

Returning of Aggregate Research Results to Study Participants

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Background

- No routine mechanism is in place in most research enterprises to share study results
 - Longstanding history in epidemiologic research, models exist
- Growing literature regarding *how* to share results or *how* patients react to the information, particularly for treatment trials

Ethical Basis

- Respect for persons
 - Respect for participants as partners in research
- Justice
 - Informed consent- willingness to continue

Potential Benefits of Offering Results

- Improving
 - Patient/Physician communication
 - Patient satisfaction
 - Quality of care
 - Potential impact on future health
 - Perception of research itself

(Markman, Cancer,2003; Partridge and Winer, JAMA, 2003)

Patient Concerns About Offering Results

- Receiving information person didn't want to receive
- Anxiety
 - Relive a difficult time
 - Learn they were in the inferior arm
 - Learn they or their child is at increased risk for health problems
- Lack of understanding of results reported and amount of detail provided

Physician Concerns About Offering Results

- Giving “unnecessary” bad news
- Concern that patients would not understand the information
- Resources including clinician and staff time
- Clinician/researcher conflict-
 - The Therapeutic Misconception

Practical Concerns

- In what context should results be shared?
 - Who
 - When
 - What
 - How
- Can a participant refuse to receive findings?
- What about next of kin, cognitively impaired, etc..?

How Many of Us Hear About Research Results

The New York Times

Amid Confusion, Journal Retracts Korean's Stem Cell Paper

TIME

BusinessWeek
Medical Guesswork



Published: December 31, 2005
Editors of the journal Science and its colleagues found it hard to record straight on a controversial paper on cloned human stem cells.

NEWS ANALYSIS Scandal for Cloning Embryos: 'A Tragic Turn' for Science

By GINA KOLATA

Published: December 16, 2005

Scientists and ethicists caution that the full story is not in, but they are staggered by how the research has unraveled so far.

Sources of Patient Information

- Health Care Providers
- Media
- Family and friends

Advocate Guidelines

- In early 2002 Patient Advisory Board developed Guidelines for Notifying Patients About Early Closure of Cancer Clinical Trials
 - Covered phase III trials
 - Closed early by the Data Safety Monitoring Board (DSMB)
 - Ethical norm
- Approved by Coalition of Cancer Cooperative Groups Board or Directors

Guidelines for Notifying Patients About Early Closure

<http://www.cancertrialshelp.org/patientAdvocates/policies/closingGuidelines.jsp>



[Advocate Training](#)

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→ PATIENT ADVOCATES

Advocacy Toolkit: Policies

GUIDELINES FOR NOTIFYING PATIENTS ABOUT EARLY CLOSURE OF CANCER CLINICAL TRIALS

Respect for the research participant is a fundamental moral requirement of human subjects research. Disclosure of information regarding the results of clinical trials in which participants are enrolled is essential to the informed consent process and to respect for participants. It is an ethical obligation of researchers.

On this basis the Patient Advisory Board of the Coalition of National Cancer Cooperative Groups offers the following guidelines for all Phase III clinical trials that are closed prematurely by a Data Monitoring Committee (DMC), Data Safety Monitoring Board (DSMB), or other Committee with these responsibilities.

1. Disclosure to individual participants of the results of clinical trials, including early disclosure, will be the ethical norm. However, disclosure must not violate any state or federal laws regarding breaking the code on anonymized data.

Guidelines

- Address the following:
 - Who should provide the information
 - When
 - How
 - Content of information provided
 - Reason for closure
 - Any change in treatment plan
 - Required follow-up

Guidelines

- Guidelines were limited
 - Focus on trials that close early where patients are still often receiving therapy
 - Lack of data to inform them
- Limited implementation
 - High profile studies closing early did not follow
 - Many barriers remain

Returning Research Results to
Study Participants:
An Evidence-Based Approach

Reactions of participants to the results of a randomised controlled trial: exploratory study

- Qualitative evaluation of parents of 24 surviving neonates enrolled in a randomized trial of ventilatory support
- Parents felt they should have access to study results, and were interested in learning results
- Several participants were upset by the information
- Parents of children who had died on study were not included in this evaluation out of concern for their emotional well-being.

(Snowdon et al., BMJ 1998)

Receiving a summary of the results of a trial: qualitative study of participants' views

- Qualitative evaluation of 20 women who participated in a RCT of antibiotics for preterm labour and preterm rupture
- Fewer than 20% of women who participated in the ORACLE trial indicated that they wished to receive the trial results
- Reactions to the results were generally positive or neutral, although some women had difficulty in understanding them
- Women requested the results because they were interested in being able to complete their own personal narrative, wishing to know to which arm of the trial they had been allocated and the implications for their own pregnancy
- They expressed disappointment with receiving a generic summary
- “Recommendations that research participants be routinely provided with the results of studies have been made without the benefit of research to show the consequences of doing this or how it should best be managed. Caution is needed”

(Dixon-Woods et al., BMJ 2006)

Impact on survivors of retinoblastoma when informed of study results on risk of second cancers

- 801 adult retinoblastoma survivors and 55 survivor parents surveyed approximately 3 years after the initial disclosure of results- response rate ~50%
- Most respondents thought the results information was understandable and useful
- A substantial minority of participants (~28%) reported increased distress after receiving results
- 1.4% reported that they would have preferred to have not received results

(Schulz et al., *Med Pediatr Oncol* 2003)

Perception of quality of life before and after disclosure of trial results: a report from the Program on the Surgical Control of the Hyperlipidemias

- 726 patients participating in a randomized phase III study of partial ileal bypass surgery versus standard care for patients with hyperlipidemias
- Patient-reported quality of life (QOL) and satisfaction with care on a trial before and after sharing aggregate results
- The treatment trial revealed that surgery resulted in more physical symptoms, but a decrease in adverse cardiovascular outcomes and possibly mortality

Perception of quality of life before and after disclosure of trial results: a report from the Program on the Surgical Control of the Hyperlipidemias (cont.)

- Learning results was associated with significant improvements in QOL among patients randomized to the surgery, with no significant change in the control group
 - Patients in the surgery group more likely to report satisfaction with randomization allocation following disclosure of results than prior to disclosure
 - Nonsignificant improvements after receiving results within both groups in:
 - satisfaction with decision to join the study
 - health since participating
 - whether or not participants would advise others to join research study
- (Buchwald et al., N Engl J Med 1990; Buchwald et al., Control Clin Trials 1993)

Our Previous Research Regarding Sharing Cancer Research Results

- Most adult patients would be interested in learning results of trials in which they have participated
- Sharing results by mail is satisfactory for the majority of patients in a “low risk” cancer situation
- Most oncology clinicians do not share results routinely, but would be willing

(Partridge et al., JNCI 2003; Partridge et al., Lancet 2005; Partridge et al., JNCI 2004)

CALGB Physician and Nurse Practices and Attitudes Regarding Offering Trial Results to Study Participants

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(Partridge et al., JNCI 2004)

Objectives

- to assess practices, preferences and attitudes among oncology clinicians about providing results of trials to patients who have participated in those trials
- to determine whether preferences and attitudes are influenced by clinician attributes and/or the characteristics of the clinical trial or patient

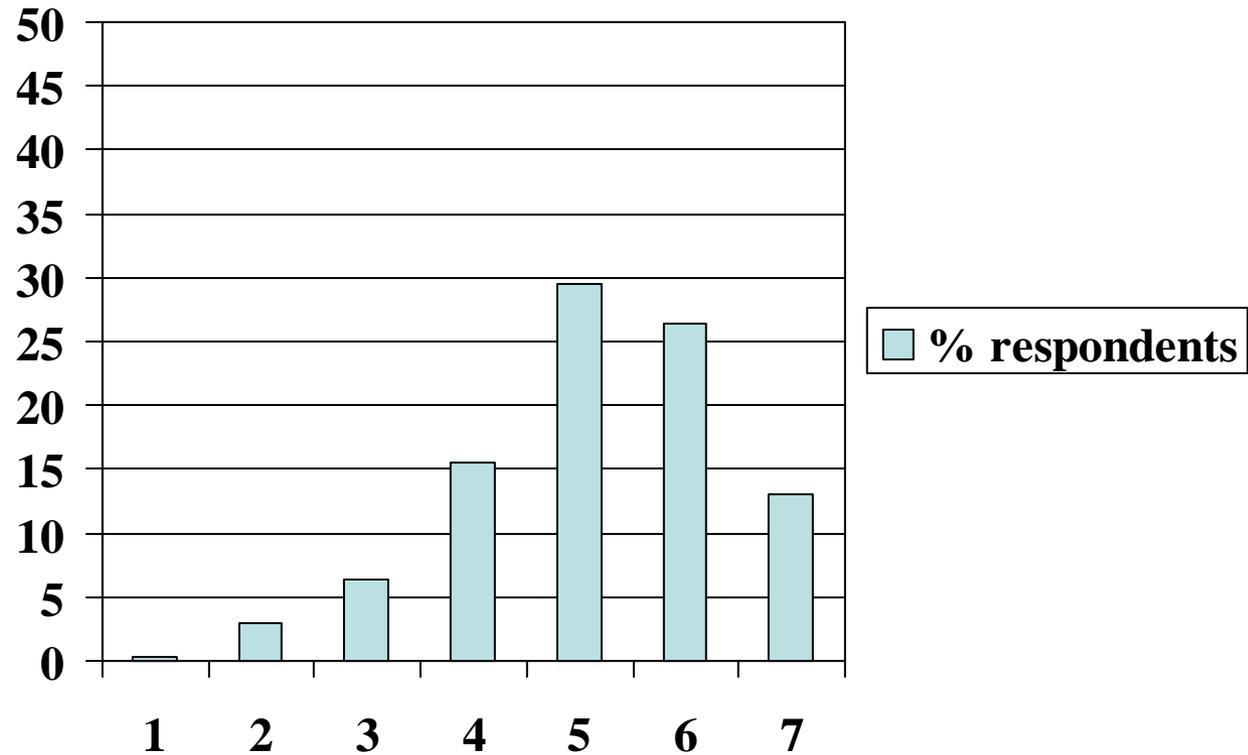
Practice and Attitudes About Offering Results

- **62% (497/796) offer results less than one-fifth of the time**
- **72% (576/796) of clinicians believe that most patients want to know results of their trials**
- **79% (628/796) of clinicians believe that trial results should be offered to most patients in trials**
- **80% (634/796) of clinicians are willing to offer trial results to most participants in the future**

Practice and Attitudes About Offering Results

- **Potential benefits most frequently cited as top 3 of routinely offering results are:**
 - **to show appreciation to patients (66%)**
 - **as a courtesy to patients (65%)**
 - **might improve patient satisfaction with care/QOL (43%)**

Enthusiasm About Offering Results



v. reluctant ----- v. enthusiastic

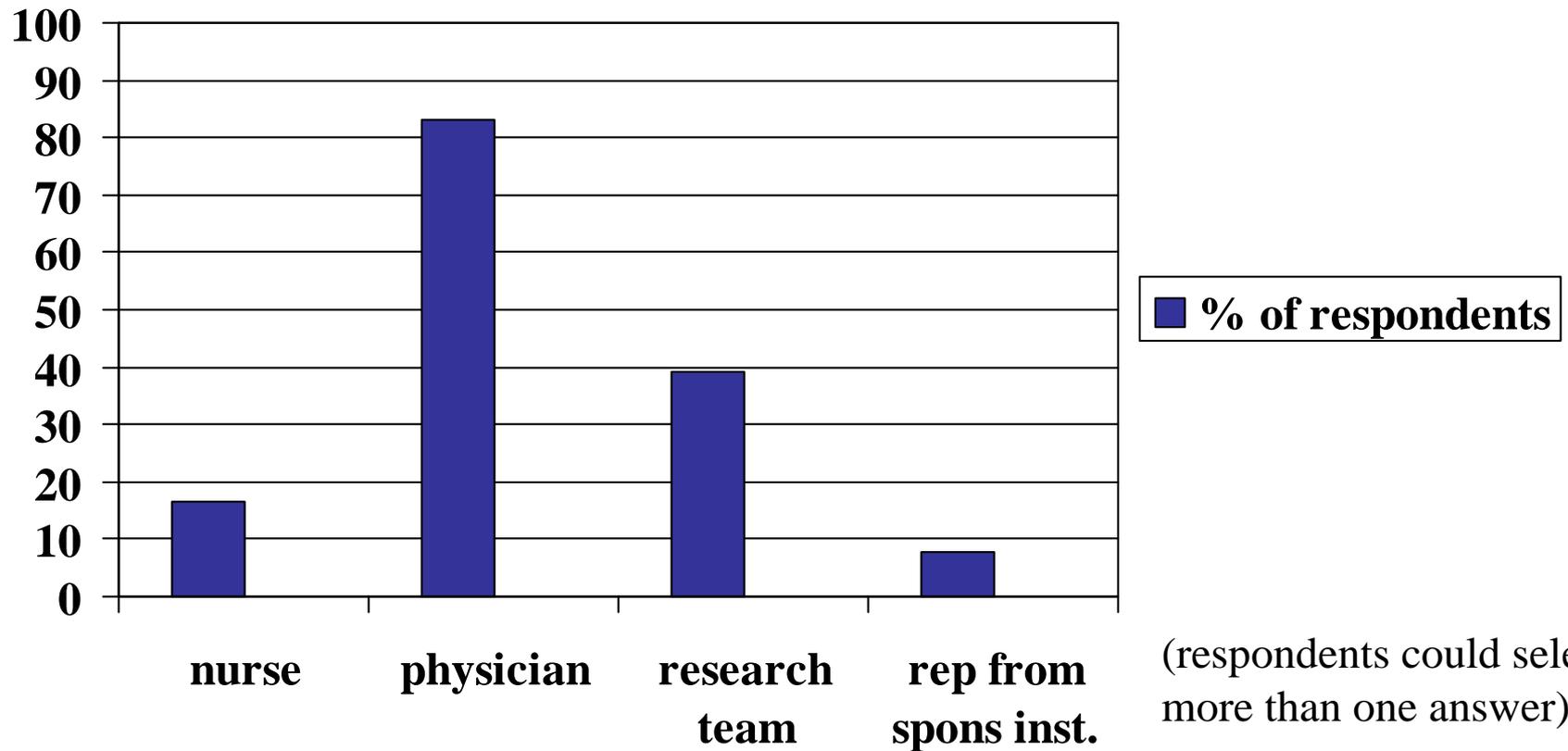
Attitudes About Offering Results

- **15% of clinicians indicated an obligation to offer results would make them less likely to enroll patients on studies; 22 % are unsure about this**
- **Concerns most frequently cited as the top 3 concerns about routinely offering results are:**
 - **potential negative emotional effect on patients (60%)**
 - **patient difficulty understanding the information (54%)**
 - **consumption of resources including \$ and clinician time (39%)**

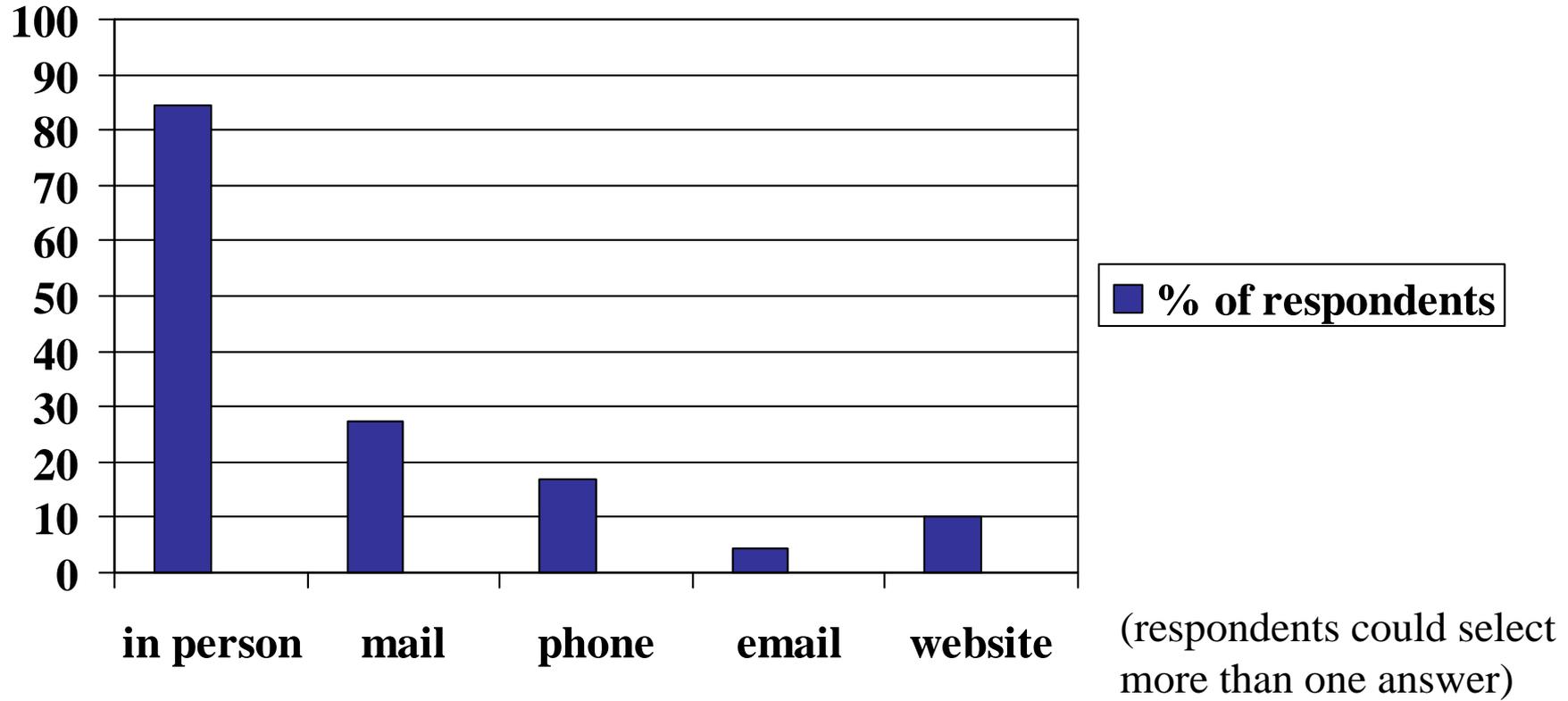
Attitudes About Offering Results

- **Only 32% (257/796) of clinicians believe trial results should be offered to next of kin if pt has died or is unavailable**
- **29% (233/796) of clinicians disagree or strongly disagree with this and 37% (292/796) neither agree nor disagree**

Who Should Provide Results?



How Should Results Be Provided?



Study Participants' Perceptions of the Process and Impact of Receiving Results of N9831, a Phase III Trial of Adjuvant Chemotherapy with or without Trastuzumab for Women with HER2+ Breast Cancer

- Results were widely disseminated in press and letter sent to study participants when the study closed early
- We evaluated living participants reactions to receipt of results

(Partridge et al, BCRT 2009)

Clinical Setting 2

- These findings were rapidly disseminated to the public as media coverage was extensive
- Institutional PIs were provided a patient letter detailing the results and potential next steps to be sent to study participants

Goals of the Study

- We sought to evaluate reactions to letter and the process of sharing results from this large cooperative group trial to evaluate
 - patient satisfaction with the process of receiving results
 - the effects of receiving results on disease-related anxiety
 - the relationship between these outcomes and sociodemographic and clinical factors

Participating Centers

- High-accruing institutions with geographic diversity were invited to participate
- Surveys were sent to all living participants from 8 institutions:
 - Dana-Farber/Partners CancerCare (DF/PCC)
 - Memorial Sloan Kettering Cancer Center (MSKCC)
 - Johns Hopkins University (JHU)
 - Dartmouth-Hitchcock Medical Center (DHMC)
 - Duke University (DU)
 - University of Chicago (UC)
 - Southeastern CCOP (SCCOP)
 - University of California at San Francisco (USCF)

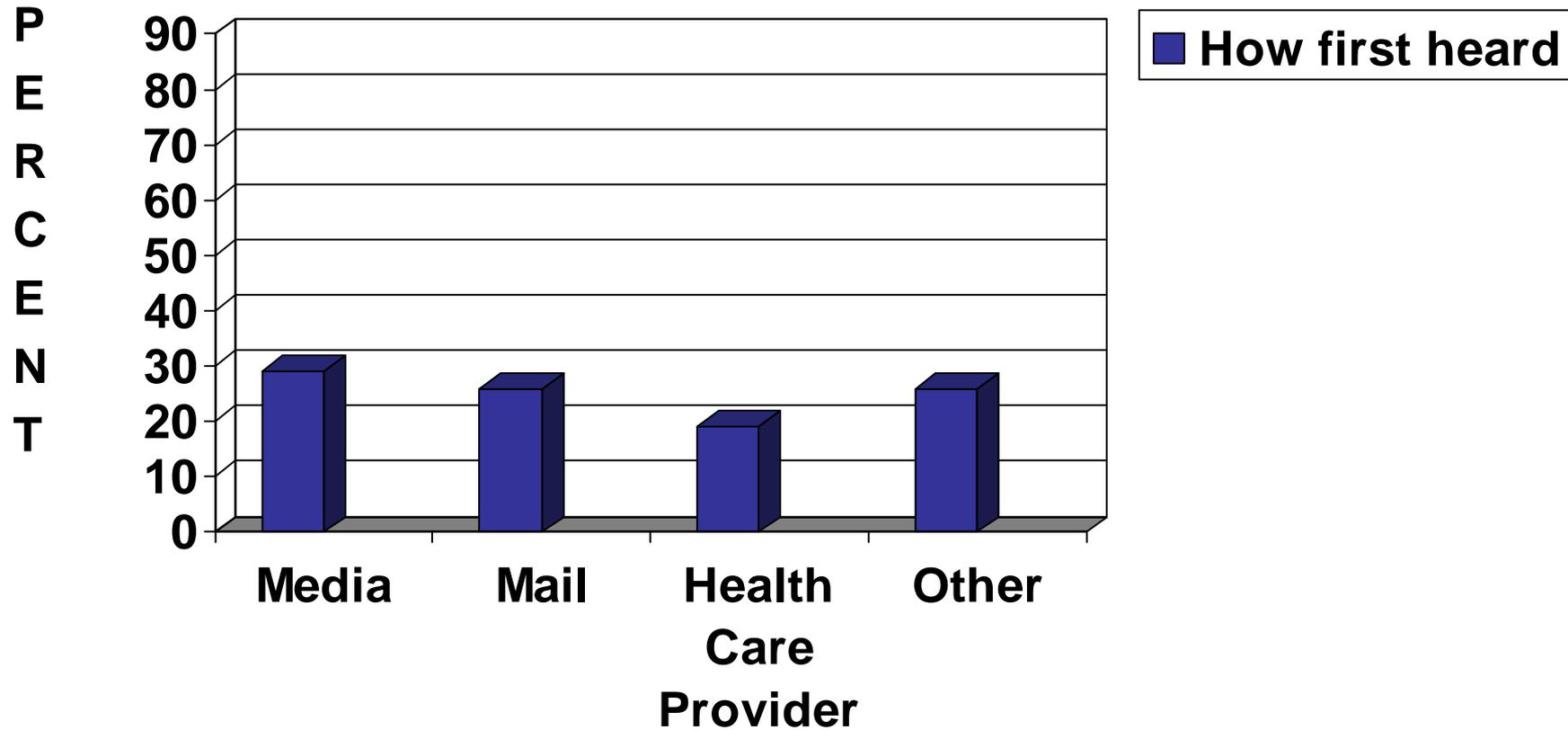
Survey Response

- All surveys were sent and returned within 6 months of when results letters were sent, most within 2 months
- 228 surveys sent (range from institutions 2-58)
- 167 surveys returned
- Response rate = 73%

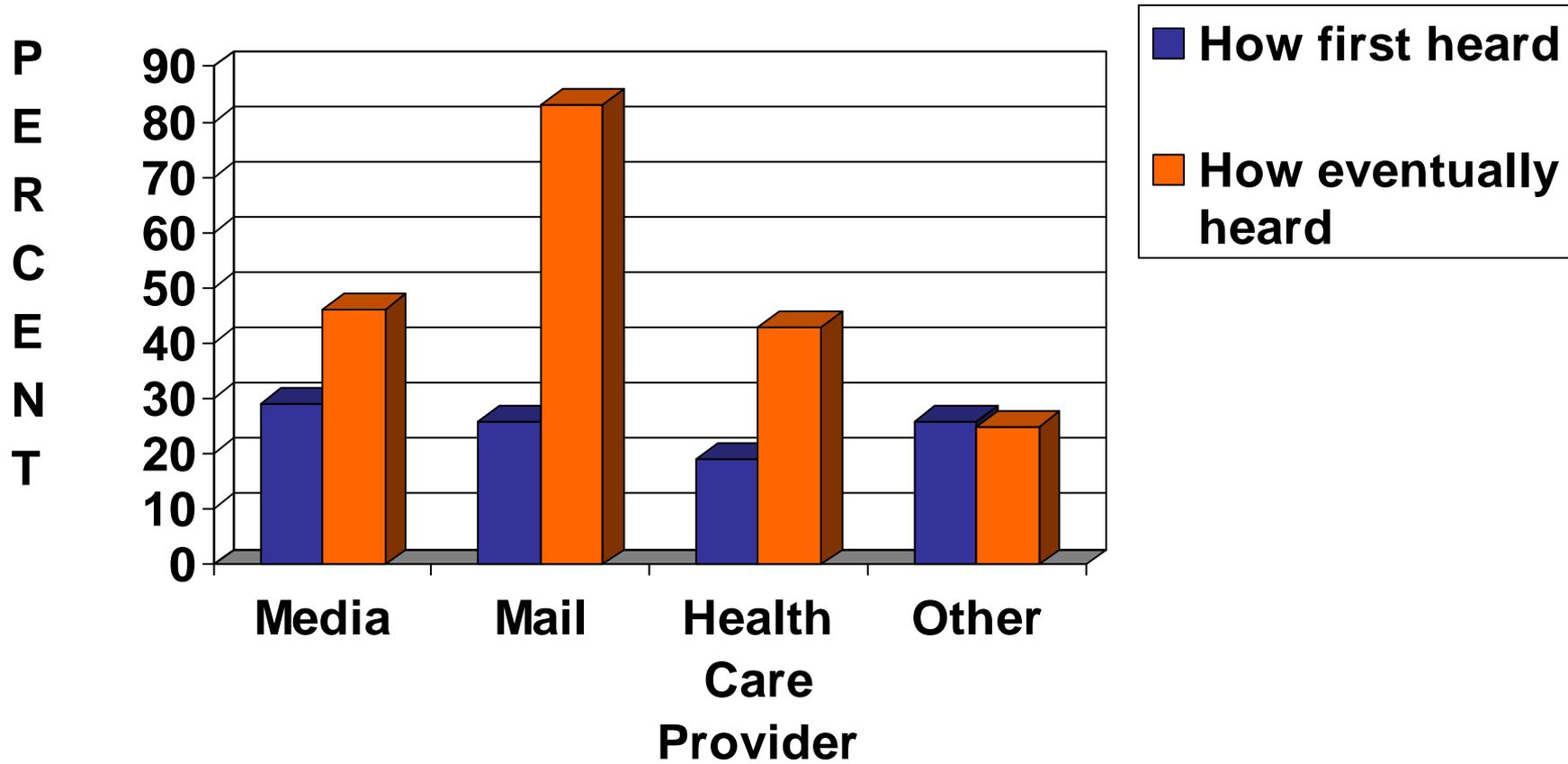
Treatment and Disease Status of Study Participants

Treatment (self-reported)	AC-TH-H	26%
	AC-T-H	35%
	AC-T	32%
	Non-protocol	7%
Recurrence		4%

First Source of Study Results



All Sources of Results



Participant Preferences About Mailed Results

Comfortable receiving
by mail 84 %

Would have preferred
to have been offered
results first 25 %
(2-step process)

If offered, would you
have declined 4 %

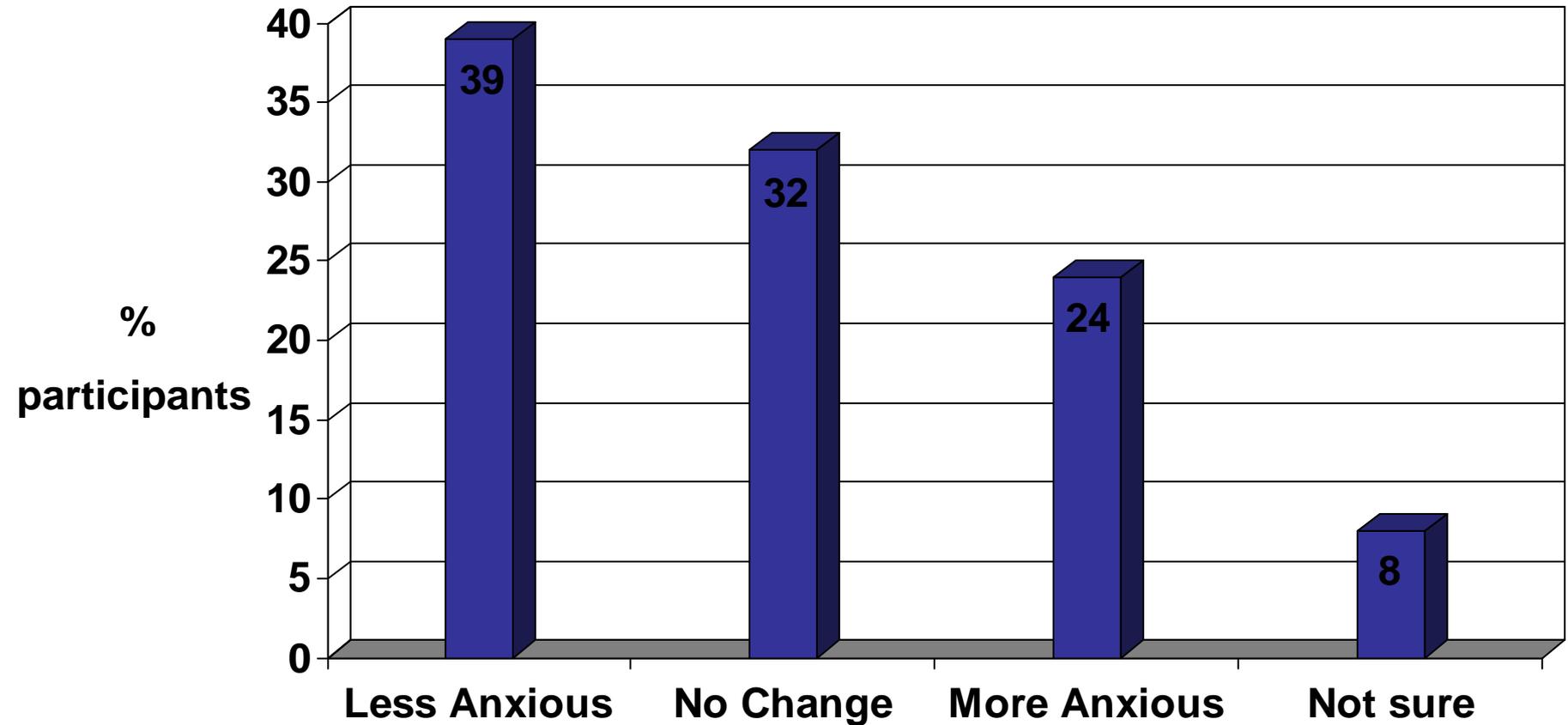
Reaction to Receiving Results

Satisfied with the process 80 %

Glad received results 95 %

Information received easy to understand 56 %

Effect of Learning Results on Anxiety



Conclusions 1

- Sharing results is met with overwhelmingly favorable responses from patients
- Some patients would prefer to be offered results first, but few would decline

Conclusions 2

- A substantial proportion of patients may not fully understand the findings
- Sharing results may increase anxiety, particularly among participants who are:
 - dissatisfied with treatment
 - did not receive the optimal therapy
 - did not understand results

Future Research Directions

- Understand patient, next of kin needs
 - diverse populations
- Provide psychosocial support, mitigate risks
- Develop “best practices” of managing the process
 - Evaluate resource use
- Share individual findings versus study summaries, especially in genetic research

Potential Solutions

- Offering not providing without consent
- Include in consent document with reinforcement of need to keep info current
- Provide results in writing and/or on web site
- Involve patient advocates
 - Provide support and resources, inc. advocate helplines and support groups
 - Material reviewed by patient advocate who “looks” like trial participants

Now Is The Time

- To create a partnership between the research and advocacy communities
- To develop and implement models to share results

Why?

- The majority of studies show patients want the results of their studies

It is the right thing to do!

My Opinion

- A plan to share results should be included in the design of phase III clinical trials
 - Tie into ClinicalTrials.gov registration
- In general, this plan should be a two-step process: first *offering* results to participants before sending them
- The potential for increased anxiety and misinterpretation of the results should be considered
- Educational and psychosocial support will be necessary for some (Partridge and Winer, JCO 2008)

Logistical concerns- Who should be offered results?

- Everyone
- Every type of study
- Every patient population
- Parents of minors, cognitively impaired
- Next of kin

Logistical concerns- What and when should results be offered?

- Timing and release of results?
- Adequate level of validity – peer-review considerations?

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**AT TIME OF ABSTRACT or
PEER-REVIEWED PUBLICATION?**

Probably depends on nature of study, result, and population;

**Prospective plan to share when appropriate-
DSMB's, advocates could be helpful here**

Logistical concerns- How should results be offered and shared?

- Duty to re-contact, consent issues
- How to share results

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- Duty to re-contact, consent issues
- How to share results

Plan to share results should be written into protocol and consent to recontact and offer results can be written into study consent

How results will be shared can also be written in; consideration of asking patients/parents to stay in contact via web?

Psychosocial Concerns

- Clearly, a substantial minority of participants or other stakeholders will experience distress upon learning study results

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Plan to assess misunderstanding and distress, and offer educational and psychosocial support via in person disclosure, support groups, appropriate referral as needed

Managing Expectations

- Explain during consent process what results might show, and differences between personal and aggregate results
- Explain during offer of results process that some patients might experience distress if applicable (e.g., a “negative” study, or patients on the “losing” arm of a positive study)

Cost Implications

- No previous study has conducted a formal cost analysis
- Sharing results from the clinical trial is a labor-intensive process
- Procedures involve:
 - drafting lay-person literature about the results
 - finding current contact information for eligible study participants
 - offering results and obtaining consent to share results information
 - sending results
 - fielding participant queries about the findings and implications
 - providing psychosocial support

Cost Implications

- Prospective incorporation of potential costs of offering and sharing results should be written into grant/study funding

Conclusion- Some parting thoughts

- Communicating with study participants after the study is a small but important part of the clinical trials process
 - Future research is clearly warranted
- Evidence suggests that the benefits may outweigh risks and costs
- Demand for change from the current “standard” needs to come from patients and advocates
 - See Liz Frank’s presentation!

Thank You