



Transparency in the Time of Constant Change

Paper RGo2

“Well, personally, I've seen enough of people who die for an idea. I don't believe in heroism; I know it's easy and I've learned that it can be murderous. What interests me is living and dying for what one loves.”

— [Albert Camus](#), [*The Plague*](#)

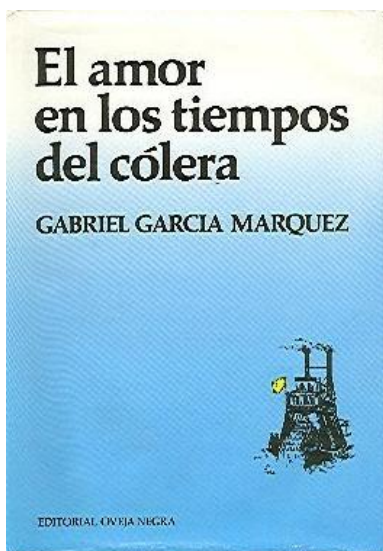


Which leads me to believe he had children...



Gabriel García Márquez

06 March 1927- 17 April 2014



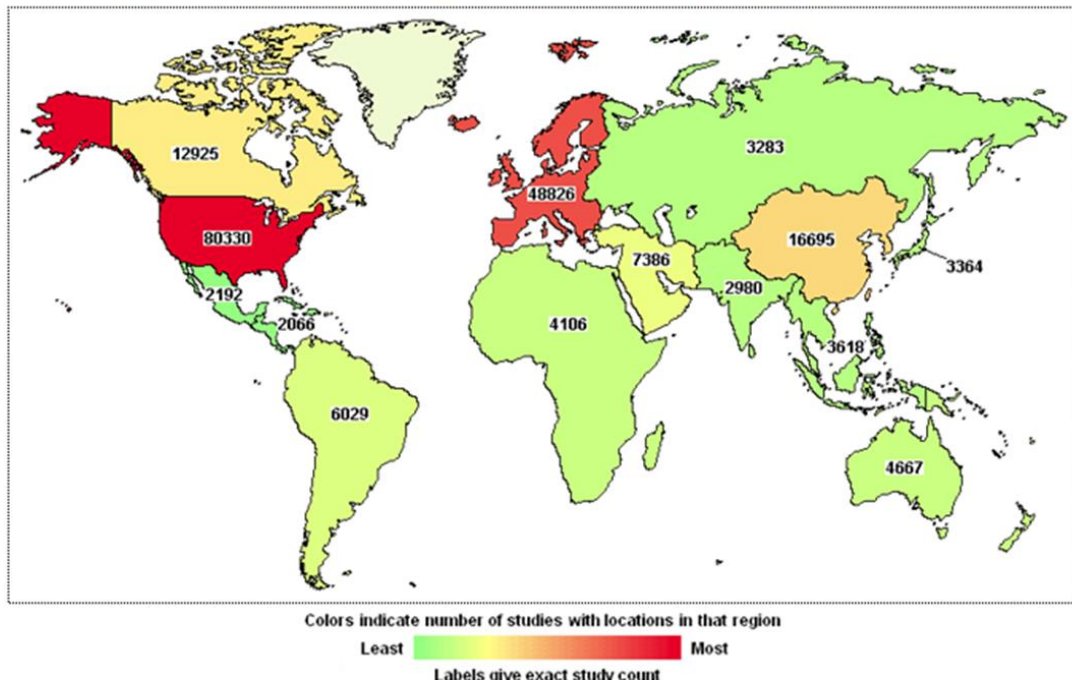
Storyline: A 50 year relationship in a time of turbulence

Storyline: 100 years in the life of family in many times of turbulence

Data Transparency

all 175684 studies found, shown on map.

Click on the map below to show a more detailed map (when available) or search for studies (when map not available).



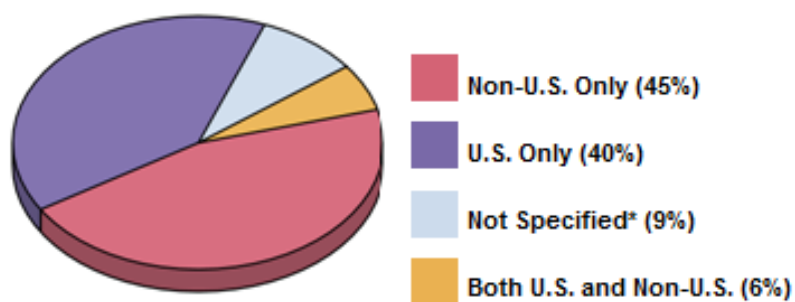
Source: <https://clinicaltrials.gov>

Storyline: Proprietary Clinical Data that will exist forever in a world full of turbulence

Clinicaltrials.gov (by region/location)

Percentage of Registered Studies by Location (as of September 18, 2014)

Total N = 175,013 studies



Location

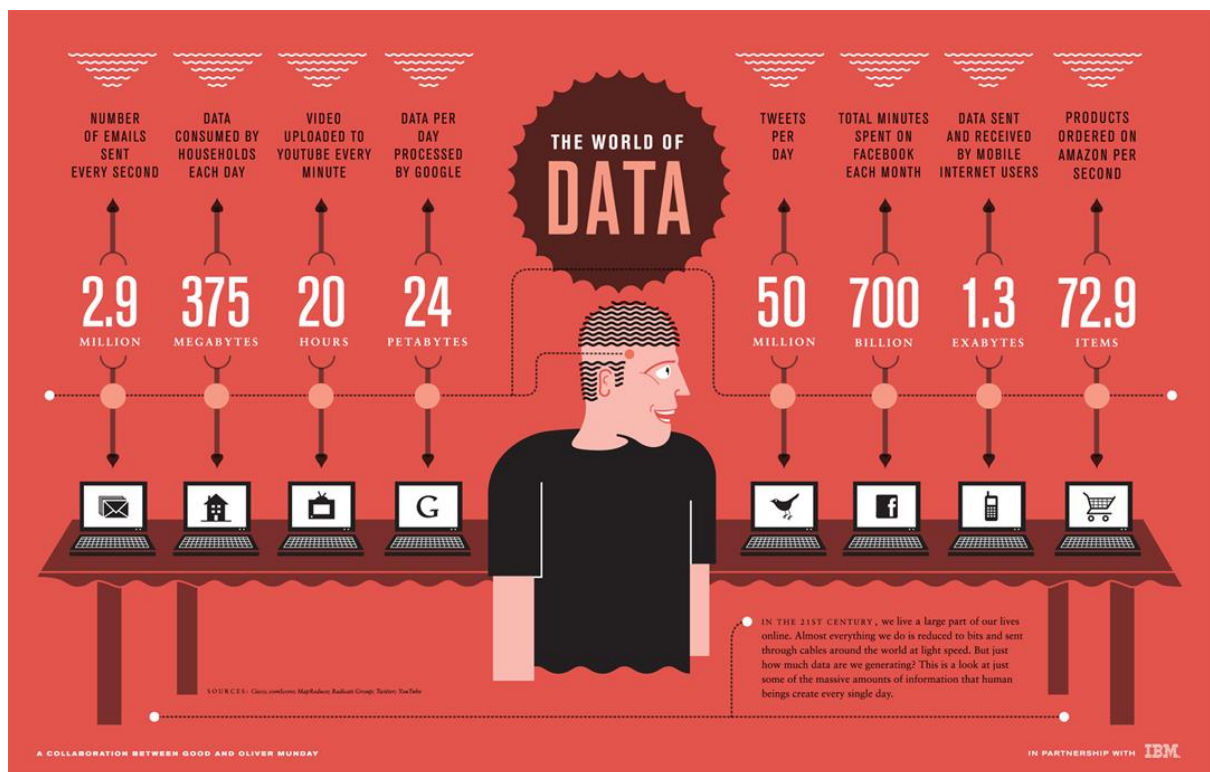
Number of Registered Studies and Percentage of Total
(as of September 18, 2014)



Background

- “Drugs are tested by the people who manufacture them, in poorly designed trials, on hopelessly small numbers of weird, unrepresentative patients, and analysed using techniques which are flawed by design, in such a way that they exaggerate the benefits of treatments... Unsurprisingly, these trials tend to produce results that favour the manufacturer. “
 - Ben

Other [transparent] Numbers...



Source: <http://awesome.good.is/transparency/web/1009/the-world-of-data/flat.html>



Overview

- Data Transparency?
- Background
 - Why now?
 - What's different?
 - Real Life Example of Transparency
- Examples
 - [ClinicalTrials.gov](#)
 - Participant Flow
 - Baseline Characteristics
 - Outcome Measures and Statistical Analyses
 - Adverse Events
 - [Alltrials.net](#)
- Challenges
- Recent Updates in Transparency



What is Data Transparency?

- A property of a communication system such that the output data stream delivered provides an output bit sequence functionally equivalent to the input bit sequence, from which the exact input bit sequence can be derived.
- Encyclopedia.com - <http://www.encyclopedia.com/doc/1O11-datatransparency.html>



Why Now?

- Principles for Responsible Clinical Trial Data Sharing
 - Three Principles
 - Safeguarding the privacy of patients
 - Respecting the integrity of national regulatory systems
 - Maintaining incentives for investment in biomedical research
- European Federation of Pharmaceutical Industries and Associations – July 18, 2013



What's Different?

1. Enhancing Data Sharing with Researchers
2. Enhancing Public Access to Clinical Study Information
3. Sharing Results with Patients Who Participate in Clinical Trials
4. Certifying Procedures for Sharing Clinical Trial Information
5. Reaffirming Commitments to Publish Clinical Trial Results



Real Life Example, Yervoy®™©

- Forbes: “Merck rival Bristol-Myers Squibb also unveiled promising melanoma drug results at ASCO from a study where patients were administered a combination of Yervoy, Bristol-Myers’ existing melanoma drug, along with its developmental drug nivolumab. *This duo resulted in a 53% response rate* (the percentage of patients who saw a decrease in tumor size) .” – italics mine. ”
- Results Released by Bristol-Myers Squibb via clinicaltrials.gov
- 46% of patients taking YERVOY alone were alive at year 1.
 - Estimated percentage, compared with 25% of patients taking an experimental drug alone.
- 24% of patients taking YERVOY alone were alive at year 2.
 - Estimated percentage, compared with 14% of patients taking an experimental drug alone.

Clinicaltrials.gov

More details available in the "Basic Results" Data Element Definitions.

August 2014

<i>Participant Flow Template</i>				<i>ClinicalTrials.gov</i>
Recruitment Details				
Pre-assignment Details				
Period ①				
* Period Title	Overall Study	①		
* Arm/Group Title				
Arm/Group Description ②				
		Number of Participants	Number of Participants	Number of Participants
* Started				
[*] Milestone Title ③				
[*] Milestone Title ③				
[*] Milestone Title ③				
* Completed				
Reason Not Completed				
[*] Adverse Event				
[*] Death				
[*] Lack of Efficacy				
[*] Lost to Follow-up				
[*] Physician Decision				
[*] Pregnancy				
[*] Protocol Violation				
[*] Withdrawal by Subject				
[*] Other Reason ③				
[*] Other Reason ③				
[*] Other Reason ③				

* Required by ClinicalTrials.gov
 [*] Conditionally required by ClinicalTrials.gov
 ① Complete a Period table for each stage of the study. If only one Period, the Title is "Overall Study". For multiple Periods, include descriptive Titles for each Period.
 ② Arm/Group Description describes details about the interventions administered (e.g., dosage, dosage form, frequency of administration) or groups evaluated.
 ③ [Optional] Add as many Milestone Title or Other Reason Not Completed rows as needed. A descriptive title for each row is required.

Clinicaltrials.gov, cont'd.

Period 2: Treated in Induction Phase

	Ipilimumab and Dacarbazine	Placebo and Dacarbazine
STARTED	247	251
COMPLETED	45 ^[1]	54 ^[2]
NOT COMPLETED	202	197
Disease Progression	88	152
Study Drug Toxicity	83	10
Death	8	15
Deterioration/Undocumented Progression	9	8
Adverse Event	6	7
Withdrawal by Subject	6	5
Physician Decision	2	0

[1] 45 participants on treatment at end of induction phase. Study undergoing closure.

[2] 54 participants on treatment at end of induction phase. Study undergoing closure.

Clinicaltrials.gov

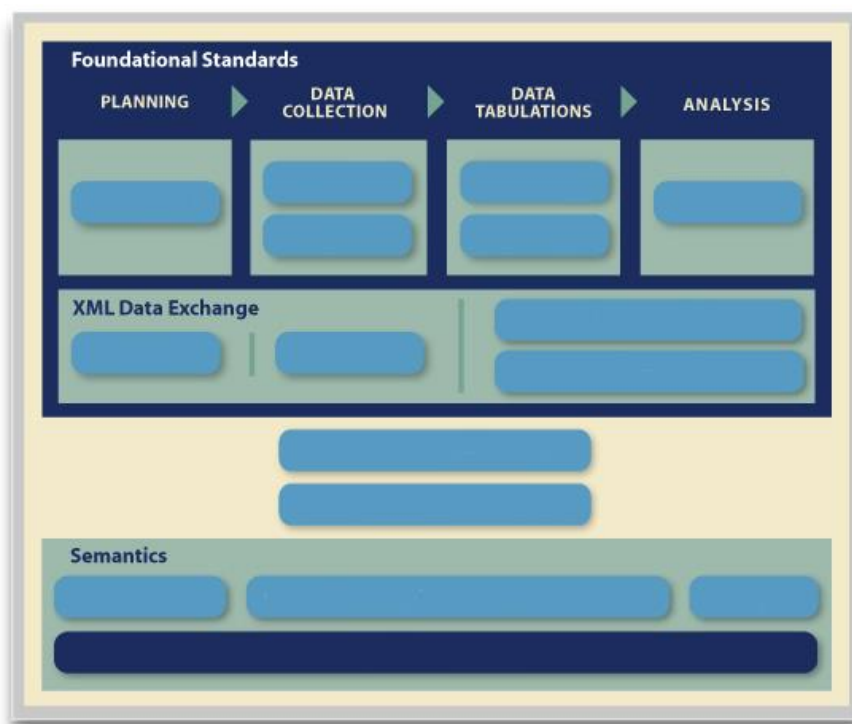
	Ipilimumab and Dacarbazine	Placebo and Dacarbazine
Number of Participants Analyzed [units: participants]	196	218
Overall Survival in Participants Randomized to Either Ipilimumab Plus Dacarbazine or Dacarbazine Plus Placebo [units: months] Median (95% Confidence Interval)	11.17 (9.40 to 13.60)	9.07 (7.75 to 10.51)



Alltrials.net

- The result in large part of Dr. Goldacre's research, books and blog) - *Note: this does not call for individual patient data to be made publicly available*
 - AllTrials calls for all past and present clinical trials to be registered and their full methods and summary results reported.
 - Large Emphasis on Previously Unpublished Trials
1. [Registration](#)
 - Self-explanatory
 2. [Summary results reporting](#)
 - summary of results should be publicly available where the trial was registered, within one year of completion of the trial. Summary results from all past trials of medicines currently in use should be made publicly available on a register now. Summary results include information on the primary and any secondary outcomes measured and statistical analysis
 3. [A full report](#)
 - In brief: Trial sponsors or others who produce a full report for marketing authorization or any other purpose should make this publicly available.
 4. Individual Patient Data - Note, again, that the AllTrials campaign is not calling for individual patient data to be made publicly available.
 - There are currently initiatives in many countries looking at how to improve sharing of this level of information for the benefit of future research. Patient groups, medical research funders and trialists have raised concerns about the inability to reuse past research. They are keen to develop consent protocols that will optimize the ability to reuse findings, and want legislators to look at whether new data protection regulations impose unnecessary burdens and restrictions on reuse of past research.

CDISC Standards and Implementation





[Very] Recent Activity

- Columbia University
 - **Transparency in Academia**
 - Approach Finds Gene that Drives Aggressive Brain Cancer (October 9, 2014)
- RAPS (October 2, 2014)
- FDA launches Sentinel programme to monitor drug safety
- PhUSE Traceability and Data Flow
- BIOGEN IDEC – Pooling of MS Data
- [http://www.phusewiki.org/wiki/index.php?title=Traceability and Data Flow](http://www.phusewiki.org/wiki/index.php?title=Traceability_and_Data_Flow).
- Resuability!



Conclusion

- Ethical Implications?
 - Randomization
 - Impacting patient recruitment/retention
- Enrollment
 - Fast?
- Patient Communities!
 - Engaging with patients
 - Enrollment based on partial data/information



References/Recommended Reading

- Encyclopedia.com -
<http://www.encyclopedia.com/doc/1O11-datatransparency.html>
- <http://transparency.efpia.eu/uploads/Modules/Documents/data-sharing-prin-final.pdf>
- www.yervoy.com
- <http://www.cdisc.org/standards-and-implementations>
- <https://clinicaltrials.gov/>
- <http://www.businessdecision-lifesciences.com>

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