Clinical Research Seminar

Using the Internet to Conduct Research and Recruit Subjects

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Boston University School of Public Health

Boston University School of Public Health
Data Coordinating Center

Types of Studies that Work Best

- Cohort Studies
  - Loss to follow up may be a problem
- Health Education
- Surveys
  - difficulty determining denominator and low response rate issues raise issues about generalizability
- Traditional Clinical Trials
  - Randomization
  - Data entry
  - Study management/communications
- Online Clinical Trials
  - “Nutriceuticals” or non-invasive interventions

Benefits of Internet in Research

- Capture data in real time
- Data collection for clinical research
  - Paperless
- Communications and management for mutli-site trials
- Subject recruitment
  - Reach greater target population

Risks

- No direct contact with subjects
  - Unable to intervene if subjects become distressed or experience other adverse events
- Breach of confidentiality
  - Most common risk
  - Via insecure transfer of data
  - Via environment in which subject is accessing Internet (e.g., Internet café, public library)

Validity

- Non-representative populations (i.e., tend to be of higher SE and educational status)
- Falsification of data
- Multiple submissions by same subject
  - "Subject naught"
- Invalid results places subjects unnecessarily at risk

Consent

- Waiver of consent
  - [45 CFR 56.116(d)]: (1) The research involves no more than minimal risk to the subjects;
  - (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
  - (3) The research could not practicably be carried out without the waiver or alteration;

  -AND-
  - (4) Subjects will be provided with additional information/results after participation

Consent

- Waiver of documentation of consent
  - [45 CFR 56.117(c)] : (1) Only record linking subject to research would be the consent document and this is the primary risk of harm (i.e., in the event of breach of confidentiality) **-OR-**
  - (2) Research presents no more than minimal risk to subjects and involves no procedures for which written consent is normally required outside of the research context
  - Can still create a consent page that subjects must read and electronically accept before proceeding
- Subjects may also print/sign consent form from Internet and fax/mail to investigator to receive password for website

Privacy

- Identifiable vs. Anonymous
  - Screen names/handles/e-mail addresses commonly used online
  - Though subject names may not appear with these, often can be “readily ascertained” via search engines
  - Online identity may be as important to a subject as real identity

Privacy

- Public vs. Private
  - Most online activity is publicly accessible
  - Federal regulations base definition of private information on the “reasonable expectation” of privacy
    - e.g., chat rooms, chatters expect privacy and not to have their chat studied

Minors as Subjects

- If research qualifies for waiver of parental permissions, no additional safeguards required
- Otherwise parental consent must be obtained unless criteria for Waiver of Informed Consent or Waiver of Documentation of Informed Consent are met
- Online services can help but none are 100% foolproof
  - AdultCheck
  - NetNanny

Confidentiality

- Breaches
  - Inadvertent disclosure (e.g., stolen laptops/computers with subject data)
  - Deliberate attempts to gain access (i.e., hackers, no documented evidence of this occurring in a research setting)
- E-mail is considered “individually identifiable information” by IRB
- Information or data transmitted by e-mail is not secure unless additional steps are taken (e.g., encryption)

Web Systems Security

- Website on secure server behind firewall
- Server housed in locked room with restricted access
- Data are encrypted (Secure Socket Layering (SSL) technology)
- Login restricted by username and password
- Automatic timeout
- Daily backup of web-server and database

Subject Compensation

- Several Different Approaches May Be Used
  - Mailed check/cash
  - E-money (e.g., PayPal)
  - Electronic gift cards (e.g., giftcertificates.com)
  - Charitable donation
- Be careful with raffles!
  - Closely scrutinized by IRB
  - Must be conducted in a way that is equitable to all subjects

Study Advertisement/Recruitment Sites

- Online search engines
  - Google
  - Yahoo
- Links on other sites
  - Gout.com
- Trial listing services
  - Centerwatch
  - Study response project
- Banner Ads
  - Gay.com
- NIH
  - ClinicalTrials.gov

Example of a Recruitment/Study Registration Site

Centerwatch Clinical Trial Site

Institutional Research Subject Recruitment

MASSACHUSETTS GENERAL HOSPITAL

CLINICAL RESEARCH PROGRAM

185 Cambridge Street
Boston, MA 02114
617.726.5500

Home

MGH's Clinical Research Day 2008 Award Winners

Clinical Innovation Award - Letter of Intent due July 11

- For Patients & Study Volunteers
- For MGH Faculty & Staff
- For Research Sponsors
- About the CRP
- Contact Us

RSVP for Health
Partner with us as a study volunteer!
Enroll Now!

View/Post Clinical Trials

For Medical Professionals Outside of MGH

Disclaimer

Disease Specific

BU ALZHEIMER'S DISEASE CENTER

Donate Contact


ABOUT US


CLINICAL CARE


OUR RESEARCH


OUR TEAM


JOBS & CAREERS

RESEARCH PARTICIPATION

Why Participate in Research?

Your participation in research provides important information regarding possible effective treatments and preventions for Alzheimer's disease. Only through community participation in research will progress be made in the fight against Alzheimer's disease.

Types of Research Studies and Their Purpose

We have several different types of ongoing studies at the ADC. Each study has its own goals. Our memory and aging studies help us to learn about the changes that occur in people's memory as they age. Clinical trials (or treatment trials) and prevention trials help to determine if new or currently used medications can prevent Alzheimer's disease or slow its progression. Our family and genetic studies look at the link between Alzheimer's disease and genetics; these studies help us to understand genetic risk factors associated with Alzheimer's disease.

Caregiving studies specifically focus on issues related to activities in daily life, such as driving, coping emotionally with caregiver activities, and support strategies for caregivers. Our imaging studies help us learn how brain images can provide more information about diagnosing and detecting Alzheimer's disease. If we can identify changes that are occurring in the brain throughout the disease process, we can help to diagnose and treat people with Alzheimer's disease as early as possible in the disease

ABOUT

- Mission
- Center Cores
- ADCRP
- Ethnicity and AD
- How Can I Help?
  - Monetary Donations
  - Research Participation


(Click on image to play video)

Craig's List

For local research studies. However, note there are many restrictions on posts:

- Cannot post continuously
- Cannot post same ad repeatedly
- Cannot post same ad in more than one city at a time
- Restrictions vary by city
  - Designated cities restrict posts to 3 days (Boston, San Francisco, New York)
  - Other cities allow posts for up to 45 days

craigslist

boston

gbs nwb bmw nos sob

post to classifieds

my account

help, faq, abuse, legal

search craigslist

for sale

event calendar

S	M	T	W	T	F	S
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	1	2	3	4	5

avoid scams & fraud

personal safety tips

craigslist blog

community

activities
artists
childcare
general
groups
pets
events
lost+found
musicians
local news
politics
rideshare
volunteers
classes

personals

strictly platonic
women seek women
women seeking men
men seeking women
men seeking men
misc romance
casual encounters
missed connections
rants and raves

discussion forums

1099
apple
arts
atheist
gifts
haiku
health
help
pets
philos
politic
psych

housing

apts / housing
rooms / shared
sublets / temporary
housing wanted
housing swap
vacation rentals
parking / storage
office / commercial
real estate for sale

for sale

barter
bikes
boats
books
business
computer
free
furniture
general
jewelry
material
rvs
sporting
arts+crafts
auto parts
baby+kids
cars+trucks
cds/dvd/vhs
clothes+acc
collectibles
electronics
farm+garden
games+toys
garage sale
household
motorcycles

jobs

accounting+finance
admin / office
arch / engineering
art / media / design
biotech / science
business / mgmt
customer service
education
food / bev / hosp
general labor
government
human resources
internet engineers
legal / paralegal
manufacturing
marketing / pr / ad
medical / health
nonprofit sector
real estate
retail / wholesale
sales / biz dev
salon / spa / fitness
security
skilled trade / craft

us cities

atlanta
austin
boston
chicago
dallas
denver
houston
las vegas
los angeles
miami
minneapolis
new york
orange co
philadelphia
phoenix
portland
raleigh
sacramento
san diego
seattle
sf bayarea
wash dc
more ...

canada

calgary
edmonton
halifax
montreal
ottawa
toronto
vancouver
victoria

us states

alabama
alaska
arizona
arkansas
california
colorado
connecticut
dc
delaware
florida
georgia
guam
hawaii
idaho
illinois
indiana
iowa
kansas
kentucky
louisiana
maine
maryland
mass
michigan
minnesota
mississippi
missouri
montana
n carolina
n hampshire
nebraska
nevada
new jersey

countries

argentina
australia
austria
bangladesh
belgium
brazil
canada
caribbean
chile
china
colombia
costa rica
czech repub
denmark
egypt
finland
france
germany
great britain
greece
hungary
india
indonesia
ireland
israel
italy
japan
korea
lebanon
malaysia
mexico
micronesia
netherlands

Craig's List "Volunteers"

Would you like to change a life in one hour a week? -

Eco Designs -

Dedicated Volunteers Needed -

Healthy Women Volunteers Needed 45-64 years old - (BWH)

Brain Imaging Research Study of the Social Brain in Autism - (Boston University School of Medicine)

Volunteers to help with hospital equipment going to poor countries - (North Andover, MA)

Fun people needed!!! - (Beverly)

Psychology study on emotional pain and self-injury - (Harvard University)

Do you have Asthma and allergy to cats or dust mites? - (BOSTON-MGH)

Participants needed for non-invasive vision studies - (Cambridge/Central Square/MIT)

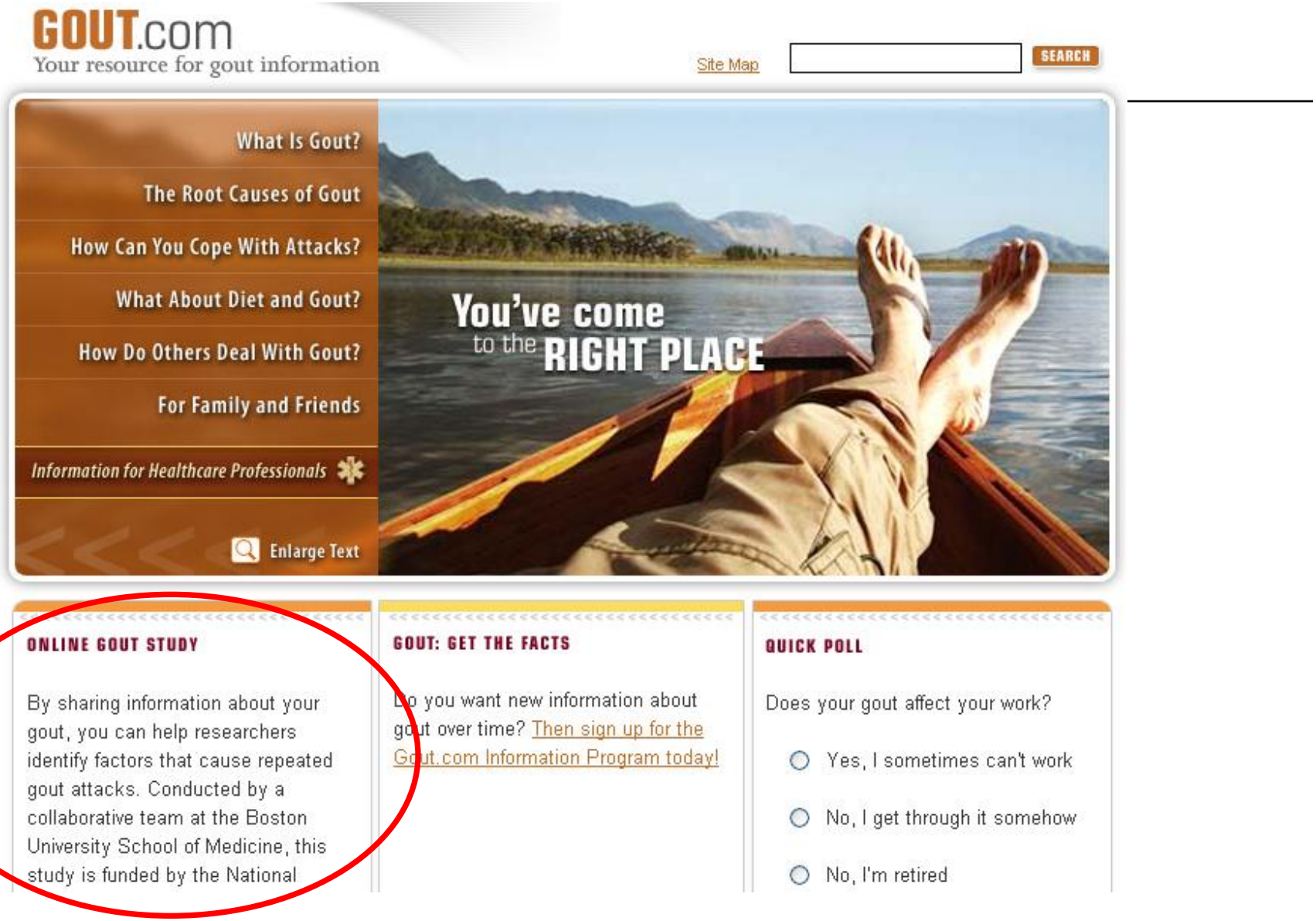
Couples Needed for Study of Veteran Relationships - (Jamaica Plain)

Has somebody suggested you cut back or quit drinking? - pic

Spend time with a needy person - (Reading)

Website for NIH Funded Research

Disease Specific Sites: Link on TAP's Gout.com

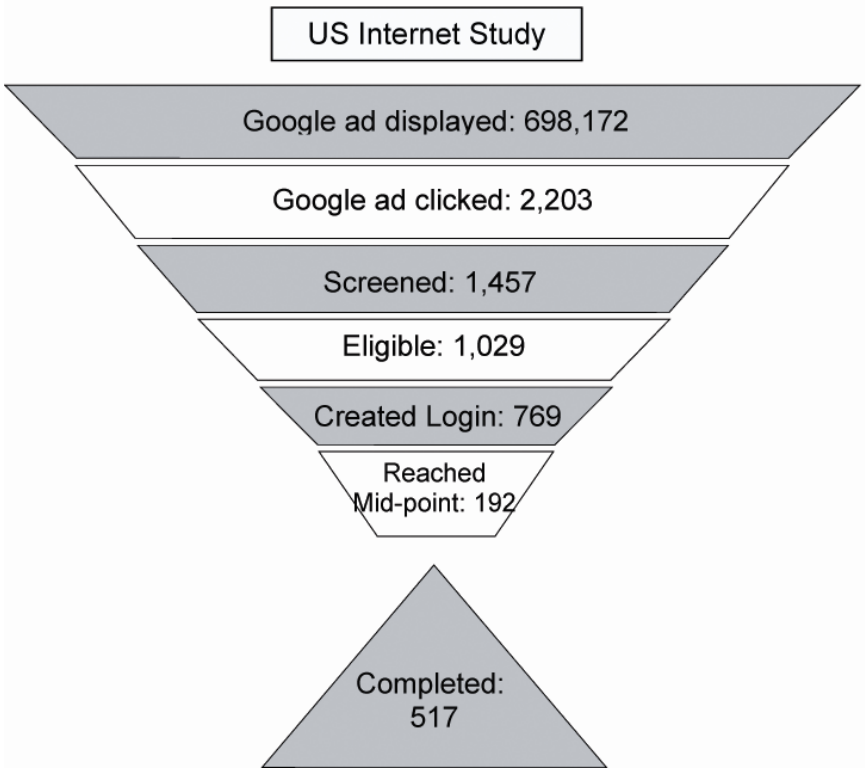


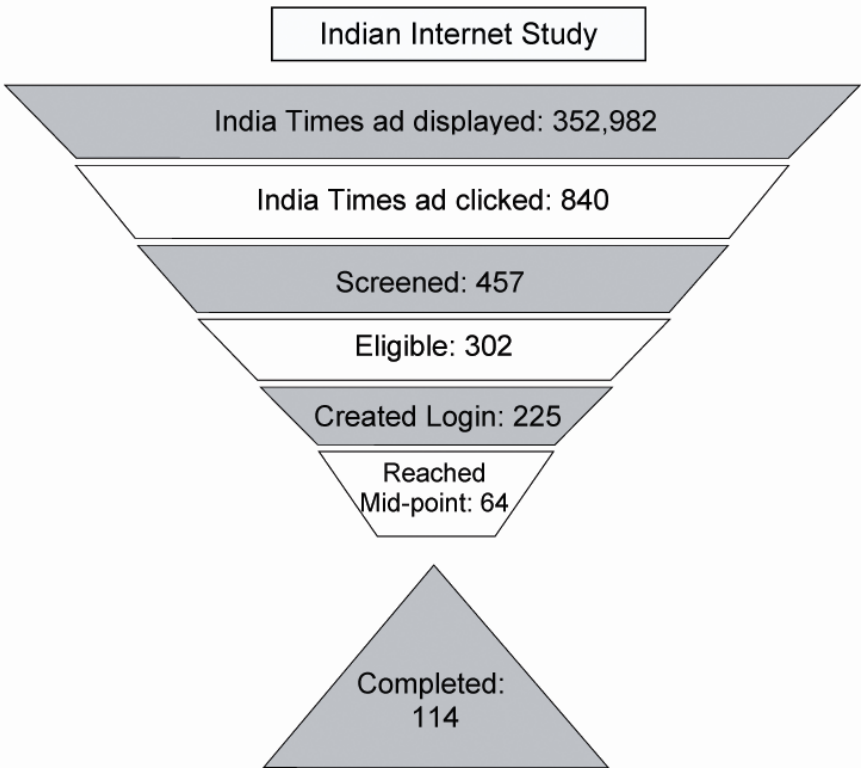
Case Study: The Non-Gay Identifying Men Who Have Sex with Men Studies (US and India)

- Compensation
  - US: giftcertificates.com
    - Eligible **AND** ineligible subjects randomly selected for online gift code
    - Code was displayed in a separate window with text warning respondent to print or carefully write down code (i.e., **NOT** e-mailed)
  - India: Used similar method with an online vendor in India

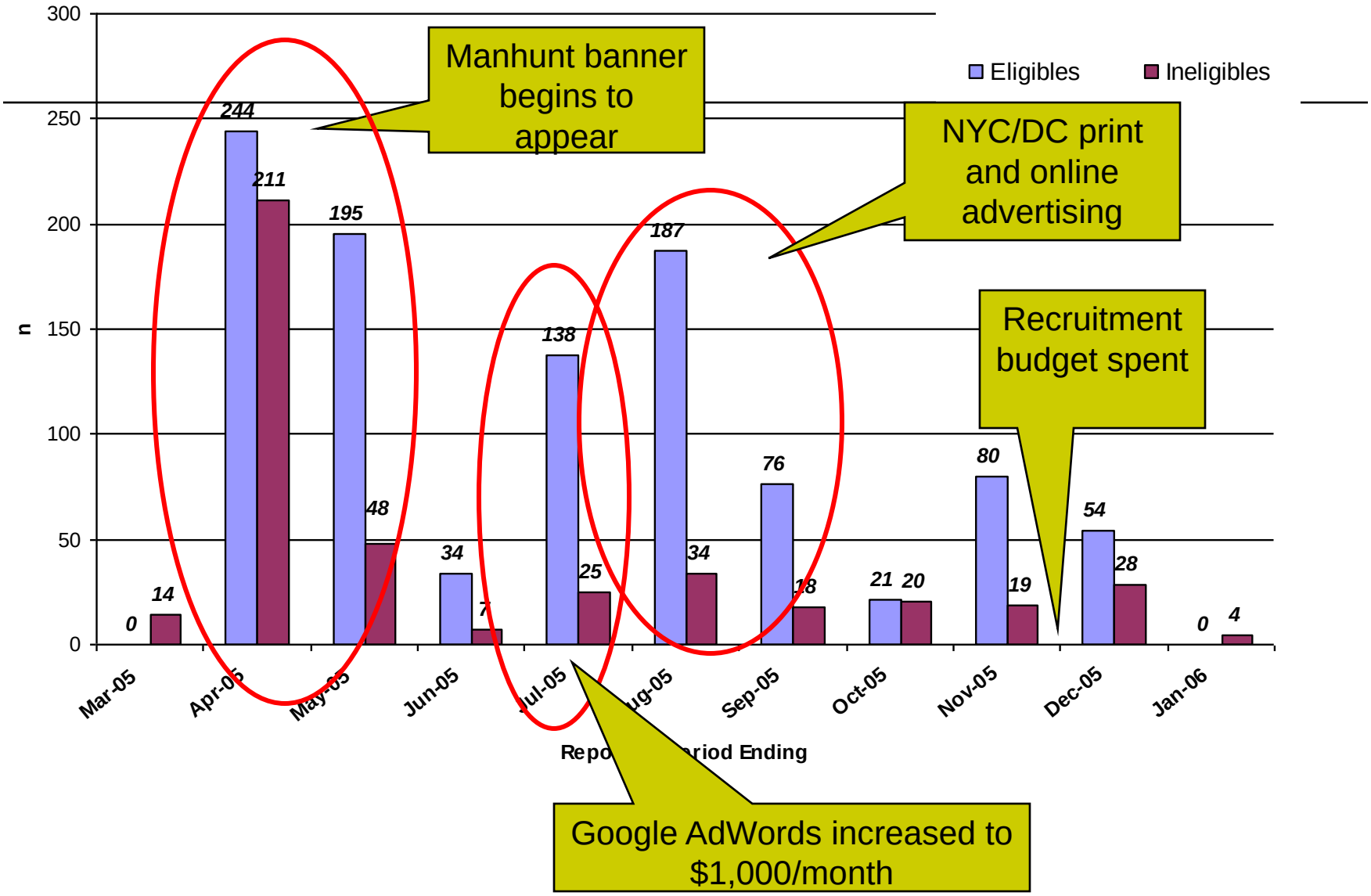
Case Study: The Non-Gay Identifying Men Who Have Sex with Men Studies (US and India)

- Recruitment
  - US: Google AdWords, gay.com, manhunt.com, African-American and gay community newspapers (Boston, NYC, Washington DC)
  - India: Banner advertising in gay chat room on indiatimes.com website


US Internet Study
Google ad displayed: 698,172
Google ad clicked: 2,203
Screened: 1,457
Eligible: 1,029
Created Login: 769
Reached Mid-point: 192
Completed: 517


Indian Internet Study
India Times ad displayed: 352,982
India Times ad clicked: 840
Screened: 457
Eligible: 302
Created Login: 225
Reached Mid-point: 64
Completed: 114

Accrual of Eligibles and Ineligibles: March 29, 2005-January 3, 2006



Internet in Clinical Trials

- Study management and communications
- Randomization
- Data collection
- Real-time SAE reporting
- Data querying
- Real-time reporting
- Form dissemination
- FAQ
- Etc.

Great for International Trials

Welcome to the DIFLUNISAL TRIAL

Participating Sites:

- Boston University, USA
- Mayo Clinic, USA
- Kumamoto University, Japan
- Shinshu University, Japan
- University Hospital San Matteo, Pavia, Italy
- Hospital Santo Antonio, Portugal
- Umea University, Sweden

Investigator Login: (•) Investigators ( ) Boston

Data Entry, Screening, Randomization, Tracking

Stratified Randomization

Randomization

Screening ID
Re-enter Screening ID

Study ID
Re-enter Study ID

Last Name, First Name

Birth Date (mmddyyyy)
Gender
Race

Hispanic
Dependence and Recent Use

Check Entries

Home

Confirm Eligibility and Randomize

HRI-Russia

Home Assign group Subject

Screening ID:	5243
Subject ID:	1032
Subject Initials:	MMR

Eligibility check list

The subject has been Randomized into the intervention group. The Subject ID is 1032.

✓	HIV diagnosis confirmed
✓	Between 18 and 70
✓	Subject has a telephone
✓	Subject lives within 150 miles
✓	Subject is not trying to become pregnant
✓	Subject can provide 2 contacts
✓	Subject does not have legal charges pending
✓	Subject meets the drinking requirements

Real-time Reporting

HRI-Russia

Home

Enrollment Report

Export PDF File

	Male	Female	TOTAL
Screened	78	29	107
Eligible	55	23	78
Consented	50	23	73
Randomized	50	23	73

	A	B	TOTAL
Randomized	38	35	73
Gender: Male	26	24	50
Gender: Female	12	11	23
IVD: Yes	19	17	36
IVD: No	19	18	37
Site: 1	38	35	73
Site: 2	0	0	0

Electronic Data Capture "Cleaner"

Interviewer Read:

Now I'm going to ask you about some symptoms or problems.

Interviewer Instruction:

If the answer to Part A is YES, ask when they had the symptoms. Note: PAST = you had the symptom or problem in the past (more than three months ago) but no longer have it. If the answer to Part A is NO, skip to the next question.

	Symptom	A Have you ever had it? Yes	No	DK	B When did you have it? Now	Past	DK
2.1	Trouble hearing	1 ◉	2 ○	8 ○	1 ◉	2 ○	8 ○
2.2	Ringing in ears	1 ○	2 ◉	8 ○			
2.3	Wear a hearing aid	1 ◉	2 ○	8 ○	1 ○	2 ○	8 ○
2.4	Trouble swallowing	1 ○	2 ○	8 ◉			

Secure, Web-based Data Querying (no faxes)

ECHO
Evaluation Center for HIV & Oral Health

Home | Data Entry | Reports | Search | Log Out |

Data Problems

☐ Include Corrected Problems?

Please click on a reason to open a particular problem and resolve it.

Site	Client	Visit Date	Reason	Corrected Value	Original Value	Created	Corrected	Problem Resolved
2	demo3	01/08/2008	Birthdate is greater than HIV date			01/10/2008		
2	Peter0808	08/08/2007	Q28 Must select an option chosen in Q27			09/27/2007		
2	SusieQ123	08/08/2007	Q28 Must select an option chosen in Q27			09/27/2007		
2	test3	01/05/2008	Birthdate is greater than HIV date			01/09/2008		

Web-based Problem Resolution

Navigation

Main
- Home Page
- Search
- Print Teleforms

Reports
- MaSBIRT Report
- Activity Report
- Report Archive

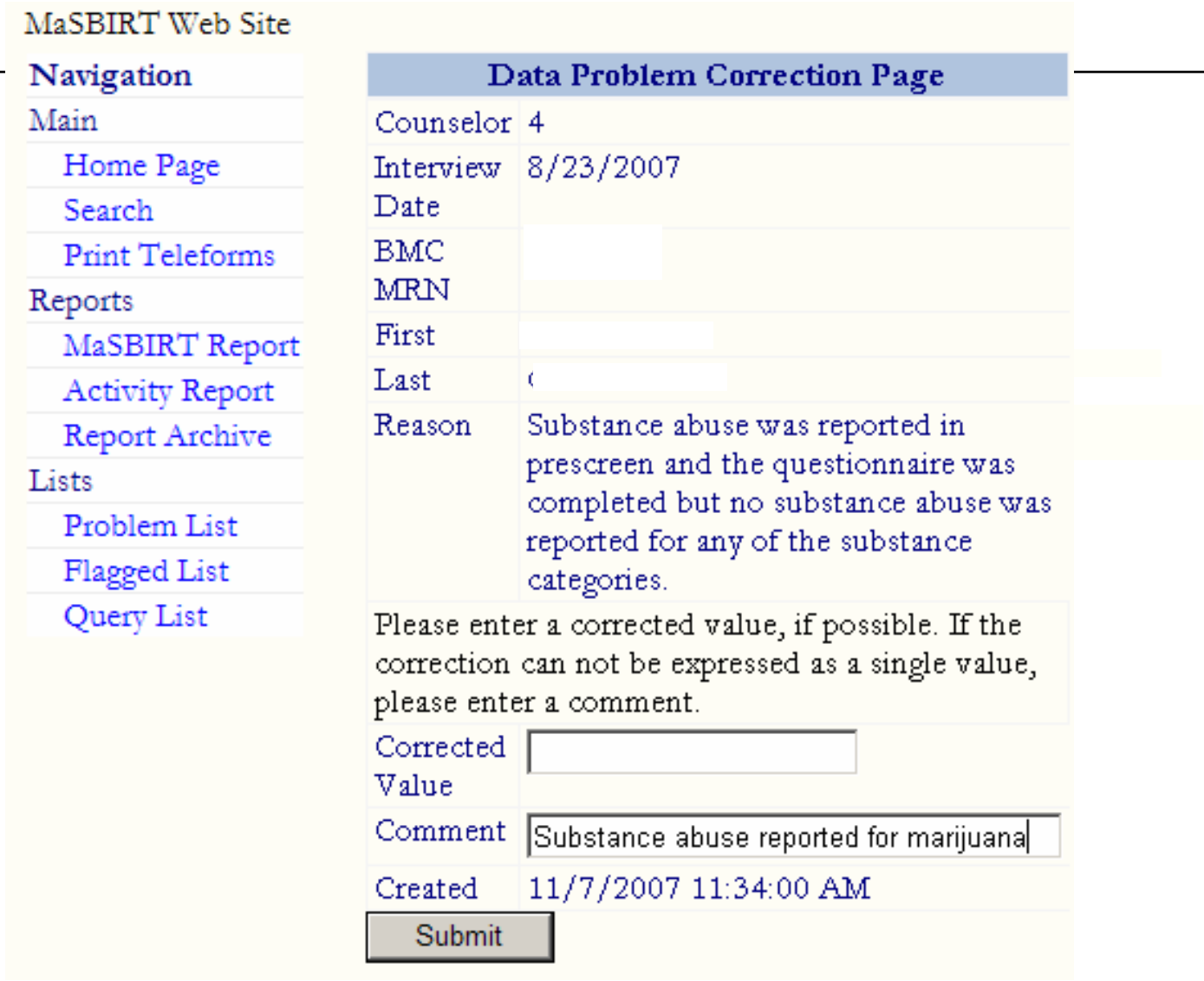
Lists
- Problem List
- Flagged List
- Query List

☐ Include Resolved Problems?

Please click on a reason to open a particular problem and resolve it.

Counselor	Interviewed	BMC MRN	First	Last	DOB	Reason	Corrected Value	Comment	Created
7	09/10/2007	3034858	A	M	'6	Alcohol AND drug use in the last 30 days > 0 but either 30 day alcohol is blank or zero OR all of the 30 day drug questions are blank or zero.			10/01/2007
3	09/25/2007	3516464			9	Duplicate last name, first name, dob, and MRN with a different SSN			10/03/2007
3	08/22/2007	3516464			9	Duplicate last name, first name, dob, and MRN with a different SSN			10/03/2007
7	09/21/2007	2130225			9	Duplicate MRN with same Interview Date and Counselor ID			10/10/2007
7	09/21/2007	2130225			9	Duplicate MRN with same Interview Date and Counselor ID			10/10/2007
5	09/19/2007	2765425			9	HQ is complete and substance abuse reported (pg.1) , but 'Alcohol in past 3 months' (pg. 1) not answered.			10/10/2007
1	09/20/2007	3340951			4	Alcohol AND drug use in the last 30 days > 0 but either 30 day alcohol is blank or zero OR all of the 30 day drug questions are blank or zero.			10/10/2007
1	10/03/2007	3514439			1	Substance abuse NOT reported (Pg.1), but BI was indicated (pg.11)			10/22/2007
4	10/09/2007	2785668			8	Substance abuse NOT reported (Pg.1), but BI was indicated (pg.11)			10/22/2007
3	05/22/2007	3544831			8	Duplicate last name, first name and dob with a different MRN			10/22/2007
3	09/19/2007	3544818			8	Duplicate last name, first name and dob with a different MRN			10/22/2007

Click-through to Correct Data



Online Clinical Trials: Nutraceuticals

IBER

Center for Internet-Based Epidemiologic Research

Home | Services | Projects

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FAQs

750 Washington St
Tufts-NEMC #406
Boston, MA 02111

866.832.1936

Progression of Knee Osteoarthritis: A Double-Blind, Placebo-Controlled Once Weekly Dosing Regimen

Vitamin D for KOA

Symptomatic knee OA has an incidence of 240/100,000 person/years and is one of the most frequent cause of dependency in lower limb tasks, especially in the elderly. It causes 68 million work loss days per year and more than 5% of the annual retirement rate1-3. It is the most frequent reason for joint replacement at a cost to the community of billions of dollars per year. No effective medical remedies for OA currently exist. However, the pharmaceutical industry is attempting to develop drugs that retard progression of OA. If efficacious, these proprietary medications will be expensive to employ in a population in which OA is endemic. Furthermore, there is evidence that vitamin D supplementation, a simple non-proprietary intervention, could slow progression of OA. Even if only modestly effective, it could have considerable impact by reducing the societal burden of OA.

This is a randomized clinical trial using Internet-based randomization, electronic data capture, coordination and monitoring. The Tufts-New England Medical Center Department of Rheumatology will be enrolling participants with knee pain to participate in this trial. Vitamin D 14,000 IU will be compared to placebo in a randomized placebo-controlled clinical trial testing the efficacy of vitamin D, 14,000 IU versus placebo taken orally once per week, as a disease-modifying agent among individuals with symptomatic knee osteoarthritis (OA). Tolerability and safety will be assed by adverse effects (AE) reporting, physical examination, vital signs, and clinical laboratory tests. The primary clinical outcome will be assessed by changes in the WOMAC questionnaire. The primary pathological process measure will be change in knee cartilage volume as measured by magnetic resonance imaging (MRI).

This study is being conducted at Tufts-New England Medical Center.

Example: Paperless Trial System

- MGH / Roche Diagnostics collaboration
- Web-based electronic data capture
- Double entry of paper forms
- Data cleaning (queries)
- Monitoring
- Reporting
- Data exporting
- Electronic Signature (21 CFR, part 11)

MGH PROTECT Study

Logout

Reports	Forms (data entry)	Queues
Visit Status Summary	Inclusion/Exclusion	Awaiting Double Entry
Baseline Demographics	Minnesota Questionnaire	Awaiting Data Checking
Interim Medical History Endpoints	Baseline Demographics	Awaiting Problem Resolution
Decompensated CHF and NYHA Classes	Interim Medical History	Awaiting Monitoring
Data Problems	Concomitant Medications	Awaiting Signing
Protocol Deviations	Living Condition/PE/EKG	Signed
View Forms By Subject ID	Treatment Decision	
	Adverse Events	
	Echocardiogram	
Excel Files	Lab Data	
Monitor Initiated Data Problems	End Lab Data	
Enrollment Date	Discontinuation	

MASSACHUSETTS GENERAL HOSPITAL

Data Coordinating Center
Boston University School of Public Health

Roche

Possibilities

"We now have the potential to conduct a cohort study of users of the World Wide Web" …

"…[the Internet] can have people recruit themselves, enter their own data into our computers, and provide for fast, convenient electronic follow-up."

Rothman KJ, Cann CI, Walker AM. Epidemiology and the internet. Epidemiology 1997; 8:123-5.

Example of Cohort Study

Internet-based study of time to pregnancy

- Elizabeth Hatch, Kenneth Rothman Laura Wise, BUSPH co-investigators
- Study taking place in Denmark where centralized medical records are available
- Subjects consent online and provide Central Population Registration # and consent to view record

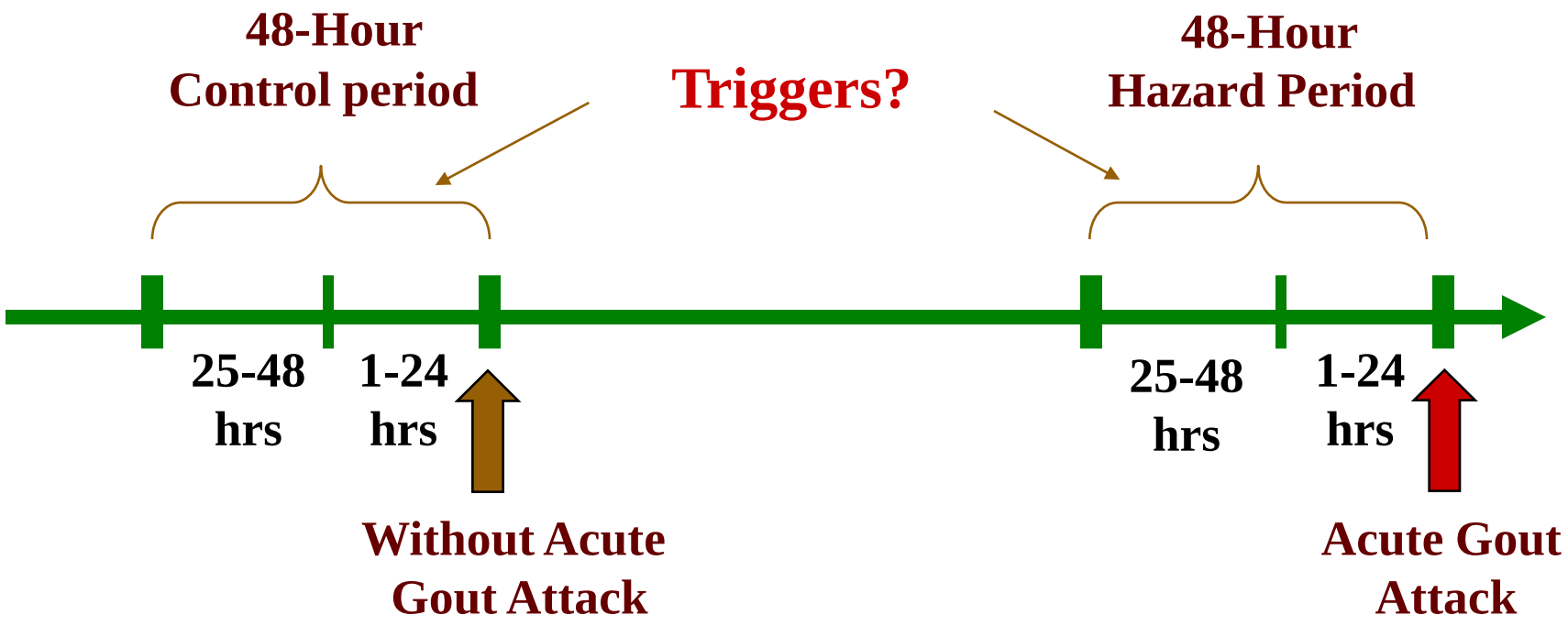
Internet-based Study of Time to Pregnancy

- Over 7,000 women screened to date
- 3,700 eligible and have consented to take part
- Subjects followed bi-monthly or until pregnant
- 85% of subjects had 4 month follow up
- Self reported medical history validated against medical record

Online Gout Study, Yuqing Zhang, PI Study

- Subjects recruited online
- Each subject serves as own control
  - control period= no symptoms
  - hazard period = acute attack
- Online consent with waiver of documentation
- All study questionnaires completed online
- Disease status and symptoms confirmed with medical records

Case-crossover Study of Triggers for Gout

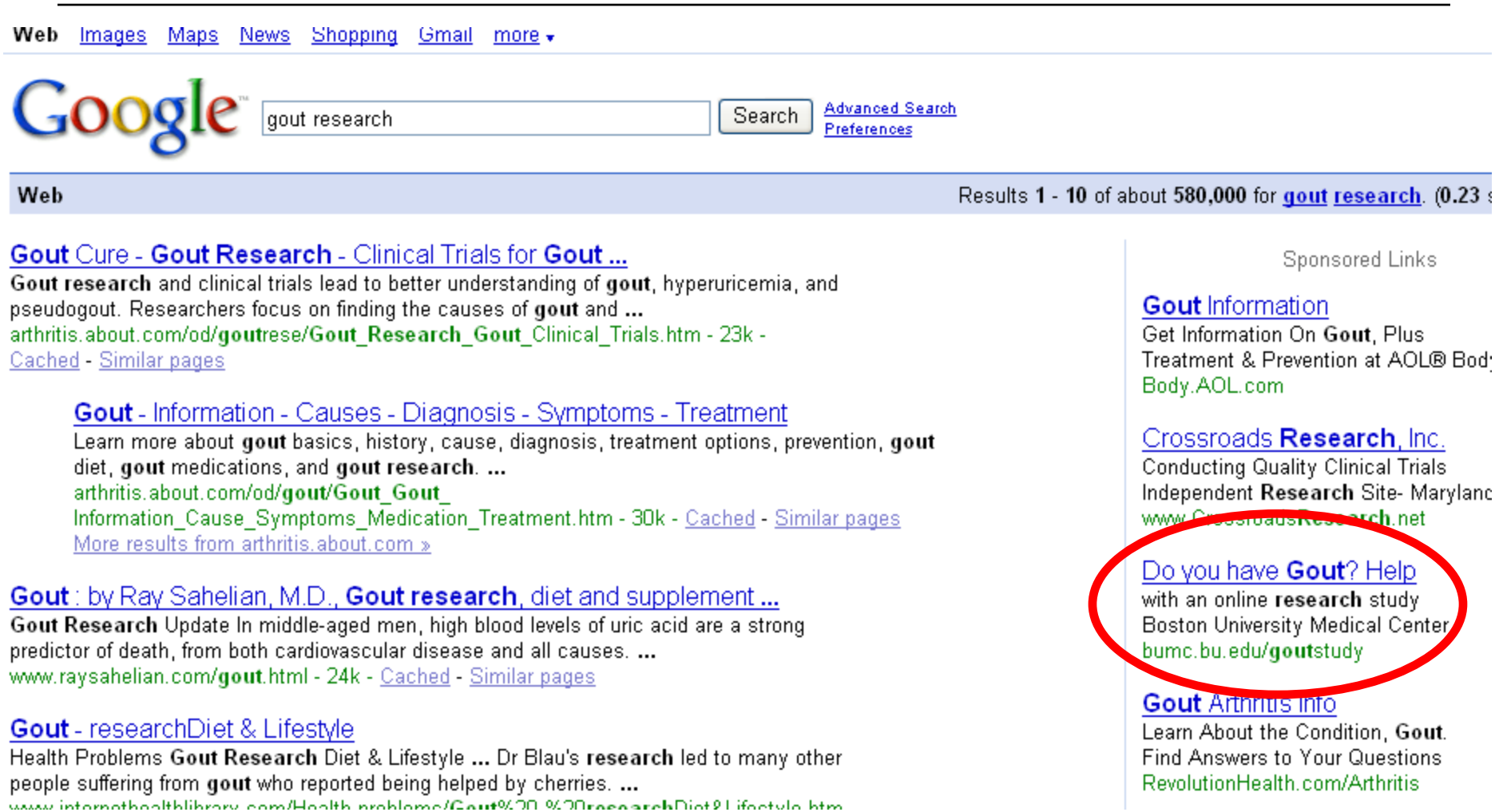


Recruitment Plan

1	Referral through former rheumatology fellows	***Only 1 subject enrolled***
2	Banners/ads and links to other sites	***Costly or difficult to get permission***
3	Search engines (link to search terms)	***Google***
4	Prevention magazine	***Lag time for publication***
5	e-Zines	***Not up to our standards***
6	Set up a chat room	***Too time intensive/ Concern re Medical questions***
7	Traditional print media	***Expensive, too many markets***

Online Search Engine

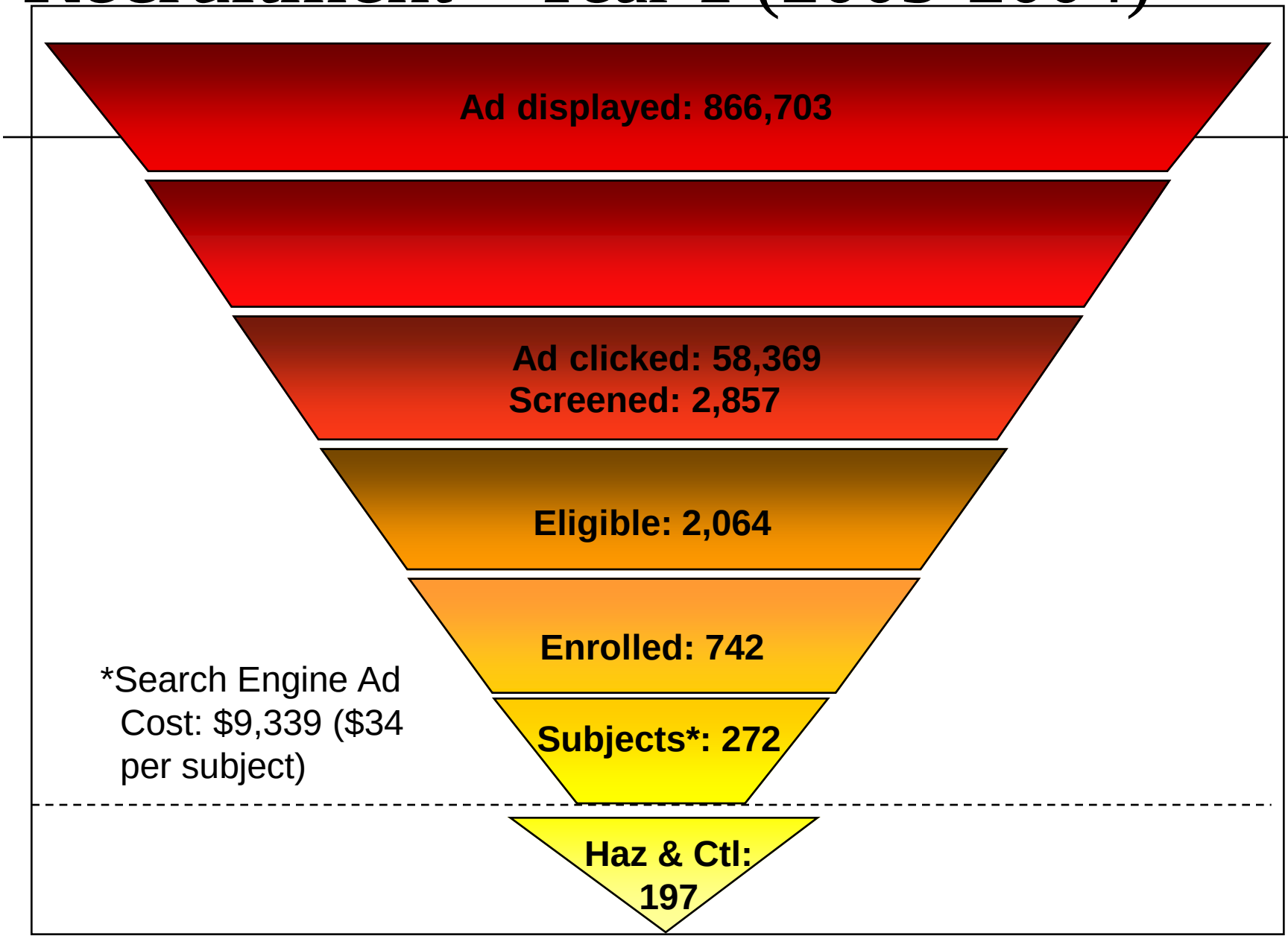
Google Ad Linked to Search Term



Incentives

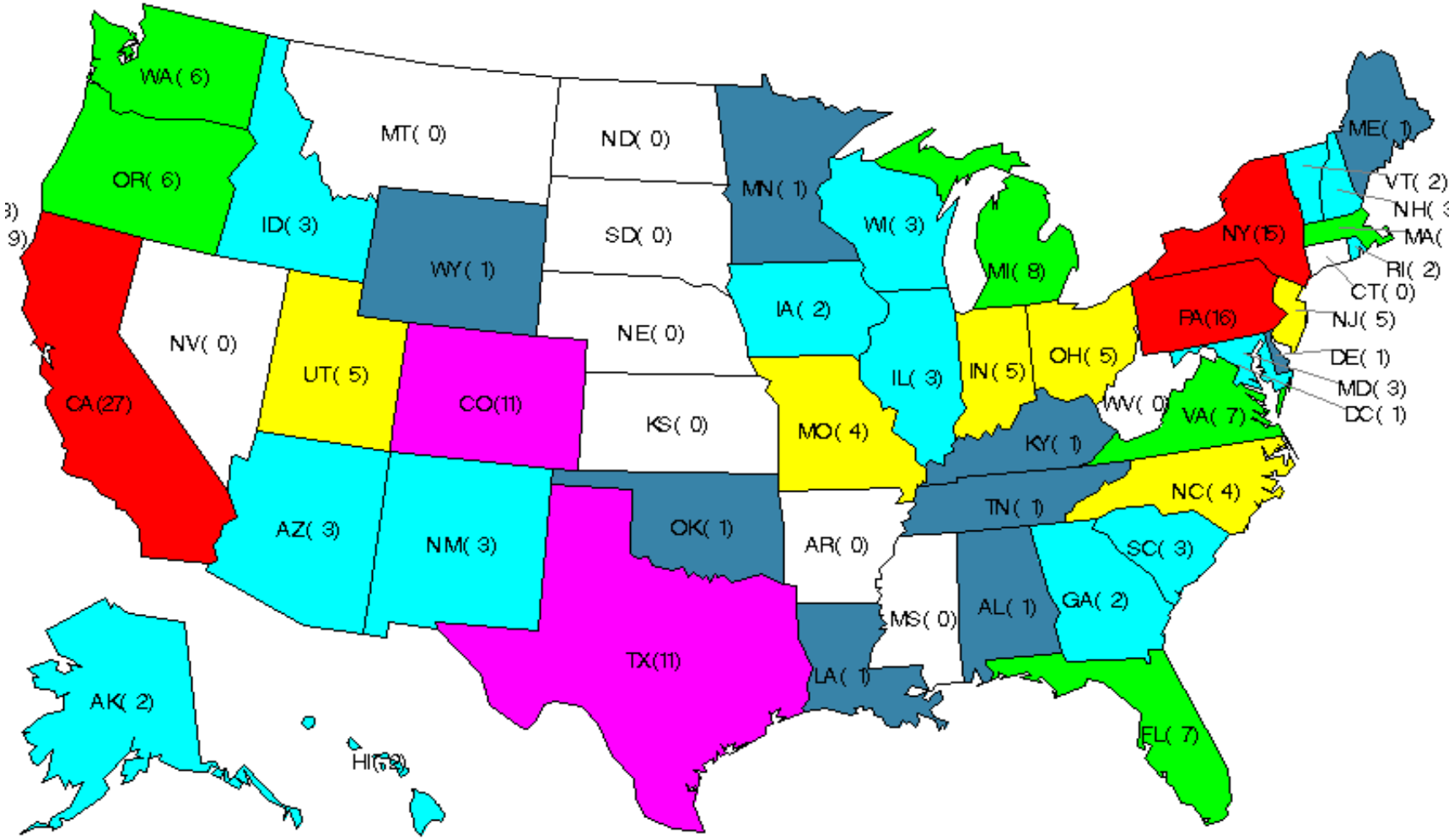
- 5 Points accumulated for each questionnaire with $1/point cash pay-out at end of study
- ‘Gout Study’ pens mailed with Medical Record Release forms as incentive to sign and return forms

Recruitment – Year 1 (2003-2004)



*Search Engine Ad Cost: $9,339 ($34 per subject)

GOUT SUBJECTS BY STATE



N= 197 Subjects with Hazard and Control Visits

Study Continues: Gout II

- Original Gout Study: 02/03 - 05/05

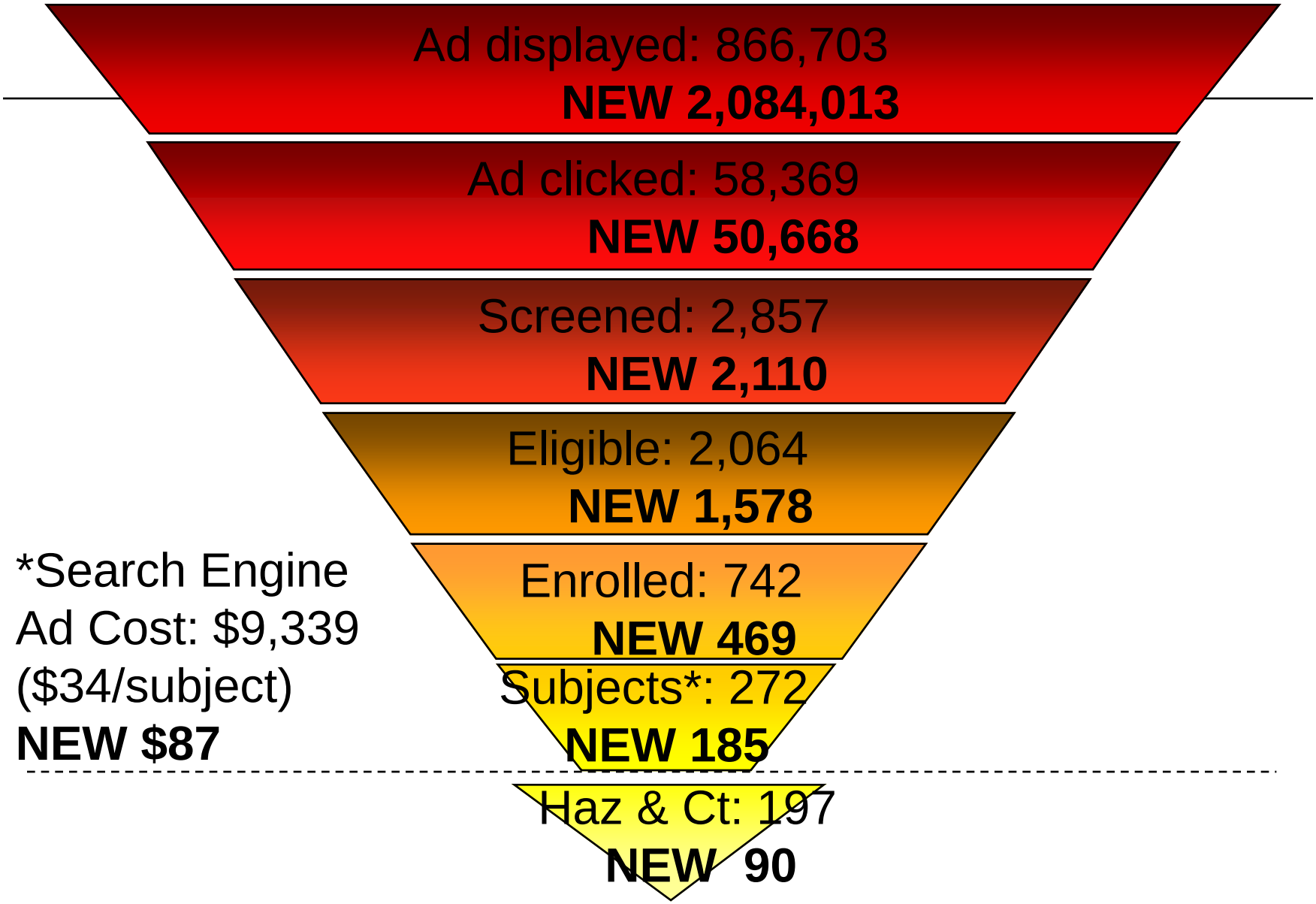
- New Gout Study: 11/05 –
  - Recruitment strategy to use Google based on results of Gout I

But Things Change…

In the meantime, Google went public and prices went up -- dramatically

- Ad placement went from first or second ad to third or fourth
- Cost/click rose from $0.16 to > $0.40
- Click-through rate dropped from 6.9% to 2.4%

RECRUITMENT: G1 VS G2



*Search Engine
Ad Cost: $9,339
($34/subject)
NEW $87

Chat
Files
Photos
Links
Database
Polls
Calendar

Promote

Reply | Forward | Delete

From: "Online Gout Study" <goutstudy@yahoo.com>
Date: Tue Nov 29, 2005 6:14 pm
Subject: Online Gout Study

goutstudy
Offline
Send Email

Hi All,

Boston University is conducting an online study to determine possible triggers for acute gout flares. If you have had an acute gout attack within the past year, reside in the US and would like to participate, we could use your help. All questionnaires are completed entirely online and all information is strictly confidential.

For more information please visit our website:
https://dcc2.bumc.bu.edu/goutstudy/

If you have questions or concerns about this study, please contact us at goutinfo@....

Thanks,
Online Gout Study

Typical Chat Room Postings

Why yes, I do have a few questions or concerns about this study.

(1) Why is the listed website close to, but not actually, a BUMC website? Why is the root site "under construction?"
(2) Why is the author or organizer of the study remaining anonymous - "Online Gout study," forsooth.
(3) What level of statistical control could you possibly expect by polling a group?

Beware that gout study. They insist on sending emails to you as attachments instead of as text and they will send annoying 'thank you' messages and 'birthday greeting' messages.

> another plek trying to milk the gout group of hard earned cash no doubt. "I"
> miss the gout police arnold and walter they would have sussed out this dodgy
> character

Current Strategies

- Google advertisements
- Link on Gout.com
- Postings under volunteer section of Craig's list (selected cities)
- Link on Centerwatch

Hits to Online Gout Study Website in Last Year

- Google Ads : 36,488
- Craigslist: 596
- TAP website, gout.com: 182
- CenterWatch : 1

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The online case-crossover study is a novel approach to study triggers for recurrent disease flares

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Conclusions

- Several types of study designs lend themselves to Internet implementation
- The Internet poses unique challenges in risk to human subjects, validity of study data, obtaining informed consent, privacy, confidentiality, and recruitment
- Important to begin with a well-defined target population to determine the feasibility of Internet recruitment and retention
- Things change quickly so be prepared to revise your strategies