Observation group	62	49	32	21	11	3	0



	0	6	12	18	24	30	36
Lenalidomide	90	83	81	72	55	42	35
Observation	92	77	67	56	34	26	19

# The number of people who can be saved by early detection



**3-5% of the general population at age 50 have MGUS**

**This rate is 2-3 times higher for individuals of African descent**

**This rate is 2 times higher for first-degree family members of myeloma patients**

**About 15 million people in the US**

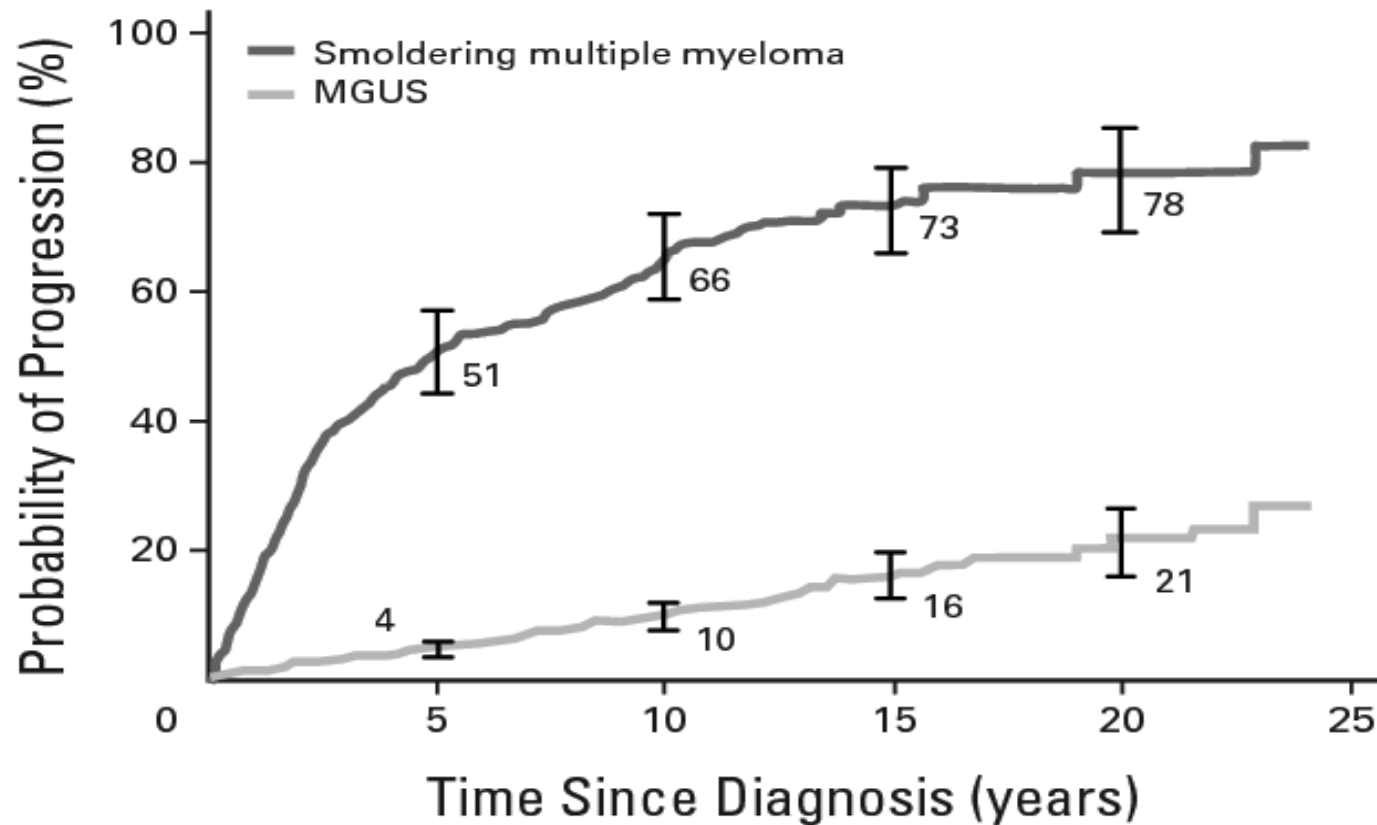
ORIGINAL ARTICLE

## Prevalence of Monoclonal Gammopathy of Undetermined Significance

Robert A. Kyle, M.D., Terry M. Therneau, Ph.D., S. Vincent Rajkumar, M.D., Dirk R. Larson, M.S., Matthew F. Plevak, B.S., Janice R. Offord, B.S., Angela Dispenzieri, M.D., Jerry A. Katzmann, Ph.D., and L. Joseph Melton, III, M.D.



# MGUS and SMM lead to MM



Published in Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2010

**Smoldering (asymptomatic) multiple myeloma: current diagnostic criteria, new predictors of outcome, and follow-up recommendations.**

J. Bladé, M. Dimopoulos, L. Rosiñol, S. V. Rajkumar, R. Kyle

# Efforts of screening for MM






Rögnavaldsson et al. *Blood Cancer Journal* (2021)11:94  
<https://doi.org/10.1038/s41408-021-00480-w>

Blood Cancer Journal

ARTICLE

Open Access

## Iceland screens, treats, or prevents multiple myeloma (iStopMM): a population-based screening study for monoclonal gammopathy of undetermined significance and randomized controlled trial of follow-up strategies

Sæmundur Rögnavaldsson <sup>1</sup>, Thorvardur Jon Love<sup>1</sup>, Sigrun Thorsteinsdottir <sup>1,2</sup>, Elín Ruth Reed<sup>1</sup>, Jón Þórir Óskarsson <sup>1</sup>, Íris Pétursdóttir<sup>1</sup>, Guðrún Ásta Sigurðardóttir<sup>1</sup>, Brynjar Viðarsson<sup>3</sup>, Páll Torfi Öundurason<sup>1,3</sup>, Bjarni A. Agnarsson<sup>1,3</sup>, Margrét Sigurðardóttir<sup>3</sup>, Ingunn Þorsteinsdóttir<sup>3</sup>, Ísleifur Ólafsson<sup>3</sup>, Ásdís Rósa Þórðardóttir<sup>1</sup>, Elías Eypórsson<sup>3</sup>, Ásbjörn Jónsson<sup>3</sup>, Andri S. Björnsson<sup>4</sup>, Gunnar Þór Gunnarsson<sup>1,5</sup>, Runólfur Pálsson<sup>1,3</sup>, Ólafur Skúli Indriðason<sup>1,3</sup>, Gauti Kjartan Gíslason <sup>1</sup>, Andri Ólafsson<sup>1</sup>, Guðlaug Katrín Hákonardóttir<sup>1</sup>, Manje Brinkhuis <sup>1</sup>,

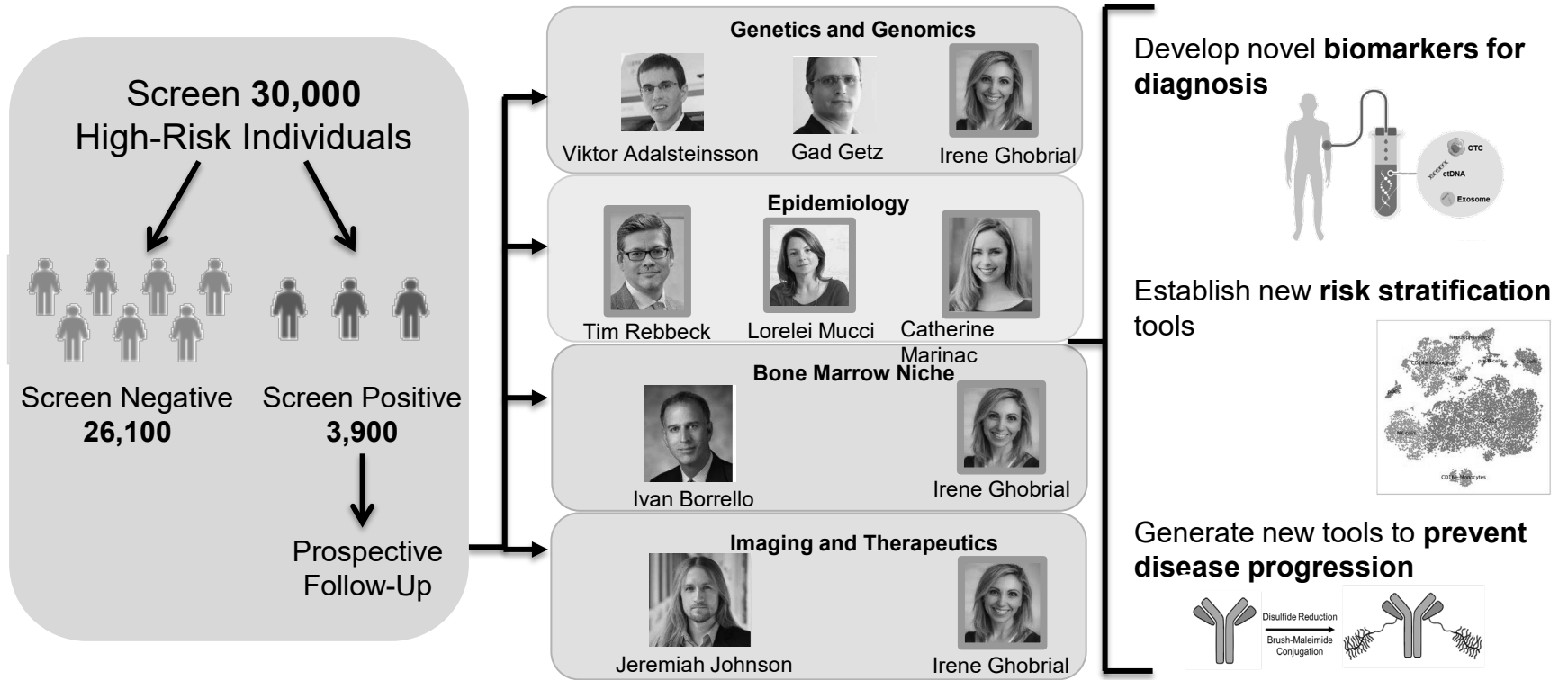
# The PROMISE study



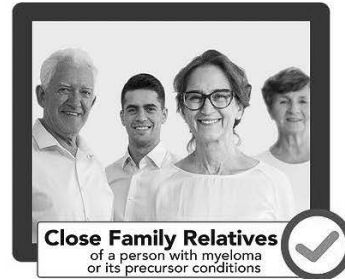
I promise  
to be there  
when he  
becomes a  
champion...

[www.promisestudy.org](http://www.promisestudy.org)

# Nationwide Study of Myeloma Screening and Prevention: PROMISE



# Eligibility Criteria



2 groups of U.S. adults, age 40-75, qualify for a free screening:

**1. African Americans**

AND / OR

**2. People of Any Race Who Have a Parent, Sibling, or Child with:  
Multiple myeloma, another blood cancer, OR one these related  
conditions:**

- Monoclonal Gammopathy of Undetermined Significance (MGUS) ⓘ
- Smoldering Multiple Myeloma ⓘ
- Waldenström Macroglobulinemia ⓘ

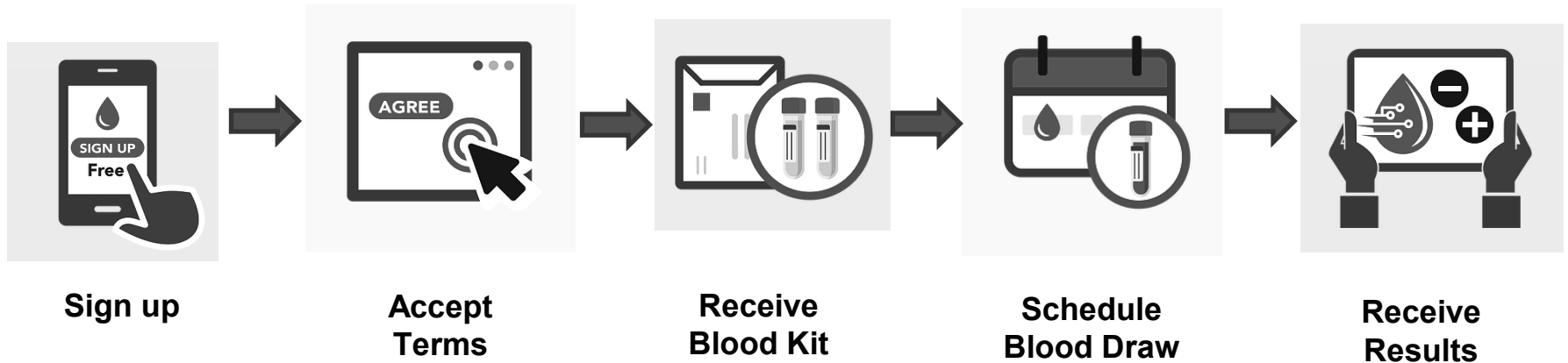
**Please sign up for the study if you qualify.**

**Note:** The PROMISE study is for people who may have higher risks,  
**but have not been diagnosed** with any of these conditions.

**If you have been diagnosed** with one of these conditions, please visit our  
[PCROWD study, a sister project for people with precursor conditions.](#)

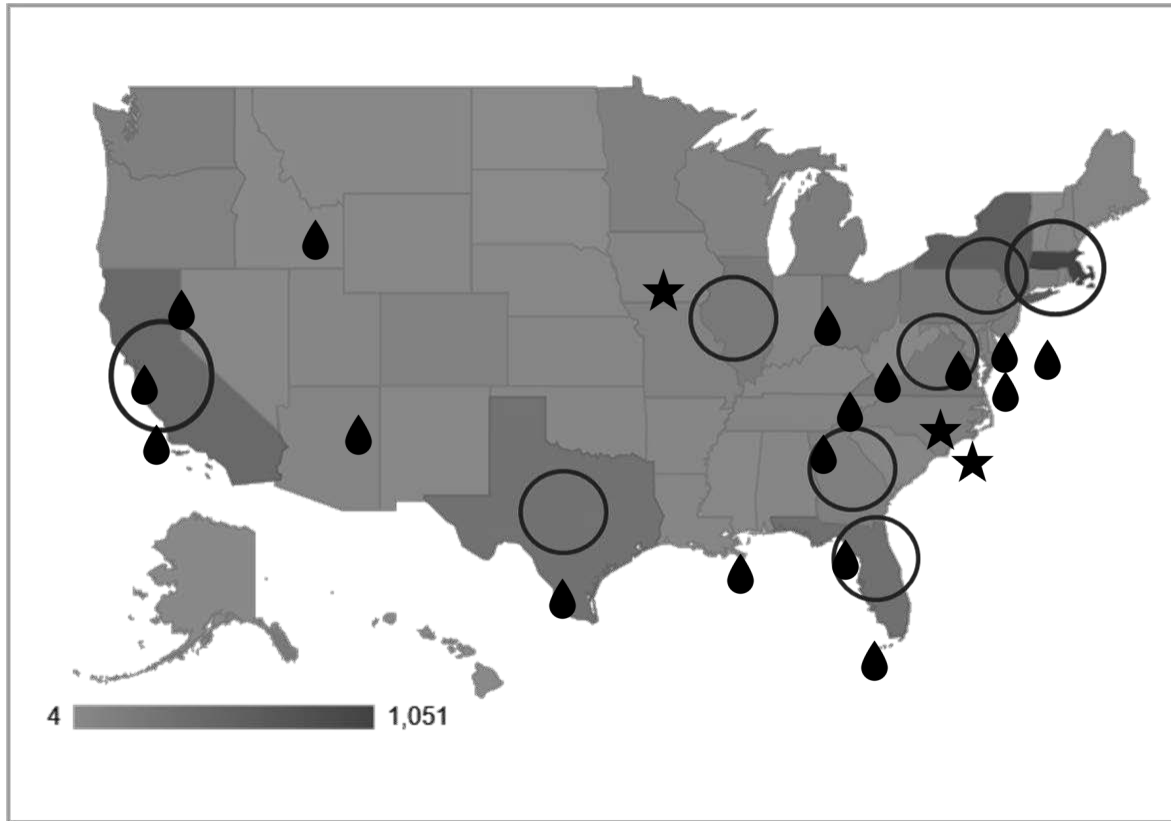
**PCROWD**

# How does the PROMISE screening process work?



# National and International PROMISE

>5600 accrued to date



**South Africa, Kenya, Israel**

# PROMISE partners with the MGB BioBank



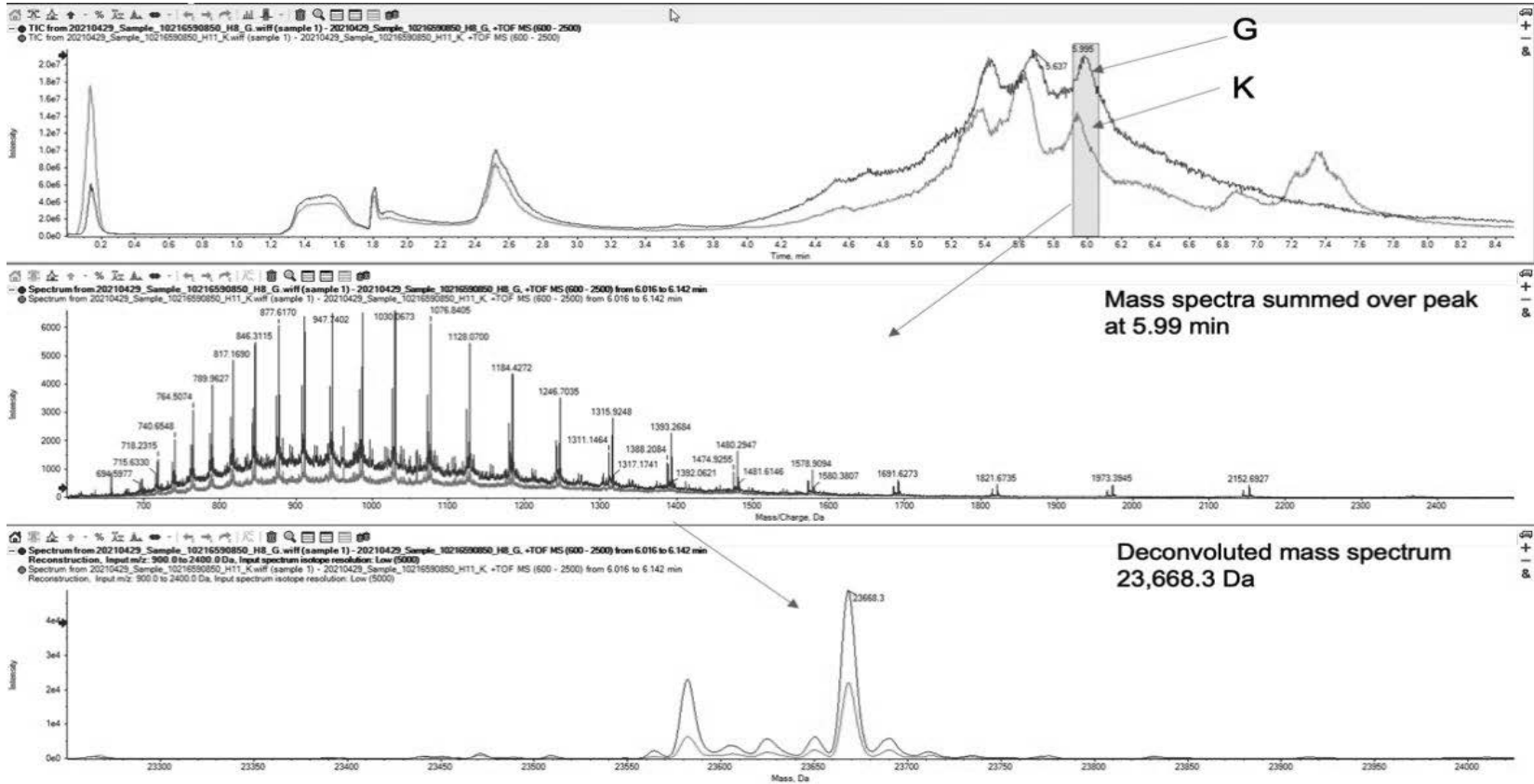
- 123,000 individuals
- 20% non-White
- 50,000 GWAS or exome sequencing data

## **PROMISE inclusion criteria applied to MGB: 4,446 samples into PROMISE**

- **2,373 individuals** self-identify as Black/African American > 30 years
- **1,868 participants** who reported to have a first-degree family relative diagnosed with a hematologic malignancy >30 years to be screened



# MALDI-TOF Mass spec is sensitive and specific



Stacked mass spectra from MALDI-TOF MS and confirmatory LC-MS of monoclonal light chains observed in the heavy chain (blue trace) and the monoclonal light chains observed in the light chain (pink trace) in a sample from a PROMISE study participant.

# No Increase in Cancer Worry after Screening Positive

**Cancer worry** assessed pre- and post-screening using 4-item scale adapted from the Lerman Breast Cancer Worry Scale

We are interested in understanding how often most people think about cancer in their daily lives. Please know that we are **NOT** asking because we think you have or will have cancer. Please answer the following questions to the best of your ability.

46. During the past month, how often have you worried about your chances of developing cancer?

Not at all or rarely       Sometimes       Often       Almost all of the time

47. During the past month, how often have you thought about your own chances of developing cancer?

Not at all or rarely       Sometimes       Often       Almost all of the time

48. During the past month, how often have your thoughts about your chances of getting cancer affected your mood?

Not at all or rarely       Sometimes       Often       Almost all of the time

49. During the past month, how often have your thoughts about your chances of getting cancer affected your ability to perform daily activities?

Not at all or rarely       Sometimes       Often       Almost all of the time

- Cancer worry assessed after receiving a diagnosis of MGUS was not significantly different than cancer worry pre-screening (paired ttest p-value=0.52)

# No Difference in Quality of Life Between Positive and Negative Participants

**Quality of Life** assessed post screening using the RAND 36-item Short Form Health Survey (SF-36)

- No significant differences observed between screen-positive vs screen-negative participants for any of the following sub-scales (all  $p > 0.2$ )
  - Physical functioning
  - Role limitations due to physical health
  - Role limitations due to emotional problems
  - Energy/Fatigue
  - Emotional well-being
  - Social functioning
  - Pain
  - General health

# Argument for screening for myeloma

- ❖ Early therapeutic intervention can improve PFS/prevents CRAB morbidity
- ❖ Early detection of MGUS can help identify those at risk of developing MM
- ❖ Screening of high-risk individuals can show a high prevalence rate >10%
- ❖ Screening is sensitive and specific
- ❖ The cost of yearly follow up is significantly lower than the cost of active therapy of MM with comorbidities (renal failure, fractures, etc)
- ❖ No evidence of increased worry or change in QOL

# A Message from our Promise Participants



[www.promisestudy.org](http://www.promisestudy.org)



# Acknowledgments

