Community Advisory Boards for patient engagement in R & D

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Declaration of interest

In the past 21 years, my life has been saved by drugs from the following companies

- Boehringer-Ingelheim
- Bristol-Myers Squibb
- Gilead Sciences
- GSK
- Merck Sharp & Dohme Chibret
- Roche
- ViiV Healthcare

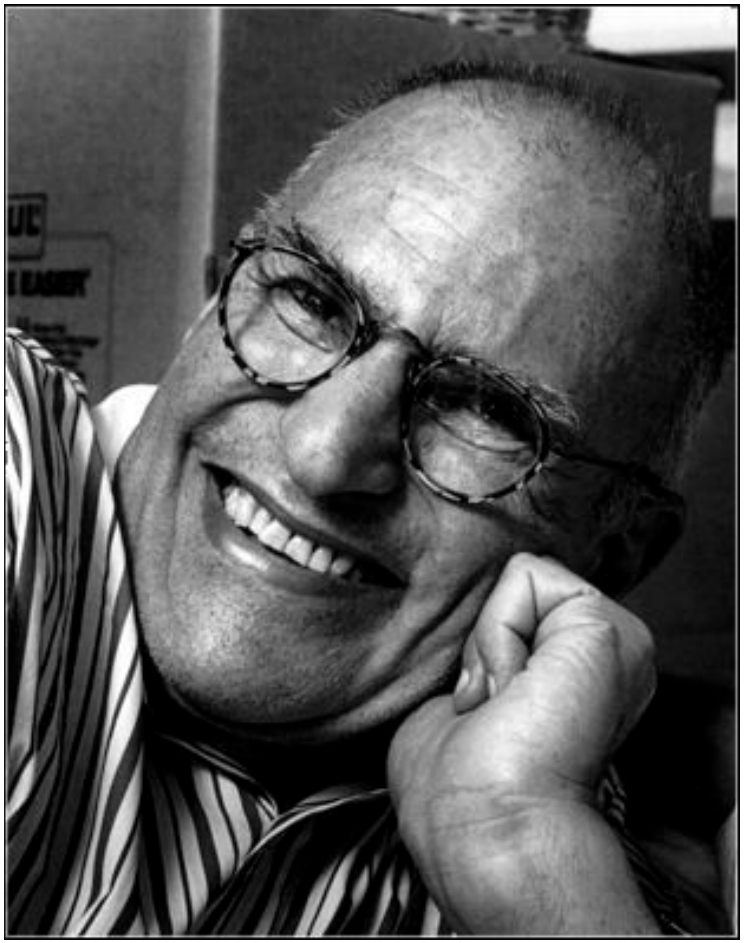
Patients & health care system – a multilevel approach

- How are patients involved in clinical trials?
- How can patients influence and improve clinical research?
- Role and influence of patient organisations, community advisory boards
- Challenges ahead

HIV history

"Our continued existence depends on just how angry you can get"

1,112 and Counting,
Larry Kramer, March 1983



The Denver Declaration 1983

- Californian & NY PWAs meet in Denver → “Denver Principles”, birth of “PWA empowerment”, as well as term “PWA”
- We recommend that people with AIDS…
  - Be involved at every level of AIDS decision-making and specifically
  - Be included in all AIDS forums with equal credibility as other participants, to share their own experiences and knowledge

"Nothing about Us, Without Us“

Pioneer 1: Project Inform

- 1985: Project Inform created (Martin Delaney & others)
- Smuggling runs to Tijuana for a cold remedy (ribavirin) Soon after, decision to take political action
- Project Inform started "medically supervised guerrilla trials" — community-based studies of the safety and efficacy of drugs, like ribavirin, without FDA approval
- Established National AIDS-treatment hotline
- Early 1990s: Delaney instrumental in introducing accelerated approval & expanded access programmes
- Delaney central figure in "Acceptable Risks" (Poseidon Press, 1992), "Who should decide which risks are acceptable, the bureaucracy in Washington or the patient whose life is on the line?"

FDA Demo
October 1988

"Storm the NIH"
May 1990

Pioneer 2: Act Up &
1st Wall Street protest March 24, 1987

To demand the following

1. Immediate release by the Federal Food & Drug Administration of drugs that might help save our lives.
   These drugs include: Ribavirin (ICN Pharmaceuticals); Ampligen (HMR Research Co.); Glucan (Tulane University School of Medicine); DTC (Merieux); ddC (Hoffman-LaRoche); AS 101 (National Patent Development Corp.); MTP-PE (Ciba-Geigy); AL 721 (Praxis Pharmaceuticals).
2. Immediate abolishment of cruel double-blind studies wherein some get the new drugs and some don't.
3. Immediate release of these drugs to everyone with AIDS or ARC.
4. Immediate availability of these drugs at affordable prices. Curb your greed!
5. Immediate massive public education to stop the spread of AIDS.
6. Immediate policy to prohibit discrimination in AIDS treatment, insurance, employment, housing.
7. Immediate establishment of a coordinated, comprehensive, and compassionate national policy on AIDS.

President Reagan, nobody is in charge!

ACT UP
AD MY LIPS

FEDERAL
DEATH
ADMINISTRA
PISD
PISD
PISD
B.S.

EATG - ECAB history

EATG founded in 1992

Purpose & mission

- Achieve effective treatment & access to experimental therapies for as many PLWHA as possible & as soon as possible
- Enable people with HIV to have maximum control over the treatment and research agenda – ***nothing about us without us***

Experimenting with early CAB models

- CABs linked to trial sites, specific trials or specific companies
- Dissatisfaction with methodology, collaboration w. industry, working model, agenda setting, minute taking, conflict resolution

1997 CAB model review with help of ethicist

- Implementation current model (ECAB)
- ECAB review – The impatient patient, 2013

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ECAB model

- Establish confidentiality internally & externally
- Business model: industry funding via unrestricted educational grants
  - ECAB = independent entity within EATG
  - Funding via meeting fees
- Establish collaboration with industry, regulators & academic societies
- 2 ½ day meetings Fri-Sun, ca. 6 per year (HIV, Hepatitis B & C, tuberculosis, prevention, diagnostics and generics)
- Agenda & minutes set by group
- Systematic member trainings
  - Training elements in every meeting
  - Peer-to-peer or by academics
- Perform policy work within EATG: complimentary activity to CAB work (since 2004)
- Membership: >150; 35 WHO Europe countries

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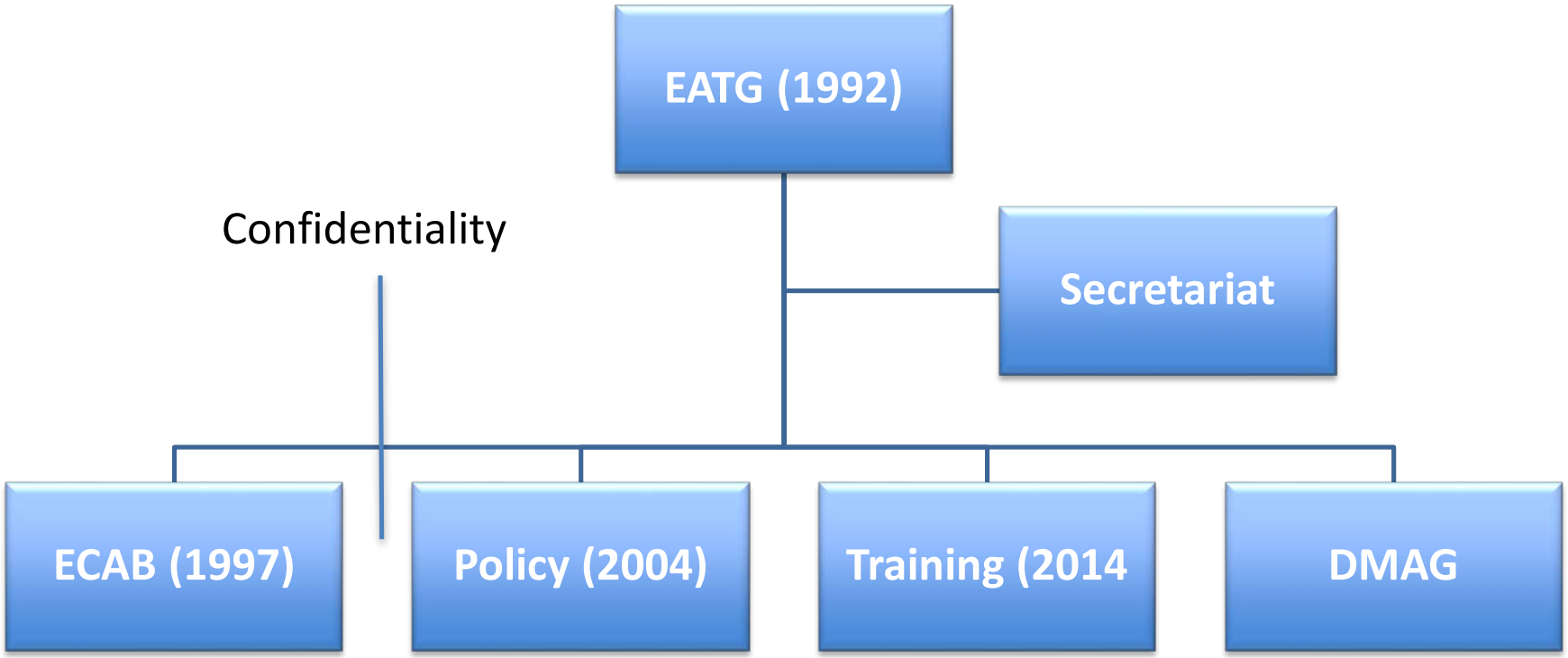
EATG – Working groups



ECAB: European Community Advisory Board
DMAG: Development & Membership Advisory Group

EATG European AIDS Treatment Group

HIV activist & ECAB achievements

1. Expanded access / compassionate use (FDA, 1987)
2. Accelerated approval for life threatening conditions (FDA, 1992)
3. Pushing for surrogate markers instead of clinical endpoints in pivotal trials (EMA, nevirapine approval 1997)

- ✧ EATG first to ring the alarm bells re. lipodystrophy in early HIV combination treatments 1997
- ✧ Influencing CD4 threshold in phII/phIII trials and other important changes in trial protocols
- ✧ Successful lobbying for a pivotal trial including two investigational compounds, ending exposure to monotherapy by multidrug resistant trial participants 2007
- ✧ Formal cooperation with EMA since 2003 (informal since 1996)
- ✧ Formal relations with WHO Europe and European Centre for Disease Control (ECDC)
- ✧ Recognised and involved in pan-European structures, conferences, clinical societies and cohort studies and EC funded research collaborations

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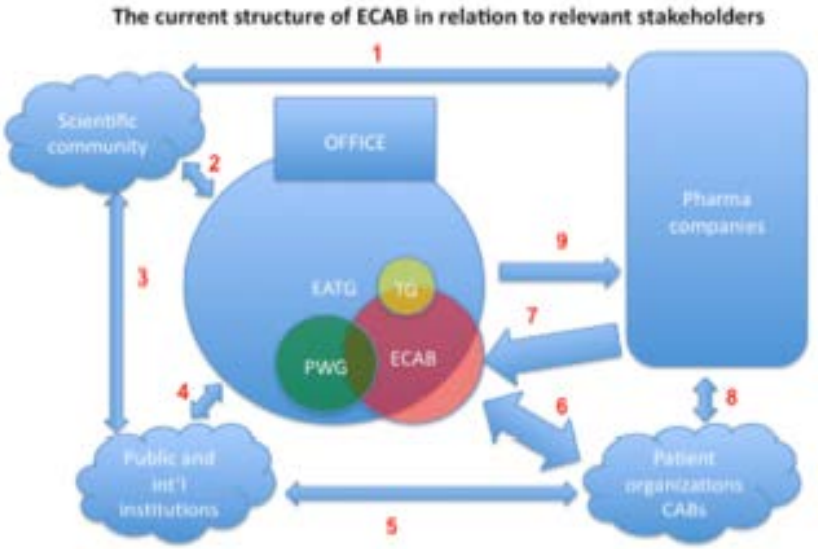
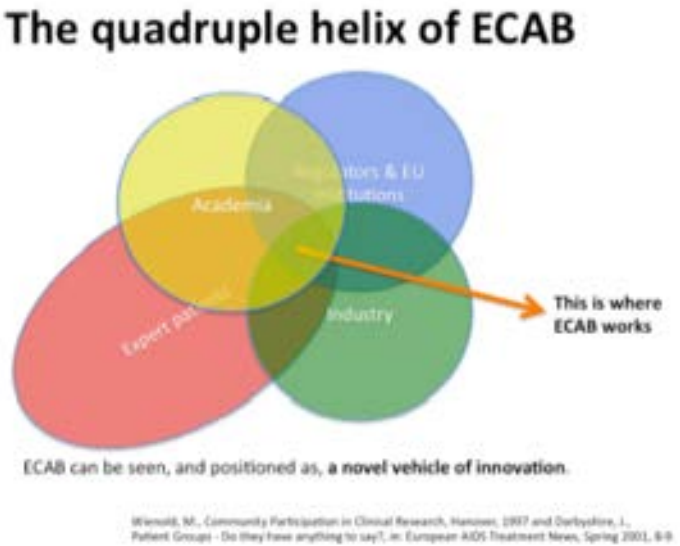
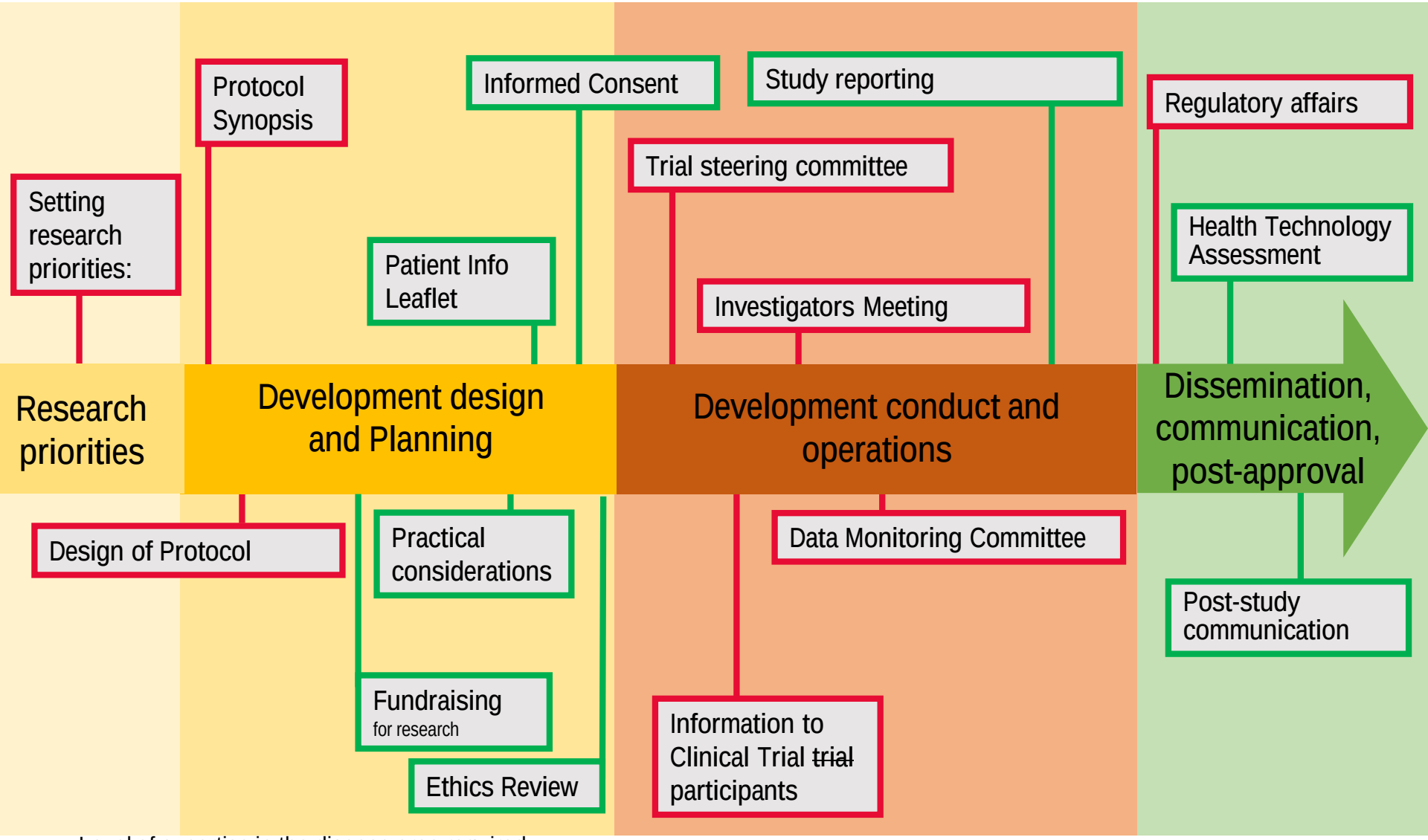
ECAB – Crossroads between patient organisations, industry, academia & regulators





European AIDS Treatment Group

Patient involvement in Research and Development (R&D) is not something new. It is reality today.



Level of expertise in the disease area required:

high | medium

Source: Geissler, Ryll, Leto, Uhlenhopp EPALCO/EUPATI (2015, unpublished)

The interaction still has challenges

- **Lack of best practice sharing and mutual learning** (across industry, across regulators, across patient organisations)
- **Lack of standardised metrics** to measure benefits and impact
- **Perceived or real legal barriers, conflict of interest, silo-thinking and finger-pointing**
- **Mushrooming of processes, rules and codes**
- **Lack of capacity** in patient organisations, lack of “universal patient experts in R&D”
- **Lack of trust**

Changing environment for CABs

- Compliance impact on previously free exchange
- All topics & questions to be agreed in advance
- R & D agenda in context with access, reimbursement & policy issues
- Current innovation model focused on hypes & patented drugs
- Off patent: no one interested, wasting resources
- Health expenditure perceived as cost, not investment. Return of investment not considered / evaluated
- No agreement on quality of life indicators
- Impact of digitalisation & real world data on drug development
- Less people in trials generate much more data
- Ethical challenges collecting, hosting, processing & sharing sensitive personal data

HIV: A lot went well

- ✧ Expanded access / compassionate use (FDA, 1987)
- ✧ Accelerated approval in life threatening indications (FDA, 1992)
- ✧ Use of surrogate markers instead of clinical end points in pivotal trials (EMA, NVP approval 1997)
- ✧ New criteria for conditional approval (Gilead first to apply, access almost 12 months accelerated)
- ✧ Cross-Atlantic lobbying for pivotal trial including 2 NCE, ending exposure to monotherapies and multidrug resistance 2007
- ✧ Single tablet regimens for convenience and adherence, while having single compounds to control toxicities, resistance and adapt drug levels

NVP: Nevirapine; NCE: Novel Chemical Entity

Systems no longer robust: impacting HCV drugs

- DAA and combination treatment: Biggest scientific breakthrough for patients since HAART introduction
- Much shorter treatment cycles, much less toxicity, a lot more effective & even cheaper
- Interaction with regulators and industry since 2007
- Despite all this: bumpy reimbursement at national level while patients continue to die
- Interesting: HTA bodies assessment in conflict (German IQWiG versus HAS & Scottish Medicines Consortium; Scotland faster than NICE) – apparent methodological discrepancies and challenges
- Current system aims too much for perfection and cost containment; fails on robustness.
- Many new drugs STR only – Gilead, Abbvie, MSD – leaving many patients without treatment options and kicking important single compound competitors out of market – HCV treatment is some weeks, not life long!

DAA: Direct Acting Agents; HAART: Highly Active Antiretrovirals; HTA: Health Technology Assessment; IQWiG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (German HTA body); HAS: Haute Autorité de Santé (France); STR: Single Tablet Regimen

What do we need

- Forget about aiming for perfection – focus on clear & agreed priorities:
  - Develop effective medicines
  - Assess properly and timely
  - Get medicines to patients quickly
  - Have patients use medicines safely
- Agree on HTA methodology in Europe
- Establish EARLY & ONGOING dialogue at EMA along product life cycle
- The secret of true innovation is that it pays out quickly; lack of stability and delaying access is poison for innovation
- A robust system, strong and trusted to face challenging situations – have the priorities right and muddle through wisely

Literature & resources

- Wienold, M., **Community Participation in Clinical Research**, Hanover, 1997
- Derbyshire, J., **Patient groups - Do they have anything to say?**, in: European AIDS Treatment News, Spring 2011, 8-9
- **The impatient patient, from anger to activism**, EATG June 2013, for download www.eatg.org/news/publication/Other
- **Patient participation in rheumatology research**, Maarten de Wit, Vrije Universiteit Amsterdam & University of Bristol, Stichting Tools 2013
- **EUPATI toolbox**, www.eupati.eu

"Never doubt that a small group of thoughtful, committed citizens can change the world; indeed it's the only thing that ever does"

Margaret Mead, 1901-1978

Thanks

- Tamas Bereczky, Giulio Maria Corbelli EATG
- Jan Geissler, EUPATI & CML Foundation
- Many colleagues & friends, alive & dead

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