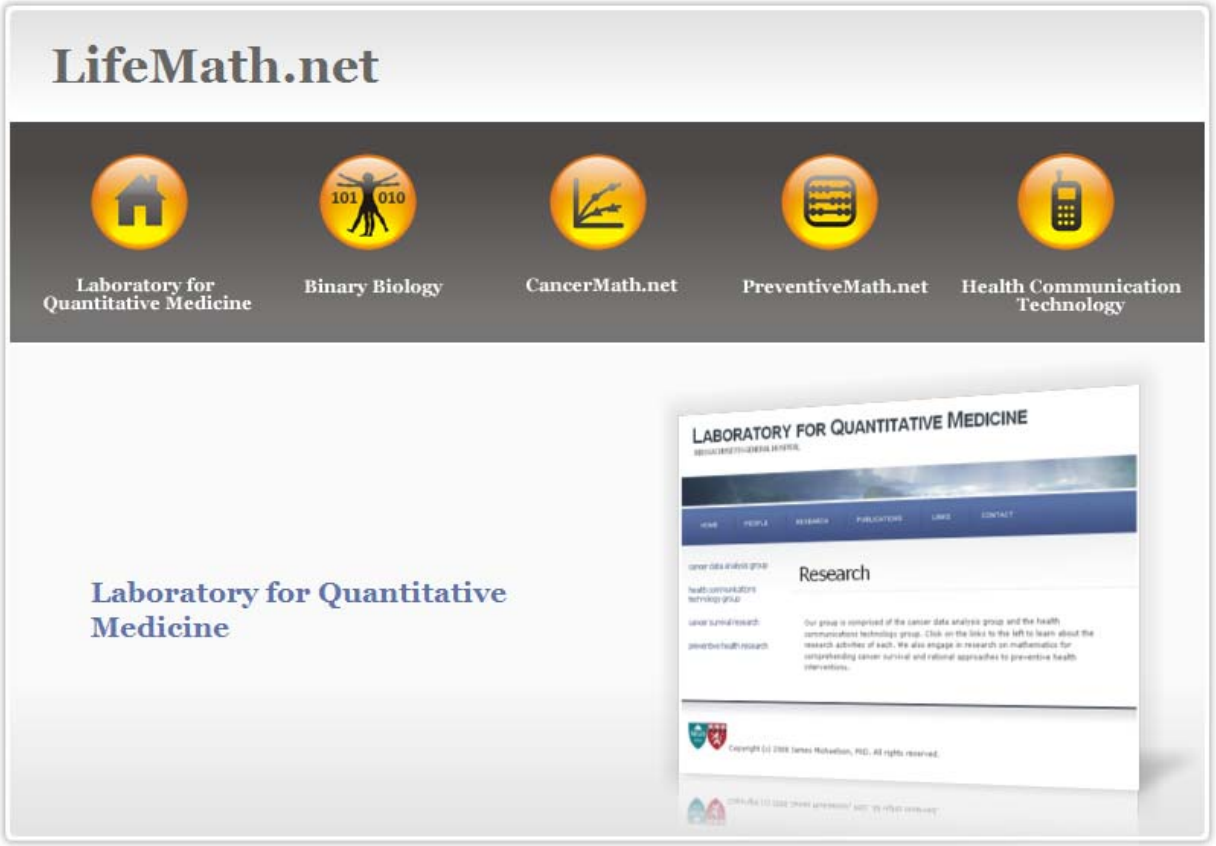
Laboratory for Quantitative Medicine

Massachusetts General Hospital
Harvard Medical School



Laboratory of Quantitative Medicine

Massachusetts General Hospital

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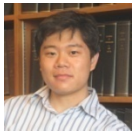
Lab for Quantitative Medicine
Scientific Director

Cancer Math Group



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Brown University

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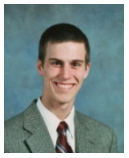

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Health Communication Technology Group

Using modern web-programing, computer speech and telephony to build systems to *recruit*, *remind*, *schedule*, and *track* patients, so as to keep them in good health

Our computer simulation studies (outlined below) told us that:

- Reaching the predicted survival level of 88% by **prompt annual attendance screening from age 40** would be an enormous reduction in breast cancer death in comparison to the current level of breast cancer survival, which is believed to be about 55-70%. Since there are more than 40,000 deaths caused by breast cancers in the USA per year, this translates into **tens-of-thousands of lives that could be saved**.

- **Twice-yearly screening from age 30** might reach breast cancer survival levels of 91%. Because of the approximately 180,000 women are found to have breast cancer in the US each year this translates into more than **5000 extra lives that might be saved** by such a strategy.

Our computer simulation studies (outlined below) told us that:

• Reaching the predicted survival level of 88% by **prompt annual attendance screening from age 40** would be an enormous reduction in breast cancer death in comparison to the current level of breast cancer survival, which is believed to be about 55-70%. Since there are more than 40,000 deaths caused by breast cancers in the USA per year, this translates into **tens-of-thousands of lives that could be saved**.

What is Our Most Powerful Tool For Reducing the Breast Carcinoma Death Rate?

Failure to Adhere to Medical Advice is a Hidden Crisis in Modern Healthcare!!

non-adherence affects many aspects of medicine, as seen in failure of patients to take their medications, missed appointments for cancer screening, hypertension control, diabetes control, immunization, …[fill in for yourself!]

Each year ~36,000 Americans, including ~ 100 children, die of influenza

In 2003, 98 otherwise normal children died of influenza…

… only one of these children had received influenza vaccine

Flu vaccine cost just ~$25, and is usually covered by health insurance, Medicaid and Medicare

Long-term Persistence in Use of Statin Therapy in Elderly Patients

Joshua S. Benner, PharmD, ScD
Robert J. Glynn, PhD, ScD
Helen Mogun, MS
Peter J. Neumann, ScD
Milton C. Weinstein, PhD
Jerry Avorn, MD

Context Knowledge of long-term persistence with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) therapy is limited because previous studies have observed patients for short periods of time, in closely monitored clinical trials, or in other unrepresentative settings.

Objective To describe the patterns and predictors of long-term persistence with statin therapy in an elderly US population.

Design, Setting, and Patients Retrospective cohort study including 34501 enrollees in the New Jersey Medicaid and Pharmaceutical Assistance to the Aged and Disabled programs who were 65 years of age and older, initiated statin treatment between 1990 and 1998, and who were followed up until death, disenrollment, or December 31, 1999.

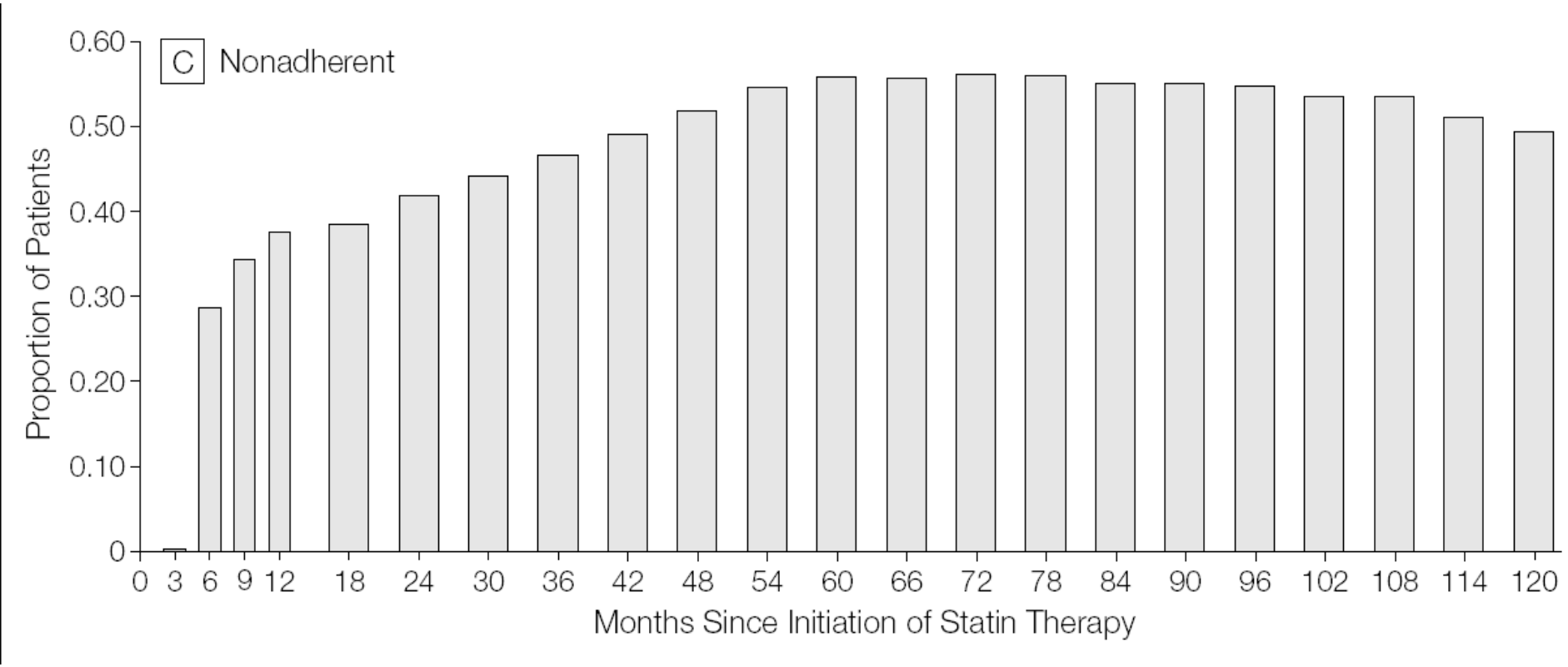
Main Outcome Measures Proportion of days covered (PDC) by a statin in each quarter during the first year of therapy and every 6 months thereafter; predictors of suboptimal persistence during each interval (PDC <80%) were identified using generalized linear models for repeated measures.

Results The mean PDC was 79% in the first 3 months of treatment, 56% in the second quarter, and 42% after 120 months. Only 1 patient in 4 maintained a PDC of at least 80% after 5 years. The proportion of patients with a PDC less than 80% increased in a log-linear manner, comprising 40%, 61%, and 68% of the cohort after 3, 12, and 120 months, respectively. Independent predictors of poor long-term persistence included nonwhite race, lower income, older age, less cardiovascular morbidity at initiation of therapy, depression, dementia, and occurrence of coronary heart disease events after starting treatment. Patients who initiated therapy between 1996-1998 were 21% to 25% more likely to have a PDC of at least 80% than those who started in 1990.

Conclusions Persistence with statin therapy in older patients declines substantially over time, with the greatest drop occurring in the first 6 months of treatment. Despite slightly better persistence among patients who began treatment in recent years, long-term use remains low. Interventions are needed early in treatment and among high-risk groups, including those who experience coronary heart disease events after initiating treatment.

JAMA. 2002;288:455-461 www.jama.com

CARDIOVASCULAR DISEASE ACcounts for 950000 deaths annually in the United States, including 460000 deaths from coronary heart disease (CHD).[1] Eighty-five percent of those who die of CHD and 72% of those who experience a stroke each year are 65 years of age and older.[1] Since 1994, 6 large clinical trials have shown that 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins) significantly reduce the incidence of CHD-related morbidity and mortality and strokes in patients undergoing treatment for an average of 5 years.[2-7] Analyses suggest that the benefits of statin treatment in patients 65 years of age and older are quite similar to those seen in younger patients.[7-10] The recent National Cholesterol Education Pro-


C Nonadherent
Proportion of Patients
0.60
0.50
0.40
0.30
0.20
0.10
0
0 3 6 9 12 18 24 30 36 42 48 54 60 66 72 78 84 90 96 102 108 114 120
Months Since Initiation of Statin Therapy

Nonadherence to Adjuvant Tamoxifen Therapy in Women With Primary Breast Cancer

By Ann H. Partridge, Philip S. Wang, Eric P. Winer, and Jerry Avorn

Purpose: **Although clinical trials have clearly demonstrated the benefits of tamoxifen in women with primary breast cancer, little is known about how this drug is actually used in the general population. We sought to estimate adherence and predictors of nonadherence in women starting tamoxifen as adjuvant breast cancer therapy.**

Patients and Methods: **Subjects were age 18 years or older initiating tamoxifen for primary breast cancer and enrolled in New Jersey's Medicaid or Pharmaceutical Assistance to the Aged and Disabled programs during the study period, from 1990 to 1996 (N = 2,378). Main outcome measures were number of days covered by filled prescriptions for tamoxifen in the first year of therapy with the 4 years after tamoxifen initiation for a subset; predictors of good versus poor adherence.**

Results: **Twenty-three percent of patients missed taking tamoxifen on more than one fifth of days studied, although on average, patients filled prescriptions for tamoxifen for 87% of their first year of treatment. The youngest, oldest, nonwhite, and mastectomy patients had significantly lower rates of adherence; patients who had seen an oncologist before taking tamoxifen had significantly higher rates of adherence. Overall adherence decreased to 50% by year 4 of therapy.**

Conclusion: **The mean level of adherence to tamoxifen is high compared with other chronic medications. However, nearly one fourth of patients may be at risk for inadequate clinical response because of poor adherence. Because of the efficacy of tamoxifen therapy in preventing recurrence and death in women with early-stage breast cancer, further efforts are necessary to identify and prevent suboptimal adherence.**

J Clin Oncol 21:602-606.

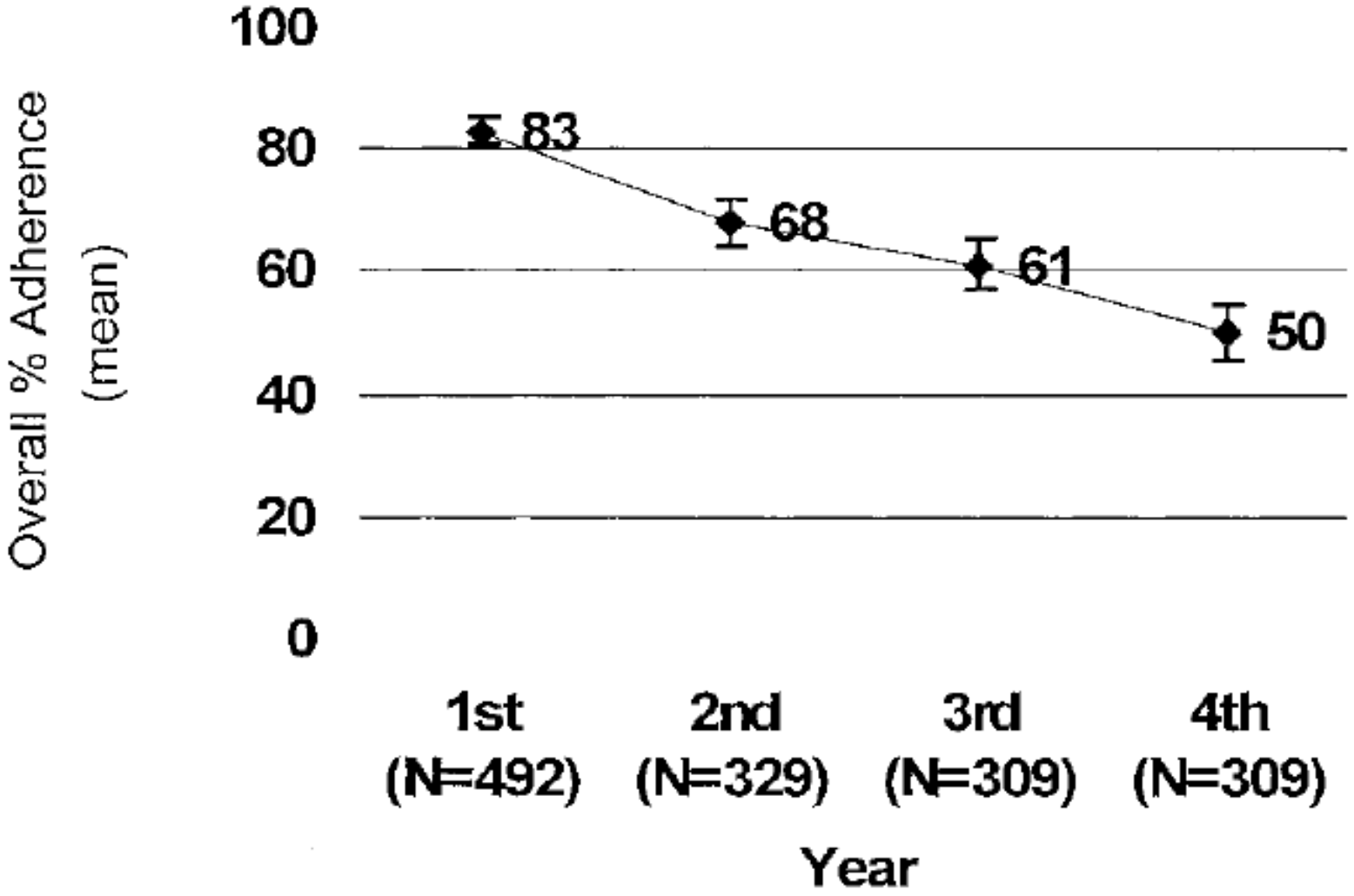


Fig 1. Long-term adherence to adjuvant tamoxifen therapy in eligible patients from 1991 index year cohort.

approximately half said that they sometimes forgot (94 of 193; 48.7%) or deliberately omitted (25 of 191; 13.1%) taking their tablets

Forgetting is an unappreciated cause of non-adherence

Which can sometimes be ameliorated by simple reminding

Reminding Patients Helps Them Adhere!

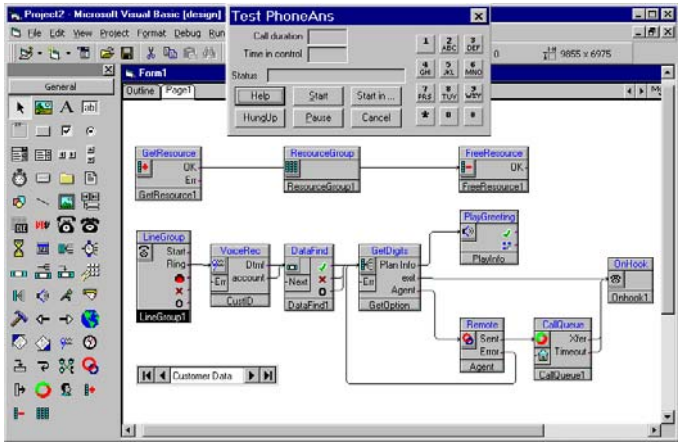
An intervention study to enhance medication compliance in community-dwelling elderly individuals.

Fulmer TT, Feldman PH, Kim TS, Carty B, Beers M, Molina M, Putnam M.

J Gerontol Nurs. 1999 Aug;25(8):6-14.

OBJECTIVE: To determine whether daily videotelephone or regular telephone reminders would increase the proportion of prescribed cardiac medications taken in a sample of elderly individuals who have congestive heart failure (CHF). METHODS: The authors recruited community-dwelling individuals age 65 and older who had the primary or secondary diagnosis of CHF into a randomized controlled trial of reminder calls designed to enhance medication compliance. There were three arms: a control group that received usual care; ***a group that received regular daily telephone call reminders***; and a group that received daily videotelephone call reminders. Compliance was defined as the percent of therapeutic coverage as recorded by Medication Event Monitoring System (MEMS) caps. Subjects were recruited from 2 sources: a large urban home health care agency and a large urban ambulatory clinic of a major teaching hospital. Baseline and post-intervention MOS 36-Item Short-Form Health Survey (SF-36) scores and Minnesota Living with Heart Failure (MLHF) scores were obtained. RESULTS: There was a significant time effect during the course of the study from baseline to post-intervention ($F[2,34] = 4.08$, $p < .05$). Over time ***the elderly individuals who were called, either by telephone or videotelephone, showed enhanced medication compliance relative to the control group***. There was a trend, but no significant difference between the two intervention groups. Both SF-36 and MLHF scores improved from baseline to post-intervention for all groups. There was no significant change in the SF-36 scores for the sample, but there was a significant change for the MLHF scores ($p < .001$). The control group had a significant fall off in the medication compliance rate during the course of the study, dropping from 81% to 57%. CONCLUSIONS: ***Telephone interventions are effective in enhancing medication compliance*** and may prove more cost effective than clinic visits or preparation of pre-poured pill boxes in the home. Technologic advances which enable clinicians to monitor and enhance patient medication compliance may reduce costly and distressing hospitalization for elderly individuals with CHF.

However, there is a cheap, easy, technological fix, in automated computer generated telephone reminder messages.



Computer Software System for Automatically Making Telephone Calls and Leaving Messages

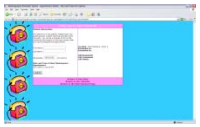
Medicine is Fragmented

Physician

Patient

Pharmacist

A Reminder System Can De-Fragment



Physician

Patient

Refill
Call-In
System

Pharmacist

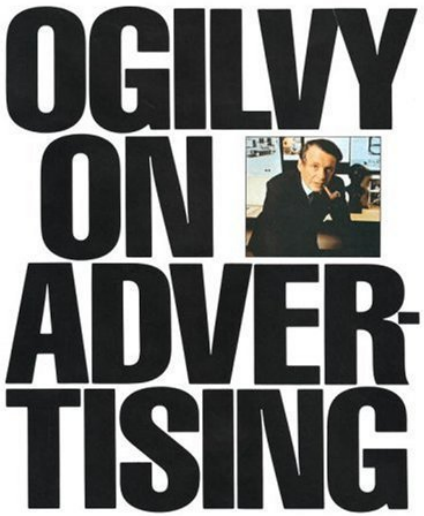
When Done Right, People LIKE Computer Speech

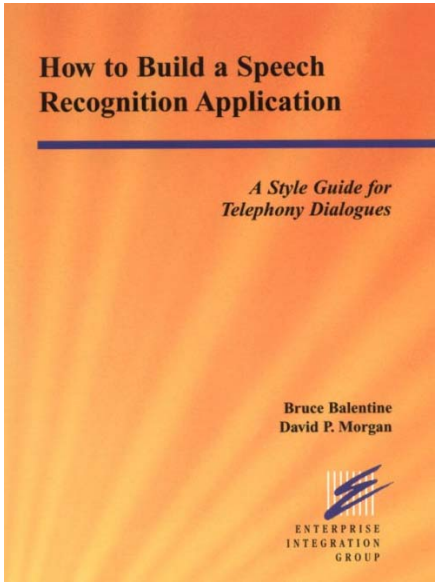
1. The reminder system creates a RELATIONSHIP between the patient and the system. A major goal is to make this a relationship that the patient LIKES, WANTS, and RESPONDS TO FAVORABLY. This means perfecting the personality and human-factors aspect of the reminder voice and message.
2. Why not let the system become a helpful friend to the patient:
    a. Allow the patient's other medications to be included
    b. Allow the patient to use the system for any other reminder that she wishes
3. Adapt the system to providing the patient with other helpful medical information
4. Create reminder systems for other medications
5. Re-engineer the cell phone to tighten the link between the cell phone and the pill

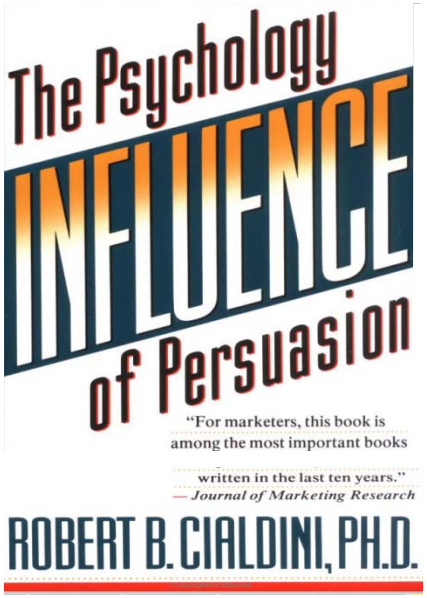
IBM Health Monitor

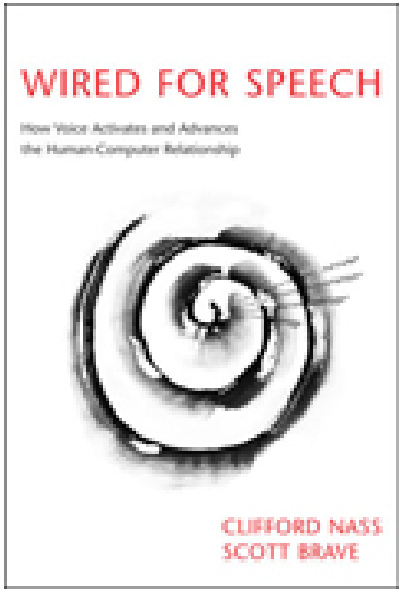
Novel mobile health monitoring devices such as the blood pressure cuff (left) and pill boxes (right) send data to the mobile phone via Bluetooth. The mobile hub software integrated into the mobile phone (center) forwards the data to a care center for monitoring (screen in the back) and returns reminders or alarms in an emergency. A Mark of Fitness MF-77 blood pressure monitor and Bang & Olufsen IDAS II patient compliance device, both modified by IBM Engineering & Technology Services to operate with Bluetooth, along with the Sony Ericsson P900 cell phone serving as the communications hub, are running software developed by IBM Research. The patient measurements are viewed in real time via a standard Web browser, are running here on an IBM Thinkpad laptop computer.

There is a Science to Persuasion









Mammography Illustrates Many of the Principles of Medical Non-Adherence

A decade of study of screening mammography has taught us:

- Annual screening saves lives (~90% survival),
- Most women begin at age 40, but then don’t come back on time.
- This cuts the life-sparing effect of mammography in half.

- Only 6% of the women with a mammogram in 1992 utilized all 10 mammograms possible over the next ten years.
- The median number of mammograms over the 10-year period utilized was 5.06 (51% of the ACS recommendation).
- By computer simulation, this underutilization should lead to a 50% higher level of breast cancer death.
- 1-in-4 women never come back.
- 26% of the women who make an appointment for a mammogram forget to show up
- Women from traditionally-underserved socio-economic, racial and ethnic groups, and women who did not speak English, had lower levels of usage, as did women attending their first mammogram or who had not previously returned promptly for screening.
- However, all sub-populations of women sorted by age, race, ethnicity, zip code, income, previous screening use, or medical history fail to return promptly for annual screening exams.

The Main Psychological Mechanism for Missing Appointments is Simple Forgetting.

More than 100 studies have shown that ordinary reminders (especially telephone reminders) will improve the use of breast cancer screening.

Why is prompt return to screening so poor?

Sending reminders to make, and then attend, mammography exams is a thankless, expensive, time-consuming, and tedious task.

Why is prompt return to screening so poor?

Sending reminders to make, and then attend, mammography exams is a thankless, expensive, time-consuming, and tedious task.

- Screening centers make their calls is the afternoon, but many women are not home till evening.
- Few screening centers have callers who speak Spanish, Chinese, and other languages in common use.
- There are no systems for sending reminders to women who have not yet made appointments, nor to women who have missed their appointments.

To solve this problem, we have developed:

An Integrated Reminder/Tracking System, for Minimizing Delay in the Diagnosis and Treatment of Breast Cancer

The system sends computer generated telephone reminder messages to women to encourage prompt attendance at annual screening visits,

and web forms to aid physicians in tracking patients with breast symptoms.

The reminder/tracking system is on a server *outside* of an individual hospital, so that it can follow a woman wherever she seeks medical care.

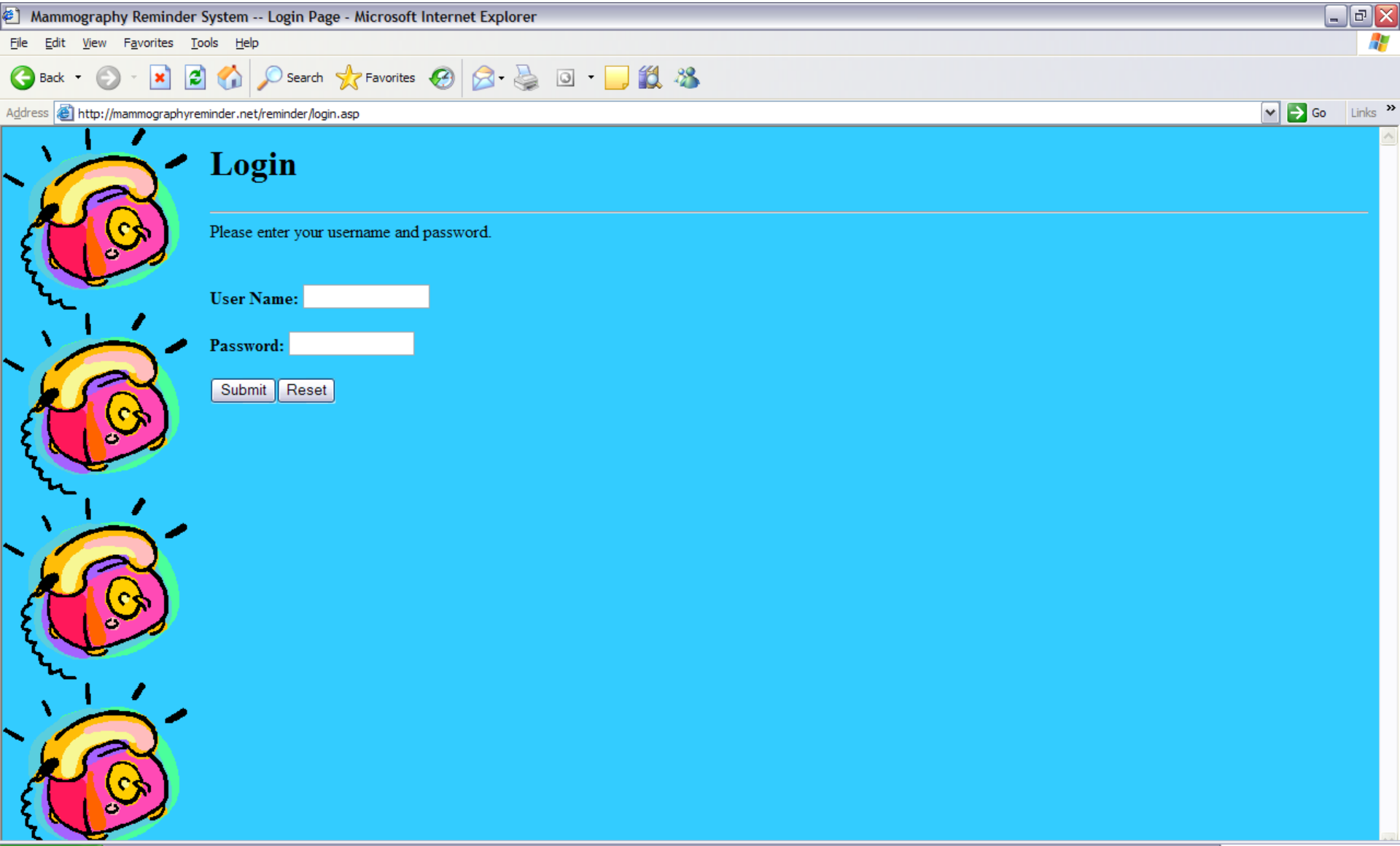
The reminder/tracking system is on a server *outside* of an individual hospital, but it will still be fully secure and HIPAA compliant.

The reminder/tracking system is on a Server *Outside* of an individual hospital, so that it can be accessed through the web, or through computer telephony, from anywhere

Let’s take a look at the system.

It’s now fully functional, capable of sending computer generated reminders to women who have made appointments for screening mammograms.

Any screening center or physician's office who has been given logon privileges and a password can use the system: all that's needed is access to the Internet.



A calendar provides a convenient tool for entering an upcoming appointment and its corresponding computer generated telephone reminder. (*Data can also be entered in bulk, if available electronically*.)

Calendar - May 2005 - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites

Address http://mammographyreminder.net/reminder/calendar/calendar.asp Go Links

« Prev | May 2005 | Next »

Sun.	Mon.	Tue.	Wed.	Thu.	Fri.	Sat.
1 **0** of 6 appts scheduled	2 **1** of 38 appts scheduled	3 **0** of 38 appts scheduled	4 **0** of 38 appts scheduled	5 **1** of 6 appts scheduled **Check patients in**	6 **0** of 38 appts scheduled	7 **0** of 6 appts scheduled
8 **0** of 6 appts scheduled	9 **0** of 38 appts scheduled	10 **0** of 38 appts scheduled	11 **6** of 38 appts scheduled	12 **0** of 6 appts scheduled	13 **0** of 38 appts scheduled	14 **0** of 6 appts scheduled
15 **0** of 6 appts scheduled	16 **0** of 38 appts scheduled	17 **0** of 38 appts scheduled	18 **0** of 38 appts scheduled	19 **0** of 6 appts scheduled	20 **1** of 38 appts scheduled	21 **0** of 6 appts scheduled
22 **0** of 6 appts scheduled	23 **0** of 38 appts scheduled	24 **0** of 38 appts scheduled	25 **0** of 38 appts scheduled	26 **1** of 6 appts scheduled	27 **1** of 38 appts scheduled	28 **0** of 6 appts scheduled
29 **0** of 6 appts scheduled	30 **0** of 38 appts scheduled	31 **0** of 38 appts scheduled				

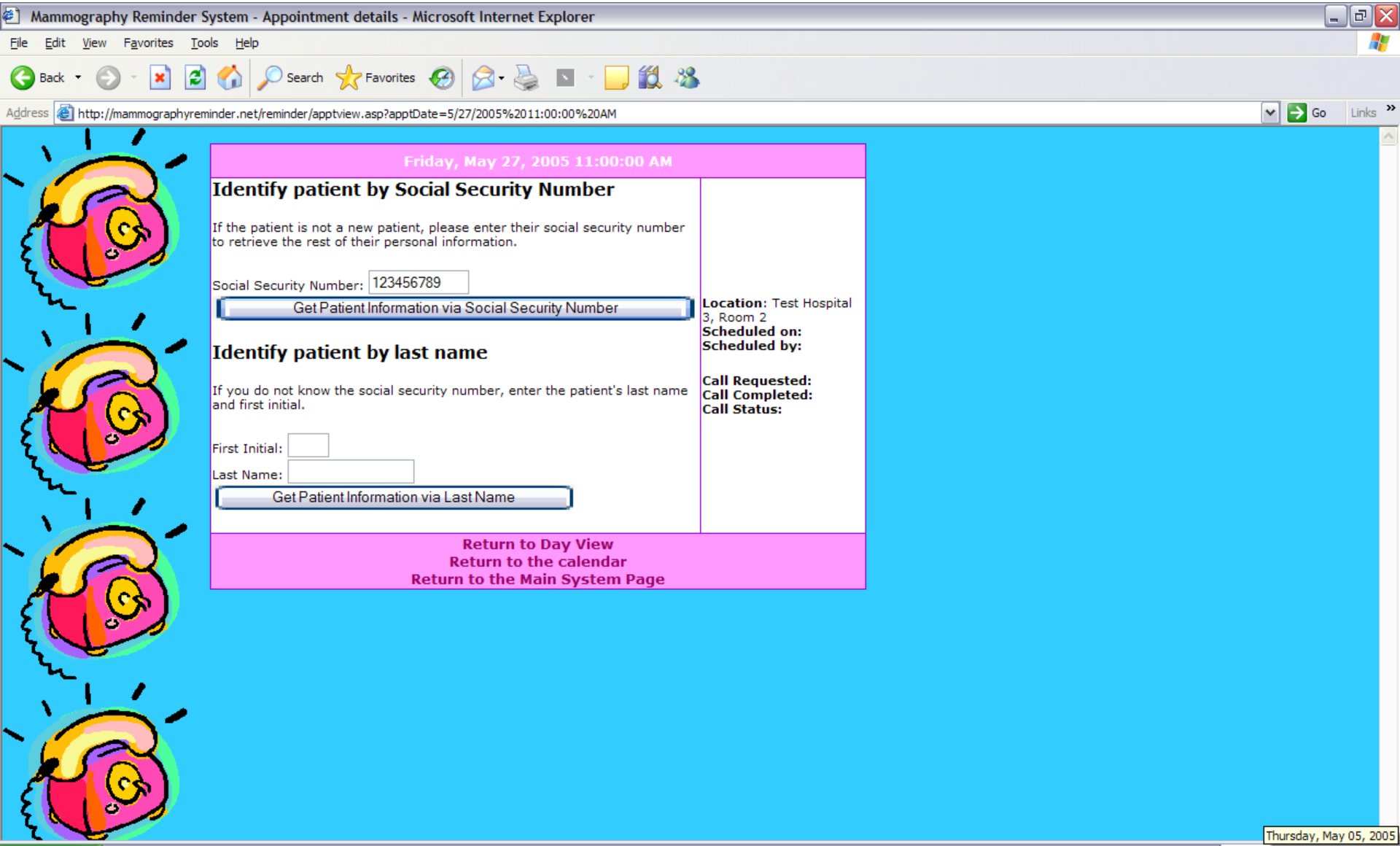
Color Key

See previous or next month	Today	Appointments Available	Appointments all booked up	No Appointments

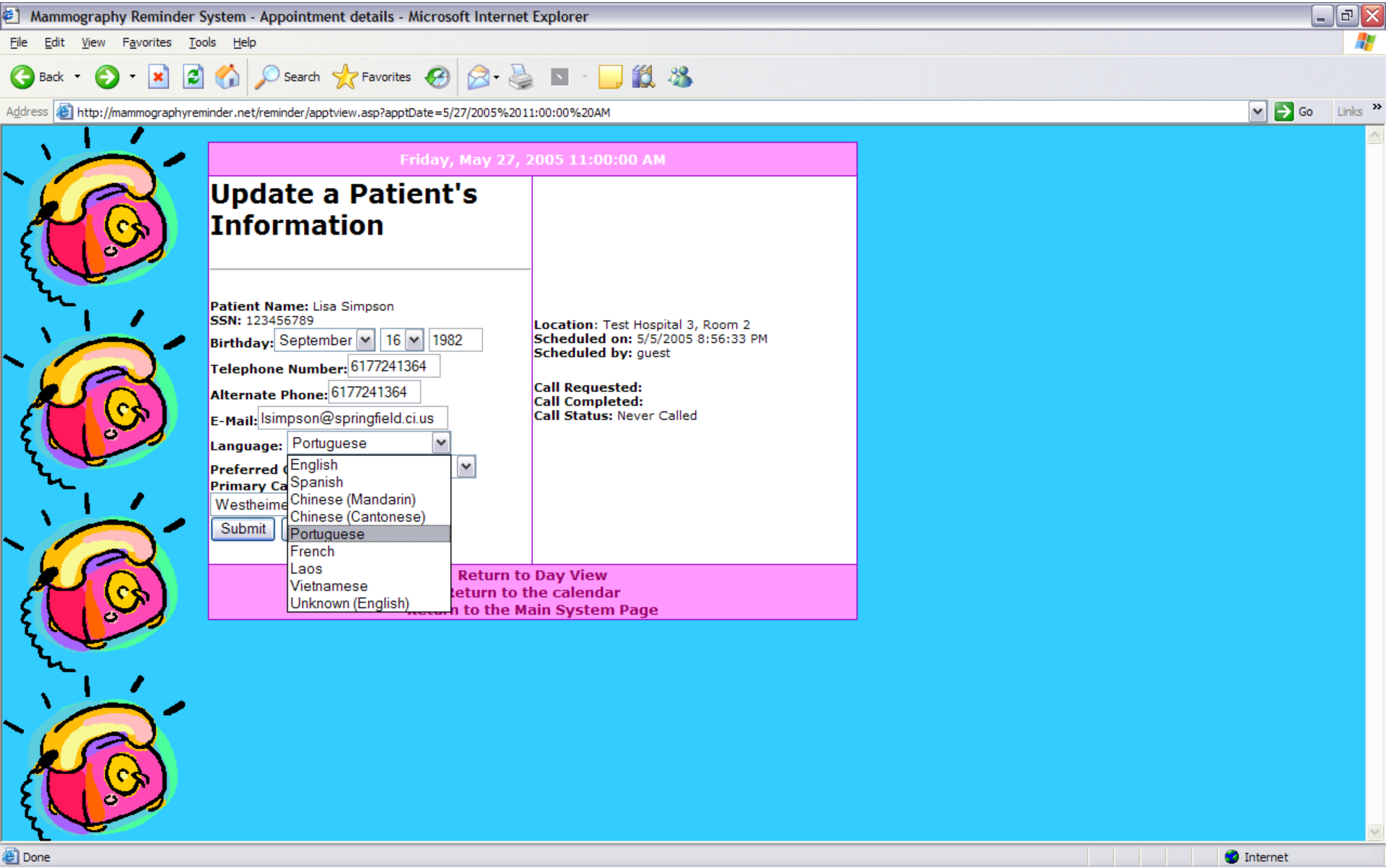
Return to the main system page

Done Internet

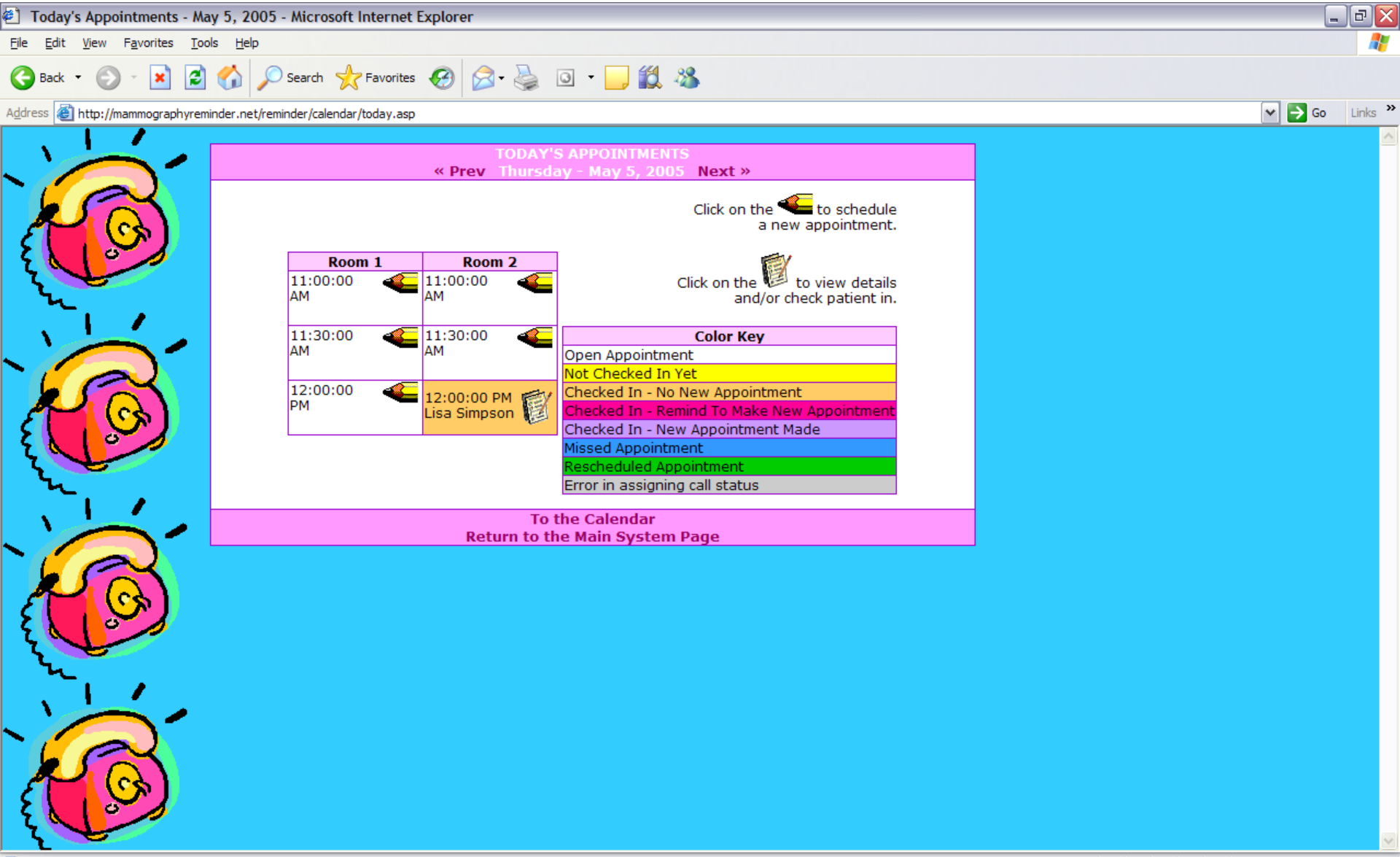
If the patient is already in the system, all you need is the social security number or first/last name.



We can send her the telephone message in any language she wishes, at any time she wishes.



When she finally comes in for this year's screening exam, it's easy to initiate the reminder for the next year's screening visit.



A scheduler initiates the telephone reminder at any desired time previous to the appointment.

Here's the script designed for the Massachusetts General Hospital Breast Imaging Center. It is now operational.

The Massachusetts General Hospital is calling with a medical appointment reminder for Ms [first name] [last name]. If this is your name, please press "1" now. Otherwise, press "2".

Nothing pressed – wait 3 seconds: This is an automated message from the Massachusetts General Hospital calling with a medical appointment reminder for Ms. [first name] [last name]. To confirm the time and day of your upcoming appointment, you may call 617-726-0985 from 9 AM to 5 PM. Thank you. Goodbye.

2 (or other key) pressed: *This is a private medical appointment reminder. Please tell Ms. [first name] [last name] that the Massachusetts General Hospital called. If Ms. [first name] [last name] wishes to confirm the date and time of her upcoming appointment, she may call 617-726-0985 from 9 AM to 5 PM. To repeat this telephone number, please press "1" now.*

If 1 is pressed: [Repeat italicized chunk of paragraph above]

If any other key is pressed or 3 seconds passes: Goodbye. [hangup]

1 pressed: I am calling to provide you with a medical appointment reminder. To insure your confidentiality, so that only you may receive this reminder, *please enter the month and day of your birthday, in numbers, followed by the pound sign. For example, if your birthday is February 14th, please press zero two one four followed by the pound key.*

Incorrect birthday (first time): I'm sorry, but that's not correct. [Repeat italicized chunk of paragraph above].

Incorrect birthday (second time): *This is a private medical appointment reminder. Please tell Ms. [first name] [last name] that the Massachusetts General Hospital called. If Ms. [first name] [last name] wishes to confirm the date and time of her upcoming appointment, she may call 617-726-0985 from 9 AM to 5 PM. To repeat this telephone number, please press "1" now.*

If 1 is pressed: [Repeat italicized chunk of paragraph above]

If any other key is pressed or 3 seconds passes: Goodbye. [hangup]

Correct birthday entered: *Thank you. Please remember that you have an appointment for your annual mammogram on [day of week] [month] [day] at [hour][minute][AM/PM]. If you have any questions, feel free to call the center at 617-726-0985 between 9 AM and 5 PM.* If you'd like to receive another telephone reminder the day before the appointment, please press 1 now, otherwise, press 2.

{If 1, any key other than 2, or nothing is pressed, set "repeat reminder" to true. If 2 is pressed, set "repeat reminder" to false. Then continue.}

To hear the date and time of your appointment again, please press 1. As you may know, the Avon Center not only provides breast cancer screening to large numbers of women, but also carries out research to improve women's health. If you would like to learn about participating in one of these studies, please press 2 and we will contact you with details. If you need directions to the center or instructions as to how to prepare for the mammogram, please press 3 now. To hear this message again, please press 4. To conclude and hang up, please press 5.

1 pressed: [Repeat italicized chunk of paragraph above *(This would be the entire paragraph, minus the section about receiving another appointment reminder)*.]

2 pressed: Thank you for your interest in being contacted about a research study. We shall be calling you in a few days. If you would like us to call you on a weekday, please press 1. If you would like us to call you on a weekend, please press 2.

1 or 2 pressed: Thank you. [Repeat the "menu" section of the previous paragraph (second italicized chunk that starts "To hear the date and time of your appointment…")]

Other or no key pressed: [Repeat the "menu" section of the previous paragraph (second italicized chunk that starts "To hear the date and time of your appointment…")]

3 pressed: The MGH Breast Imaging Division is located on the Second Floor of the Wang Building at the Massachusetts General Hospital, Blossom Street, Boston, Massachusetts. Please arrive 10 minutes early to the Avon Center and do not apply any deodorants, lotions, or powders to your skin that day. [Repeat the "menu" section of the previous paragraph (second italicized chunk that starts "To hear the date and time of your appointment…")]

4 pressed: [Repeat the "menu" section of the previous paragraph (second italicized chunk that starts "To hear the date and time of your appointment…")]

5, other, or no key pressed: Goodbye. [hangup]

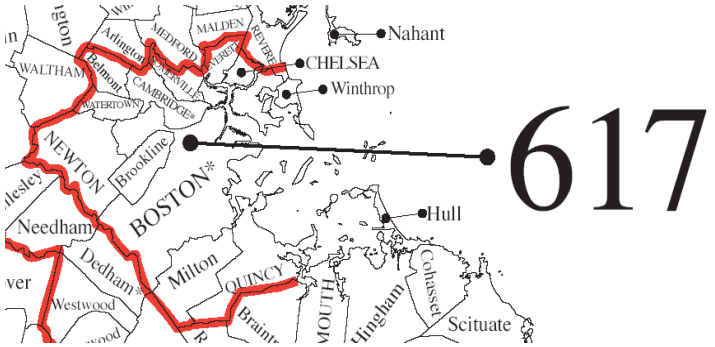
A scheduler initiates the telephone reminder at any desired time previous to the appointment.

The telephone reminder is a hosted service:
The screening center needs
no special telephone equipment.

We Are Funded by the Komen Foundation To Provide Mammography Reminders to All Women in Massachusetts, and Test Their Impact on Screening Use

TABLE: Features of the population in the greater Boston (617 area code) region

City	Population	% of Massachusetts Populatio
Boston	589,141	9.3%
Winthrop	18,303	0.3%
Chelsea	34,106	0.5%
Brookline	57,107	0.9%
Newton	84,323	1.3%
Milton	26,062	0.4%
Quincy	89,059	1.4%
Somerville	76,296	1.2%
Everett	37,540	0.6%
Belmont	24,194	0.4%
Watertown	32,915	0.5%
Cambridge	101,587	1.6%
TOTAL POPULATION	1,106,267	18.4%
Estimated number of woman age 40+	220,000	
Estimated number of mammo calls/year (2 per woman)	442,506	
Estimated Line Cost/year (BrCa) (2 calls per@$0.05/call)	$22,000	
Estimated number of potential screening colonoscopies[122]	221,253	
Estimated number of CoCa calls/year (2 per patient)	442,506	
Estimated Line Cost/year (CoCa) (2 calls per@$0.05/call)	$22,125	



Mammography facilities in the greater Boston (617 area code) region

Facility	Phone Number	City	Zip Code	Phone Number	Harvard Affiliatio
BETH ISRAEL DEACONESS MEDICAL CENTER	330 BROOKLINE AVENUE	BOSTON	02215	617-667-7160	Yes
BOSTON'S MAMMOGRAPHY VAN	44 BINNEY STREET	BOSTON	02115	617-632-1974	Yes
BRIGHAM & WOMEN'S AMBULATORY	850 BOYLSTON STREET/ST 60	CHESTNUT HILL	02467	617-732-9801	Yes
BRIGHAM & WOMEN'S HOSPITAL	75 FRANCIS STREET	BOSTON	02115	617-732-8525	Yes
CAMBRIDGE HEALTH ALLIANCE	1493 CAMBRIDGE STREET	CAMBRIDGE	02139	617-665-1312	Yes
DANA FARBER CANCER INSTITUTE	44 BINNEY STREET	BOSTON	02115	617-632-3215	Yes
FAULKNER HOSPITAL-SAGOFF CENTER	1153 CENTRE STREET	BOSTON	02130	617-983-7090	Yes
HARVARD MEDICAL FACULTY, PHYSICIANS D.B.A. BETH ISRAEL RADIOLOGY	25 BOYLSTON STREET, STL	CHESTNUT HILL	02467	617-754-0300	Yes
HARVARD MEDICAL PHYSICIANS GROUP DBA B.I. RADIOLOGY	1101 BEACON STREET, 3 WEST	BROOKLINE	02146	617-731-5250	Yes
HARVARD UNIVERSITY HEALTH SERVICES	75 MOUNT AUBURN ST.,	CAMBRIDGE	02138	617-496-0689	Yes
HARVARD VANGUARD MEDICAL ASSOCIATES	291 INDEPENDENCE DRIVE	WEST ROXBURY	02467	617-541-6395	Yes
HARVARD VANGUARD MEDICAL ASSOCIATES	40 HOLLAND STREET	SOMERVILLE	02144	617-629-6110	Yes
HARVARD VANGUARD MEDICAL ASSOCIATES -KENMORE CENTER	133 BROOKLINE AVENUE	BOSTON	02215	617-421-8990	Yes
HARVARD VANGUARD MEDICAL ASSOCIATES -QUINCY	1250 HANCOCK STREET	QUINCY	02169	617-774-0710	Yes
MGH AVON COMPREHENSIVE BREAST CENTER	15 PARKMAN STREET, ST240	BOSTON	02114	617-726-5005	Yes
MT. AUBURN HOSPITAL	330 MT. AUBURN STREET	CAMBRIDGE	02138	617-499-5070	Yes
NEWTON-WELLESLEY HOSPITAL	2014 WASHINGTON STREET	NEWTON	02162	617-243-6065	Yes
1180 BEACON IMAGING, LLC	1180 BEACON STREET	BROOKLINE	02446	617-232-1485	No
BIOCARE DIAGNOSTICS	300 CONGRESS STREET	QUINCY	02169	617-770-9300	No
BOSTON IMAGING ASSOCIATES	ONE BROOKLINE PL, ST105	BROOKLINE	02146	617-754-6500	No
BOSTON MEDICAL CENTER DOCTOR'S OFFICE BUILDING	720 HARRISON AV, ST703	BOSTON	02118	617-638-8139	No
BOSTON MEDICAL CENTER	850 HARRISON AV	BOSTON	02118	617-414-4854	No
CODMAN SQUARE HEALTH CENTER	637 WASHINGTON STREET	DORCHESTER	02124	617-825-9660	No
DORCHESTER HOUSE MULTI-SERVICE CENTER	1353 DORCHESTER AVENUE	DORCHESTER	02122	617-288-3230	No
EAST BOSTON NEIGHBORHOOD HEALTH CENTER	10 GOVE STREET	EAST BOSTON	02128	617-569-5800	No
LEMUEL SHATTUCK HOSPITAL	170 MORTON STREET	JAMAICA PLAIN	02130	617-971-3366	No
MEDICAL CARE CENTER NORTH	1000 BROADWAY	CHELSEA	02150	617-660-6302	No
MILTON HOSPITAL	92 HIGHLAND STREET	MILTON	02186	617-696-4600	No
MIT HEALTH SERVICE CENTER	25 CARLETON STREET	CAMBRIDGE	02139	617-253-4481	No
NEW ENGLAND MEDICAL CENTER HOSPITAL DEPT OF RADIOLOGY	750 WASHINGTON ST	BOSTON	02111	617-636-0040	No
QUINCY MEDICAL CENTER	114 WHITWELL STREET	QUINCY	02169	617-376-4135	No
SCHATZKI ASSOCIATES, INC.	725 CONCORD AVENUE	CAMBRIDGE	02138	617-876-8630	No
SCHATZKI ASSOCIATES, INC.	521 MOUNT AUBURN STREET	WATERTOWN	02172	617-924-5210	No
SOMERVILLE HOSPITAL RAD DEPT.	230 HIGHLAND AVENUE	SOMERVILLE	02143	617-591-4150	No
SOUTH BOSTON COMMUNITY HEALTH CENTER	409 WEST BROADWAY,	SOUTH BOSTON	02127	617-269-7500	No
SOUTH COVE COMMUNITY HEALTH CENTER	885 WASHINGTON STREET	BOSTON	02111	617-521-6864	No
ST. ELIZABETH'S MEDICAL CENTER OF BOSTON	736 CAMBRIDGE STREET	BOSTON	02135	617-789-2762	No
THE CARNEY HOSPITAL, INC.	2100 DORCHESTER AVENUE	DORCHESTER	02124	617-296-4000	No
UPHAMS CORNER HEALTH CENTER	415 COLUMBIA ROAD	DORCHESTER	02125	617-287-8000	No
WHIDDEN MEMORIAL HOSPITAL	103 GARLAND STREET	EVERETT	02149	617-389-6270	No
WOMEN'S HEALTH CENTER	96 GARLAND STREET	EVERETT	02149	617-381-7196	No

Other Projects...

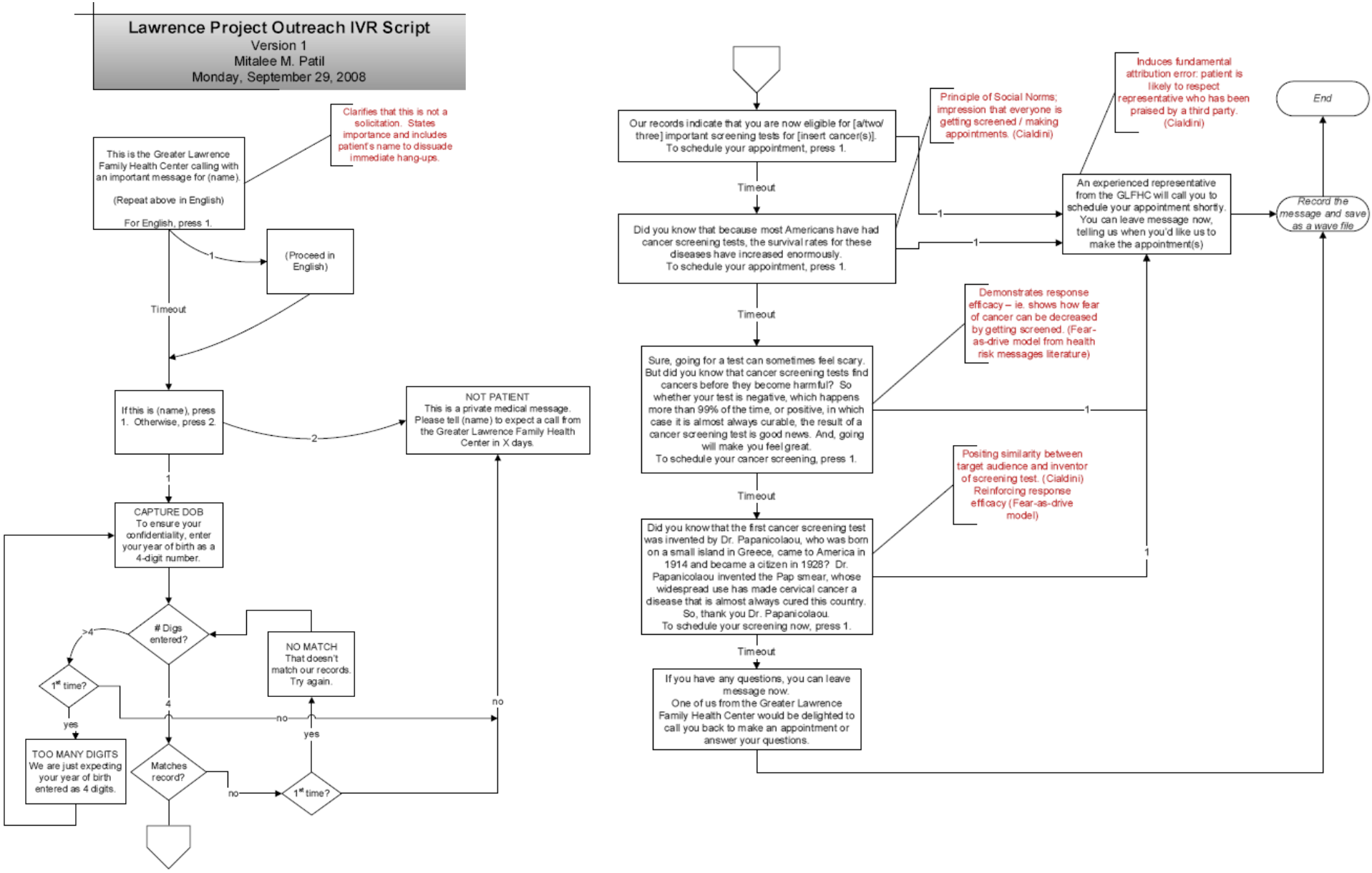
… Ongoing

A randomized trial at the Greater Lawrence Family Health Center of a systems that will launch computer generated telephone messages to recruit patients to come in for cancer screening tests (Karen Emmons DFCI PI)

- Lawrence Is the Poorest City in Massachusetts
- Many Immigrants
- Many Undocumented
- 2nd Largest Dominican Population in US
- 90% Spanish Speaking
- 60% Do Not Understand English
- 30% Illiterate in all Languages
- Deeply Committed to Good Health for All
- Research Oriented

Lawrence Project Outreach IVR Script

Version 1
Mitalee M. Patil
Monday, September 29, 2008



Other Projects...

… Planned

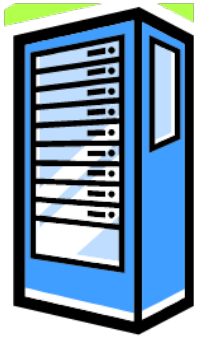
TRACKING/REMINDER SYSTEM FOR INCREASING RATES OF INFLUENZA IMMUNIZATION

"Hello, this is a medical reminder message from the [STATE] Department of Health, with information about the availably of flu vaccine in your area ..."

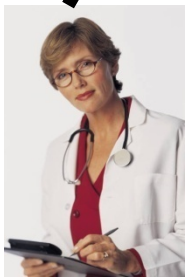
Reminder System Server

800-xxx-xxxx
Please call when the flu vaccine becomes available

Immunization Registry

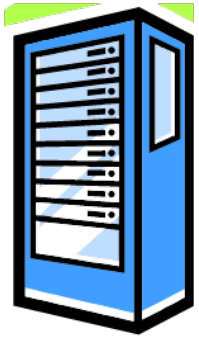


Telephone Directory Database
(Available from Commercial Sources)



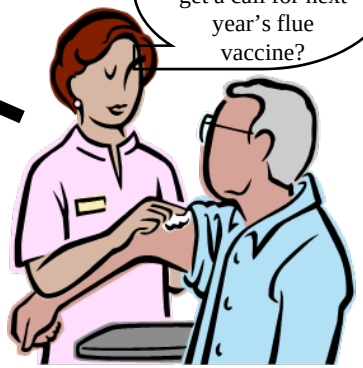
Physician's Offices, HMO's, etc

Pharmacies



Mammography Reminder System

Would you like to get a call for next year's flue vaccine?



The Patient

AN APPOINTMENT-MAKING/REMINDING/TRACKING SYSTEM FOR COLORECTAL CANCER SCREENING

James S. Michaelson Ph.D.

COLLABORATORS

- Blake Cady MD, Massachusetts General Hospital, Division of Surgical Oncology, Harvard University
- Paul C. Schroy III, MD, MPH, Director of Clinical Research for the Section of Gastroenterology, Section of Gastroenterology, Boston Medical Center
- Robert Mayer M.D. Stephen B. Kay Family Professor of Medicine, Department of Medicine, Harvard Medical School, Vice Chair for Academic Affairs, Department of Medical Oncology, Dana-Farber Cancer Institute
- James C. Cusack, Jr, MD, Massachusetts General Hospital, Division of Surgical Oncology, Harvard University
- William R. Brugge, M.D, Director, Massachusetts General Hospital GI Endoscopy Unit, Harvard University
- Daniel Chung M.D, Director, Massachusetts General Hospital GI Cancer Genetics Clinic, Harvard University
- David L Carr-Locke, MD, FRCP, Director of Endoscopy, Brigham & Women's Hospital, Harvard University
- Wendy Atkin PhD, Population Screening Research Group, Colorectal Cancer Unit, St Mark's Hospital, London,
- Clifford I. Nass PhD, Professor and Director of the Institute for Communication Research, Stanford University
- Joseph R. Betancourt, MD, MPH, Senior Scientist, Institute for Health Policy in Medicine and Program Director for Multicultural Education, Massachusetts General Hospital
- Alexander R. Green, MD, MPH, Senior Scientist, Institute for Health Policy, Massachusetts General Hospital

OUTLINE

Failure of large numbers of patients to make, and then attend, appointments for colorectal cancer screening is a major contributor to colorectal cancer death. The modern technologies of computer speech and telephony make it possible to launch, for pennies a call, computer generated telephone messages that can help patients make, and then keep, appointments colorectal cancer screening. Here, we propose to create just such an appointment-making/reminding/tracking system for colorectal cancer screening. The system will launch computer generated telephone messages to recruit patients for screening as well as reminder messages to help patients remember to attend screening visits. The system will also provide web-forms for medical professionals to initiate appointments for screening and to track patients with symptoms found at screening. We propose to test the reminder system by implementation in Greater Boston (area code 617), but the long-term goal of this work is to create a system that can be used nationally. This work builds upon the expertise we have gained during the construction of an integrated appointment-making/reminding/tracking system of breast cancer screening. The work we propose here will also have a strong research component, so as to analyze the patterns of colorectal cancer screening usage, with special emphasis on the process of appointment making and keeping, and the impact of the system on attendance at screening.

HealthTalker Home - Windows Internet Explorer

http://healthtalker.hct.lifemath.net/

HealthTalker Home

HealthTalker ALPHA

An IVR System for Preventive Health Interventions

Please log in below.

Login

E-mail: dfghjklrd@erf.edu

Password: ••••••••••

Log In

Recover Password

Welcome to HealthTalker

HealthTalker is an interactive voice response (IVR) system for recruiting and reminding patients to schedule preventive health visits, such as cancer screening (mammography, colorectal cancer screening, and pap tests), immunizations, diabetes control, or hypertension control.

Why use HealthTalker?

Sends computer-generated telephone messages.

- **Recruiting** calls encourage patients to make an appointment.
- **Confirming** calls notify patients of the scheduled appointment time.
- **Reminding** calls ensure patients do not forget appointments.

Helps schedulers book appointments.

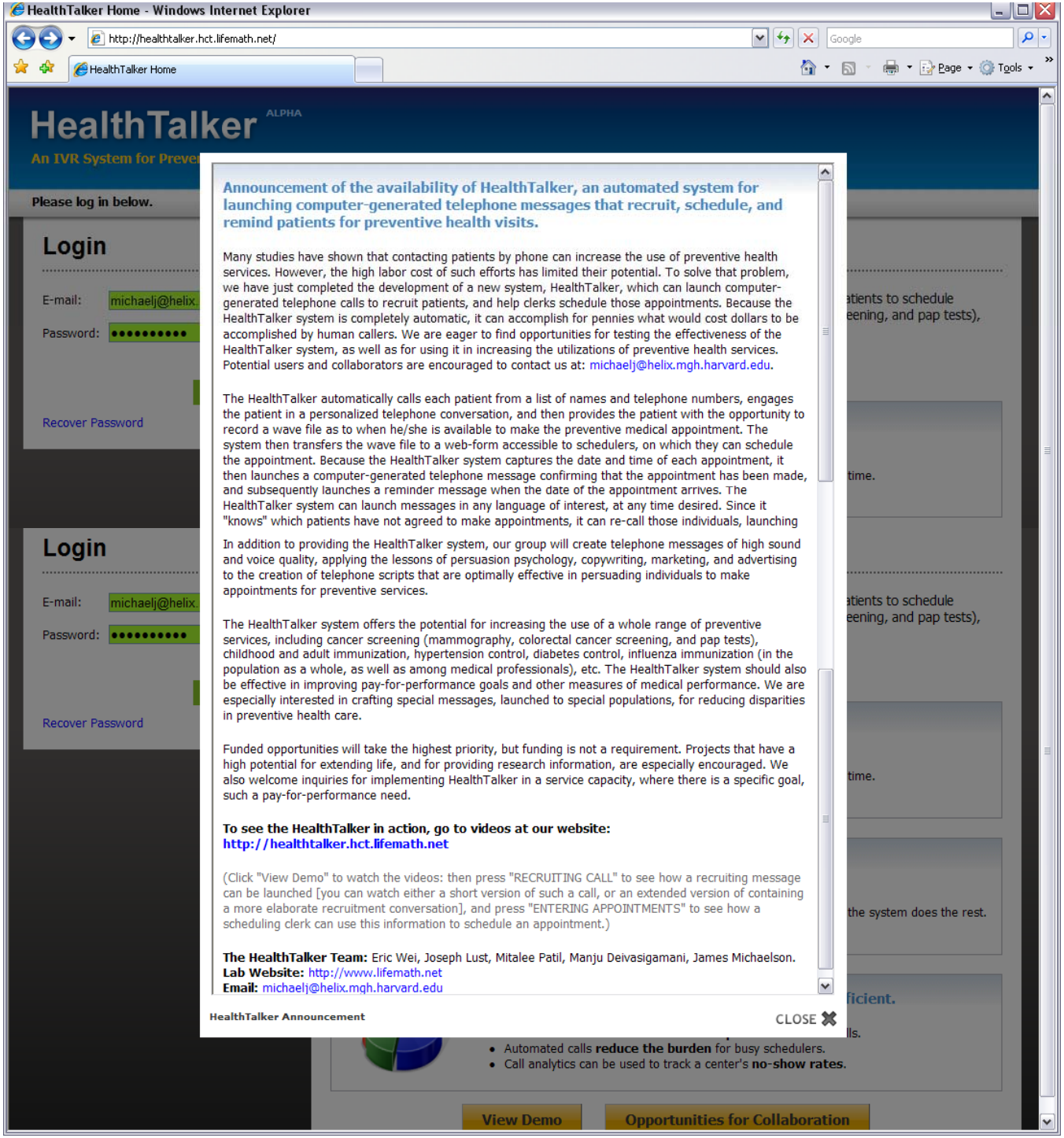
- **Audio recordings** notify schedulers of patient's availability.
- Simply enter **date, time, and location** of appointments, and the system does the rest.
- **Detailed analytics** are provided for each call.

Helps medical centers save money and be more efficient.

- Automated calls cost a **fraction of the price** of traditional calls.
- Automated calls **reduce the burden** for busy schedulers.
- Call analytics can be used to track a center's **no-show rates**.

View Demo

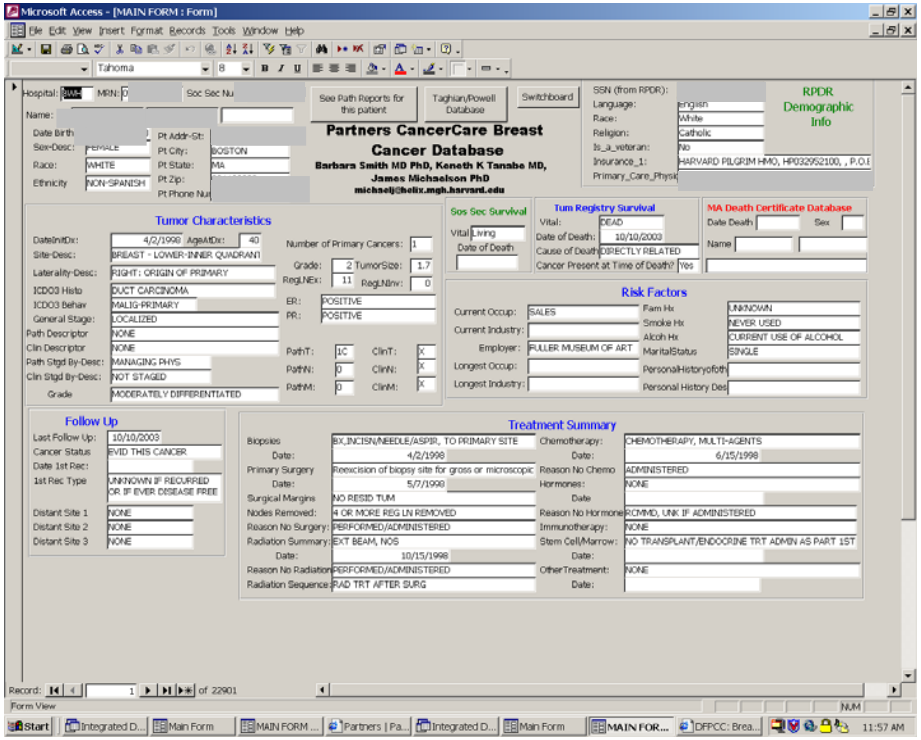
Opportunities for Collaboration


HealthTalker Home - Windows Internet Explorer
http://healthtalker.hct.lifemath.net/
HealthTalker Home
HealthTalker
ALPHA
An IVR System for Preve
Please log in below.
Login
E-mail:
michaelj@helix.
Password:
Recover Password
Login
E-mail:
michaelj@helix.
Password:
Recover Password
Announcement of the availability of HealthTalker, an automated system for launching computer-generated telephone messages that recruit, schedule, and remind patients for preventive health visits.
Many studies have shown that contacting patients by phone can increase the use of preventive health services. However, the high labor cost of such efforts has limited their potential. To solve that problem, we have just completed the development of a new system, HealthTalker, which can launch computer-generated telephone calls to recruit patients, and help clerks schedule those appointments. Because the HealthTalker system is completely automatic, it can accomplish for pennies what would cost dollars to be accomplished by human callers. We are eager to find opportunities for testing the effectiveness of the HealthTalker system, as well as for using it in increasing the utilizations of preventive health services. Potential users and collaborators are encouraged to contact us at: michaelj@helix.mgh.harvard.edu.
The HealthTalker automatically calls each patient from a list of names and telephone numbers, engages the patient in a personalized telephone conversation, and then provides the patient with the opportunity to record a wave file as to when he/she is available to make the preventive medical appointment. The system then transfers the wave file to a web-form accessible to schedulers, on which they can schedule the appointment. Because the HealthTalker system captures the date and time of each appointment, it then launches a computer-generated telephone message confirming that the appointment has been made, and subsequently launches a reminder message when the date of the appointment arrives. The HealthTalker system can launch messages in any language of interest, at any time desired. Since it "knows" which patients have not agreed to make appointments, it can re-call those individuals, launching
In addition to providing the HealthTalker system, our group will create telephone messages of high sound and voice quality, applying the lessons of persuasion psychology, copywriting, marketing, and advertising to the creation of telephone scripts that are optimally effective in persuading individuals to make appointments for preventive services.
The HealthTalker system offers the potential for increasing the use of a whole range of preventive services, including cancer screening (mammography, colorectal cancer screening, and pap tests), childhood and adult immunization, hypertension control, diabetes control, influenza immunization (in the population as a whole, as well as among medical professionals), etc. The HealthTalker system should also be effective in improving pay-for-performance goals and other measures of medical performance. We are especially interested in crafting special messages, launched to special populations, for reducing disparities in preventive health care.
Funded opportunities will take the highest priority, but funding is not a requirement. Projects that have a high potential for extending life, and for providing research information, are especially encouraged. We also welcome inquiries for implementing HealthTalker in a service capacity, where there is a specific goal, such a pay-for-performance need.
To see the HealthTalker in action, go to videos at our website:
http://healthtalker.hct.lifemath.net
(Click "View Demo" to watch the videos: then press "RECRUITING CALL" to see how a recruiting message can be launched [you can watch either a short version of such a call, or an extended version of containing a more elaborate recruitment conversation], and press "ENTERING APPOINTMENTS" to see how a scheduling clerk can use this information to schedule an appointment.)
The HealthTalker Team: Eric Wei, Joseph Lust, Mitalee Patil, Manju Deivasigamani, James Michaelson.
Lab Website: http://www.lifemath.net
Email: michaelj@helix.mgh.harvard.edu
HealthTalker Announcement
CLOSE
atients to schedule
eening, and pap tests),
time.
atients to schedule
eening, and pap tests),
time.
the system does the rest.
ficient.
lls.
Automated calls reduce the burden for busy schedulers.
Call analytics can be used to track a center's no-show rates.
View Demo
Opportunities for Collaboration

Cancer Math Group

Building and Using Cancer Databases

Partners CancerCare
Retrospective
Breast Cancer Database



27,000 patients
27 million records!

Largest
(in terms of total data)
and most accurate
(in terms of follow up)
source of information on breast cancer in the world

We have built similar databases for melanoma and hematolgical malignancies.
Databases for other cancers are in preparation.

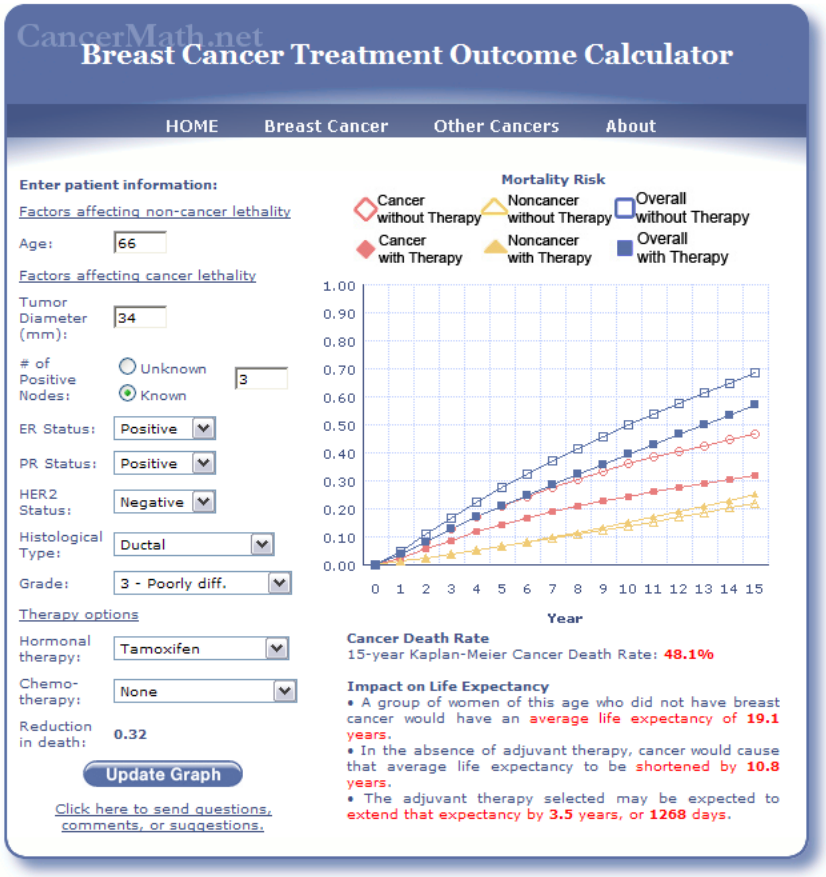
One Use of These Data

Part of our work concerns the development of improved mathematical methods for predicting the risk of cancer death…

… and the application of these methods to the development of practical web-calculators, which can aid medical professionals in estimating the risk of breast carcinoma death, and the impact of various treatment options on that risk of death

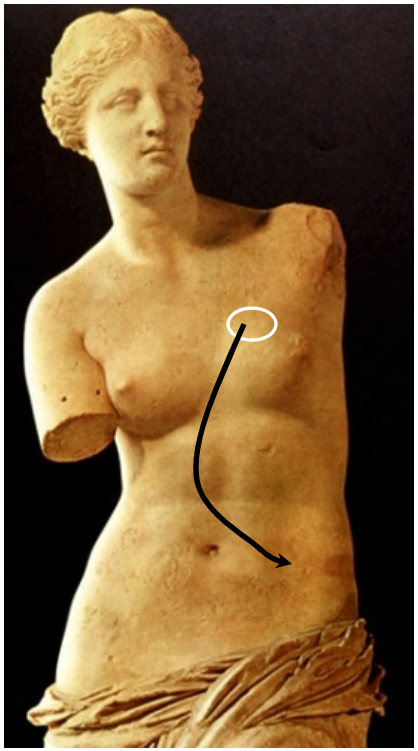
Web-Based Calculators For Estimating the Risk of Cancer Death (and Other Features of Cancer Outcome), and the Impact of Various Treatment Choices on that Risk

http://www.cancer-math.net



The Math Behind the Calculators…

… Is Based on a Mathematical Consideration of the Most Generally Recognized Mechanism of Cancer Death By the Spread of Cancer Cells



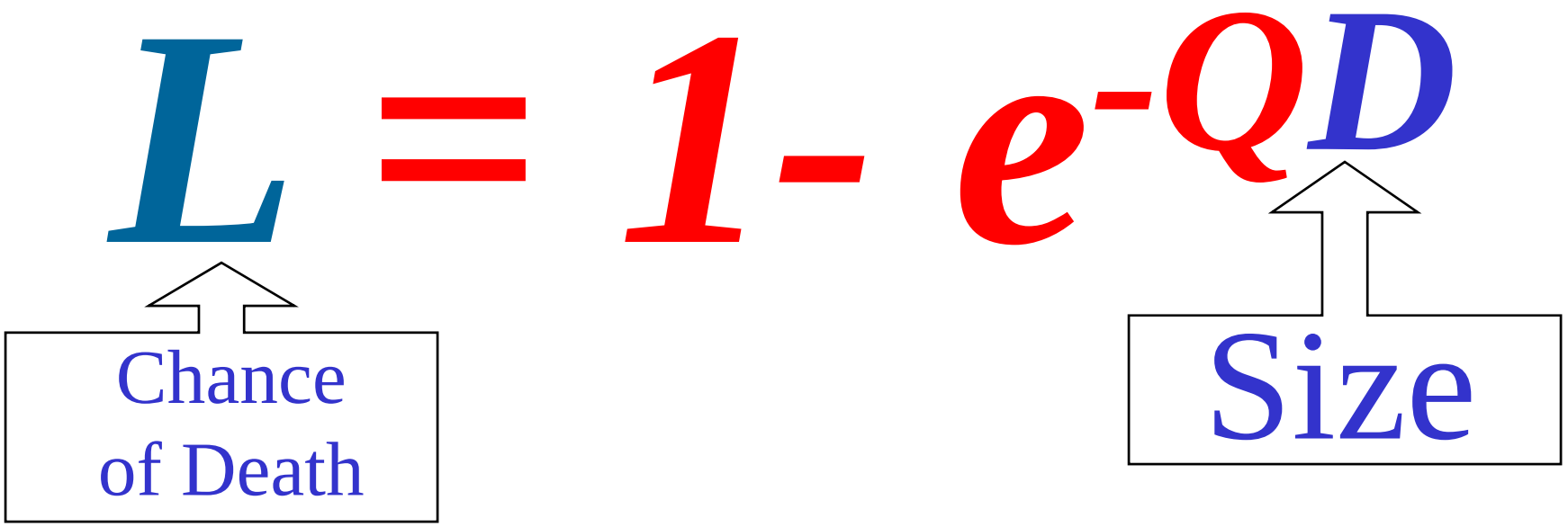
Let us define

p

as the probability of the lethal spread of a breast cancer cell from the primary site to the periphery, leading to death

From this, we can build an expression that relates the chance that the patient will die of the cancer (*L*) to the size of the cancer *(D*)

The *sSizeOnly* Equation



The *sSizeOnly* Equation

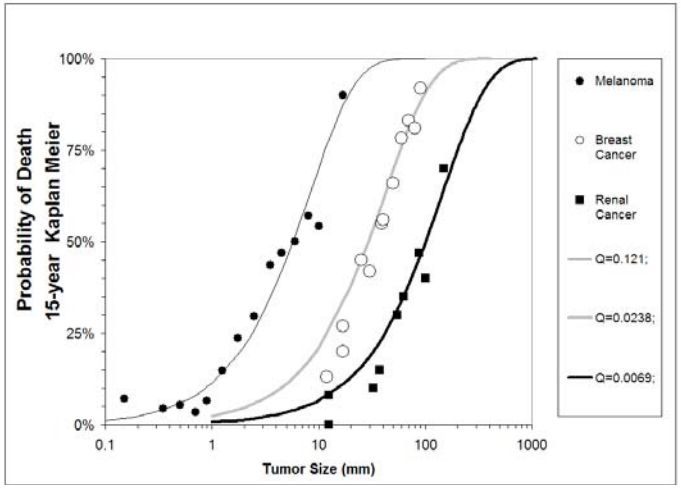
$$L = 1 - e^{-QD}$$

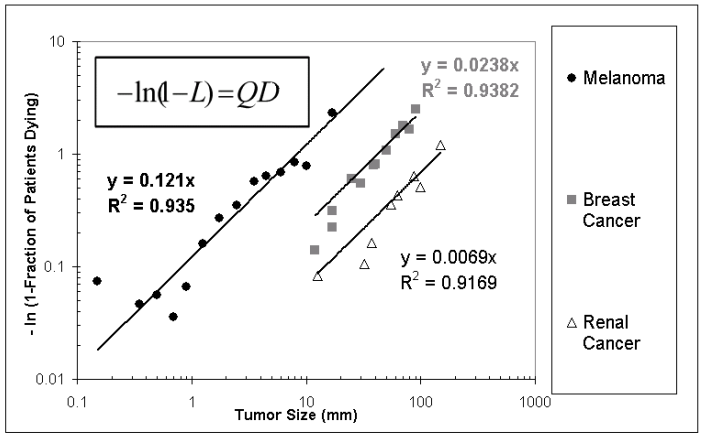
The Q parameter
is a measure
of the probability
of the spread
of cancer cells

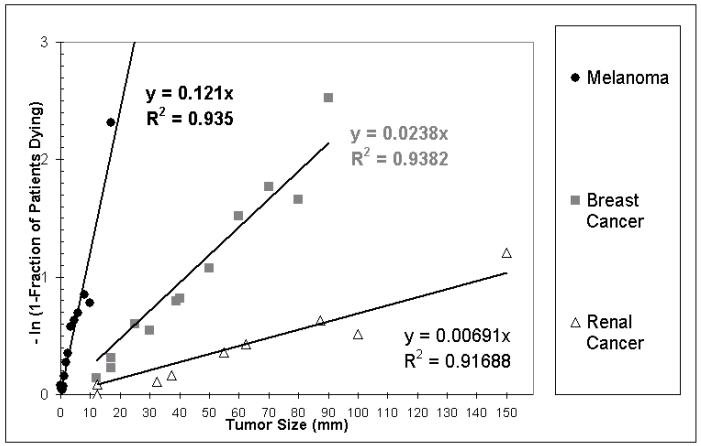
The *sSizeOnly* Equation

$$L = 1 - e^{-QD}$$

But does it work?


Probability of Death
15-year Kaplan Meier
100%
75%
50%
25%
0%
0.1
1
10
100
1000
Tumor Size (mm)
Melanoma
Breast Cancer
Renal Cancer
Q=0.121;
Q=0.0238;
Q=0.0069;


$-\ln(1-L)=QD$
y = 0.0238x
R² = 0.9382
y = 0.121x
R² = 0.935
y = 0.0069x
R² = 0.9169
- ln (1-Fraction of Patients Dying)
10
1
0.1
0.01
0.1
1
10
100
1000
Tumor Size (mm)
Melanoma
Breast Cancer
Renal Cancer


y = 0.121x
R² = 0.935
y = 0.0238x
R² = 0.9382
y = 0.00691x
R² = 0.91688
- ln (1-Fraction of Patients Dying)
3
2
1
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
Tumor Size (mm)
Melanoma
Breast Cancer
Renal Cancer

YES

$$L = 1 - e^{-QD}$$

The *sSizeOnly* Equation is expandable,
so as to include information
on additional prognostic factors

The -*Q* parameter
is a measure
of the probability
of the spread
of cancer cells

$$L = 1 - e^{-Q(g1*g2*g3)D}$$

The *sSizeOnly* Equation is expandable,
so as to include information
on additional prognostic factors

How much extra lethality is associated with other prognostic factors?

g Parameters

Prognostic factors (#)	SEER	Partners	Mel updated
LATERALITY			
Left (258885/5825)	1.0325	0.9955	
Right (249458/5523)	1.029	1.0055	
Bilateral (397)	1.845		
RACE/ETHNICITY			
Asian (/139/)		0.5195	
Black (39809/553)	1.2435	1.071	
White (437101/9960)	1.0326	0.921	
American Indian/Alaska Native (1746)	1.0995		
Asian Indian, Pakistani (1988+) (1135)	0.861		
Chinese (5575)	0.8258		
Filipino (6524)	0.781		
Hawaiian (2502)	0.9373		
Japanese (7488)	0.6575		
Kampuchean (1988+) (93)	1.1009		
Korean (1988+) (1253)	0.536		
Vietnamese (1988+) (993)	0.7775		
HORMONAL THERAPY			
No (8160)		0.9995	
Yes (3110)		1.008	
RADIATION THERAPY			
No (6020)		1.035	
Yes (5250)		0.932	
CHEMOTHERAPY			
No (7586)		0.9375	
Yes (3684)		1.165	
TYPE OF SURGERY			
Breast Conserving (6009)		0.89	
Mastectomy (4582)		0.955	
None (499)		2.2925	
HORMONAL STATUS/TUMOR BIOLOGY			
ER-/PR- (992/431)		1.382	1.215
Basal-like (ER-/PR-/Her2-) (98)			0.7305
luminal B (ER+ and/or PR+, Her2+) (138)			2.146
Luminal A (ER+ and/or PR+, Her2-) (581)			0.975
Her2+, ER- (83)			1.4755

g Parameters

Prognostic factors (#)	SEER	Partners	Mel updated
RECURRENCE			
Local recurrence (Taghian Powell (210)/217)		3.715	1.8273
Local recurrence (Partners – 181pts)		1.16	
No local recurrence (2496)			0.903
HER2 STATUS			
Neg (668)			0.9662
Pos (221)			1.515
Not stated (1822)			
METHOD OF DETECTION			
Nonpalp (666)			0.6424
Palp (2012)			1.0254
LVI			
No (1891)		0.8895	0.8187
Yes (604)		1.1936	1.42
STAGE			
1 (1249)			0.7878
2 (1153)			1.126
3 (237)			0.9726
4 (10)			2.957
Distant Metastasis (295)		6.22	
Localized (5711)		0.5305	
Regional (2963)		1.161	
SEX			
Male (3518/89)	1.2462	1.304	

g Parameters

Prognostic factors (#)	SEER	Partners	Mel updated
AGE			
Less than 40 (30886/1114/362)	1.0918	1.0196	1.362
40to49 (84819/2602/783)	0.8863	0.8379	0.864
50to59 (110408/2748/674)	1.028	0.971	0.949
60to69 (115861/2477/530)	1.066	1.0555	0.786
70to79 (107475)	1.0655		
70plus (2330/351)		1.1518	1.5465
80plus (59412)	1.1815		
HISTOLOGY			
Inflammatory (688/44)	2.244	1.356	
Ductal and lobular (30889/927)	0.9155	0.6651	
Ductal (364695/8864/2396)	1.082	1.0405	1.0455
Lobular (38427/795/317)	1.0097	0.9378	0.7352
Adenocarcinoma/Adenoma (79)		1.825	
Atypical Medullary Carcinoma (58)		0.893	
Carcinoma/Epithelial Tumor (70)		1.235	
Comedocarcinoma (36)		1.102	
Mucinous Adenocarcinoma/Adenoma (164)		0.7615	
Mucinous adenocarcinoma (12685)	0.4331		
Mucin-producing adenocarcinoma (672)	0.6795		
Paget disease (2708/32)	1.17	1.0205	
Tubular Adenocarcinoma/Adenoma (7220/122)	0.394	0.12402	
ER			
Negative (66948/1346/520)	0.9525	1.149	1.3145
Positive (239988/5015/1449)	0.7845	0.798	0.9845
PR			
Negative (97868/1458/712)	0.95	1.557	1.2775
Positive (199967/4154/1233)	0.763	0.6795	0.9302
FAMILY HX			
No (2082)		0.852	
Yes (4017)		0.7825	
GRADE			
1 - Well differentiated (64600/1420/636)	0.4585	0.2735	0.3205
2 -Moderately differentiated (149413/3425/524)	0.866	0.8563	1.064
3 -Poorly differentiated (133189/2946/350)	1.139	1.0625	1.142
Undifferentiated (11607/85)	1.2035	2.25	

The *SNP* (*Size+Nodes+PrognosticMarkers*) Method for Estimating the Risk of Cancer Death from Information on Tumor Size, Nodal Status, and Other Prognostic Factors

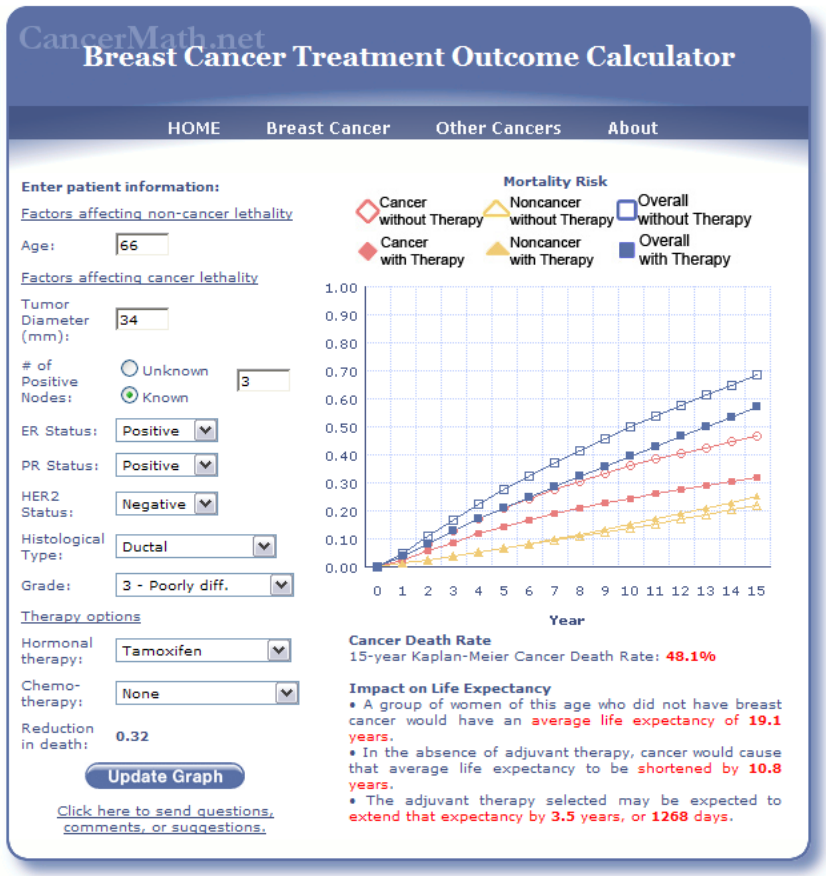
$$L_{overall} = L_{primary} + L_{nodes} - (L_{primary} * L_{nodes})$$

(eq. (3))

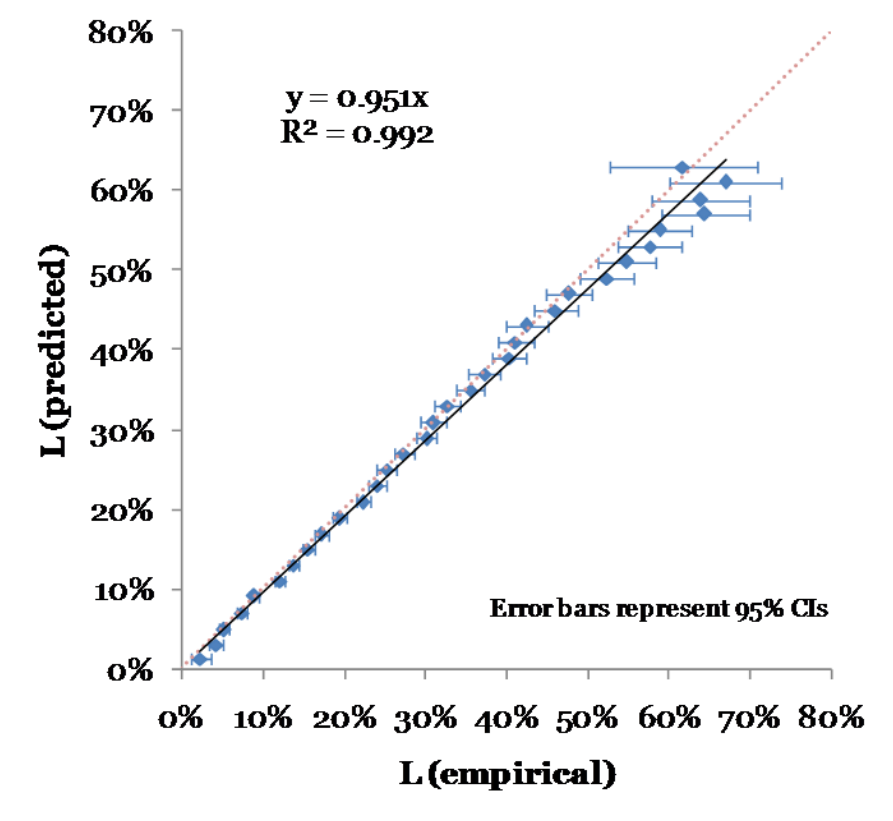
Source of Lethality	*Method of Estimation*	*Independent Variable*	*Parameters*	*Interpretation*
The lethal contribution from cancer at the primary site	$L_{primary} = 1 - e^{-(Q * j_{nodes} * g_1 * g_2 ...) D^Z}$ eq. (1d)	D = Tumor Thickness (mm)	*For Breast Cancer:* Q= 0.0062 Z=1.34 j_{nodes}=0.661if nodal status is known j_{nodes} =1 if nodal status is unknown *For Melanoma:* Q= 0.1428 Z= 0.89 j_{nodes} =0.801 if nodal status is known j_{nodes} =1 if nodal status is unknown g_1=1.206 if male g_1=0.771 if female g_2=1.229 if ulcerated g_2=0.887 if not ulcerated g_2=1 if ulceration unknown	*The lethal contribution of the primary mass increases gradually with tumor size, and the amount of that lethal contribution is influenced by prognostic factors, as captured by the g parameters in Equation 1d*
The lethal contribution from cancer in the lymph nodes	$L_{nodes} = 1 - e^{-(M * R)}$ eq. (2)	M = The Number of Positive Nodes	*For Breast Cancer:* R= 0.0608 *For Melanoma:* R= 0.2253	*The presence of each positive lymph node contributes approximately "R" extra chance of death*

The *SNP* (*Size+Nodes+PrognosticMarkers*) method reduces to:

- **the *Size+Nodes* method, when only size and nodal status are known.**
- **the *SizeOnly* method, when only size is known.**

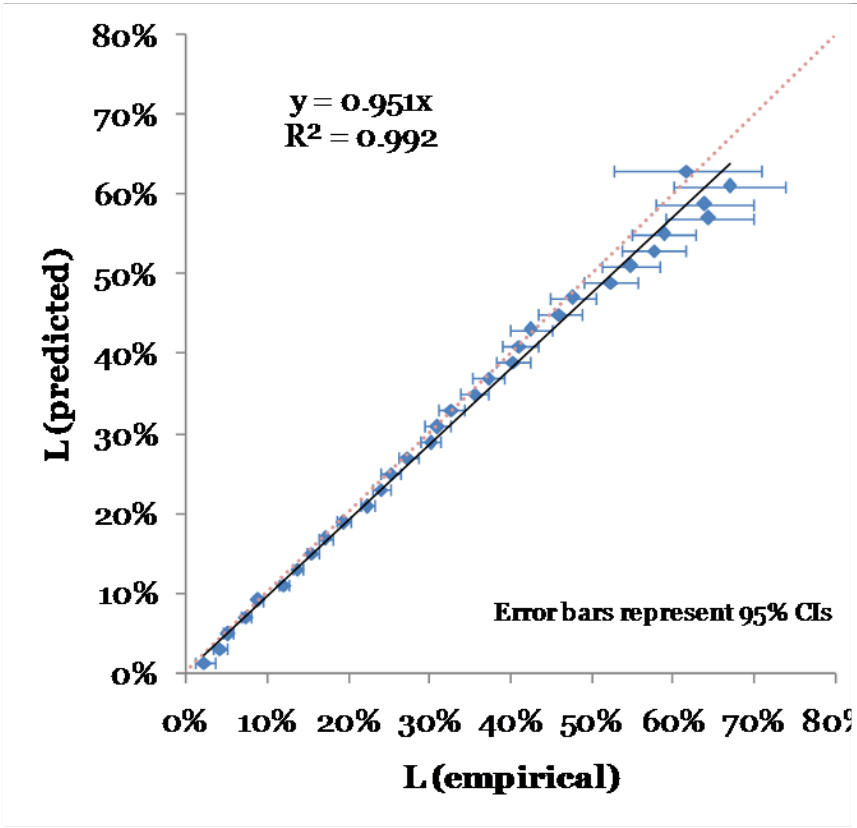


How Accurate Is It?

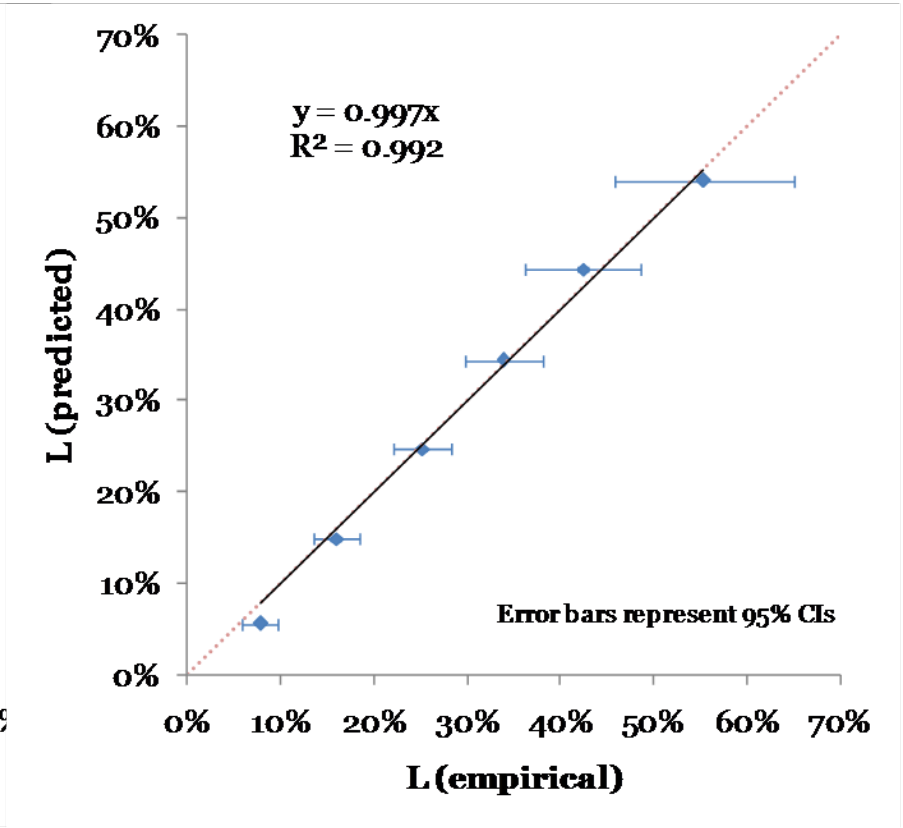


SEER, Stratified into Groups Differing by 2% Risk of Death

How Accurate Is It?



SEER, Stratified into Groups Differing by 2% Risk of Death

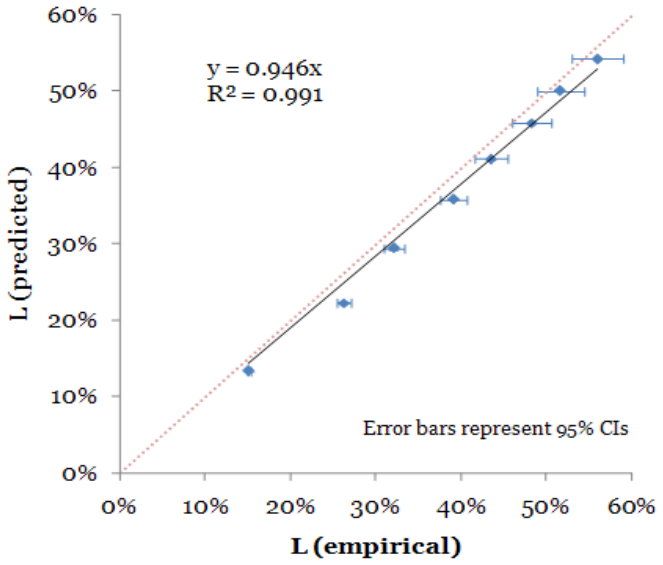


Partners, Stratified into Groups Differing by 10% Risk of Death

How Accurate Is It?

Grouped by number of positive lymph nodes

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
0	263544	15.09% (0.12%)	13.34% (0.02%)	-1.75%
1	44002	26.21% (0.42%)	22.32% (0.04%)	-3.89%
2	21367	32.06% (0.59%)	29.46% (0.06%)	-2.60%
3	12319	39.05% (0.80%)	35.86% (0.07%)	-3.19%
4	7934	43.40% (0.98%)	41.17% (0.08%)	-2.23%
5	5699	48.28% (1.17%)	45.90% (0.09%)	-2.39%
6	4296	51.63% (1.38%)	50.11% (0.09%)	-1.51%
7	3330	55.99% (1.53%)	54.25% (0.10%)	-1.74%
			Mean (std. dev.)	-2.41% (0.81%)
			Mean weighted by N (std. dev.)	-2.13% (3.47%)
			Root Mean Square (std. dev.)	2.53% (2.09%)
			Root Mean Square weighted by N (std. dev.)	3.88% (6.01%)

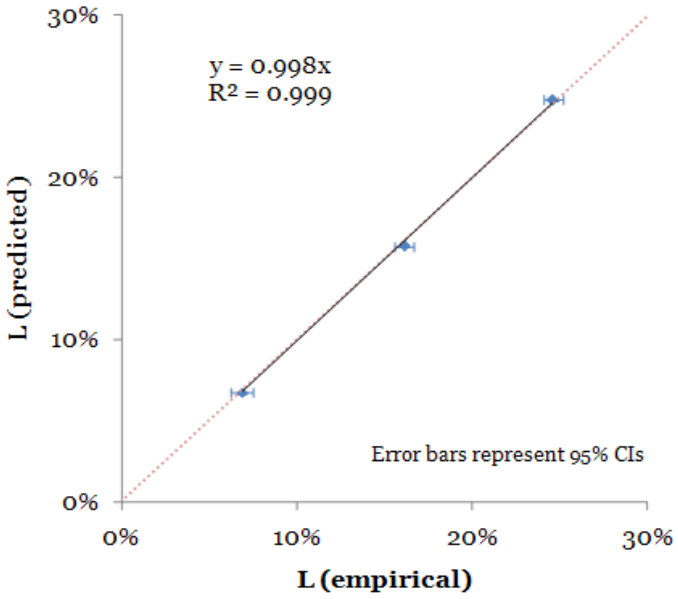


How Accurate Is It?

Grouped by tumor grade

Group†	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
grade 1	51159	6.84% (0.27%)	6.74% (0.03%)	-0.11%
grade 2	114415	16.10% (0.27%)	15.77% (0.03%)	-0.33%
grade 3	95092	24.61% (0.27%)	24.79% (0.04%)	0.19%
			Mean (std. dev.)	-0.08% (0.26%)
			Mean weighted by N (std. dev.)	-0.10% (0.32%)
			Root Mean Square (std. dev.)	0.23% (0.22%)
			Root Mean Square weighted by N (std. dev.)	0.28% (0.31%)

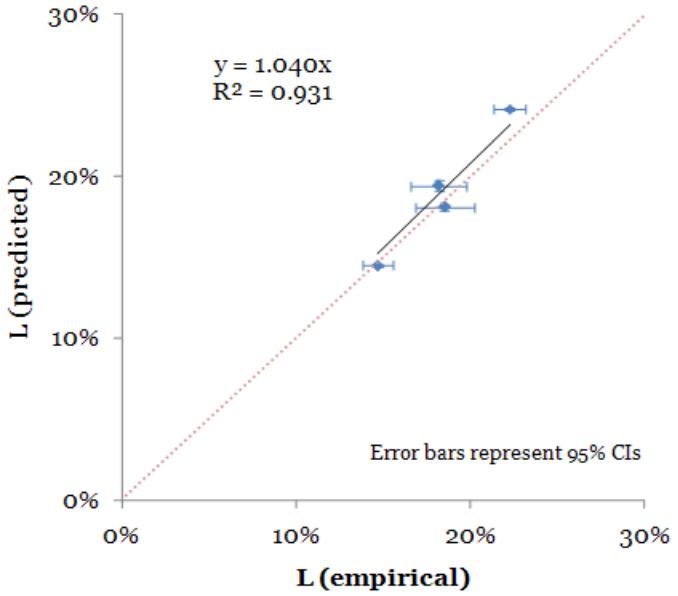
†grade 4 also exists in the dataset, but is not included in the calculation of the mean or displayed on graph; grade 4 no longer exists



How Accurate Is It?

Grouped by estrogen and progesterone receptor status

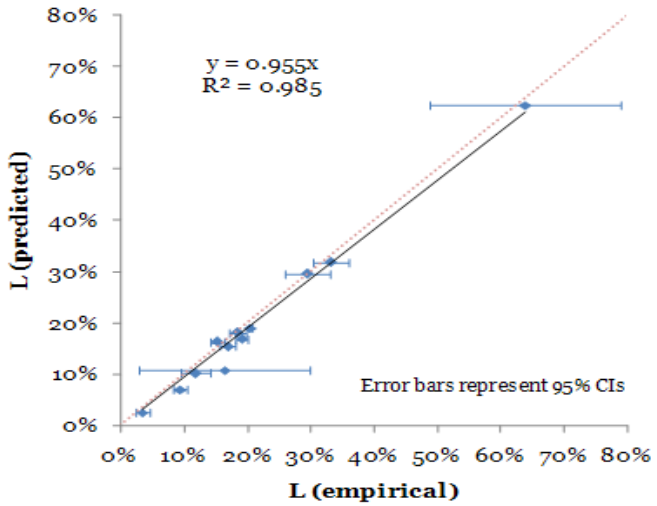
Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
ER+/PR+	151742	14.68% (0.43%)	14.49% (0.03%)	-0.19%
ER+/PR-	28880	18.51% (0.87%)	18.10% (0.08%)	-0.41%
ER-/PR+	5519	18.16% (0.81%)	19.44% (0.17%)	1.27%
ER-/PR-	44672	22.25% (0.48%)	24.17% (0.06%)	1.92%
			Mean (std. dev.)	0.65% (1.13%)
			Mean weighted by N (std. dev.)	0.23% (0.88%)
			Root Mean Square (std. dev.)	1.17% (1.30%)
			Root Mean Square weighted by N (std. dev.)	0.79% (1.03%)



How Accurate Is It?

Grouped by histological type

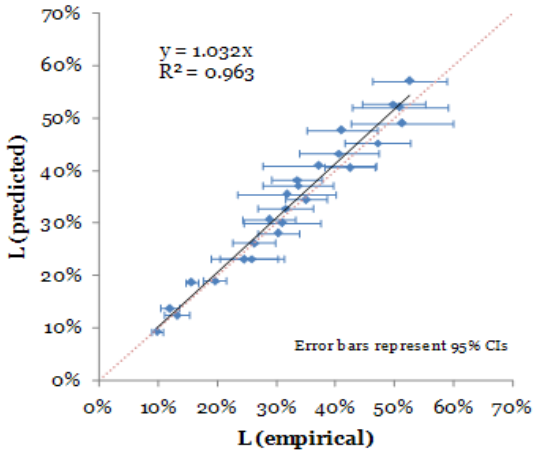
Group	N	L empirical (SEM)		L predicted (SEM)		Difference (pred – emp)
Ductal	264692	20.51%	(0.13%)	18.96%	(0.02%)	-1.56%
Lobular	25117	19.13%	(0.49%)	16.84%	(0.07%)	-2.29%
Intraductal+ LCIS	23449	16.90%	(0.64%)	15.44%	(0.07%)	-1.45%
Mucinous	9374	9.39%	(0.56%)	7.00%	(0.06%)	-2.39%
Medullary	5675	15.21%	(0.57%)	16.33%	(0.12%)	1.12%
Tubular	4992	3.46%	(0.55%)	2.50%	(0.06%)	-0.96%
Comedo	4184	18.48%	(0.72%)	18.07%	(0.18%)	-0.41%
Scirrhous	1577	33.26%	(1.42%)	31.79%	(0.35%)	-1.48%
Inflammatory	147	63.85%	(7.74%)	62.45%	(1.41%)	-1.40%
Paget's disease	1266	29.51%	(1.83%)	29.61%	(0.44%)	0.10%
Papillary	1991	11.92%	(1.16%)	10.18%	(0.18%)	-1.75%
Cribriform	722	16.41%	(6.88%)	10.74%	(0.32%)	-5.67%
				Mean (std. dev.)		-1.51% (1.65%)
				Mean weighted by N (std. dev.)		-1.56% (4.10%)
				Root Mean Square (std. dev.)		2.18% (2.97%)
				Root Mean Square weighted by N (std. dev.)		4.23% (7.75%)



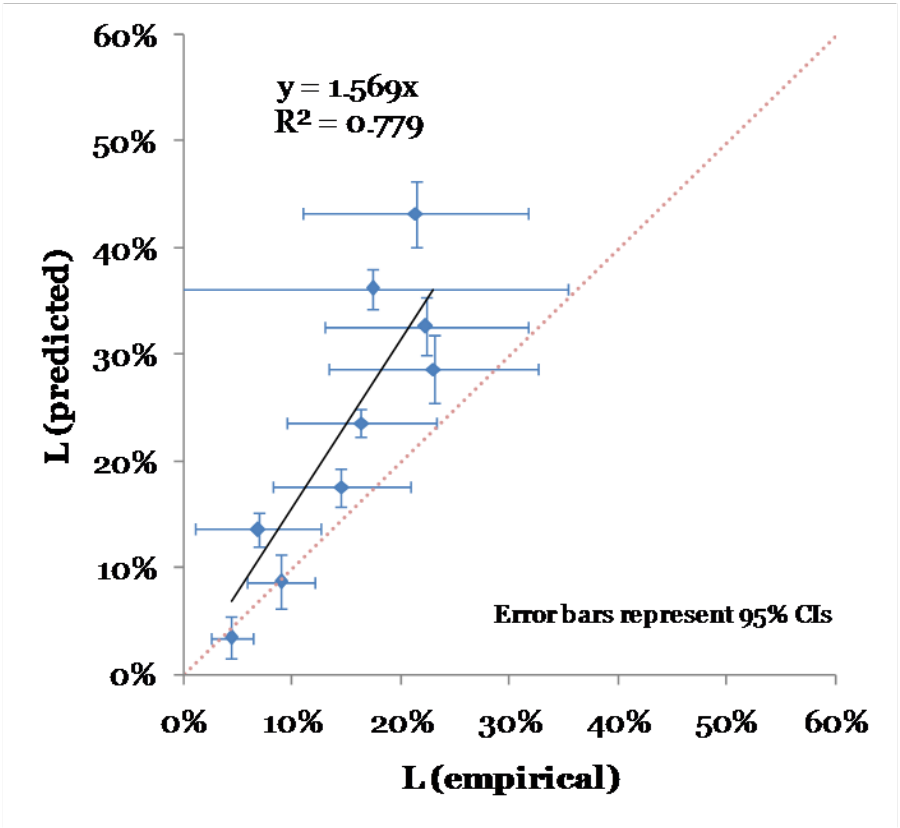
How Accurate Is It?

Permutations of number of positive lymph nodes and estrogen/progesterone receptor status

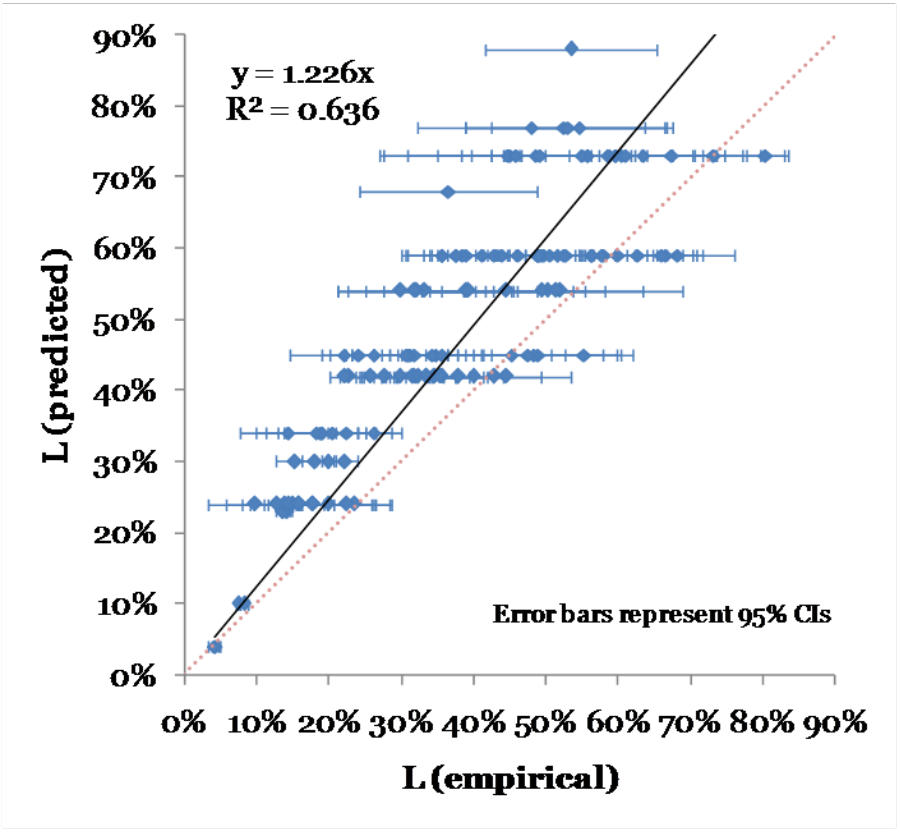
Nodes	Group† ER/PR status	N	L empirical (SEM)		L predicted (SEM)		Difference (pred – emp)
0	ER+/PR+	106881	9.74%	(0.51%)	9.23%	(0.02%)	-0.50%
1	ER+/PR+	20980	19.56%	(1.00%)	18.96%	(0.05%)	-0.60%
2	ER+/PR+	9637	26.18%	(1.81%)	26.19%	(0.07%)	0.01%
3	ER+/PR+	5446	31.56%	(2.42%)	32.77%	(0.08%)	1.21%
4	ER+/PR+	3369	33.45%	(2.18%)	38.22%	(0.10%)	4.76%
5	ER+/PR+	2369	40.57%	(3.47%)	43.25%	(0.11%)	2.67%
6	ER+/PR+	1742	41.08%	(3.05%)	47.67%	(0.13%)	6.59%
7	ER+/PR+	1318	50.92%	(4.15%)	52.10%	(0.14%)	1.18%
0	ER+/PR-	20228	13.15%	(1.07%)	12.43%	(0.06%)	-0.72%
1	ER+/PR-	3994	24.56%	(2.84%)	23.11%	(0.14%)	-1.45%
2	ER+/PR-	1817	28.79%	(2.28%)	30.68%	(0.19%)	1.89%
3	ER+/PR-	1040	33.66%	(3.04%)	37.16%	(0.25%)	3.50%
0	ER-/PR+	3754	11.97%	(0.86%)	13.74%	(0.14%)	1.77%
1	ER-/PR+	749	25.92%	(2.79%)	23.20%	(0.31%)	-2.72%
2	ER-/PR+	406	30.97%	(3.34%)	30.01%	(0.40%)	-0.97%
3	ER-/PR+	207	31.74%	(4.22%)	35.49%	(0.56%)	3.75%
4	ER-/PR+	146	37.27%	(4.87%)	40.95%	(0.57%)	3.68%
0	ER-/PR-	30538	15.62%	(0.53%)	18.69%	(0.06%)	3.07%
1	ER-/PR-	6119	30.28%	(1.82%)	28.07%	(0.12%)	-2.21%
2	ER-/PR-	2959	35.07%	(1.83%)	34.49%	(0.16%)	-0.58%
3	ER-/PR-	1781	42.41%	(2.15%)	40.60%	(0.20%)	-1.81%
4	ER-/PR-	1195	47.14%	(2.82%)	45.20%	(0.22%)	-1.93%
5	ER-/PR-	843	51.27%	(4.46%)	49.08%	(0.25%)	-2.19%
6	ER-/PR-	703	49.87%	(2.73%)	52.65%	(0.24%)	2.78%
7	ER-/PR-	534	52.53%	(3.24%)	57.16%	(0.27%)	4.64%



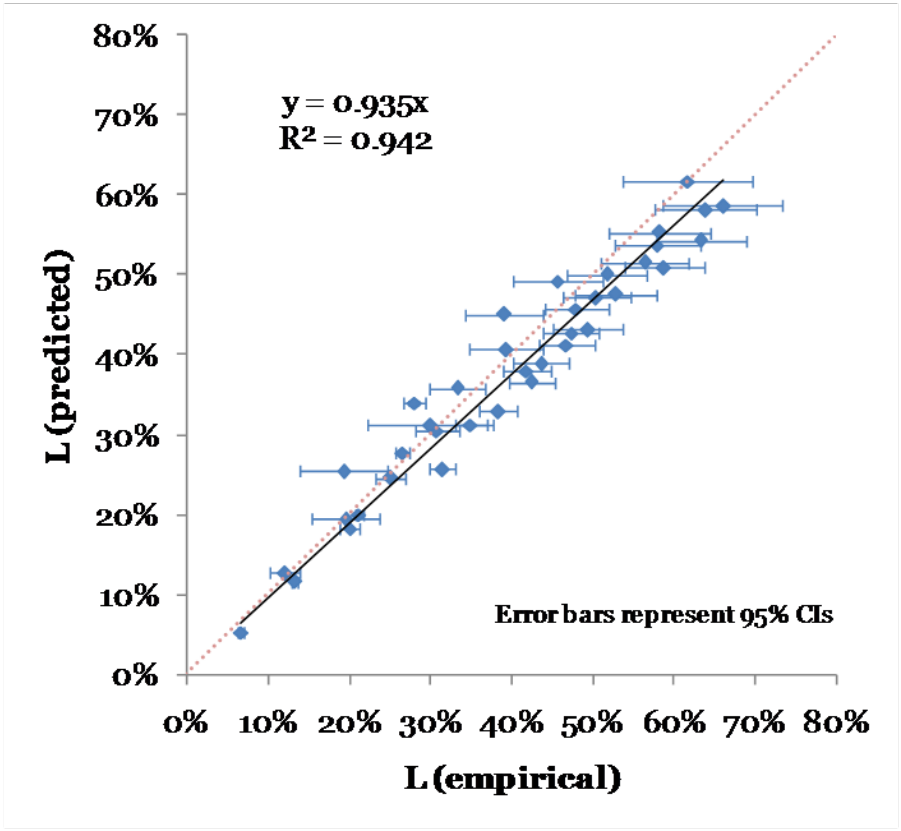
On The Other Hand, Adjuvant!Online is Quite inaccurate



And, Adjuvant!Online Does a Poor Job of Stratifying

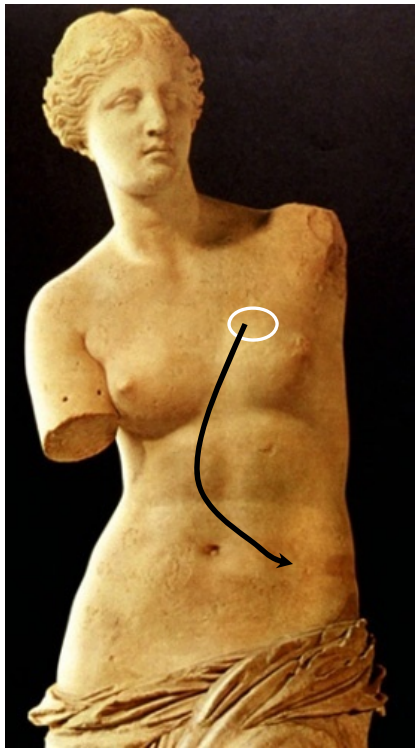


Adjuvant!Online,
Patients Sorted By Size and Number of Positive Nodes



SNP Method,
Patients Sorted By Size and Number of Positive Nodes

This Mathematical Framework Can Answer Many Practical Questions About Cancer



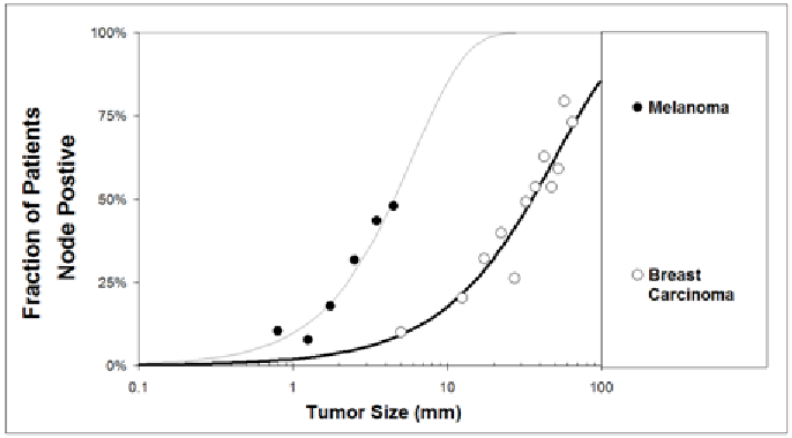
This Mathematical Framework Can Answer Many Practical Questions About Cancer

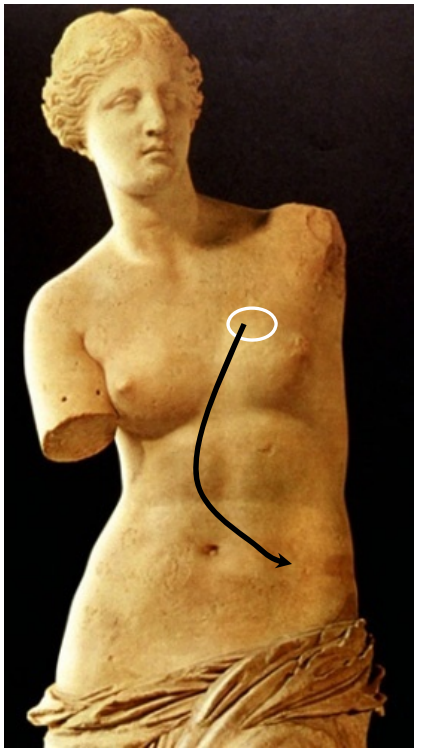
What is the Chance That a Patient Will Have Cancer in the Nodes?

Tumor size and cancer in the nodes
(the *NodalSizeOnly* equation)

$$L_{to-nodes} = 1 - e^{-Q_{Nodes} D^Z}$$

where $L_{to-nodes}$ on of patients with cancer in the nodes, and is the tumor D.

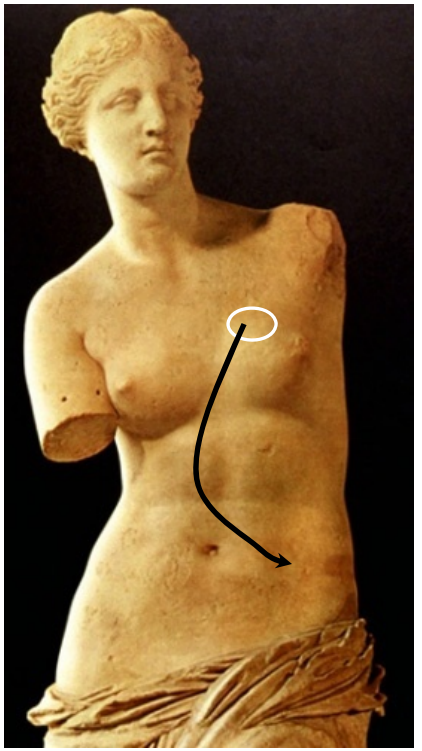




This Mathematical Framework Can Answer Many Practical Questions About Cancer

How Often Should Women Go For Mammograms?

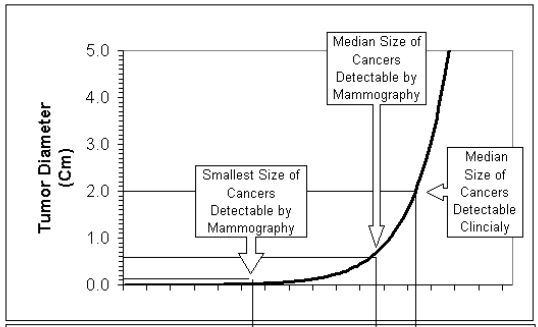
Country	**Screening Recommendation**
United States	Every year from age 40
Canada, Australia, Europe	Every second year
United Kingdom	every three years from age 50



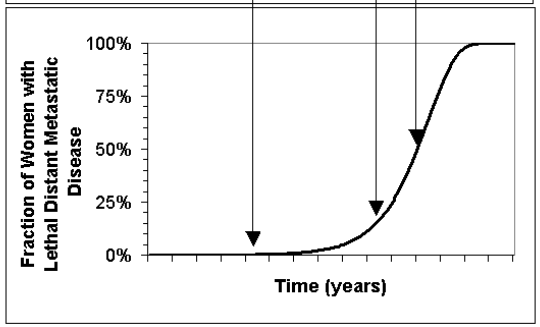
This Mathematical Framework Can Answer Many Practical Questions About Cancer

How Often Should Women Go For Mammograms?

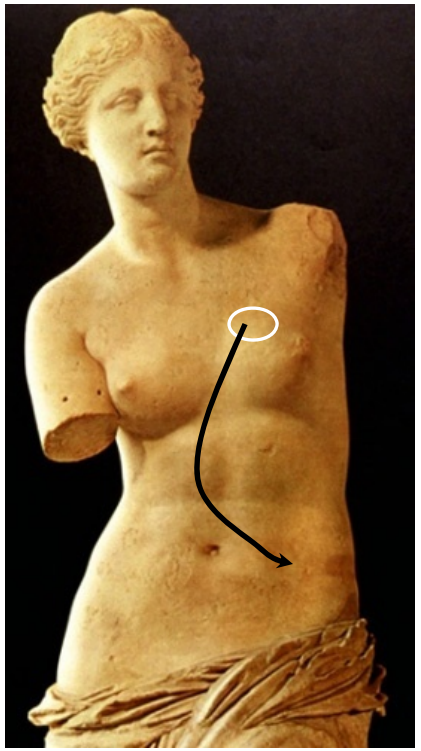
Simulation of Breast Cancer Growth



Simulation of Breast Cancer Spread



$L=1-e^{-QD}$

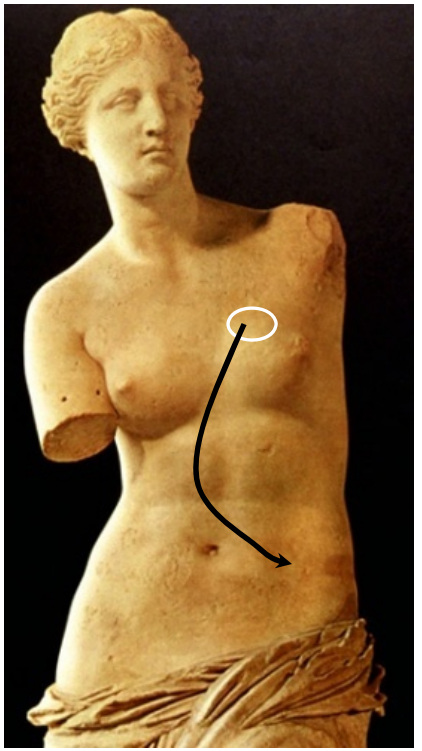


This Mathematical Framework Can Answer Many Practical Questions About Cancer

How Often Should Women Go For Mammograms?

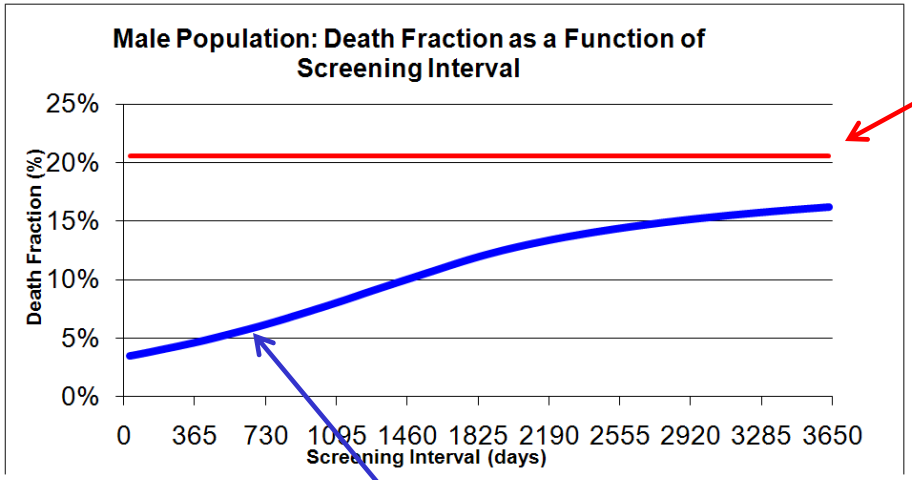
The Consequences of Various Life-Long Screening Breast Cancer as Determined by Computer Simulation Analysis

	SCREENING INTERVAL (MONTHS)							Reduction in Br Ca death (un-age-structure-adjusted)	Survivors	Average Screening Costs (in dollars per cancer free years of life saved) (USA population)	Program Screening Costs (screening dollars per woman per year averaged over the whole USA population of women over age 20)
	age 20	age 30	age 40	age 50	age 60	age 70	age 80				
UK	none	none	none	36	36	none	none	12%	68.9%	$1,353	$4
MGH-actual	none	none	none	17	17	17	17	56%	84.6%	$1,707	$14
ACS	none	none	12	12	12	12	12	66%	88.1%	$2,978	$30
12 months 40-70	none	none	12	12	12	12	none	33%	76.4%	$3,489	$24
NCI	none	none	none	12	12	12	12	60%	85.9%	$2,225	$19
12 months 50-70	none	none	none	12	12	none	none	25%	73.7%	$2,473	$13
2 COUNTY	none	none	24	33	33	33	none	29%	75.0%	$1,916	$11
6 month from 40	none	none	6	6	6	6	6	71%	89.8%	$5,415	$59
6 month from 30	none	6	6	6	6	6	6	74%	90.7%	$8,948	$82



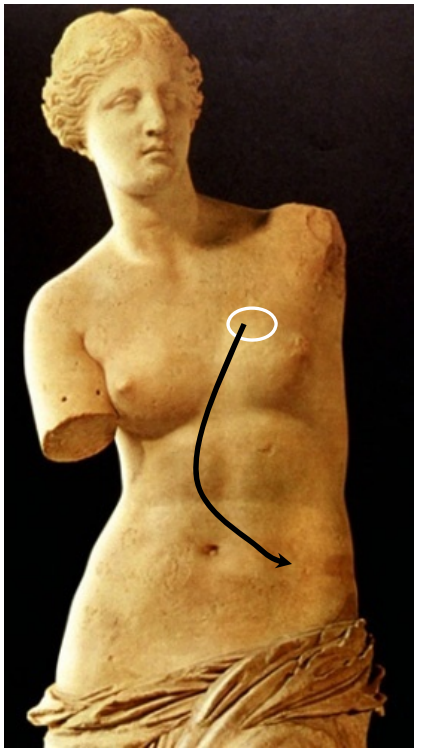
This Mathematical Framework Can Answer Many Practical Questions About Cancer

Should we Screen for Melanoma, and if so, How?



Death Rate in the Absence of Screening

Regular screening should result in a enormous reduction in the melanoma death rate!

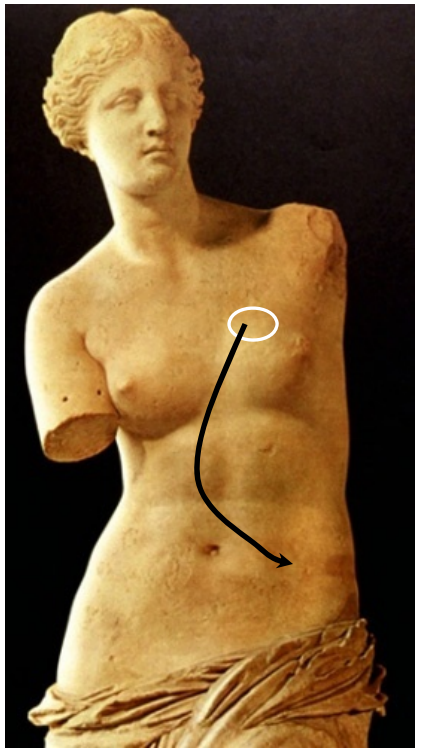


This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

…design systems that optimize patient scheduling, tracking, and reminding, so as to achieve the maximal reduction in cancer death with the resources available:

- ONGOING:
  - •Komen Mammography Reminder Project
  - •Lawrence Health Center Cancer Screening Messaging Project
- NEXT:
  - •Colo-Rectal Cancer Screening Reminder Project
  - •Breast Cancer Tracking System Project
  - •Skin Cancer Screening Project.
  - • …



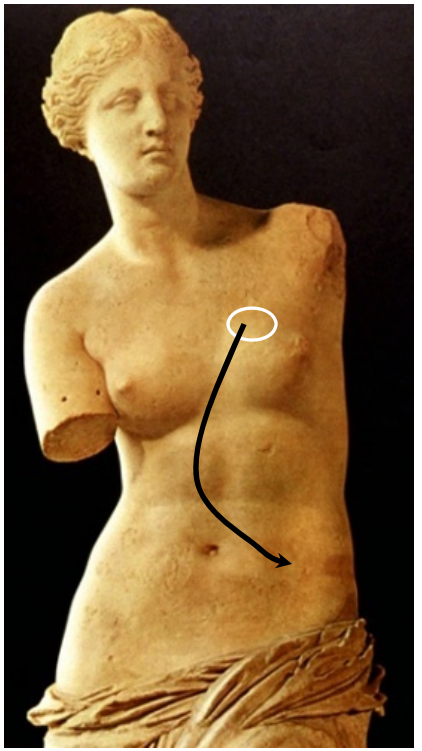
This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

… analyze the Nature of the Events of Spread that Underlie Metastasis

Br J Cancer. 2005 Nov 28;93(11):1244-9. Links
Spread of human cancer cells occurs with probabilities indicative of a nongenetic mechanism.Michaelson JS, Cheongsiatmoy JA, Dewey F, Silverstein MJ, Sgroi D, Smith B, Tanabe KK.
Department of Pathology, Massachusetts General Hospital, Boston, MA 02114, USA. michaelj@helix.mgh.harvard.edu

There has been much uncertainty as to whether metastasis requires mutation at the time of spread. Here, we use clinical data to calculate the probability of the spread of melanoma and breast cancer cells. These calculations reveal that the probability of the spread of cancer cells is relatively high for small tumours (approximately 1 event of spread for every 500 cells for melanomas of 0.1 mm) and declines as tumours increase in size (approximately 1 event of spread for every 10(8) cells for melanomas of 12 mm). The probability of spread of breast cancer cells from the lymph nodes to the periphery is approximately 1 event of spread for every 10(8) cells in the nodal masses, which have a mean diameter of 5 mm, while the probability of spread of cancer cells from the breast to the periphery when the primary masses are 5 mm is also approximately 1 event of spread for every 10(8) cells. Thus, the occurrence of an event of spread from the breast to the lymph nodes appears not to increase the propensity of the progeny of those cells to spread from the lymph nodes to the periphery. These values indicate that the spread of human breast cancer and melanoma cells is unlikely to occur by a mechanism requiring mutation at the time of spread.



This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

…indentify The Causes of the Reductions in Cancer Death Rates that Have Occurred Over the Past Decades

The Impact of Breast Cancer Screening Practices on Survival over Three Decades: A Proposal for Improving Survival

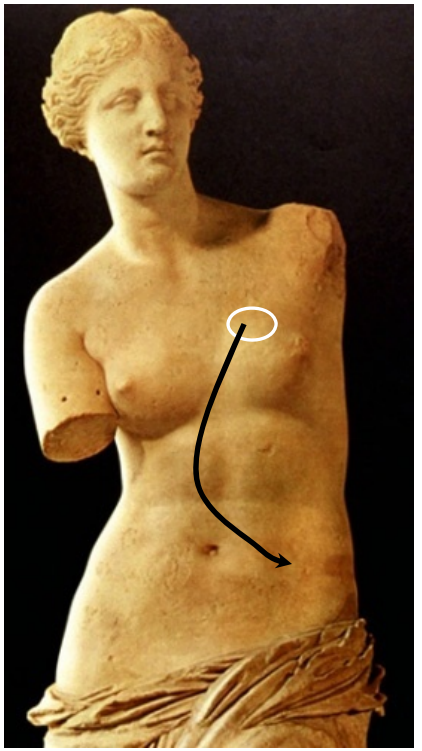
Amanda Wheeler, MD, Barbara L. Smith, MD, PhD, …. James Michaelson PhD

Introduction:
While breast carcinoma (BrCa) lethality has declined over the past three decades, the relative contributions of screening and adjuvant therapy have been uncertain. A recently developed mathematical method, the *SizeOnly* equation, makes it possible to determine the impact of tumor size on the risk of cancer death, and thus the impact of screening on the BrCa death rate.

Methods:
Data were derived from a modified SEER dataset of 402,240 BrCa patients from and a "LOCAL" dataset of 22,901 patients from a consortium of tertiary care hospitals.

Results:
When examined by year of death, the BrCa death rate has declined steadily since the early 1990s. When examined by year of detection, the BrCa case fatality rate has declined from 44% in 1974 to 29% in 1991, remaining stable since 1991 (SEER & LOCAL datasets). The average tumor diameter declined from 30 mm in the 1970s to 22 mm in 1991, remaining stable since 1991 (SEER & LOCAL). The fraction of BrCa's detected by mammography increased from 18% in 1980 to 73% in 1993, remaining stable since 1993 (LOCAL). The fraction of women receiving adjuvant chemotherapy/hormone therapy increased from 25% in 1987 to 70% in 1991, remaining stable since 1991 (SEER). *SizeOnly* calculations indicate that reduction in BrCa size can account for 2/3rds of the reduction in the case fatality rate over the past 3 decades. Similarly, 80% of the reduction in the case fatality rate occurred before 1987 when few patients (12%) received adjuvant therapy (SEER). Among the very few women (1-in-20) who consistently attend annual screening, the average tumor size is 10.9 mm (LOCAL), roughly half the size (and, by the *SizeOnly* equation, half the lethality) of both the cancers in the population as a whole (SEER) and the cancers in the women who utilize screening intermittently (LOCAL).

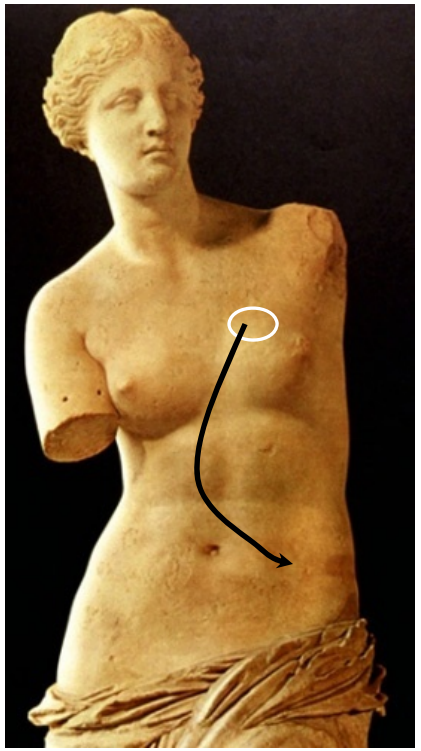
Conclusions:
Despite its widespread underutilization, screening mammography has been the principal mechanism for the reduction in BrCa lethality over the past three decades, with adjuvant chemotherapy/hormone therapy making a smaller contribution. If utilized to its full extent, mammographic screening has the further potential for cutting the BrCa death rate in half.



This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

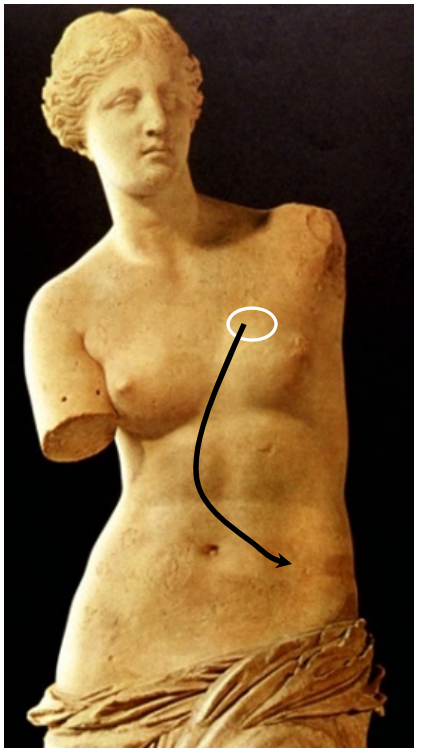
.. . tease out and Quantify the Contributions of Gene Expression Array Patterns to Cancer Lethality



This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

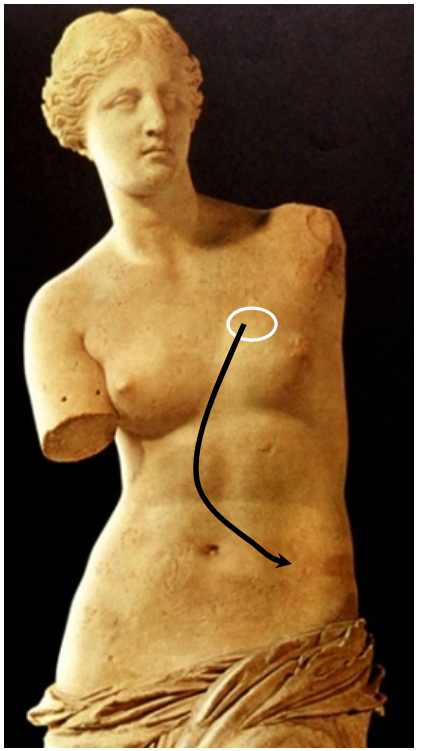
.. . tease out and Quantify the Contributions of Local Recurrence and Second Cancers to Cancer Lethality



This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

.. . Model The Spread of Cancer in the Nodes, and From the Nodes, so as to Provide Physicians with better Tools For Estimating the Chance of Nodal Metastasis, and to Quantify It's Lethal Consequence.



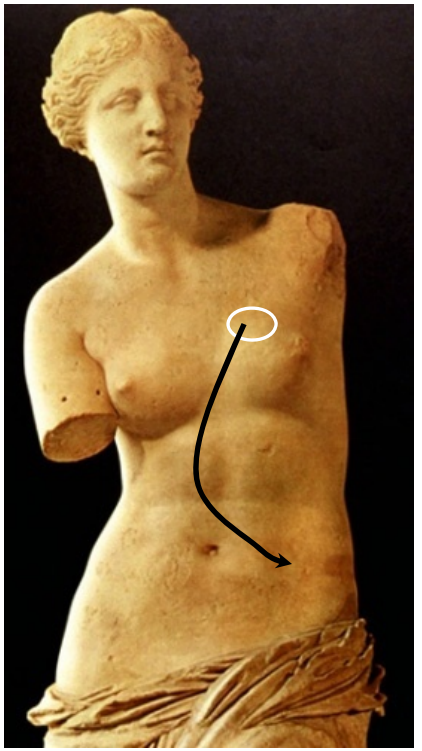
This Mathematical Framework Can Answer Many Practical Questions About Cancer

We have used this framework to…

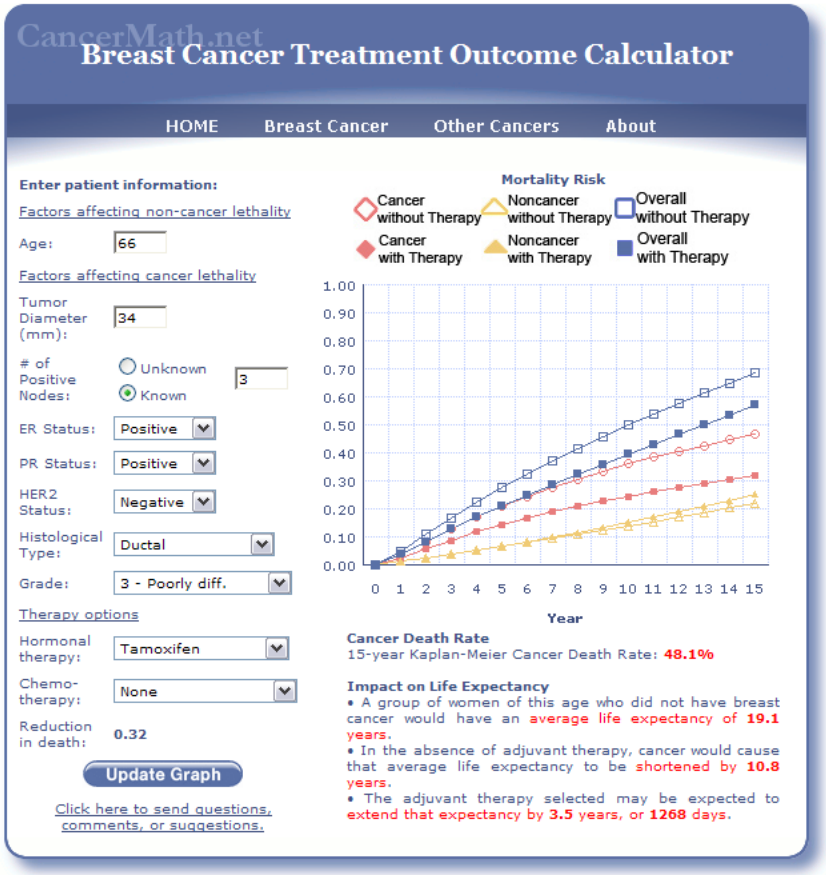
- …Understand the Time Course of Metastatic Disease, the Tumor Dormancy Period, and the Cancer Hazard Function.

&

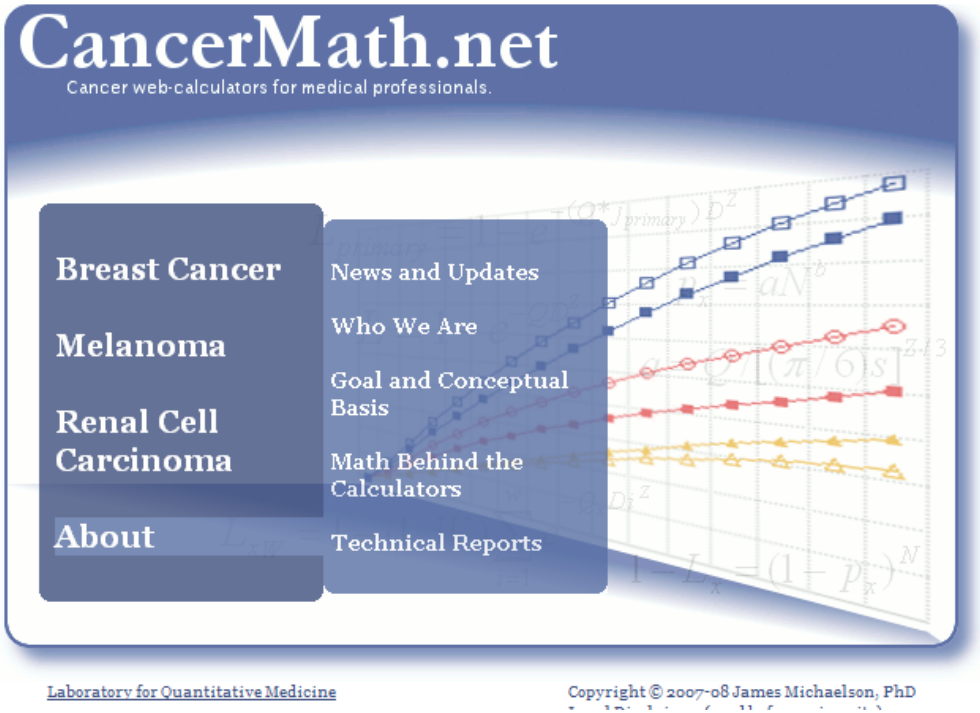
- …Model Chemotherapy, so as to Indentify the Dosages and Schedules for Achieving the Greatest Possible Extension (or Extinction) of Metastatic Disease



Let’s Return to Our Calculators



We Provide a Lot of Information



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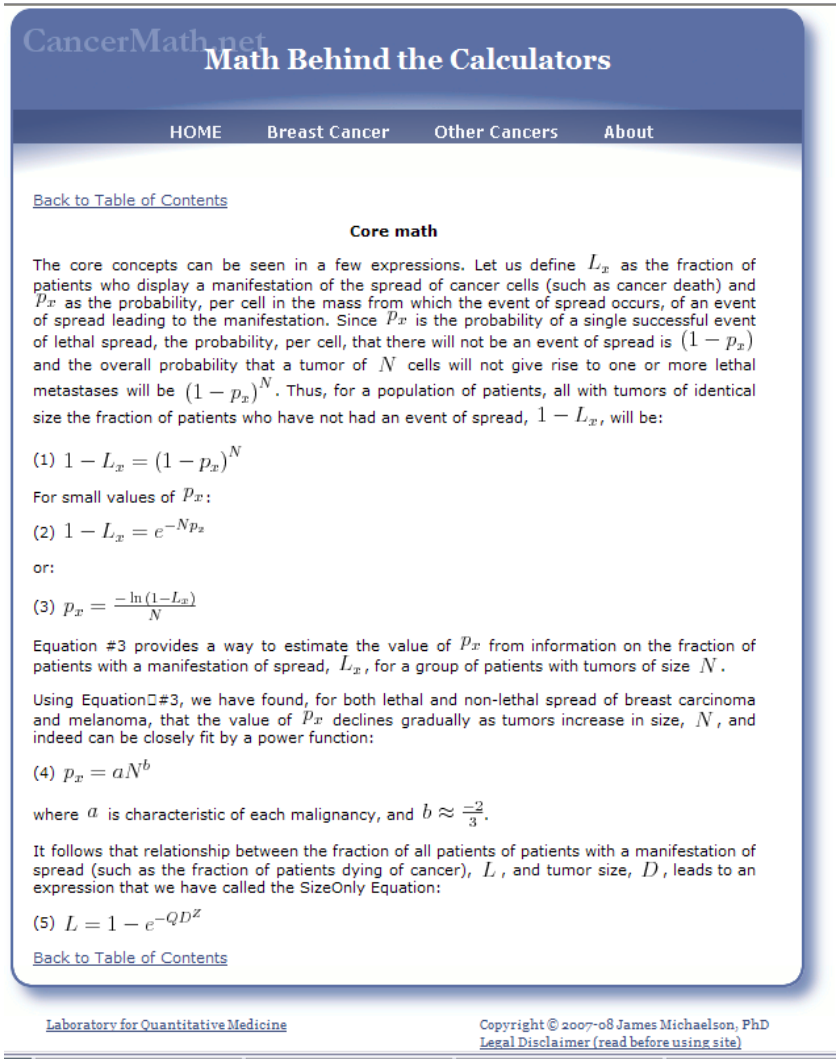

CancerMath.net

Math Behind the Calculators

HOME Breast Cancer Other Cancers About

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Core math

The core concepts can be seen in a few expressions. Let us define L_x as the fraction of patients who display a manifestation of the spread of cancer cells (such as cancer death) and p_x as the probability, per cell in the mass from which the event of spread occurs, of an event of spread leading to the manifestation. Since p_x is the probability of a single successful event of lethal spread, the probability, per cell, that there will not be an event of spread is $(1 - p_x)$ and the overall probability that a tumor of N cells will not give rise to one or more lethal metastases will be $(1 - p_x)^N$. Thus, for a population of patients, all with tumors of identical size the fraction of patients who have not had an event of spread, $1 - L_x$, will be:

(1) $1 - L_x = (1 - p_x)^N$

For small values of p_x:

(2) $1 - L_x = e^{-Np_x}$

or:

(3) $p_x = \frac{-\ln(1-L_x)}{N}$

Equation #3 provides a way to estimate the value of p_x from information on the fraction of patients with a manifestation of spread, L_x, for a group of patients with tumors of size N.

Using Equation #3, we have found, for both lethal and non-lethal spread of breast carcinoma and melanoma, that the value of p_x declines gradually as tumors increase in size, N, and indeed can be closely fit by a power function:

(4) $p_x = aN^b$

where a is characteristic of each malignancy, and $b \approx \frac{-2}{3}$.

It follows that relationship between the fraction of all patients of patients with a manifestation of spread (such as the fraction of patients dying of cancer), L, and tumor size, D, leads to an expression that we have called the SizeOnly Equation:

(5) $L = 1 - e^{-QD^Z}$

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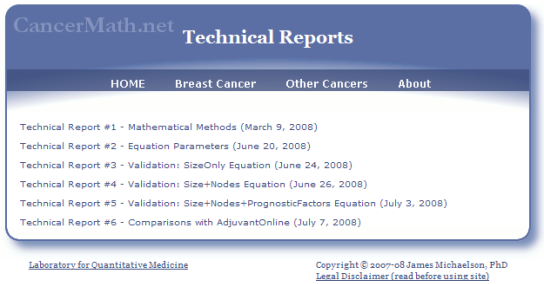
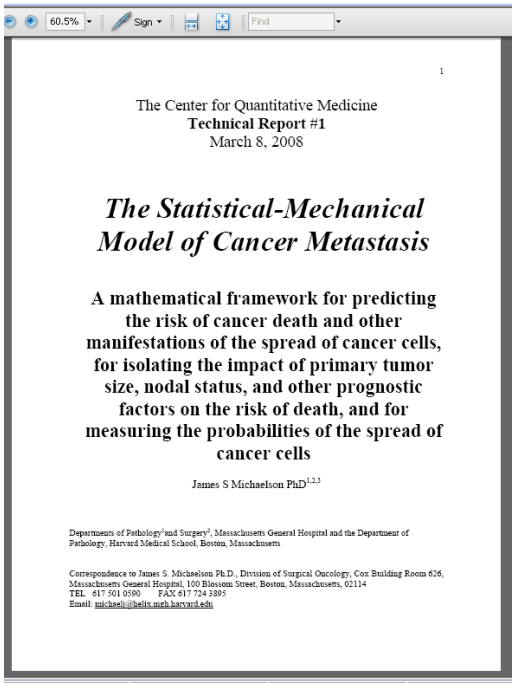
We Provide a Lot of Information

We Provide a Lot of Information





1

The Center for Quantitative Medicine
Technical Report #1
March 8, 2008

The Statistical-Mechanical Model of Cancer Metastasis

A mathematical framework for predicting the risk of cancer death and other manifestations of the spread of cancer cells, for isolating the impact of primary tumor size, nodal status, and other prognostic factors on the risk of death, and for measuring the probabilities of the spread of cancer cells

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Departments of Pathology[1] and Surgery[2], Massachusetts General Hospital and the Department of Pathology, Harvard Medical School, Boston, Massachusetts

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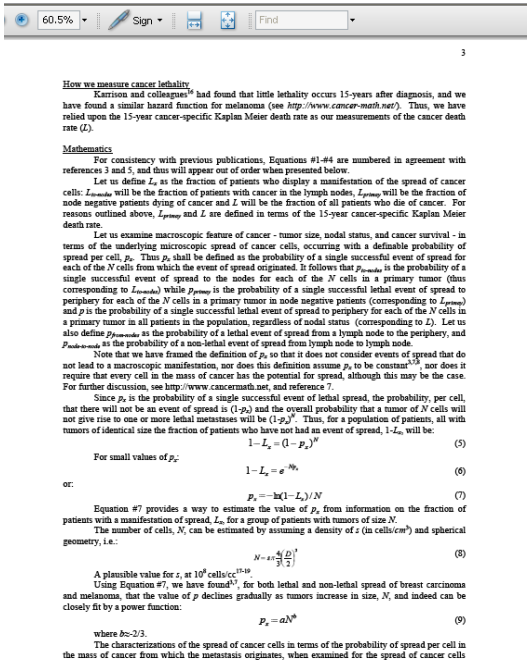


3

How we measure cancer lethality

Karrison and colleagues[16] had found that little lethality occurs 15-years after diagnosis, and we have found a similar hazard function for melanoma (see *http://www.cancer-math.net/*). Thus, we have relied upon the 15-year cancer-specific Kaplan Meier death rate as our measurements of the cancer death rate (L).

Mathematics

For consistency with previous publications, Equations #1-#4 are numbered in agreement with references 3 and 5, and thus will appear out of order when presented below.

Let us define L_x as the fraction of patients who display a manifestation of the spread of cancer cells: $L_{in\text{-}nodes}$ will be the fraction of patients with cancer in the lymph nodes, $L_{primary}$ will be the fraction of node negative patients dying of cancer and L will be the fraction of all patients who die of cancer. For reasons outlined above, $L_{primary}$ and L are defined in terms of the 15-year cancer-specific Kaplan Meier death rate.

Let us examine macroscopic feature of cancer - tumor size, nodal status, and cancer survival - in terms of the underlying microscopic spread of cancer cells, occurring with a definable probability of spread per cell, p_x. Thus p_x shall be defined as the probability of a single successful event of spread for each of the N cells from which the event of spread originated. It follows that $p_{in\text{-}nodes}$ is the probability of a single successful event of spread to the nodes for each of the N cells in a primary tumor (thus corresponding to $L_{in\text{-}nodes}$) while $p_{primary}$ is the probability of a single successful lethal event of spread to periphery for each of the N cells in a primary tumor in node negative patients (corresponding to $L_{primary}$) and p is the probability of a single successful lethal event of spread to periphery for each of the N cells in a primary tumor in all patients in the population, regardless of nodal status (corresponding to L). Let us also define $p_{from\text{-}node}$ as the probability of a lethal event of spread from a lymph node to the periphery, and $p_{node\text{-}to\text{-}node}$ as the probability of a non-lethal event of spread from lymph node to lymph node.

Note that we have framed the definition of p_x so that it does not consider events of spread that do not lead to a macroscopic manifestation, nor does this definition assume p_x to be constant[3,5,8], nor does it require that every cell in the mass of cancer has the potential for spread, although this may be the case. For further discussion, see http://www.cancermath.net, and reference 7.

Since p_x is the probability of a single successful event of lethal spread, the probability, per cell, that there will not be an event of spread is $(1\text{-}p_x)$ and the overall probability that a tumor of N cells will not give rise to one or more lethal metastases will be $(1\text{-}p_x)^N$. Thus, for a population of patients, all with tumors of identical size the fraction of patients who have not had an event of spread, $1\text{-}L_x$, will be:

$$1-L_x=(1-p_x)^N \tag{5}$$

For small values of p_x:

$$1-L_x=e^{-Np_x} \tag{6}$$

or:

$$p_x=-\ln(1-L_x)/N \tag{7}$$

Equation #7 provides a way to estimate the value of p_x from information on the fraction of patients with a manifestation of spread, L_x, for a group of patients with tumors of size N.

The number of cells, N, can be estimated by assuming a density of s (in cells/cm^3) and spherical geometry, i.e.:

$$N=s\frac{4}{3}\pi\left(\frac{D}{2}\right)^3 \tag{8}$$

A plausible value for s, at 10^9 cells/cc[17-19]

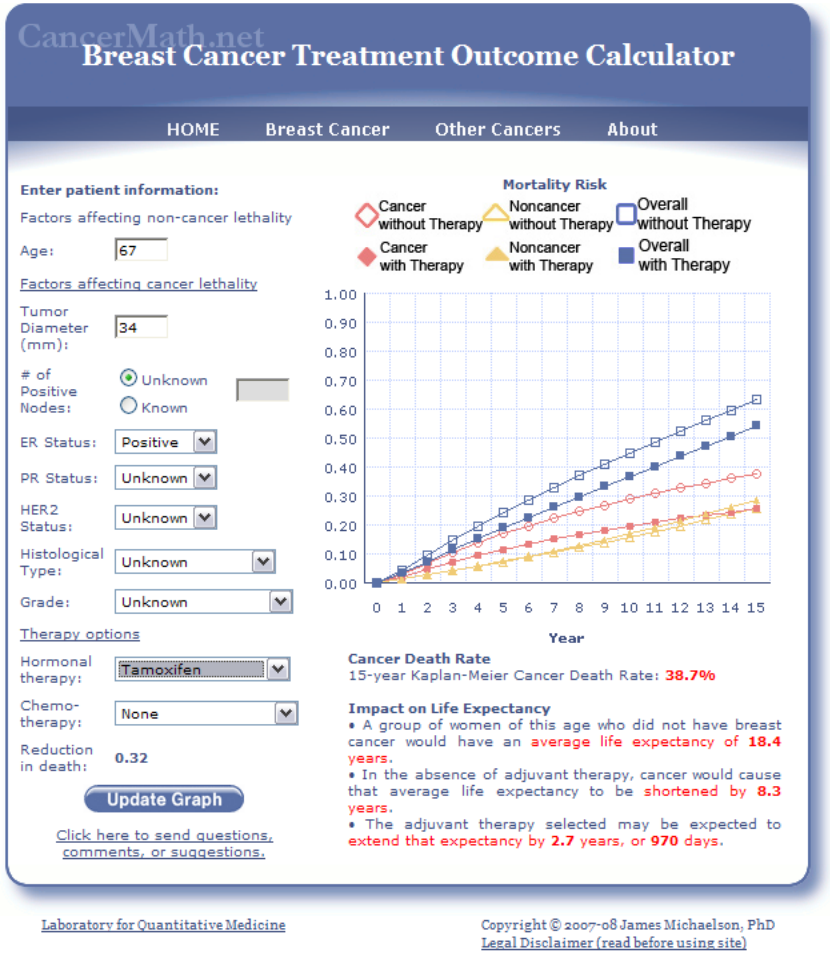
Using Equation #7, we have found[4,7], for both lethal and non-lethal spread of breast carcinoma and melanoma, that the value of p declines gradually as tumors increase in size, N, and indeed can be closely fit by a power function:

$$p_x=aN^b \tag{9}$$

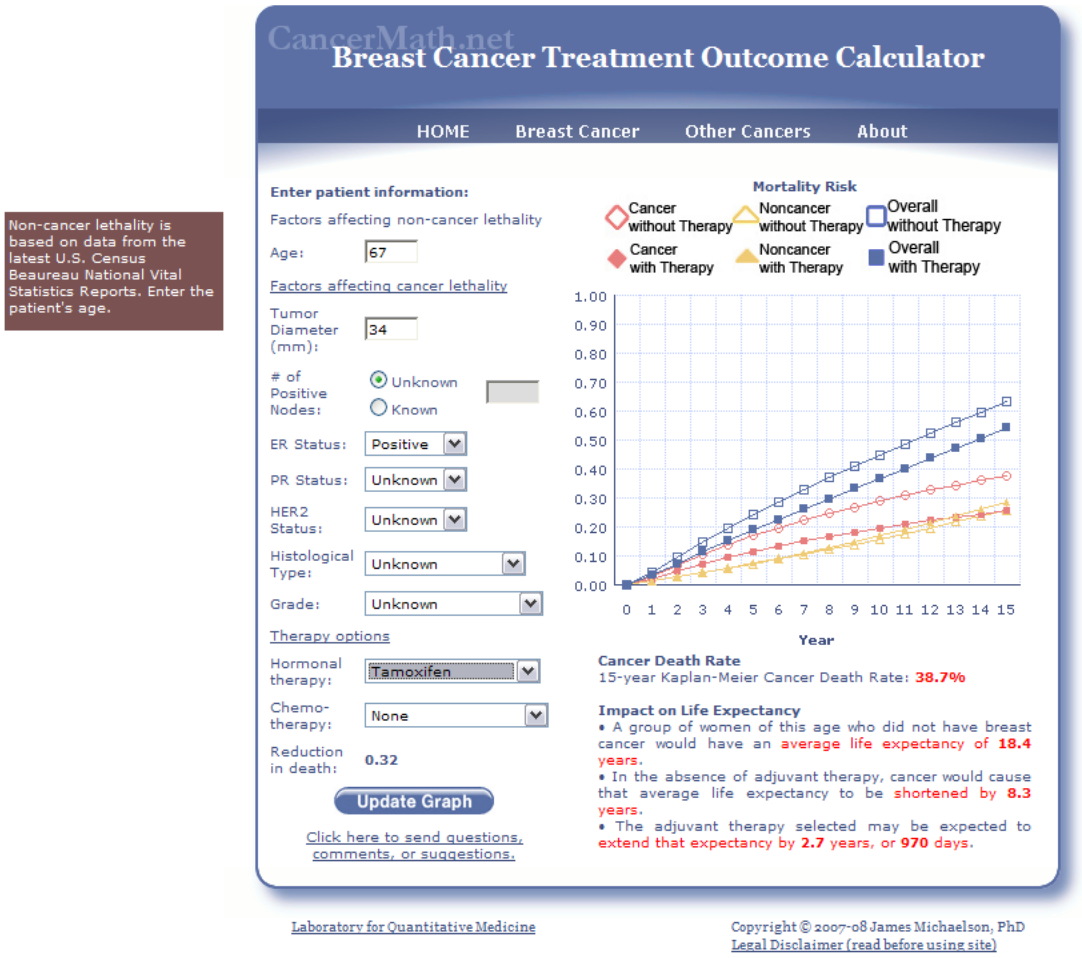
where $b\approx -2/3$.

The characterizations of the spread of cancer cells in terms of the probability of spread per cell in the mass of cancer from which the metastasis originates, when examined for the spread of cancer cells

The Calculators Are Thoroughly Explained

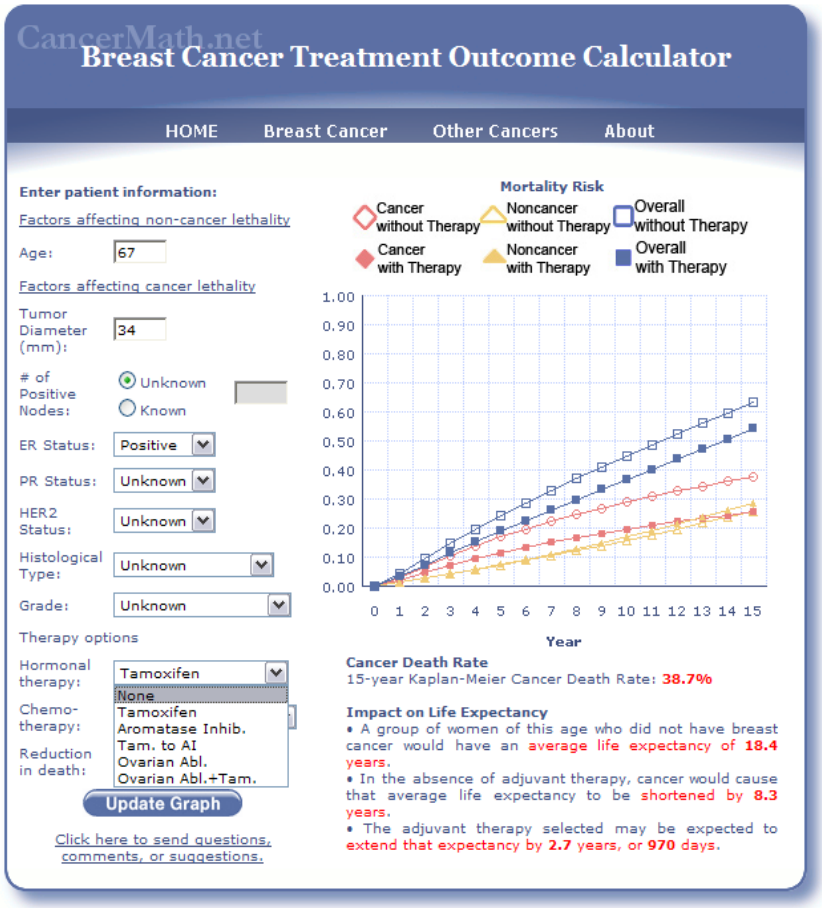


The Calculators Are Thoroughly Explained



The Calculators Are Thoroughly Explained

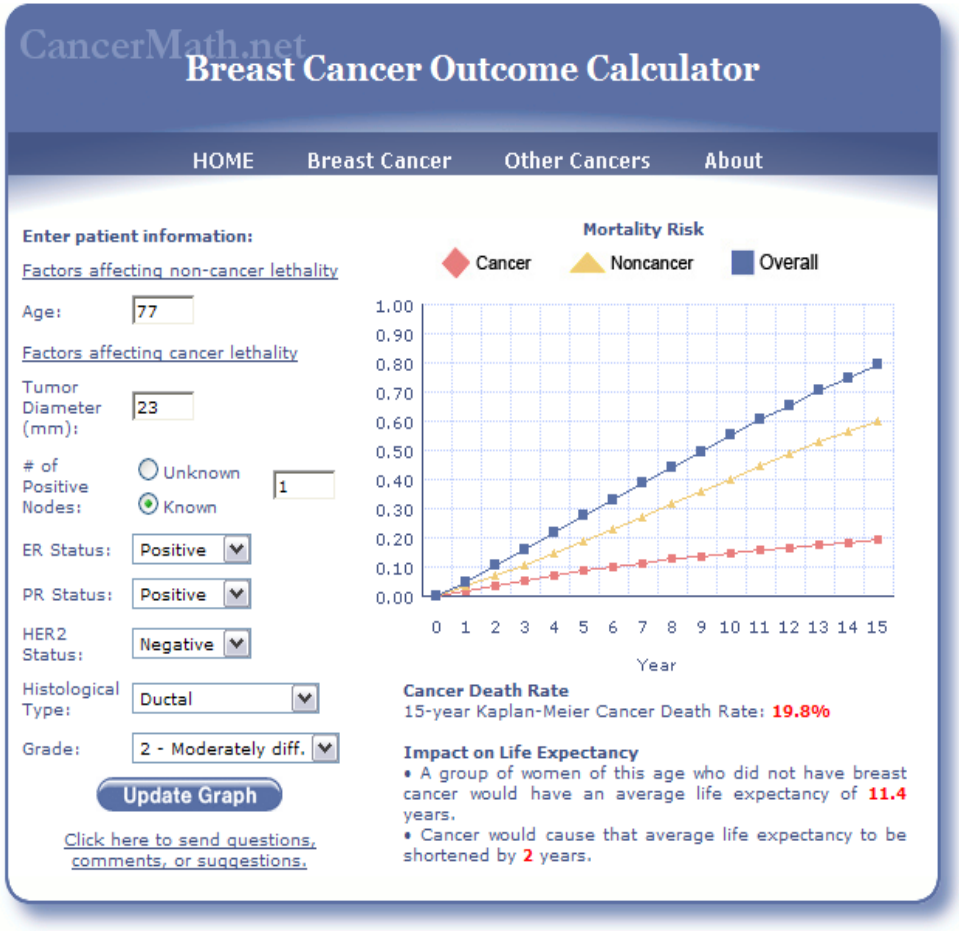
A proportional risk reduction model is used in determining the effects of adjuvant therapy. NOTE: we have adopted the same reduction in death values that were adopted by AdjuvantOnline.



We Provide a Whole Range of Calculators

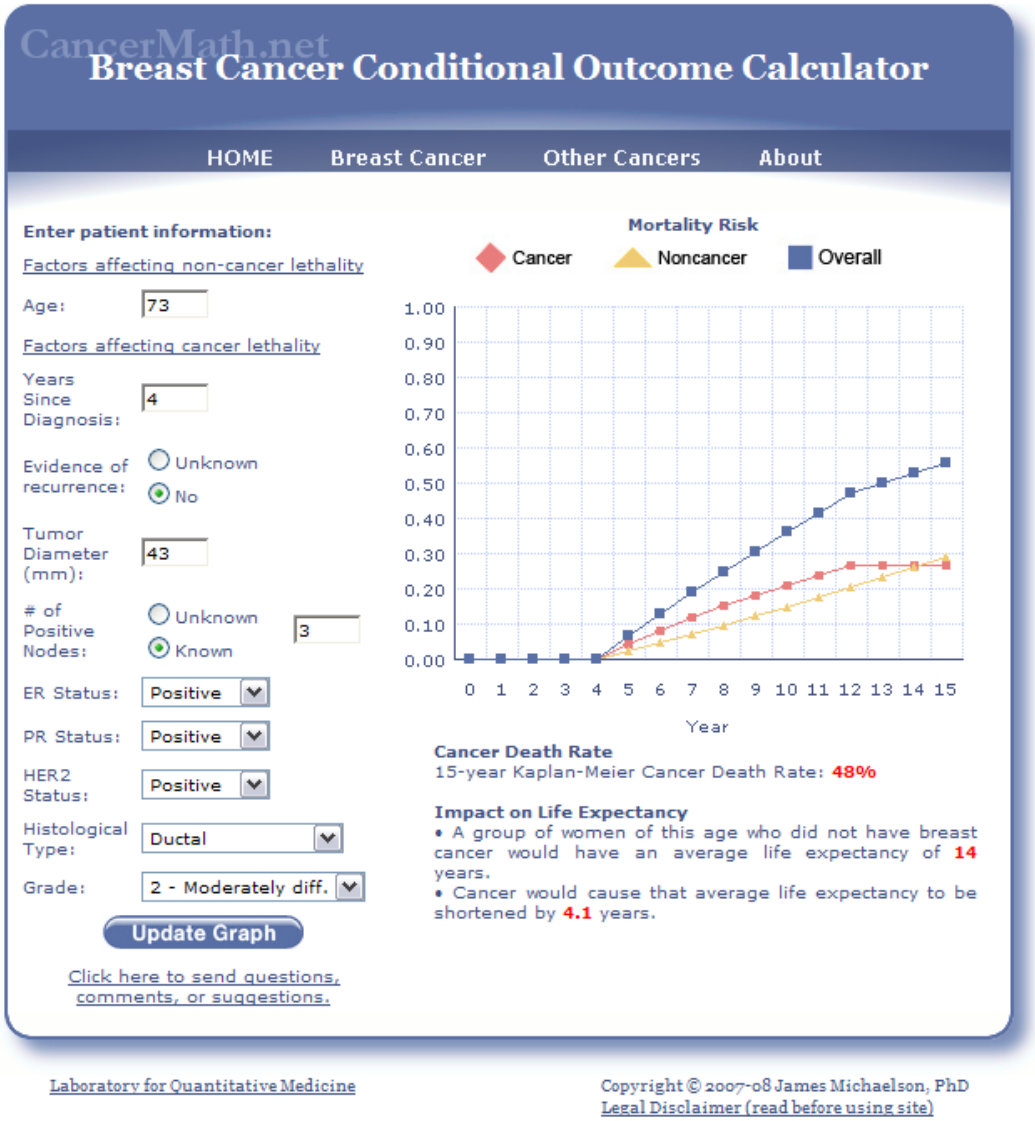
We Provide a Whole Range of Calculators

This calculator gives the breast cancer survival and other information, projected over time, that reflects expectations at the current time.



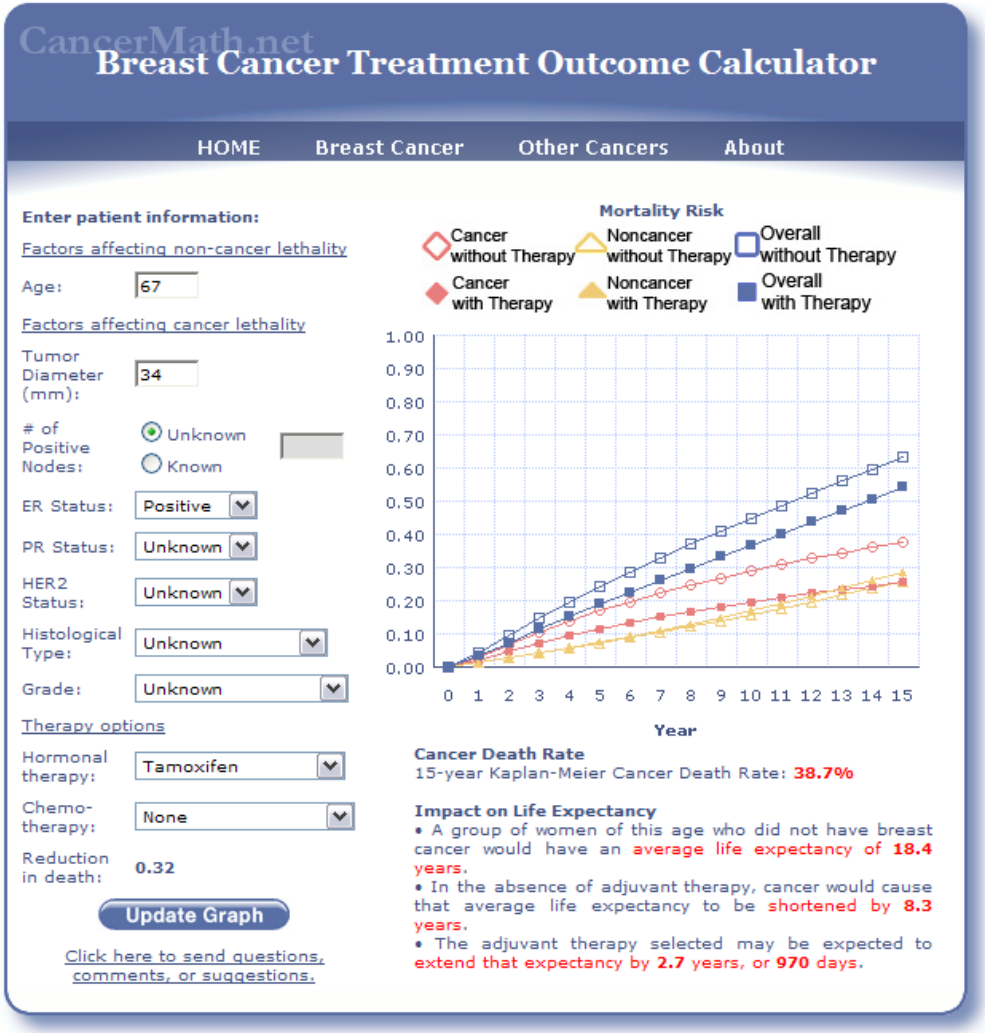
We Provide a Whole Range of Calculators

This calculator gives the breast cancer survival and other information, projected over time, that reflects expectations at the current time. The number of years since diagnosis can be specified, as well as whether or not during this period of time the patient was known to be recurrence-free.



We Provide a Whole Range of Calculators

This calculator gives the breast cancer survival and other information, projected over time, with and without various adjuvant chemo- and hormonal therapies, presuming the same reduction in death values that were adopted by AdjuvantOnline.



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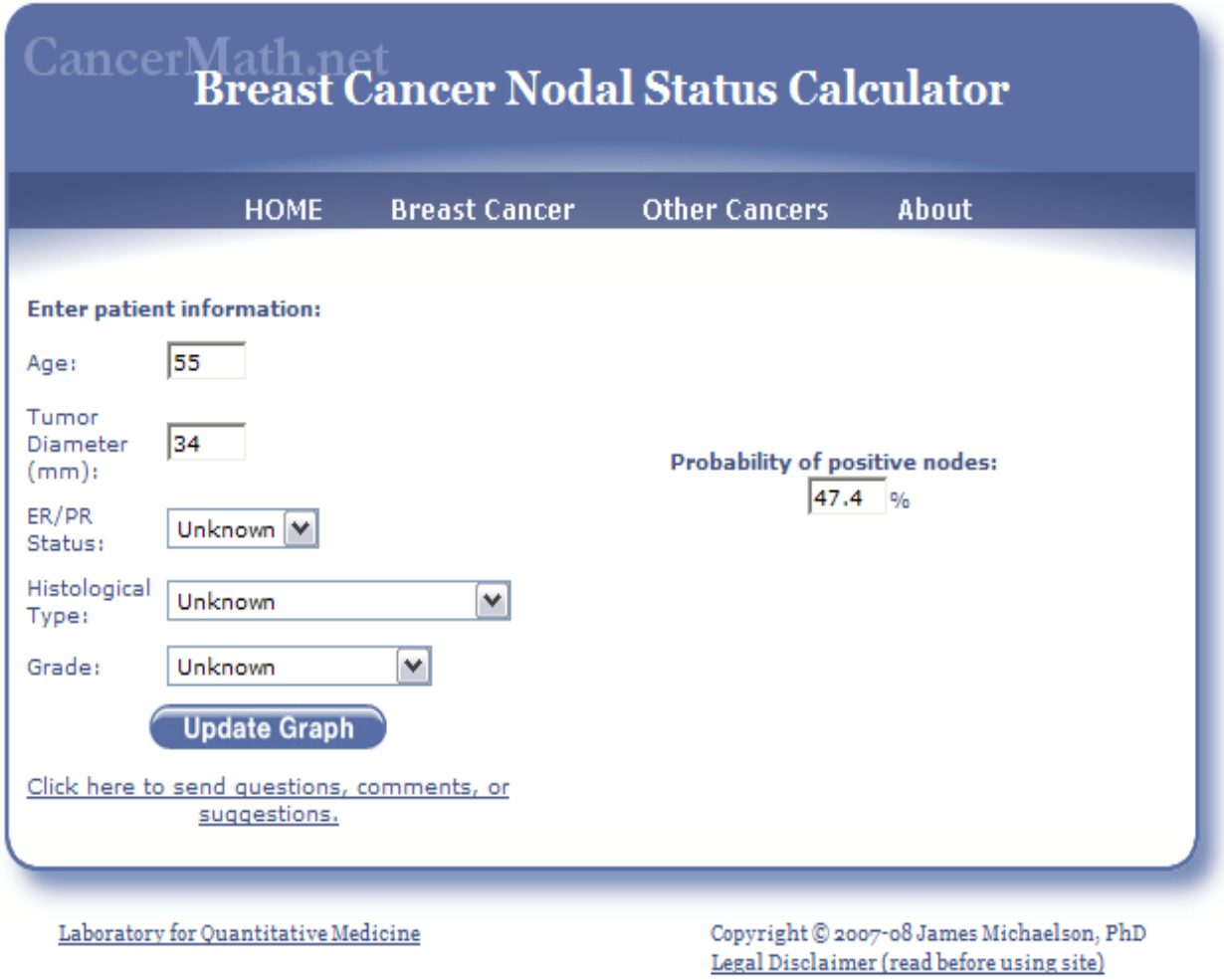


We Provide a Whole Range of Calculators

This calculator gives the risk of cancer in the nipple, for assistance in deciding on nipple-sparing mastectomy.

CancerMath.net

Breast Cancer: Nipple Involvement Calculator

HOME | Breast Cancer | Other Cancers | About

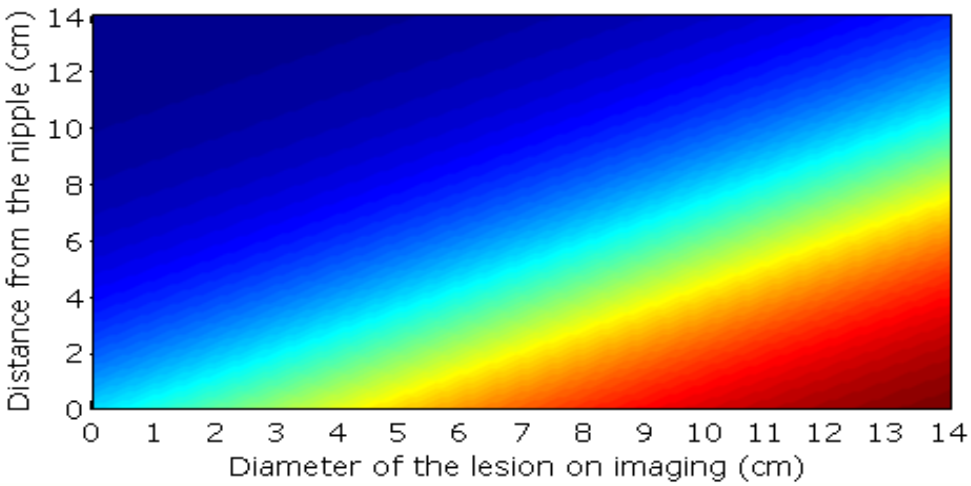
Information

Tumor Diameter (cm):	6.1
Tumor Distance (cm):	7.5
Probability of Nipple Involvement:	0.163

Reset Information

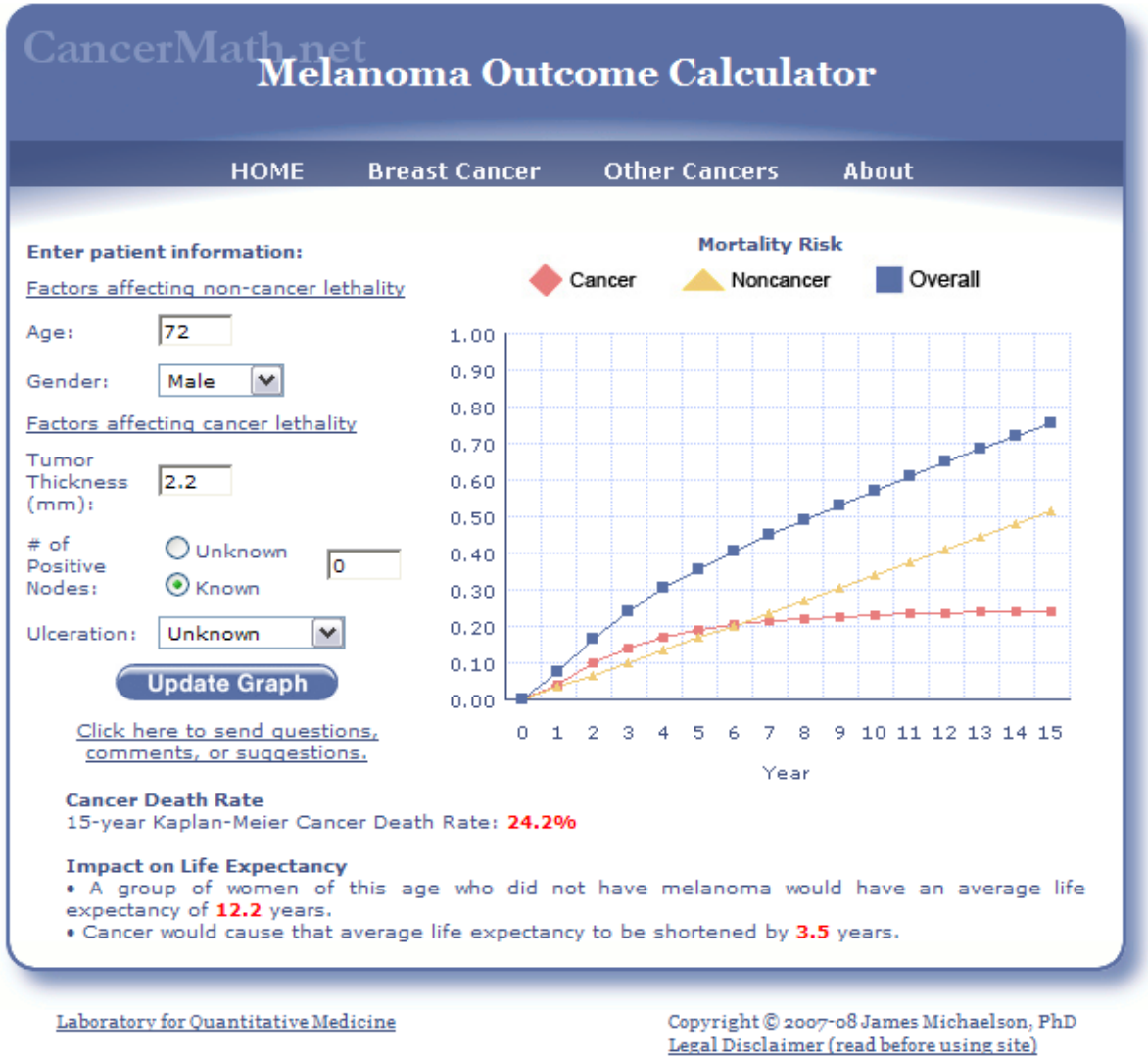
Click here to send questions, comments, or suggestions.

Move mouse over graph:



Laboratory for Quantitative Medicine

We Provide a Whole Range of Calculators



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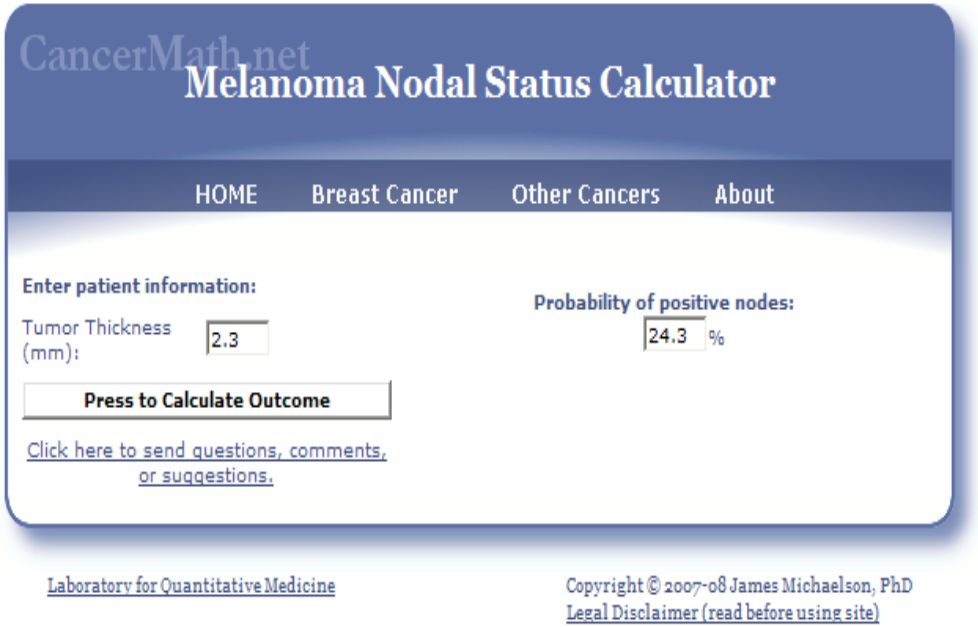

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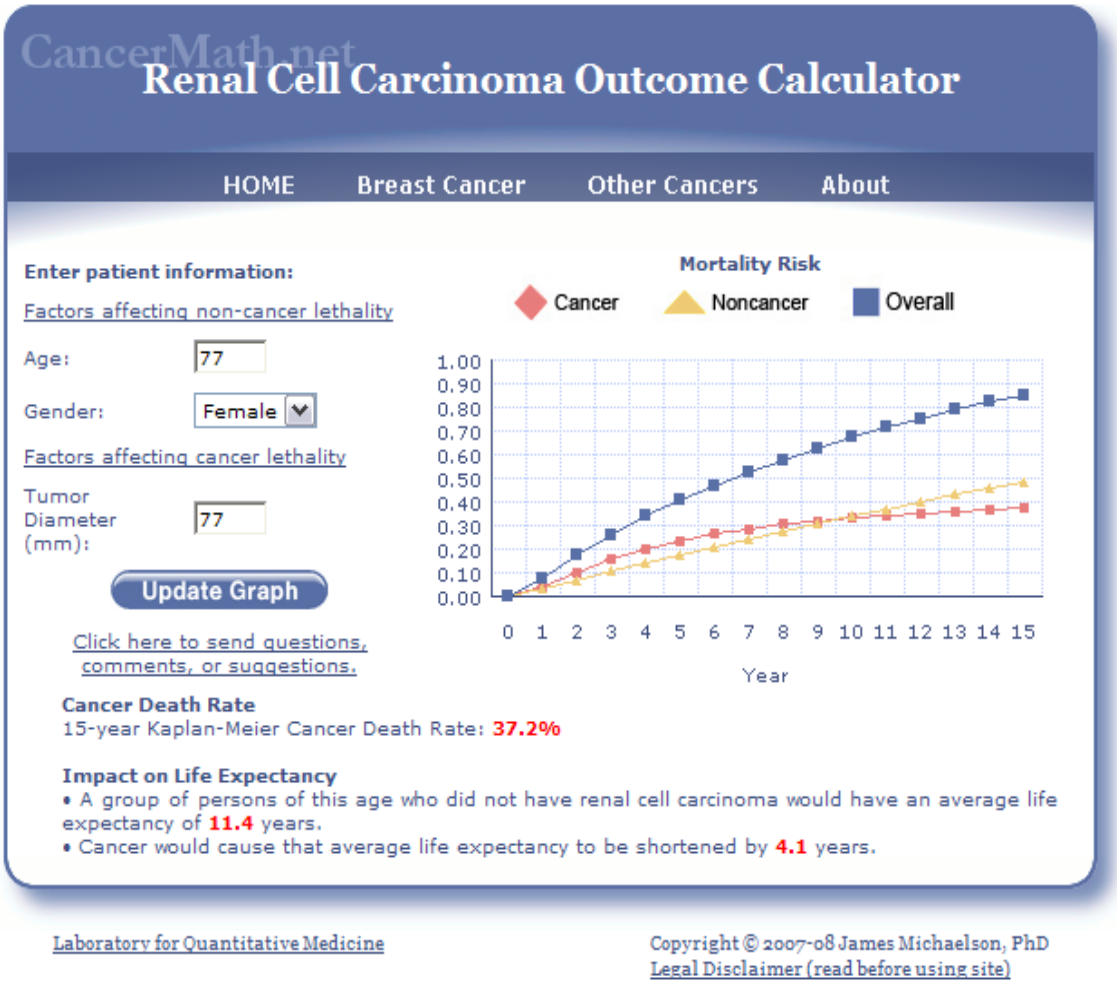

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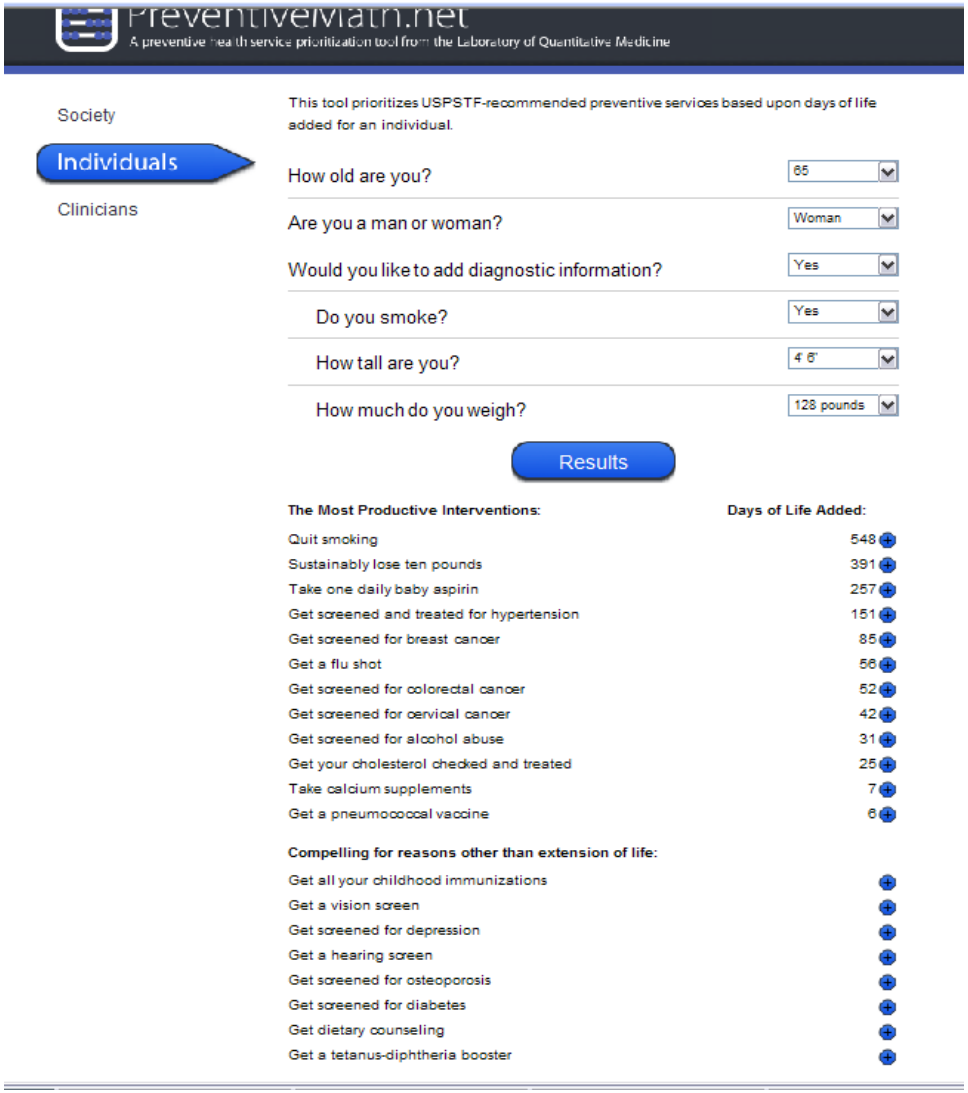

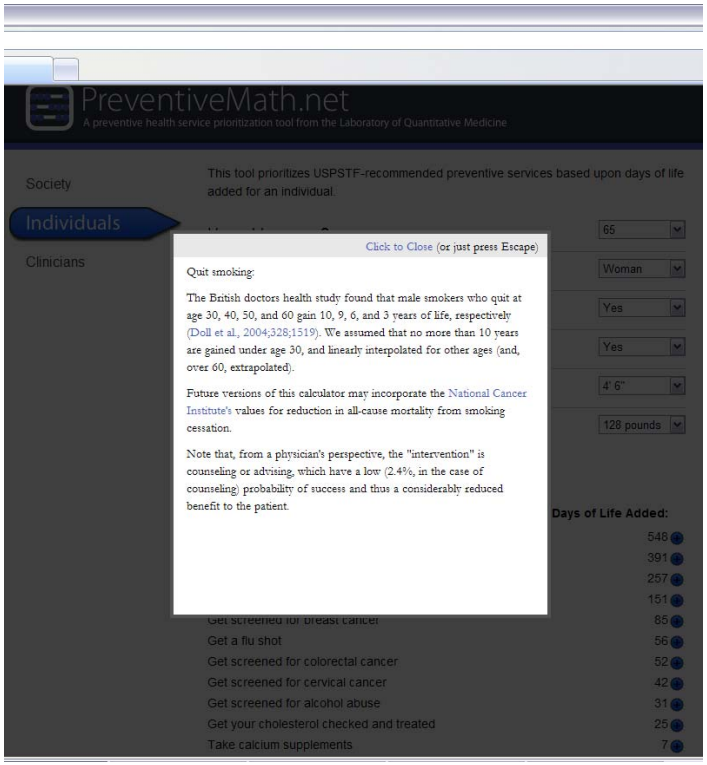

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Massachusetts General Hospital
Harvard Medical School