Patients & clinical trials or…

How we can make better clinical trials together

SITC Immunotherapy Winter School

February 22, 2019

Deborah Collyar

PAIR: Patient Advocates In Research

The U.S. ~~healthcare~~ disease crisis system

Patients are PEOPLE

Congratulations! You have…

It’s like a new planet with:

- No roadmap
- No dictionary
- No survival training

Patient dilemmas & decisions

Invasive? Non-invasive? Biopsy?

2nd pass? Am I Going to Die?

Risk? Genomics?

Personalized? Precision?

Academic Center? Local?

Tissue donation? Biospecimen?

Family genetics? Which treatment?

Targeted Therapies?

Informed consent? Eligible?

Ineligible?

Biomarker?

EGFR Inhibitor? Proteomics? Kras?

Insurance? Radiation?

Immunotherapy?

What is it like to be a “patient”?

People need better treatments… but not at all costs

Issues start with:

- (mis) Diagnosis
- Confusion at each step
- Technology for ‘big data,’ not patient results
- Costs (many kinds)
- Clinical trials?

The Real World of BC

- Composite of hundreds
  - Family, job, insurance
- 15 steps < diagnosis
- 19 steps < clinical trial
  - Doesn't join a trial
- Ends w/50th birthday
  - New metastasis

The REAL World of Breast Cancer

EVENT	RESULT/QUESTIONS	REACTION	DECISIONS	CONSEQUENCES
Healthy 40ish	Enjoy activities, family, leisure, work, No known risk factors	Life is good	Normal ones	Family provider, Good job, Career aspirations, Has insurance
Lump	What is it?	Concern Must be cyst	Find out Schedule PCP	Work schedule, Life Responsibilities
PCP	Yep, it's a lump: Aspirate or Punt?	Concern Hassle	Schedule GYN	Lunch hour, sick leave, or vacation
GYN	Before visit: Liquid or Solid?	Nuisance It's nothing	Schedule ultrasound	Lunch hour, sick leave, or vacation
Radiology	Solid: Benign or Cancer? "9 out of 10, it's benign"	Denial Belief in odds	Schedule mammogram	Lunch hour, sick leave, or vacation
Radiology	Mammogram "suspicious," need biopsy: FNA, Core, or Surgical?	Scared & confused Insurance?	Call PCP & GYN See Surgeon	Lunch hour, sick leave, or vacation When to tell family?
Surgeon	Biopsy info: When do I find out? Anesthesia: local or general?	Fear Read Insurance Pray	Schedule biopsy	Work schedule Life responsibilities Listen to others' "trivial" complaints
Pre-Op	Blood work, EKG, etc. Report says "suspicious"	Anxiety Doubt	Think positively	Deny cancer possibility
Biopsy	It's Cancer, "good" kind Lumpectomy or mastectomy? Prophylactic on other side? Reconstruction? Radiation? Chemo? Both? Before or after surgery?	Hope: "good?" Aloneness Death Shock Loss of control Betrayal by own body	Go into information overdrive	Changes in all relationships, including: Family Work Friends Acquaintances Doctors Life
Info Quest	Who helps me through this? What is a Pathologist? What are my options? How much time to decide? Why don't doctors coordinate my care?	Intimidated Confused Alone Mistrust	Get 2nd opinions	Do I tell my employer? When? Children, mother &/or sisters scared Husband/partner: protect? feels powerless

Research (PAIR)

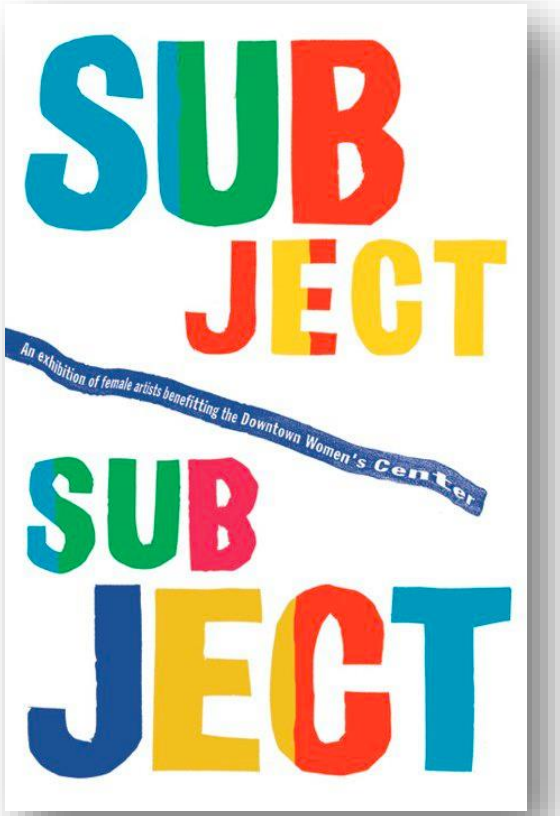
Words matter: Terms 101

Term	Scientific/Medical	Public Definition
Negative test	**That's too bad**	**This is good, right?**
Positive test	**That's too bad**	**This is good, right?**
Cure	**5 year survival rate**	**Never again**
Tumor Mutation Burden	Good!	Bad?
Support services	Help science	Fit medical condition into life
Lay	**All non-scientists**	**Down?**
Environment	Patient controlled	External forces
Community	Non-academic center	Where I live
Medical advance	Incremental adjustment	A cure

i.e. Informed Consent

What do patients want to know?

- ✓ I am not alone (others before me)
- ✓ What to expect
- ✓ How bad can it get?
- ✓ What's the 'safe' word to get out?



Low health literacy is a big problem

93 million Americans lack the health literacy skills to understand and use health information

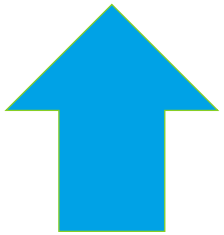
1 in 5 adults have health literacy skills considered to be “below basic”

NAAL, 2003

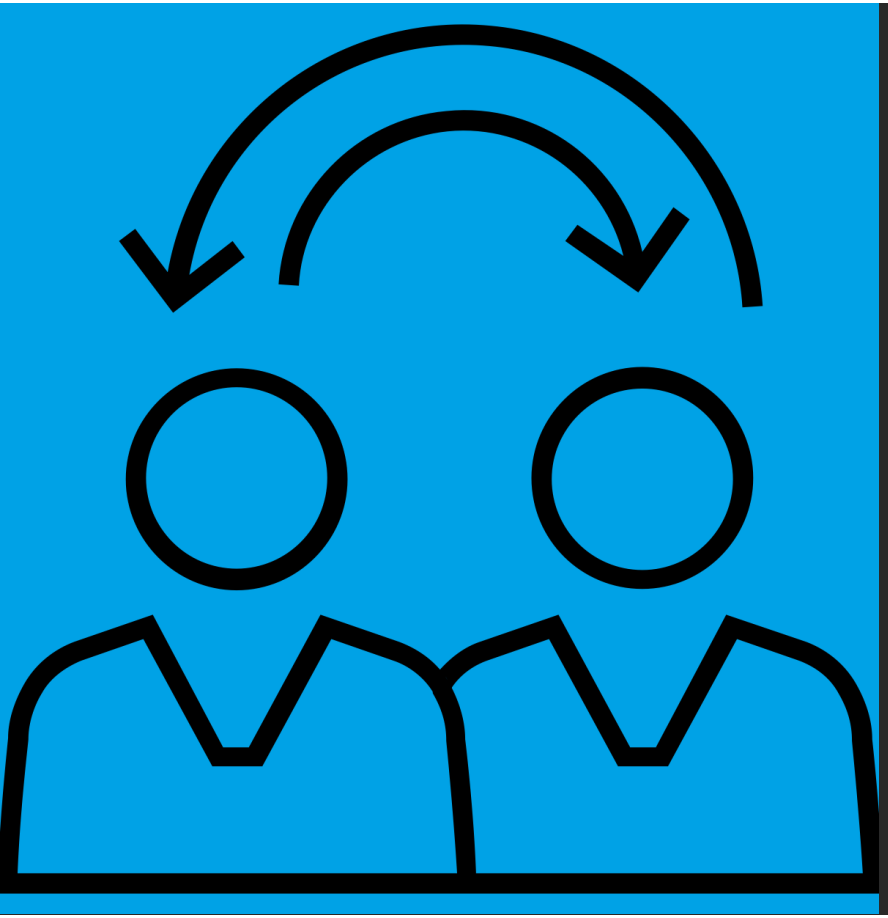
Which statement is correct?

A. “the patient failed the treatment”

B. “the treatment failed the patient”



Please **stop** using this one!



Research/healthcare only works

when the system plays fair

Not:

- We’re there when WE need patients

This!

- We’re there when PATIENTS need us

Speaking of immunotherapy… as of 2019

The “latest greatest” (again)

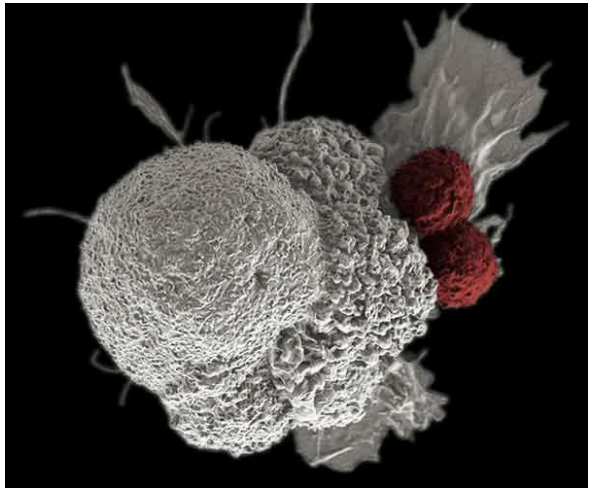
A minority of cancer patients are treated with IO

- Most still get surgery, radiation, and/or chemotherapy

Immunotherapy promising, but…

- Many tumors don’t respond
- Not a total replacement therapy
- Side effects
- Trial results don’t transfer to commercial use

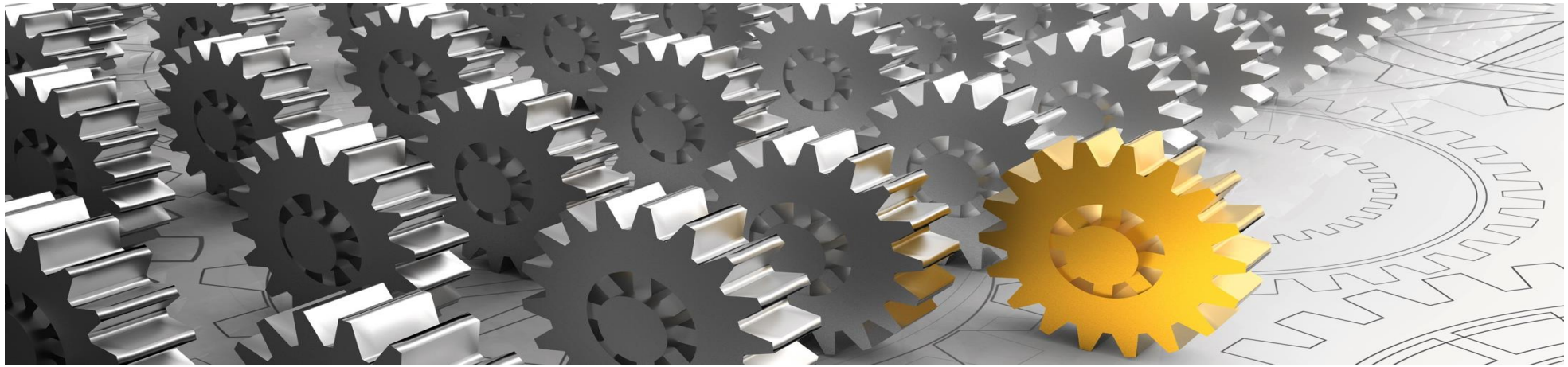
Please set reasonable expectations!



What do patients want?

Patients want ***BETTER***,
not just more treatments.

And answers that work for them,
not just other people.



What do patients want from immunotherapy?

Less hype, more realism

- Compared regimens > guidelines
- Integration w/other treatments
- Better care
- “C” word issue (cure)

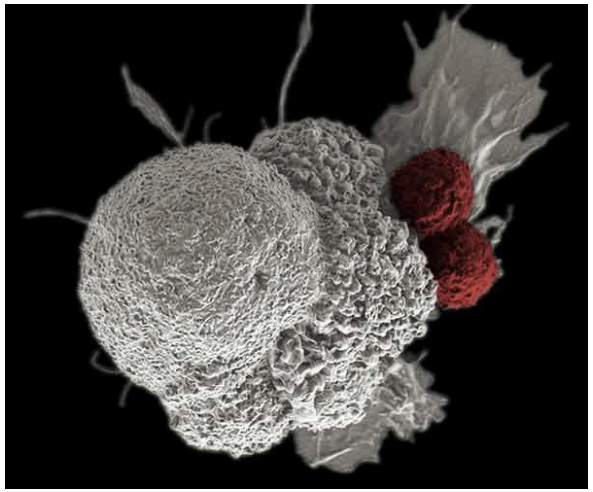
Fewer irAEs

- ≥ grade 2 can be serious
- Autoimmune is serious
- Possible age factors?

Report additional info

- Response rates
  - Comparable to chemotherapy
- Duration of response
- Financial toxicities
- QOL & PROs

CONTEXT



https://www.inspire.com/groups/american-lung-association-lung-cancer-survivors/discussion/opdivo-beware-the-hype-and-commercials/

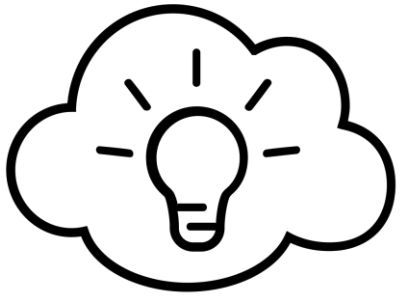
https://jitc.biomedcentral.com/articles/10.1186/s40425-017-0300-z

http://yourcenter.uvacancercenter.com/autoimmune-disorders-and-cancer-whats-the-connection/

https://www.medscape.com/viewarticle/897946

http://bit.ly/2LD4YPX

I have a dream…



Create future clinical trials + products that meet patient needs

Analyze past trials/summaries

What can we do better?

What patient questions could've been answered?

Learn from real world use

Incorporate lessons into new trials

e.g. Study design, endpoints, eligibility, PD, biomarkers

Patient Advocates in Research (**PAIR**)

Where research meets reality

Patient-focused peers = Partners

- Patient experiences/issues into research
- Practice respectful irreverence
- Resolve research barriers
- Relevance for results

Déjà vu, all over again

Research silos

Chasing $$$

Biospecimens

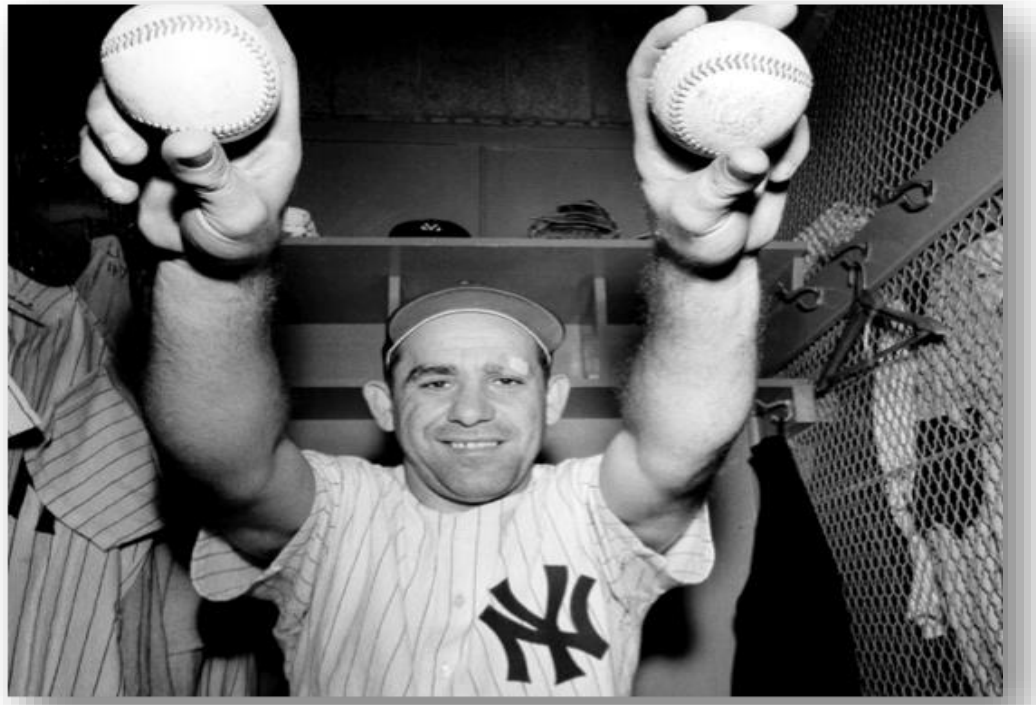
Reproducibility

Informed consent

Recruitment/retention
(aka clinical trial mantra)

Data sharing

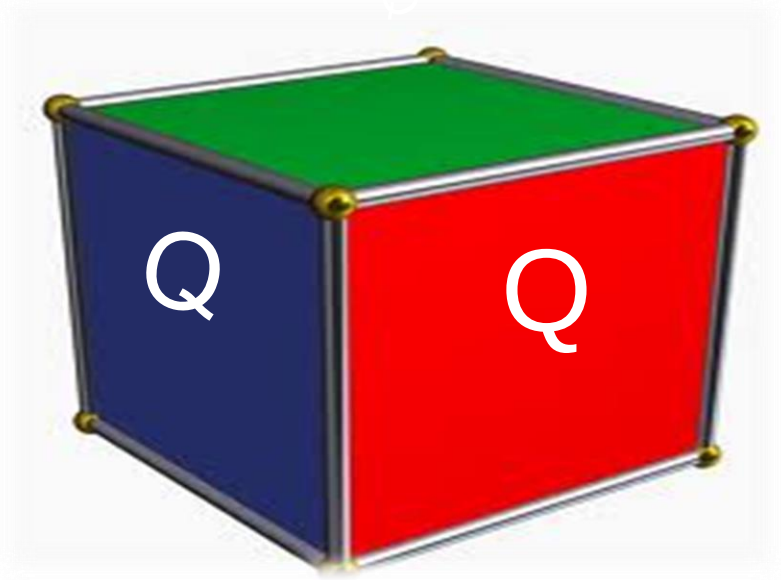
Need **CHANGES**, not tweaks!



Same problems 20+ years ago

Why we need to work together…

Scientists: experts on "Q"

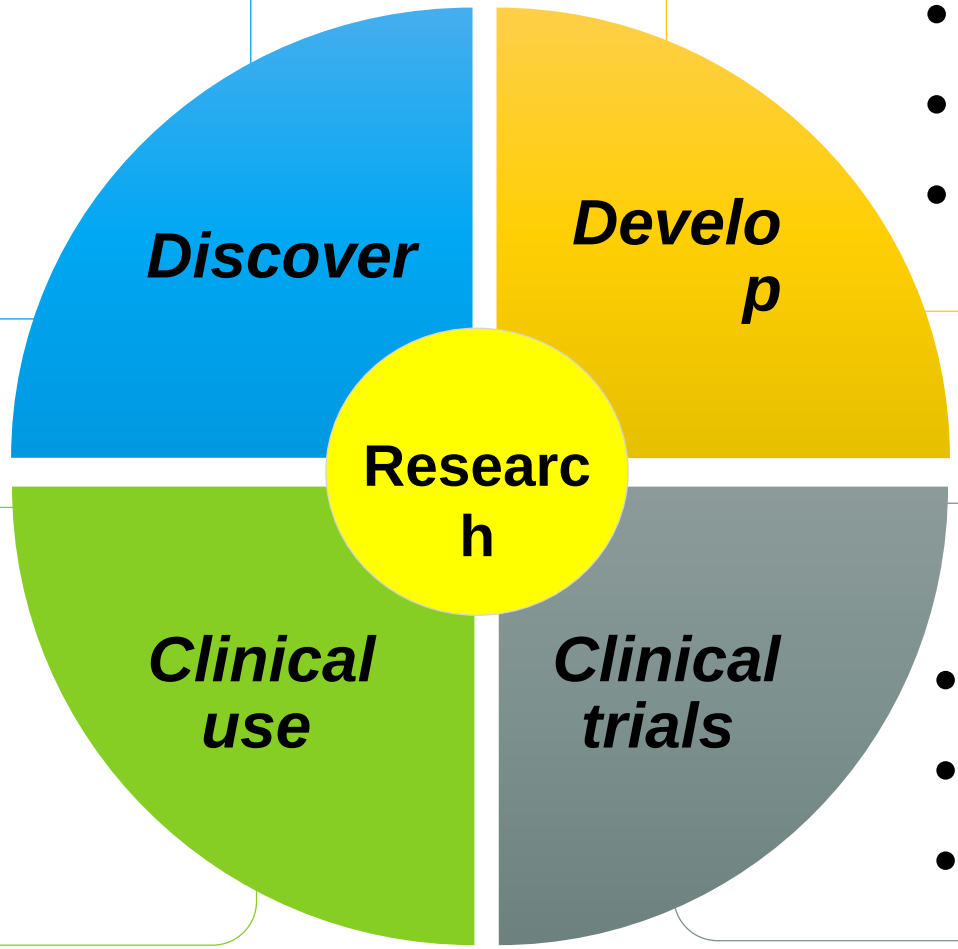


Patients: whole alphabet

Where patient advocates fit

- Projects
- Proof
- Preclinical

- Plans
- Concept
- Protocol



- Results
- Value
- Adoption

- Activation
- Recruitment
- Retention

Nature Reviews Cancer, 2005

SCIENCE AND SOCIETY

How have patient advocates in the United States benefited cancer research?

Deborah Collyar

Abstract | Cancer patient advocates represent those affected by cancer and have a broad view of cancer research. They are involved in many diverse cancer research committees, where they can help tackle old problems from new perspectives that often differ from government, academic, medical and scientific approaches. In this role, patient advocates have aided the development of educational dialogue between investigators and patient communities and assisted in streamlining cancer research policies and clinical trials.

A standard definition for an advocate is "One who pleads on another's behalf"[1]. The term 'patient advocate' therefore refers to people who act on a patient's behalf. Cancer patient advocates have existed for many years in the United States, and most have embarked on this path because of an experience with cancer, either personally or through a loved one. This experience has reinforced their need to provide cancer patients with support and navigate them through the treatment process. While many patient advocates continue to focus on patient care, others have set up their own advocacy organizations, hosted fundraising events, pressured politicians to increase cancer research funding or helped to solve systemic problems like insurance denials, or become involved with the cancer research system (FIG. 1). Others have fought to protect the rights of patients or have been members of advisory boards in federal committees — for example, the National Cancer Institute (NCI) National Cancer Advisory Board (NCAB; see online links box) — and professional societies such as the American Cancer Society (ACS) and the American Society of Clinical Oncology[2,3].

Cancer patient advocates come from diverse backgrounds, as shown in FIG. 2, and cancer patient advocacy has reached global proportions, with people working to improve cancer patients' lives and treatments in many countries such as Australia, Canada, China, India, Japan, Malaysia, parts of South America, many countries in Europe and in some developing countries[4,5]. Cancer patient advocacy has come a long way from its origins in 1950s America.

Pioneering cancer patient advocates

Today, patients with cancer are frequently helped by non-scientists and non-clinicians in local hospitals and patient support groups, but the views of these 'lay' people were often ignored by the medical community in the past. However, in 1952, Terese Lasser succeeded in influencing the American Cancer Society to create the Reach to Recovery programme for women diagnosed with breast cancer through persistent efforts and respectful discussions with the clinicians of the day[6]. In the 1970s, the former First Lady Betty Ford and journalist Betty Rollin[7] raised the issues surrounding breast cancer to new heights by making them a public issue rather than a personal tragedy. Also at this time, Rose Kushner (see 'Rose Kushner Breast Cancer Advisory Centre' in the online links box) had substantial impact on the well-being of patients with cancer through her books and an organization she helped found — the National Alliance of Breast Cancer Organizations (see online links box). Importantly, she also helped to change the way women with breast cancer were treated by demanding a study to compare mastectomy and lumpectomy surgical procedures while serving on a NCI Consensus Conference in 1979 (REF. 8).

Grass roots cancer patient advocacy groups formed throughout the United States in the 1980s and 1990s, starting with breast cancer organizations, such as the Susan G. Komen Breast Cancer Foundation, the National Breast Cancer Coalition (NBCC) and the Y-ME National Breast Cancer Organization (see online links box). Today, many advocacy organizations have developed for almost all types of cancer, including brain, colorectal, gastrointestinal, genitourinary, gynaecological, head and neck, lung, pancreatic and skin cancer, and leukaemia, lymphoma and myeloma. This article cannot list every individual who helped form patient advocacy in the United States, but a brief sample is represented in a 1998 MAMM

Figure 1 | **The world of cancer patient advocacy.** Cancer patient advocates work in many different environments to ensure that cancer patients receive the best clinical care and support during their illness and that this process remains fair. They are involved in fundraising and lobbying politicians to help ensure that cancer research remains high on the political agenda. They are also involved in directing aspects of both scientific and clinical research so that new therapeutic developments can reach cancer patients as efficiently as possible.

NIH intramural board served from 1998–2003 and was involved in the review of the NCI's intramural laboratories within the Center for Cancer Research, the Division of Cancer Epidemiology and Genetics, and in policy decisions for the NCI intramural programme. At the end of her term, another patient advocate was appointed, clearly showing that the value of patient advocates had become apparent to top NCI intramural officials. In 1998, Harold Varmus established the Director's Council of Public Representatives (see online links box) following the release of a United States Institute of Medicine report, 'Scientific Opportunities and Public Needs'[14], which urged the council "to facilitate interactions between NIH and the general public".

Patient advocates now sit on key government committees in the United States along with scientists, physicians and ethicists to guide important research programmes. The Food and Drug Administration (FDA) includes patient advocate input in discussions with companies once an Investigational New Drug application is submitted, in addition to creating appointments on committees like the Oncology Drug Advisory Committee. The NCI has also engaged cancer patient advocates into many levels of its advisory and operation-level committees — it includes patient advocates on its extramural review boards, from presidential appointments on the NCAB[15] to specific task-oriented panels such as the Clinical Trials Working Group. In addition, two patient advocate programmes, the Director's Consumer Liaison Group and the Consumer Advocates in Research and Related Activities (CARRA; see online links box) were established to review programmes dedicated to improving treatment, patient care, long-term survival and prevention, and to solidify their involvement throughout the peer-review system of the NCI.

Why request advocate involvement?

The underlying reason for the increasing number of requests for patient advocate involvement is quite simple. Leland Hartwell, the 2001 Nobel Prize laureate in physiology and medicine and President and Director of the Fred Hutchinson Cancer Research Center, noted, while addressing a 2004 American Association of Cancer Research general session, "As a basic scientist, I was often satisfied if I could provide an answer to the question put to me…'What are you learning about cancer?' But that knowledge has had surprisingly little impact on cancer outcomes. Now, as a cancer center director, I am asked a different question…'What are you doing to cure cancer?' It's a fair question…Congress and the public are not paying $4.7 billion a year just to learn about cancer. They are paying to cure the disease"[16]. Public and private funding sources have become increasingly impatient regarding the results of cancer research and how advances can ensure a positive impact on patient outcome.

Researchers have traditionally been rewarded for being experts in ever-narrowing areas of science. Although this is a crucial element in building knowledge about the causes of cancer, it can sometimes cause a recurrently narrow focus that often keeps researchers from seeing the 'big picture', and therefore can hinder meaningful breakthroughs for patients.

The recent progress made through the successful mapping of the human genome could improve patient diagnosis and treatment, but only if someone involved can focus on end results for patients. Patient advocates who participate on genomic policy committees can facilitate this process, and have often connected specific geneticists and clinical researchers to work on joint projects. The Human Genome Project also illustrates the need for multidisciplinary collaborations to generate advances, as well as the need for sizeable research grants to cover all the parties involved. Successes with new biological agents, such as trastuzumab (Herceptin; effective in certain kinds of breast and lung cancers) and imatinib (Gliver; effective for gastrointestinal tumours and chronic myeloid leukaemia), have included new levels of collaboration in research and unprecedented levels of patient advocate involvement[17,18].

Since the 1990s, patient advocates, using both customary and innovative strategies, have improved epidemiological studies and helped revamp the protracted drug-development process at national, regional and local research levels[19]. Patient advocates who participate in research efforts do so to foster environments

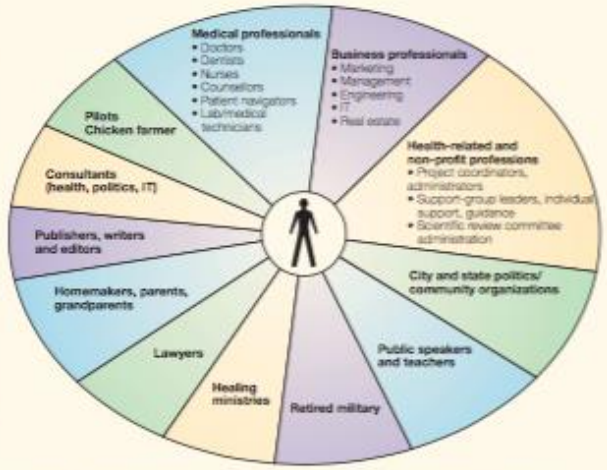


Figure 2 | **Patient advocate backgrounds.** Cancer patient advocates have come from diverse backgrounds, reflecting that people from all walks of life are affected by cancer, either personally or through a loved one. This often leaves them determined to help others in a similar situation and patient advocacy is one way of achieving this.

NCI SPORE
Patient Advocate Research Teams (PART)

Planning

Direction

Decisions

Discovery

Observation

Proof of concept

Development

Preclinical

Tissue + trials

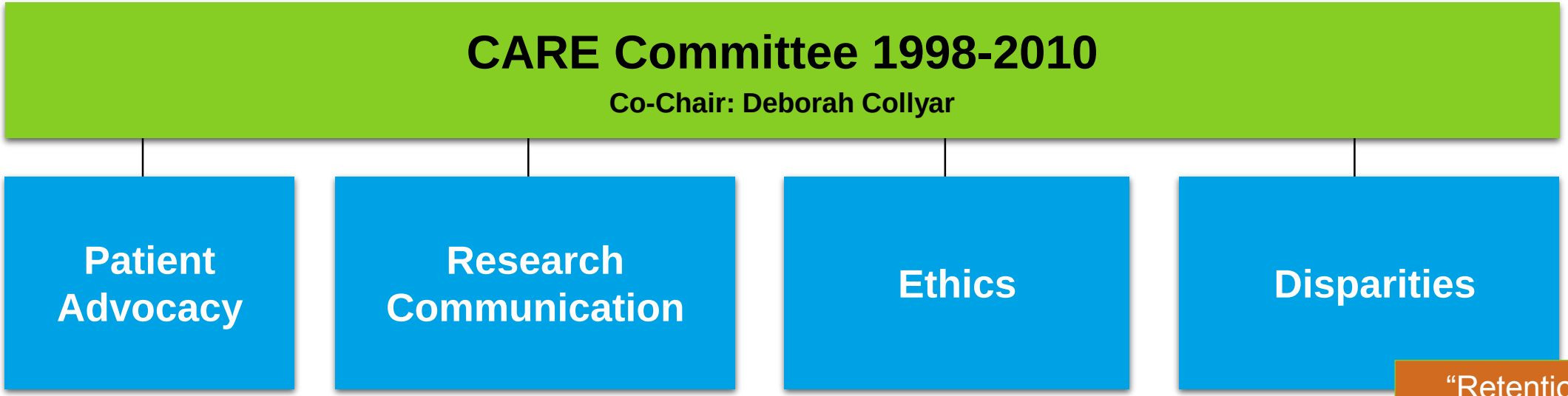
Barriers

Intellectual Property

Interoperability

Collyar D, Nature Reviews Cancer 2005

e.g. Cancer & Leukemia Group B



Themes: Service, educational, and research activities

"Retention"
"Adherence"
"Compliance"

Development → **Approval** → **Activation** → **Recruitment** → **Endurance** → **Results**

Reviews:
Operational
Concept
Protocol

Informed consent:
Templates
Lexicons

Recruitment plan:
Tools
Special populations

Tracking and advice:
Resource networks
Protocol evaluation
Accrual Plan adjustments

Participant communication:
Thank you letters
Research summaries

Helping all patients…

Race ≠ ethnicity ≠ minority

Race

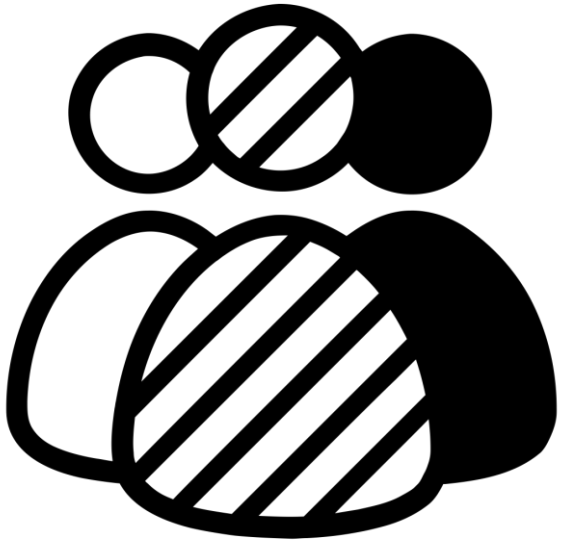
Differences/similarities in biological traits

Ethnicity

A shared cultural heritage that is learned

Minority

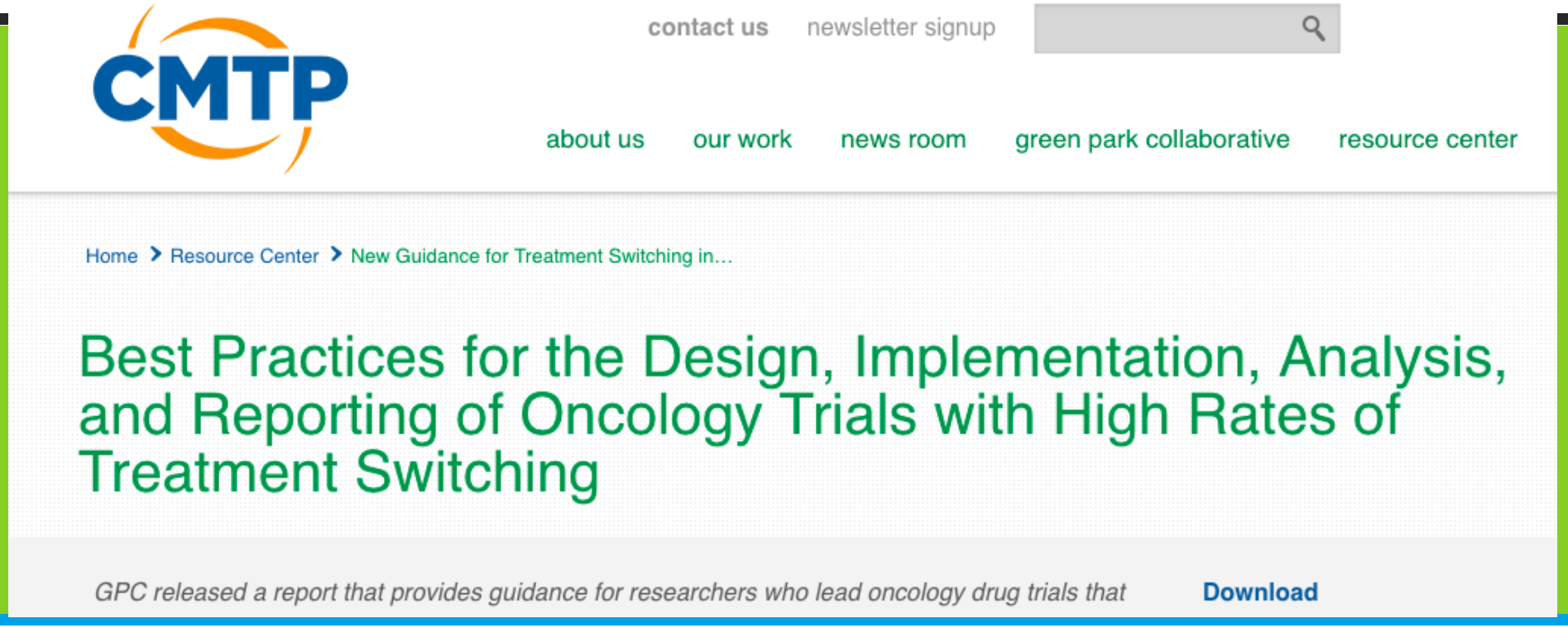
Smaller population than the controlling majority



Ageism: pervasive

Socioeconomic status (SES) matters

e.g. Crossover (treatment switching) 2016



International consortium

Australia (IRB), UK (NICE),
US (FDA)

Multi-stakeholders

Clinicians, regulators, companies,
patient advocates, payers

PAIR represents **patients** first, then research

Concept and protocol design & review ➔ feasibility

Recruitment plans & materials ➔ understanding

FDA, all phases, collaborators, etc. ➔ speed

Ethics/Institutions Review Boards ➔ risk

Communities and populations ➔ influence

Plain language summaries ➔ results

Data can help, but not alone

Patients may help, but won't be used!

Data ≠ Knowledge ≠ Results

Un-validated info harms people

Bias, false positive or negative results

Wastes time and money

Erodes trust and costs lives

We HAVE to get this right

Data sharing resolution

- Signed by all NCTN adult patient advocate committees
  - 127 total patient advocates
- Articles in media
- Requested by U.S. VP
- Presented to CEO Roundtable
- Project Data Sphere

Bertinoloi M et al NIJM 2017

A Resolution to Share Legacy Cancer Clinical Trial Data; a Right of Consented Patients

Submitted by the Patient Advocate Committee of the Alliance for Clinical Trials in Oncology on the behalf of all patients who have participated in cancer clinical trials to improve treatments and outcomes for all cancer patients in the future.

Sharing data is essential to bring together vast amounts of legacy cancer clinical trial data to advance medical discoveries. Discoveries made through collaborations and sharing data are discoveries that cannot be made using small isolated data sets. Barriers to sharing data must be resolved so that all legacy NCTN clinical trial data can be shared in a way that benefits all patients.

WHEREAS, patients volunteer to participate in clinical trials for many reasons, including to help themselves, others, and to help improve treatments for future patients;

WHEREAS, patients who volunteer to participate in clinical trials;

- are informed about potential benefits and risks, including the risk of the loss of confidentiality;
- have signed an informed consent document indicating knowledge and acceptance of potential risks (including potential loss of confidentiality) and receive printed copies for future reference;
- voluntarily donate their personal information, tissue, blood, and other biological samples for future research while participating in clinical trials;
- expect that the samples and information they submit will be used to further understand and improve the treatment of future patients in a way that is concordant with current research practices;

WHEREAS, current technology permits data sharing to collect data from various clinical trials to gain better knowledge, understanding, and improve the treatment of future patients;

WHEREAS, patients acknowledge that loss of confidentiality, identification of individuals and misuse are potential risks of data sharing;

WHEREAS, data sharing projects (e.g., Project Data Sphere) take high security measures to ensure that there is minimal possibility of loss of confidentiality or misuse of data collected.

Therefore, be it

RESOLVED, that patients who participate in clinical trials are aware of the potential loss of confidentiality and signed an informed consent document acknowledging this as a possibility and,

RESOLVED, that patients who participate in clinical trials expect their samples and information to be used to benefit future patients. Not allowing data sharing in an open and transparent process could negatively affect the potential to discover new medical and scientific advancements translating to future patients' treatment and,

RESOLVED, that sharing patient data collected in clinical trials is essential, and would be a disservice to patients not to use their data in the most productive and efficient way possible to advance treatments and preventive measures for future patients,

And be it finally

RESOLVED, that barriers of federal agencies and research institutions to restrict the sharing of clinical trial data should be immediately resolved, and full support granted to National Cancer Institute's National Clinical Trials Network (NCTN) groups and other accredited cancer research organizations to allow and encourage sharing of legacy cancer clinical trial data.

Change: embrace or get out of the way!

Informed Consent

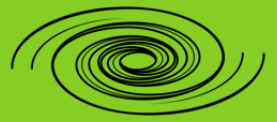
For patients? Really?

Electronic?

IOE

Who needs doctors?

What's a control group?



RWE (data)

Who benefits? Really?

Who pays for?

Right to Try

How many states now?

Who need clinical trials?

Note: these are still about the **system,** not patients

What ***should*** clinical trials really be about?

Re-think traditional phases

Design & conduct with ***clinical use*** in mind

Connect trials together

Technology for patient results, not ‘big data’

Get out of comfort zones

PROs = more than AEs

Let’s make patient-centered **change** happen!

Critical learning after clinical trials

Shorter FDA approvals leave questions

- What long-term impact & issues? When to give treatment?
- How to achieve best results? Who else?

Conditional approvals/REMS are important

- Make these count
- Access is crucial (after clinical trials, label, etc.)
- Patients, providers, & payers need more information

Plan on real world studies

- Patient needs/preferences: before, during & after trials
- Partner with us to provide real value on pricing

How can we help with immunotherapy?

Decision points

Biospecimens

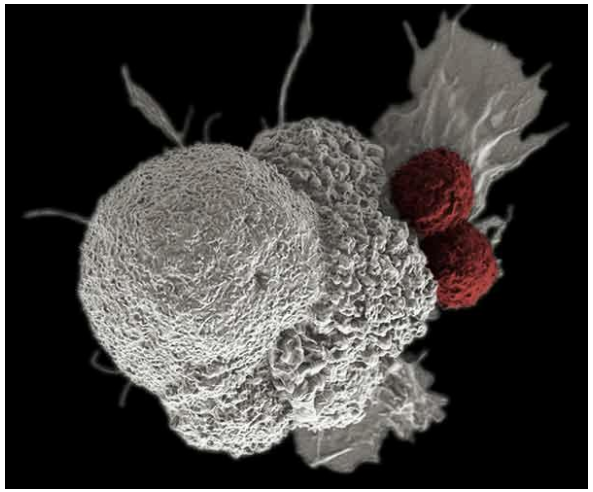
Data sharing (reciprocal)

Trial design

- Bayesian, etc.

Consent/trial strategies

ImmunoScore?



Patient Advocates In Research (PAIR)

Where research meets reality

Thank you! Get in touch

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