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1 DEFINITIONS of "Experiment"

- (WMS5) "the process by which an observation is made"
- (MRT2, p 18-19) "any act that can be repeated under given conditions"
- (M&M3, p 234) "an observational study observes individuals and measures variables of interest but does not attempt to influence the responses. An experiment, on the other hand, deliberately imposes some treatment on individuals in order to observe their responses"
- (FPPA2**, p 11) "In a controlled experiment (the title of the authors' chapter 1, with the Salk vaccine field trial as their example), the investigators decide who will be in the treatment group and who will be in the control group.
  By contrast in an observational study (the title of the authors' chapter 2*, with studies of the effect of cigarette smoking on humans as their first example) it is the subjects who assign themselves to the different groups: the investigators just watch what happens."

  *Introduced with the quote, from Sir Ronald Fisher "That's not an experiment you have there, that's an experience"
- (OED3, 1944)

  1. The action of trying anything; a test, trial; 2. A procedure adopted in uncertainty whether it will answer the purpose; 3. An action or operation undertaken in order to discover something unknown, to test a hypothesis, or establish or illustrate some known truth.
- (Miettinen, 1985)

  A study in which a determinant is intentionally perturbed for reasons none other than the goals of the study itself.
- See also..
  * Program 12 in Against All Odds Video series.
  * Handouts: Cox, **Freedman, Rothman & Greenland, vanBelle. ...
  * Hill AB (1953) Observation and Experiment. NEJM 248 995-1001

2 "Natural Experiments - example 1"

On the Mode of Communication of Cholera

by John Snow, M.D.

London: John Churchill, New Burlington Street, England, 1855

INTIMATE MIXTURE OF THE WATER SUPPLY OF THE LAMBETH WITH THAT OF THE SOUTHWARK AND VAUXHALL COMPANY

[text taken from `http://www.ph.ucla.edu/epi/snow/snowbook3.html`]

Although the facts shown in the above table afford very strong evidence of the powerful influence which the drinking of water containing the sewage of a town exerts over the spread of cholera, when that disease is present, yet the question does not end here; for the intermixing of the water supply of the Southwark and Vauxhall Company with that of the Lambeth Company, over an extensive part of London, admitted of the subject being sifted in such a way as to yield the most incontrovertible proof on one side or the other. In the sub-districts enumerated in the above table as being supplied by both Companies, the mixing of the supply is of the most intimate kind. The pipes of each Company go down all the streets, and into nearly all the courts and alleys. A few houses are supplied by one Company and a few by the other, according to the decision of the owner or occupier at that time when the Water Companies were in active competition. In many cases a single house has a supply different from that on either side. Each company supplies both rich and poor, both large houses and small; there is no difference either in the condition or occupation of the persons receiving the water of the different Companies. Now it must be evident that, if the diminution of cholera, in the districts

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partly supplied with the improved water, depended on this supply, the houses receiving it would be the houses enjoying the whole benefit of the diminution of the malady, whilst the houses supplied with the water from Battersea Fields would suffer the same mortality as they would if the improved supply did not exist at all. **As there is no difference whatever, either in the houses or the people receiving the supply of the two Water Companies, or in any of the physical conditions with which they are surrounded, it is obvious that no experiment could have been devised which would more thoroughly test the effect of water supply on the progress of cholera than this, which circumstances placed ready made before the observer.**

OPPORTUNITY THUS AFFORDED OF GAINING CONCLUSIVE EVIDENCE OF THE EFFECT OF THE WATER SUPPLY ON THE MORTALITY FROM CHOLERA

The experiment, too, was on the grandest scale. No fewer than three hundred thousand people of both sexes, of every age and occupation, and of every rank and station, from gentlefolks down to the very poor, were divided into two groups without their choice, and, in most cases, without their knowledge; one group being supplied with water containing the sewage of London, and, amongst it, whatever might have come from the cholera patients, the other group having water quite free from such impurity.

To turn this grand experiment to account, all that was required was to learn the supply of water to each individual house where a fatal attack of cholera might occur. I regret that, in the short days at the latter part of last year, I could not spare the time to make the inquiry; and, indeed, I was not fully aware, at that time, of the very intimate mixture of the supply of the two Water Companies, and the consequently important nature of the desired inquiry.

When the cholera returned to London in July of the present year, however, I resolved to spare no exertion which might be necessary to ascertain the exact effect of the water supply on the progress of the epidemic, in the places where all the circumstances were so happily adapted for the inquiry. I was desirous of making the investigation myself, in order that I might have the most satisfactory proof of the truth or fallacy of the doctrine which I had been advocating for five years. I had no reason to doubt the correctness of the conclusions I had drawn from the great number of facts already in my possession, but I felt that the circumstance of the cholera-poison passing down the sewers into a great river, and being distributed through miles of pipes, and yet producing its specific effects, was a fact of so startling a nature, and of so vast importance to the community, that it could not be too rigidly examined, or established on too firm a basis.

I accordingly asked permission at the General Register Office to be supplied with the addresses of persons dying of cholera, in those districts where the supply of the two Companies is intermingled in the manner I have stated above. Some of these addresses were published in the "Weekly Returns," and I was kindly permitted to take a copy of others. I commenced my inquiry about the middle of August with two sub-districts of Lambeth, called Kennington, first part, and Kennington, second part. There were forty-four deaths in these sub-districts down to 12th August, and I found that thirty-eight of the houses in which these deaths occurred were supplied with water by the Southwark and Vauxhall Company, four houses were supplied by the Lambeth Company, and two had pump-wells on the premises and no supply from either of the Companies.

ACCOUNT OF THE INQUIRY FOR OBTAINING THIS EVIDENCE

As soon as I had ascertained these particulars I communicated them to Dr. Farr, who was much struck with the result, and at his suggestion the Registrars of all the south districts of London were requested to make a return of the water supply of the house in which the attack took place, in all cases of death from cholera. This order was to take place after the 26th August, and I resolved to carry my inquiry down to that date, so that the facts might be ascertained for the whole course of the epidemic. I pursued my inquiry over the various other sub-districts of Lambeth, Southwark, and Newington, where the supply of the two Water Companies is intermixed, with a result very similar to that already given, as will be seen further on. In cases where persons had been removed to a workhouse or any other place, after the attack of cholera had commenced, I inquired the water supply of the house where the individuals were living when the attack took place.

The inquiry was necessarily attended with a good deal of trouble. There were very few instances in which I could at once get the information I required. Even when the water-rates are paid by the residents, they can seldom remember the name of the Water Company till they have looked for the receipt. In the case of working people who pay weekly rents, the rates are invariably paid by the landlord or his agent, who often lives at a distance, and the residents know nothing about the matter. It would, indeed, have been almost impossible for me to complete the inquiry, if I had not found that I could distinguish the water of the two companies with perfect certainty by a chemical test. The test I employed was founded on the great difference in the quantity of chloride of sodium contained in the two kinds of water, at the time I made the inquiry. On adding solution of nitrate of silver to a gallon of the water of the Lam-

beth Company, obtained at Thames Ditton, beyond the reach of the sewage of London, only 2.28 grains of chloride of silver were obtained, indicating the presence of 0.95 grains of chloride of sodium in the water. On treating the water of the Southwark and Vauxhall Company in the same manner, 91 grains of chloride of silver were obtained, showing the presence of 37.9 grains of common salt per gallon. Indeed, the difference in appearance on adding nitrate of silver to the two kinds of water was so great, that they could be at once distinguished without any further trouble. Therefore when the resident could not give clear and conclusive evidence about the Water Company, I obtained some of the water in a small phial, and wrote the address on the cover, when I could examine it after coming home. The mere appearance of the water generally afforded a very good indication of its source, especially if it was observed as it came in, before it had entered the water-butt or cistern ; and the time of its coming in also afforded some evidence of the kind of water, after I had ascertained the hours when the turncocks of both Companies visited any street. These points were, however, not relied on, except as corroborating more decisive proof, such as the chemical test, or the Company's receipt for the rates.

A return had been made to Parliament of the entire number of houses supplied with water by each of the Water Companies, but as the number of houses which they supplied in particular districts was not stated, I found that it would be necessary to carry my inquiry into all the districts to which the supply of either Company extends, in order to show the full bearing of the facts brought out in those districts where the supply is intermingled. I inquired myself respecting every death from cholera in the districts to which the supply of the Lambeth Company extends, and I was fortunate enough to obtain the assistance of a medical man, Mr. John Joseph Whiting, L.A.C., to make inquiry in Bermondsey, Rotherhithe, Wandsworth, and certain other districts, which are supplied only by the Southwark and Vauxhall Company. Mr. Whiting took great pains with his part of the inquiry, which was to ascertain whether the houses in which the fatal attacks took place were supplied with the Company's water, or from a pump-well, or some other source.

RESULT OF THE INQUIRY AS REGARDS THE FIRST FOUR WEEKS OF THE EPIDEMIC OF 1854

Mr. Whiting's part of the investigation extended over the first four weeks of the epidemic, from 8th July to 5th August; and as inquiry was made respecting every death from cholera during this part of the epidemic, in all the districts to which the supply of either of the Water Companies extends, it may be well to consider this period first. There were three hundred and thirty-four deaths from cholera in these four weeks, in the districts to which the water supply of the Southwark and Vauxhall and the Lambeth Company extends. Of these it was ascertained, that in two hundred and eighty-six cases the house where the fatal attack of cholera took place was supplied with water by the Southwark and Vauxhall Company, and in only fourteen cases was the house supplied with the Lambeth Company's water; in twenty-two cases the water was obtained by dipping a pail directly into the Thames, in four instances it was obtained from pump-wells, in four instances from ditches, and in four cases the source of supply was not ascertained, owing to the person being taken ill whilst traveling, or from some similar cause. The particulars of all the deaths which were caused by cholera in the first four weeks of the late epidemic, were published by the Registrar-General in the "Weekly Returns of Births and Deaths in London," and I have had the three hundred and thirty-four above enumerated reprinted in an appendix to this edition, as a guarantee that the water supply was inquired into, and to afford any person who wishes it an opportunity of verifying the result. Any one who should make the inquiry must be careful to find the house where the attack took place, for in many streets there are several houses having the same number.

According to a return which was made to Parliament, the Southwark and Vauxhall Company supplied 40,046 houses from January 1st to December 31st, 1853, and the Lambeth Company supplied 26,107 houses during the same period; consequently, as 286 fatal attacks of cholera took place, in the first four weeks of the epidemic, in houses supplied by the former Company, and only 14 in houses supplied by the latter, the proportion of fatal attacks to each 10,000 houses was as follows. Southwark and Vauxhall 71. Lambeth 5. The cholera was therefore fourteen times as fatal at this period, amongst persons having the impure water of the Southwark and Vauxhall Company, as amongst those having the purer water from Thames Ditton.

It is extremely worthy of remark, that whilst only five hundred and sixty-three deaths from cholera occurred in the whole of the metropolis, in the four weeks ending 5th August, more than one half of them took place amongst the customers of the Southwark and Vauxhall Company, and a great portion of the remaining deaths were those of mariners and persons employed amongst the shipping in the Thames, who almost invariably draw their drinking water direct from the river.

It may, indeed, be confidently asserted, that if the Southwark and Vauxhall Water Company had been able to use the same expedition as the Lambeth Company in completing their new works, and obtaining water free from the contents of sewers, the late epidemic of cholera would have been confined in a great measure to persons employed among the shipping, and to poor people who get water by pailsful direct from the Thames or tidal ditches.

The number of houses in London at the time of the last census was 327,391. If

TABLE VII.

The mortality from Cholera in the four weeks ending 5th August.

Sub-Districts.	Population in 1851.	Deaths from Cholera in the four wks. ending 5th August.	Water Supply.				
			Southwark & Vauxhall.	Lambeth.	Pump-wells.	River Thames, ditches, etc.	Unascertained.
St. Saviour, Southwark	19,709	26	24	—	—	2	—
St. Olave, Southwark .	8,015	19	15	—	—	2	2
St. John, Horsleydown	11,360	18	17	—	—	1	—
St. James, Bermondsey	18,899	29	23	—	—	6	—
St. Mary Magdalen .	13,934	20	19	—	—	1	—
Leather Market .	15,295	23	23	—	—	—	—
Rotherhithe . .	17,805	26	17	—	—	9	—
Battersea . . .	10,560	13	10	—	1	2	—
Wandsworth . .	9,611	2	—	—	—	2	—
Putney . . .	5,280	1	—	—	1	—	—
Camberwell . .	17,742	19	19	—	—	—	—
Peckham . . .	19,444	4	4	—	—	—	—
Christchurch, Southwk.	16,022	3	2	1	—	—	—
Kent Road . .	18,126	8	7	1	—	—	—
Borough Road . .	15,862	21	20	1	—	—	—
London Road . .	17,836	9	5	4	—	—	—
Trinity, Newington .	20,922	14	14	—	—	—	—
St. Peter, Walworth .	29,861	20	20	—	—	—	—
St. Mary, Newington .	14,033	5	5	—	—	—	—
Waterloo Road (1st) .	14,088	5	5	—	—	—	—
Waterloo Road (2nd) .	18,348	5	5	—	—	—	—
Lambeth Church (1st)	18,409	5	2	1	—	1	1
Lambeth Church (2nd)	26,784	10	7	2	—	—	1
Kennington (1st) .	24,261	11	9	1	1	—	—
Kennington (2nd) .	18,848	3	3	—	—	—	—
Brixton . . .	14,610	1	—	1	—	—	—
Clapham . . .	16,290	5	4	—	1	—	—
St.George, Camberwell	15,849	9	7	2	—	—	—
Norwood . . .	3,977	—	—	—	—	—	—
Streatham. . .	9,023	—	—	—	—	—	—
Dulwich . . .	1,632	—	—	—	—	—	—
Sydenham . .	4,501	—	—	—	—	—	—
	486,936	334	286	14	4	26	4

Figure 1: From Snow 1855

the houses supplied with water by the Southwark and Vauxhall Company, and the deaths from cholera occurring in these houses, be deducted, we shall have in the remainder of London 287,345 houses, in which 277 deaths from cholera took place in the first four weeks of the epidemic. This is at the rate of nine deaths to each 10,000. But the houses supplied with water by the Lambeth Company only suffered a mortality of five in each 10,000 at this period; it follows, therefore, that these houses, although intimately mixed with those of the Southwark and Vauxhall Company, in which so great a proportional mortality occurred, did not suffer even so much as the rest of London which was not so situated.

3 "Natural Experiments - example 2"

The Dutch Hunger Winter of 1944-1945 [`Google dutch famine natural experiment`] from "Famine, third-trimester pregnancy weight gain, and intrauterine growth: The Dutch famine birth cohort study" Human Biology, Feb 1995 by Stein et al.

The Dutch Hunger Winter of 1944-1945 is a unique episode in human history: a severe famine clearly delineated in place and time and occurring in a society with a well-developed administrative structure and where food supplies had previously been generally adequate (Trienekens 1985). The famine was the result of an embargo on transport of food supplies imposed by the German occupying forces in early October 1944 in reprisal for a wave of partisan activity. Official rations, which by the end of the famine consisted almost exclusively of bread and potatoes, declined rapidly, dropping below 1000 kcal/day by January 1945 and reaching as low as 500 kcal/day by April 1945. Although pregnant women were allocated some additional food rations over those available to nonpregnant women, the extent to which redistribution of these additional rations occurred within families is not known. The famine ceased immediately with the liberation in May 1945, when Allied food supplies became widely available. The severity of the famine and its widespread nature have been fully documented (Stein et al. 1975). Trends in postpartum weight (Stein et al. 1975), weight gain late in pregnancy ...) over the famine period have been previously reported .

*Susser E. et al. Neurodevelopment Disorders after Prenatal Famine. The Story of the Dutch Famine Study. Americal J Epi Vol 146, pp 213-216. 1998.

*LH Lumey et al. . Cohort Profile: the Dutch Hunger Winter Families Study IJE online on June 25, 2007 Int J Epi, doi:10.1093/ije/dym126 `http://ije.oxfordjournals.org/cgi/content/full/dym126v1`