HEROES AND MARTYRS OF QUALITY AND SAFETY

Shuffle the deck, flip that coin: randomization comes to medicine

D Neuhauser, M Diaz

There is a lot of confusion about the first use of randomization in an experiment and the first use of randomization in medicine. Some writers think that the great statistician R A Fisher carried out the first randomized trial (in agriculture) and published the results in 1923. Others think that the first medical trial was carried out by the British National Research Council in the 1940s. But there are earlier examples and we think we have found the oldest.

To resolve this debate we have to be precise in our definition of randomization in experiments.

The word “randomization” does not exist in the Oxford English Dictionary or its supplement. It has two frequent uses in social science and clinical research. The first is a “random sample” from a larger population. Here randomization is used to ensure that the sample is representative of the population as a whole. The second use of randomization in experimental design is our focus here. There is an experiment, purposefully and prospectively designed; there are control and experimental interventions on patients purposefully designed to eliminate every observable and unobservable difference between the two except for the experimental intervention; and there is a method of assignment which is out of the control of any human and their potential biases. This is done by flipping a coin, shuffling a deck of cards, drawing lots, the use of tables of (pseudo) random numbers or today by computer generated random numbers. The study is carried out and the results of the intervention are evaluated by comparing the differences.

Those readers who wish to argue against our “firsts” may be able to find older studies using our definition or they can use another definition and argue for earlier studies. Here are the oldest two studies fitting this definition known to us.

CHARLES PEIRCE SHUFFLES THE CARDS IN 1883

Charles Peirce (1839–1914) graduated at the bottom of his class at Harvard (79th out of 90) in 1859 and went on to make major scientific contributions in astronomy, geodetics, psychology, and philosophy (as the founder of “pragmatism”). He suffered from repeated bouts of depression and his worldly career was not successful. In 1879 he was fired from John Hopkins the next year. The reasons are not clear, but, seemingly, were in part due to his divorcing his abused first wife and remarrying. His cocaine addiction (unproved) probably did not help. It must be said that opiates were legally dispensed at the time.

Today you can visit the Peirce Edition Project website and join the Peirce International Society of Scholars. The 150th anniversary conference proceedings discuss his contributions to philosophy and make no reference to his first knowledgeable, explicit use of randomizing experimental interventions.

J BURNS AMBERSON FLIPS A COIN FOR PATIENTS IN 1926

Where in the world did the first randomized trial in medicine occur? If you ask your friends this question, you have a safe bet they will not know. The answer is Detroit, Michigan at the Detroit Municipal Tuberculosis Sanatorium which no longer exists. Its site is now a public park and no monument marks this contribution to clinical evidence.

J Burns Amberson (1890–1979) was on the staff of this hospital in 1926–1927 when he carried out a clinical trial of a drug for tuberculosis (sodium gold-thiosulfate or sanocrisin). He had moved to Bellevue Hospital in New York City when it was published in 1931 in the American Review of Tuberculosis.

To quote from this paper: “On the basis of clinical, X-ray and laboratory findings the 24 patients were then divided into two approximately comparable groups of 12 each. The cases were individually matched one with another in making this division. Obviously, the matching could not be precise but it was as close as possible, each patient having been studied independently by two of us. Then, by a flip of the coin, one group became identified as group I (sanocrisin treated) and the other as group II (control). The members of the separate groups were known only to the nurse in
charge of the ward and the two of us. The patients themselves were not aware of any distinction in the treatment administered.”

Today we would not have “flipped the coin” once to divide these groups in two but would use a table of random numbers 24 times to assign each individual to one of the groups. Amberson’s group found no difference in outcomes and this treatment was abandoned.

Unlike Peirce, Amberson in his lifetime gained all the honors his field had to offer: Professor at Columbia University Medical School and head of the Chest Service at Bellevue with devoted, excellent resident physicians; President of the National Tuberculosis Association in 1942; winner of the Trudeau Medal in 1952; an honorary degree from the University of Pennsylvania in 1953; and over 70 publications.

He lived to see the end of the sanatorium era from the University of Pennsylvania in 1953; and over 70 publications. Amberson’s group found no difference in outcomes these groups in two but would use a table of randomization to human experimentation.

Today we would not have “flipped the coin” once to divide these groups in two but would use a table of random numbers 24 times to assign each individual to one of the groups. Amberson’s group found no difference in outcomes and this treatment was abandoned.

Unlike Peirce, Amberson in his lifetime gained all the honors his field had to offer: Professor at Columbia University Medical School and head of the Chest Service at Bellevue with devoted, excellent resident physicians; President of the National Tuberculosis Association in 1942; winner of the Trudeau Medal in 1952; an honorary degree from the University of Pennsylvania in 1953; and over 70 publications, 20–22 He lived to see the end of the sanatorium era of tuberculosis treatment, due to the introduction of streptomycin which led to ambulatory treatment and the hope that tuberculosis could be eradicated. Since his death, HIV/AIDS and drug resistant tuberculosis have dashed this hope for now.

Peirce is now honored and Amberson nearly forgotten, but they are heroes for their explicit, purposeful introduction of randomization to human experimentation.

ACKNOWLEDGEMENTS
The authors acknowledge the help of Preeti Rout MD, Steven Nosack, Lucinda Klein, and Dzwinka Holian.

Authors’ affiliations
D Neuhauser, M Diaz, Department of Epidemiology and Biostatistics, Case School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA

Correspondence to: M Diaz PhD, Department of Epidemiology and Biostatistics, Case School of Medicine, Case Western Reserve University, 10900 Euclid Ave, Cleveland, OH 44106, USA; mcd8@cwru.edu

REFERENCES


22 Waring JJ. The Chest Service at Bellevue Hospital: a better mouse trap (The first J Burns Amberson Lecture. This whole issue was dedicated to Dr Amberson). Am Rev Tuberc 1956;74:821–9.
Shuffle the deck, flip that coin: randomization comes to medicine

D Neuhauser and M Diaz

*Qual Saf Health Care* 2004 13: 315-316
doi: 10.1136/qshc.2004.011593

Updated information and services can be found at:
http://qualitysafety.bmj.com/content/13/4/315

**References**

This article cites 9 articles, 4 of which you can access for free at:
http://qualitysafety.bmj.com/content/13/4/315#BIBL

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

BMJQS Heroes and martyrs of quality and safety (32)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/