Causality in the Time of Cholera: John Snow and the Process of Scientific Inquiry

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Abstract

John Snow in 1849 proposed the intestinal fecal-oral theory for cholera and provided substantial evidence supporting the theory and particularly the prediction that cholera was water-borne. Snow's analysis fits naturally within a Neyman-Rubin causal framework, and Snow is credited with two tools (randomization as an instrumental variable and difference-in-differences design) widely used in causal analysis today. Nonetheless, although water was widely accepted in the 1850s as a causal factor, Snow's *theory* was not. This seeming puzzle cannot be resolved within the Neyman-Rubin framework and requires a broader conception of abductive scientific inquiry, as advocated by Peirce (and recently Heckman and Singer 2017). The *methodology of scientific research programmes* of Lakatos (1980) provides a concrete framework for such a broader conception of scientific inquiry, and for understanding the competition among theories in the 1850s. A "rational reconstruction" of the case of cholera illustrates the logic of inquiry: alternative theories (rationally) protected against refutation by incorporating water as a causal factor, but Snow's theory was superior (*progressive* in Lakatos's terms) – producing new predictions corroborated by new facts. Besides illustrating how the abductive process of scientific inquiry works with an important history of science example, we hope to encourage quantitative social scientists, especially those who rely on potential outcome frameworks, to see their research in this larger context. Finally, this is part of an effort to support teaching statistical data analysis as part of the broader process of scientific inquiry. [237 words]

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1 Introduction

Cholera is a horrible and often deadly disease. Victims experience diarrhea, vomiting, and rapid dehydration; without treatment the mortality rate is roughly 50 percent. It was a scourge of the 19^{th} century – Tumbe (2020) estimates that between 1817 and 1920 it killed 50 million people in a world of about 1.2 billion – and it visited London in 1831, 1849, 1854, and 1866. Today we know cholera is caused by a bacterium, *Vibrio cholerae*, but in the 19^{th} century the underlying cause was uncertain and discovering it was of the highest priority and represented one of the outstanding achievements of 19^{th}-century science. Debate in England over cholera was robust and usually reasoned. Participants used evidence to develop and refine their ideas, and also to advance their theories within the medical and public sphere. The goal, sometimes stated explicitly, was to use evidence to understand the causes of cholera, to develop theories of the disease that would lead to policies to ameliorate its impact. The evidence was often anecdotal (particularly prior to the 1850s) but there was an understanding that evidence was crucial to understanding the disease, discriminating between competing theories, and developing effective public policies.

John Snow (1813-1858) was a London doctor who in 1849 (Snow, 1849a) proposed the intestinal (fecal-oral) theory.[1] Nonetheless, despite substantial supporting evidence, Snow's theory received only modest acceptance during the 1850s, and the intestinal fecal-oral theory was not generally accepted until the end of the 19^{th} century. The lack of early recognition of Snow's theory – in spite of substantial supporting evidence – has puzzled many authors (including the present authors), as a case of "smart people cling[ing] to an outlandishly incorrect idea despite substantial evidence to the contrary" (Johnson, 2007, 125). The puzzle arises, however, from a too-narrow conception of

[1] Snow and the story of cholera has long exercised a fascination over both the popular imagination and academic inquiry. A very limited sampling of recent books and papers devoted to the topic is Johnson (2007); Freedman (1999, 1991); Hempel (2007); Vinten-Johansen et al. (2003); Vinten-Johansen (2020); McLeod (2000); Rothman (2002).

causal and scientific inquiry. It is resolved by embracing a broader view of scientific inquiry as the dynamic interplay of data and theory, a conception of scientific inquiry that is even more necessary today than it was 170 years ago.

The dominant paradigm today for causal analysis and "identification" of causal effects is a Neyman-Rubin potential outcomes or "treatment-control" approach (Neyman, 1923; Cox, 1958; Rubin, 1974; Holland, 1986). Some "treatment" is hypothesized as causal, for example consumption of contaminated water that causes higher probability of disease and thus higher observed aggregate cholera mortality. Each individual is either treated or not and so there is no way to directly measure the counterfactual (what mortality would be for those drinking contaminated water *if* they were instead to drink clean water) but one can envision the hypothetical potential outcome or counterfactual (everyone drinking clean water). Under certain circumstances and with certain research designs, one can identify and estimate say the average treatment effect, the causal effect of contaminated versus clean water.

Snow's fecal-oral theory seems to fit neatly within the potential outcome (treatment-control) framework. A key prediction, possibly the signature prediction of the theory, was waterborne transmission: contaminated water consumption would be an important (causal) factor for cholera mortality. Alternative theories had no such strong prediction, and prior to the 1849 outbreak water was little discussed as a cause of cholera.[2]

If one can demonstrate that water is causal in a potential outcome framework, it seems to follow that alternative theories are contradicted and Snow's theory supported, and the rational outcome would be to switch to the fecal-oral theory. And indeed, there was strong support in the 1850s for water as causal. Snow (1849a) provided strong evidence that cholera was associated with contaminated water, as did others examining the 1849 epidemic – see Sutherland (1851, 14) and Grainger (1851, 91). Snow (1855) provided substantial additional evidence, and Simon (1856) even stronger evidence.[3]

And yet, in spite of strong evidence for water and even widespread acceptance of water as a causal factor, there was scant acceptance of the fecal-oral *theory*. To make sense of this seeming puzzle we need to move beyond a treatment effects or simple hypothesis-testing framework, beyond the dominant potential outcome paradigm for causal analysis. We must embrace a process of abductive scientific inquiry, akin to that advocated by Charles Sanders Peirce in the early 20^{th} century and more recently by Heckman and Singer (2017), which pushes us to recognize that scientific inquiry is a dynamic back-and-forth between data and theory that is not decided by a single hypothesis or test.

Charles Sanders Peirce was an American philosopher, mathematician, and scientist and the founder of pragmatism. Peirce proposed scientific inquiry as comprising three stages: abduction (generating theories or hypotheses), deduction (deriving predictions from theory), and induction (testing against

[2]Wakley (1831, 281) mentions water as one among a long list of predisposing causes: "poverty, filth, ... habits of intemperance, defective clothing." Parkin (1832) was unusual in proposing water-borne transmission, but did not seem to gain much attention. General Board of Health (1848) seems to be typical: "The chief predisposing causes of every epidemic, and especially of cholera, are damp moisture, filth, animal and vegetable matters in a state of decomposition, and, in general, whatever produces atmospheric impurity."

[3]As discussed more fully below and in Coleman (2020), Snow is credited with the first use of two research designs widely used today for demonstrating causal effects – randomization as an instrumental variable and difference-in-differences. See Greene (2018, 228), and also Deaton (1997); Grootendorst (2007), for randomization, and Angrist and Pischke (2014, 205) and Angrist and Pischke (2008, 227) for differences-in-differences. Arguably, Simon (1856, Table 1) is an even cleaner early example of difference-in-differences.

evidence). Figure 2 shows a schematic for the process. The overall process of scientific inquiry incorporates all three of Peirce's stages.

For a practical framework of the process of abductive scientific inquiry we use Lakatos (1980), with the concepts of *scientific research programmes* and *sophisticated falsification*. Lakatos argues that science is built upon "a developing series of theories" rather than an isolated hypothesis (or conjunction of hypotheses) (Lakatos, 1980, 178). He argues that theories are never decided by a single crucial experiment, contrary to the *naive falsification* of Karl Popper. Existing theories incorporate contrary evidence by developing protective "auxiliary hypotheses";new and existing theories predict new facts which are then either corroborated or contradicted. Replacement of one theory by another is not simple or quick, but "a complicated war of attrition, starting long before, and ending after, the alleged 'crucial experiment' " Lakatos (1980, 133). Importantly, "There is no falsification before the emergence of a better theory" Lakatos (1980, 35).

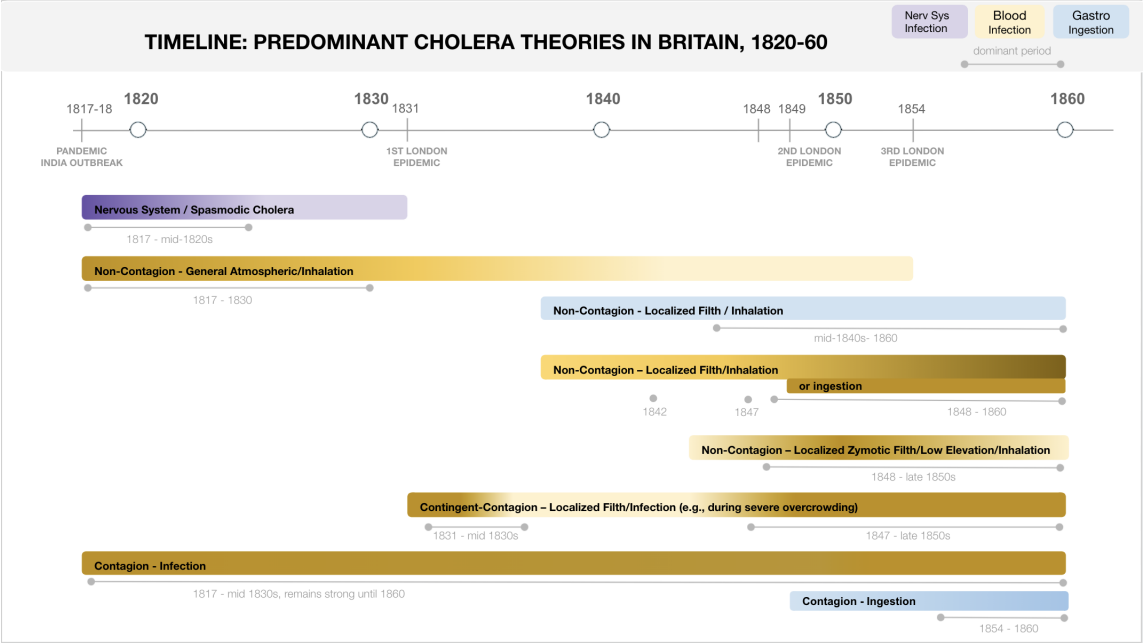
We undertake (following Lakatos, 1980, 52-53) a *rational reconstruction* of the development of John Snow's fecal-oral theory of cholera and its competition with alternative theories during the 1850s. Doing so illustrates the dynamic interplay between theory, data, and testing and makes explicit the logic of scientific inquiry. Such logic is absent (or at best implicit) in much teaching of statistical and computational methods in the social sciences today, thus risking mechanical application of such tools. The story of cholera contradicts popular understandings of science as a one-off experiment or test of theory that decisively demonstrates a causal effect. There was no single, definitive experiment or test that proved cholera was an intestinal disease transmitted by fecal contamination and oral ingestion. Even an *experimentum crucis* such as the South London "Grand Experiment" of 1854 only occurred after several years of analyses at individual and neighborhood scales (including the famous Broad Street pump outbreak) and even then did not on its own decide between the competing theories. "Identification" of the underlying causal theory required, not one crucial experiment, but consideration of a wide range of evidence across alternative models and theories.

The rational reconstruction also explains the slow acceptance of the fecal-oral theory, showing that it was unfortunate but in no way irrational. Falsification and eventual refutation of a theory is not a simple or quick process. We adopt Lakatos's *methodology of scientific research programmes* as a practical framework for scientific inquiry. Comparing across theories in 1855 in Section 5 – undertaking a formalized attempt at falsification – shows that Snow's theory was better-supported by the evidence. Alternatives were not outright refuted because of adjustments that were added to the alternative (airborne) theories that incorporated water - but these were not illogical or unscientific. Nevertheless, even though we can easily judge today that Snow's theory was superior, the comparison in Section 5 also provides a strong argument that Snow's theory was superior to alternatives using evidence available in 1855-56.

Conducting this rational reconstruction of an important history of science case to illustrate how the abductive process of scientific inquiry works is one goal of this article. In this context, we also hope to encourage quantitative social scientists, especially those who rely on potential outcome frameworks, to see their research in this larger context. Finally, this is part of a larger project to support teaching statistical data analysis as part of the broader process of scientific inquiry.

We view Snow (1855) (together with Snow 1856b) as an attempt at falsification, which Section 5 formalizes. We lay out the most important theories of the 1850s, and detail their predictions. We

Figure 1: Timeline for Theories of Cholera in Nineteenth Century England



follow the methodology of Katz and Singer (2007) to assemble a range of evidence that allows one to discriminate among the alternate theories. We argue that the evidence available at the time was sufficient to demonstrate that the fecal-oral theory was correct and alternative airborne theories were not. In Section 6 we show that the fecal-oral theory was eventually decided towards the end of the 19^{th} century, after the bacterium was widely recognized and the disease mechanism could be more clearly delineated.

2 Cholera Theories and Predictions

In this section we summarize the theories of cholera, which are discussed in more detail in Appendix A. For present purposes we can collapse the non-Snow alternative theories into one broad category – inhaled blood disease – which then split into two depending on whether the airborne cholera poison is contagious (generated in and transmitted from one person to another) or non-contagious / contingent-contagious (generally created by localized environmental conditions but sometimes capable of being contagious).

The important second step is making explicit the predictions from *all* theories being considered. This was not done in the 1850s although the predictions are implicit throughout the writings of Snow and contemporaries.

2.1 Cholera Theories in 1849 and After

Figure 1 shows a timeline summarizing cholera theories in the 19^{th} century. In late 1848 Snow, in line with most of his colleagues, believed cholera was an inhaled disease of the the blood.[4] By late 1849, Snow "had been led, contrary to the usual opinion, to consider cholera as being ... a local affection of the mucous membrane of the alimentary canal" (Snow, 1849b, 431). In other words, between late 1848 and late 1849 Snow had developed and adopted a new theory of cholera as a gastrointestinal disease, the theory that we recognize today as correct. From Snow's writings we can trace his thinking and create a "rational reconstruction" of the development of his theory (to use Lakatos's phrase).

The prominent theories in 1848 assumed transmission was via airborne inhalation, but diverged on whether cholera was contagious or non-contagious. The divergence reflected contradictory evidence, with some observations supporting airborne contagion and others supporting non-contagion. In a formal sense, all airborne inhaled theories were refuted by the evidence and had been from the early days.[5] In fact, the hypothesis of contingent contagion had been introduced in the 1830s specifically to adjust the non-contagious theories to (or protect them from) the evidence supporting airborne contagion.

Snow explicitly laid out a theory for cholera, as an intestinal disease transmitted from person-to-person via the inadvertent swallowing of contaminated matter: "That a portion of the ejections or dejections must often be swallowed by healthy persons is, however, a matter of necessity" Snow (1849a, 9). Alternatives were generally not so explicit as to the disease or mechanism of transmission. In Appendix A we attempt, from a wealth of sometimes contradictory contemporary accounts, to construct historically honest but cogent descriptions of alternative theories.

The three important dimensions along which we can categorize theories of the 1850s are: 1) the mode of transmission, either inhaled or ingested; 2) whether contagious or non-contagious; 3) the "seat of the disease" – the nervous system, blood, or the gastrointestinal tract; . The major alternatives to Snow were all inhaled diseases. A major point of debate (prior to but continuing after 1849) was whether cholera was contagious or not, with important implications for predictions. By 1849 it was widely assumed that cholera was a blood disease, but for observations on mortality the distinction between blood and nervous system disease is not especially relevant – airborne and contagion were the important characteristics.

There are important distinctions – for example between general atmospheric non-contagious and localized non-contagious – but these do not have any large impact on the predictions from the alternate theories for the epidemiological data on observed mortality.

[4] We can sse this in Snow (1848, 507-508), where he discusses treatments, presuming that cholera affects the lungs, "in some points resembling [asphyxia], as far as the internal congestion is concerned."

[5] Blane and Corbyn (1821) cited evidence on both sides: For example pro-contagious was an episode from Mauritius where cholera seemed to be imported by the frigate Topaz from Cylon (Blane and Corbyn, 1821, 148-150, 152-153); anti-contagious was a case of three Sepoys in Seroor hospital who escaped disease despite being in close proximity to patients (Blane and Corbyn, 1821, 143)

2.2 Predictions

Snow's core theory posited cholera as a disease of the intestine, transmitted by some unknown material that passed out of one individual (vomit or more commonly diarrhea) and was then inadvertently ingested by others. This core theory or hypothesis implied three modes of communication or transmission: (1) person-to-person ordinary or normal transmission; (2) neighborhood transmission when a local water (or food) source becomes contaminated; and (3) municipal transmission when a municipal water source becomes contaminated. These predict what we should observe about patterns of mortality.

Fecal-Oral Predictions

- **Person-to-Person** or **Normal** Transmission: People in the same room and sharing air would tend to get cholera unless they are in close physical contact or share food and drink but not otherwise (for example, doctors attending patients would tend not to become ill); Once a case of cholera occurs in a house or neighborhood, it will tend to transmit to others in close physical contact; Cholera "may be conveyed to a distance, and into quarters having apparently no communication with the sick" when "the patient, or those waiting on him, are occupied in the preparation or vending of provisions" Snow (1849a, 10).
- **Neighborhood** Transmission: Explosive growth in a local area when a localized source (say a pump-well) becomes contaminated. Cases will rise very quickly, but tail off quickly.
- **Municipal** Transmission: Widespread cholera in a city or area when a common water-source such as a river or a water company is contaminated. Large differential in mortality rate at the beginning of the outbreak, diminished differential as cholera spreads more widely through normal transmission.

The core of the airborne theories predicted that cholera would be transmitted via air. Auxiliary hypotheses stated that local or environmental factors would cause or amplify cholera disease, for example local dampness or filth generating or amplifying the cholera poison. The split between contagious and non-contagious could also by treated as an auxiliary hypothesis.

Airborne Predictions

- **Person-to-Person** Transmission:
  - **Non-Contagious** & **Contingent Contagious**: No – People in the same room will not necessarily become sick. In the 1830s, an auxiliary hypothesis of *Contingent Contagion* was introduced to account for contrary observations, that cholera person-to-person airborne contagion was sometimes observed, sometimes not.
  - **Contagious**: Yes – People in the same room will likely become sick.
- **Transmitted via Air**: People sharing the same air should suffer the same mortality, those not sharing the same air should experience different mortality.

- **Factors Increasing Mortality**: Predisposing causes and susceptibilities increase cholera mortality, and these factors will be associated with higher mortality. The list is extensive and includes: decomposing vegetation, soil contamination, overcrowding, dampness, filth, poor ventilation, proximity to graveyards, bad water, bad sanitation, poverty, unhealthy & moist living conditions. (Predisposing causes may generate or amplify the lethality of the cholera poison, and susceptibilities increase susceptibility to cholera illness.)
- **Water** (post-1849): Added as an auxiliary hypothesis – Water as a, possibly the most important, predisposing cause. Additionally, the airborne cholera poison may dissolve in water and be ingested (thus adding ingestion and water as a mode of transmission).

Appendix B (Table 3) lays out the detailed predictions that correspond to the evidence and mortality observations available at the time.

3 The Abductive Process of Scientific Inquiry: Snow's Cholera Theory 1849-66

The limited reception of Snow's theory in the 1850s presents something of a puzzle if one starts (as did the current authors, see Coleman (2018)) from a simple treatment-control approach to testing and discriminating between theories. Theories prior to 1849 did not consider water an important cause of cholera. Snow (1849a) proposed the fecal-oral theory, whose signature prediction was waterborne transmission. Snow and others (see Grainger 1851, 14; Sutherland 1851, 91) provided substantial evidence that water was an important, possibly the most important factor, in mortality. By 1852 water was widely (although not universally) acknowledged as at least a contributing and sometimes a major cause of cholera.[6] Nonetheless, Snow's fecal-oral theory saw scant acceptance.

3.1 Theory-Data Interplay and Falsification of Research Programmes

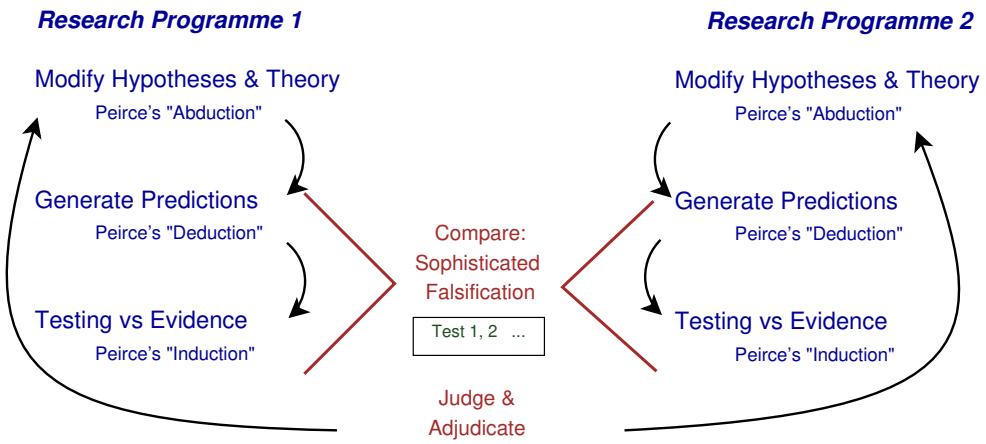
The puzzle of strong empirical support for Snow's theory but scant acceptance is resolved by recognizing that scientific inquiry is an on-going interplay between data and theory, with theories modified in response to new evidence, and new facts in turn predicted by theory. We use a framework that combines Peirce's idea for the stages of scientific inquiry together with Lakatos's methodology of *scientific research programmes*. Figure 2 provides an schematic overview.

For the abductive process of scientific inquiry we use Peirce's three stages of inquiry: abduction[7] (generating and modifying theory and hypotheses); deduction (deducing or generating predictions from the theory); induction (testing the theory and hypotheses against evidence) – see Misak (2004,

[6] There is a good quote from about 1851 discussing the 2 or 3 contemporary theories, but I am not sure who and cannot find it at present - TSC

[7] We face a challenge regarding terminology. Heckman and Singer, along with some others, use the term *abduction* more broadly than did Peirce, for the entire dynamic process of scientific inquiry, where "the analyst ... engage[s] models and data in an iterative dynamic process, using multiple models and sources of data in a back and forth where both models and data are augmented as learning evolves" (Heckman and Singer, 2017, unpublished abstract). Peirce's use of abduction was limited to the first stage of the on-going and dynamic process of inquiry, with abduction being "the process of forming an explanatory hypothesis" (Peirce 1960, vol 5, para 171, 1903, quoted in Misak 2004, 93). We have settled on the term "abductive inquiry" to emphasize the dynamic interplay of data and theory.

Figure 2: Schematic for The Abductive Process of Scientific Inquiry



We combine Peirce's three stages of scientific inquiry with Lakatos's *scientific research programmes*. Scientific inquiry involves a dynamic back-and-forth of data and theory, from theory generation to predictions to comparing against data, and back again to theory generation and modification. Scientists work with research programmes, which are collections of theories & hypotheses. Sophisticated falsification is the criterion to appraise and compare across programmes, and may involve testing various hypotheses and predictions (*Test 1, 2, ...*) within a Neyman-Rubin potential outcome framework.

93-94). Any sharp distinction between the three stages is something of an exaggeration, but captures important aspects of the process.

In this context, we need to consider the *working unit* for inquiry. Rather than a single hypothesis or theory, we use Lakatos's *research programme*, a structured set of theories and hypotheses: "my unit of appraisal is not an isolated hypothesis (or a conjunction of hypotheses): a research programme ... consists of a developing series of theories [with] ... a structure. It has a tenacious *hard core* ... a *heuristic*, [a set of rules for analyzing the theory and data] ... [and] a vast belt of auxiliary hypotheses [that translate from the core to the world of observations" Lakatos (1980, 178).

There is an important component of the inquiry process that Peirce does not address, and that is the comparison across and adjudication between theories and programmes. Abductive scientific inquiry is an undertaking of a scientific community rather than an individual process. The core theory is not subject to refutation or contradiction, until and unless the complete programme is replaced by another – to which we turn shortly when we discuss *sophisticated falsification* and the comparison across programmes. The belt of auxiliary hypotheses, in contrast, may be refuted, altered, and added to. This belt of auxiliary hypotheses and theories provides the translation from the core to the world of observed phenomena, while also protecting the core from refutation.

A research programme, consisting of a core theory and a belt of auxiliary (protective) hypotheses, provides a realistic framework for how science and scientific inquiry actually works. We know, according to the Duhem-Quine thesis (Quine 1953, chapter 11; Lakatos 1980, 93-101), that a contradictory observation can be accommodated by an adjustment to the theory. We know from experience that science is practiced in this way, and we will see an example with airborne cholera theories accommodating to water as a cause. The adjustment of auxiliary hypotheses provides the way to incorporate such adjustment into the process of scientific inquiry, providing a more realistic framework for understanding scientific inquiry.

Comparison across programmes shows us how and why we should replace one programme (set of theories) with another. Our initial thought might be to a simple comparison of a theory's predictions versus observations or facts. If the predictions pass, the theory is (provisionally) accepted, if not then the theory is summarily rejected. This is what Lakatos calls dogmatic or naive falsification.[8] But the adjustment of theories to accommodate conflicting facts raises substantial problems for a naive approach to falsification (including Popper's). Lakatos emphasizes that "Popper's great negative crucial experiments disappear" Lakatos (1980, 111) and that, "Contrary to naive falsification, *no experiment, experimental report, observation statement or well-corroborated low-level falsifying hypothesis alone can lead to falsification*" Lakatos (1980, 35).

Separating between *theories* and *programmes* – rejecting one theory (or collection of hypotheses) and replacing by an alternative – requires more than testing for a single hypothesis or demonstrating a single causal effect within the potential outcome framework. The case of water and cholera shows how the auxiliary belt of hypotheses may be adjusted to accommodate recalcitrant facts and "protect" the core theory from rejection. A more comprehensive approach is necessary, one that compares across a range of predictions and evidence.

Lakatos (1980, 179) provides the criterion for replacing one research programme (collection of core and auxiliary theories) by another:

> Having specified that the unit of mature science is a research programme, I now lay down rules for appraising programmes. A research programme is either progressive or degenerating. It is *theoretically progressive* if each modification leads to new unexpected predictions and it is *empirically progressive* if at least some of these novel predictions are corroborated. It is always easy for a scientist to deal with a given anomaly by making suitable adjustments to his programme (e.g. by adding a new epicycle). Such manoeuvres are *ad hoc*, and the programme is *degenerating*, unless they not only explain the given facts they were intended to explain but also predict some new fact as well.
>
> ...
>
> One research programme *supersedes* another if it has excess truth content over its rival, in the sense that it predicts progressively all that its rival predicts and some more besides.

Research programmes are thus fundamentally dynamic, being a series of theories and hypotheses that progress (or degenerate) over time. A progressive research programme provides a good working definition of effective scientific inquiry, what Heckman and Singer (2017) call the "abductive approach". A degenerating programme does not produce excess content or predict new facts; it is not effective scientific inquiry. The distinction between progressive and degenerating research programmes resolves the problem (at least in the long run) for how to choose between theories or research programmes: (1) scientific progress requires discarding degenerating programmes, and (2) adjustments to auxiliary hypotheses that protect a theory "are *ad hoc*, and the programme is degenerating, unless they not only explain the given facts they were intended to explain but also predict some new fact as well" (Lakatos, 1980, 179).

[8] See Lakatos (1980, Section 1.2) and also page 93 ff for more detail on various flavors of falsification.

Lakatos (1980, 32) proposes *sophisticated falsification* as the specific criterion for separating between theories:[9]

> a scientific theory T is falsified if and only if another theory T' has been proposed with the following characteristics: (1) T' has excess empirical content over T: that is, it predicts novel facts, that is, facts improbable in the light of, or even forbidden by, T; (2) T' explains the previous success of T, that is, all the unrefuted content of T is included (within the limits of observational error) in the content of T'; and (3) some of the excess content of T' is corroborated.

Note that an important implication (maybe not obvious from the way that Lakatos stated the criterion) is the importance of *both* corroborations of the new T' (3) *and* contradictions of the original T (1). In other words, sophisticated falsification requires contradiction of the existing (or parts of the existing) theory, which looks something like a form of naive or even dogmatic falsification. But with two important additions. First, additional empirical content that is corroborated is also required, and second "falsification" is always provisional and cannot immediately or automatically lead to rejection of the original theory T.

This last condition, that adjustments must predict new facts (increase the empirical content of the theory) manages the problem that any theory may be adjusted to accommodate contradictory evidence (the Duhem-Quine thesis). Lakatos's framework of research programmes recognizes and embraces the fact that theories – particularly the protective belt of auxiliary hypotheses – may and indeed *should* be adjusted to incorporate and subsume "anamolies" and new evidence. The challenge is to distinguish between *ad hoc* adjustments that adjust only to accommodate inconvenient observations and should be disallowed, versus "legitimate" adjustments that refine and enhance the overall programme. Rather than provide *a priori* conditions to distinguish between disallowed versus allowed adjustments, here the focus is on the result and whether an adjustment improves the theory by predicting new facts (increasing empirical content). Failure to predict new facts does not immediately disqualify a theory or programme, but does separate between progressive programmes that increase scientific knowledge, versus degenerating programmes that, ultimately, do not.

Below we will consider the incorporation of water as a predisposing cause (after 1849) as an adjustment of airborne theories. We will see that such an adjustment fails this condition. Specifically, the adjusted theories predict that water will be a cause (thus bringing the theories into accord with observation), but also predict that other factors (crowding, poverty, etc.) will be causal. The evidence is that, yes, water is causal for cholera mortality (in a large municipal outbreak) but other factors are not, contradicting the prediction. We may consider this as either a failure to predict a new fact, or a prediction that is contradicted by evidence.

The development and progress of Snow's intestinal fecal-oral theory from 1849 to 1866 demonstrates the abductive process of inquiry, and particularly the use of auxiliary hypotheses in protecting the airborne theories. In the next section we provide an overview of the overall process. In Section 5 we focus specifically on the comprehensive comparison (process of sophisticated falsification) undertaken

[9]Lakatos distinguishes between three forms of falsification: *dogmatic*, *naive* or methodological, and *sophisticated* – see Lakatos (1980, 12-47). Both dogmatic and naive falsification are open to the Duhem-Quine critique (Quine 1953, chapter 11; Lakatos 1980, 93-101). Lakatos discusses rules for the falsification of research programmes (as opposed to theories within a programme) on page 69 and page 179, quoted above.

in the 1855 2^{nd} edition of *On the mode of communication of cholera*. In Section 4 we drill down to examine one piece of evidence in the 1855 falsification effort, illustrating the application of the potential outcome (treatment-control) framework for demonstrating the causal effect of water.

3.2 Snow's Cholera Theory 1849-1866 and Scientific Inquiry

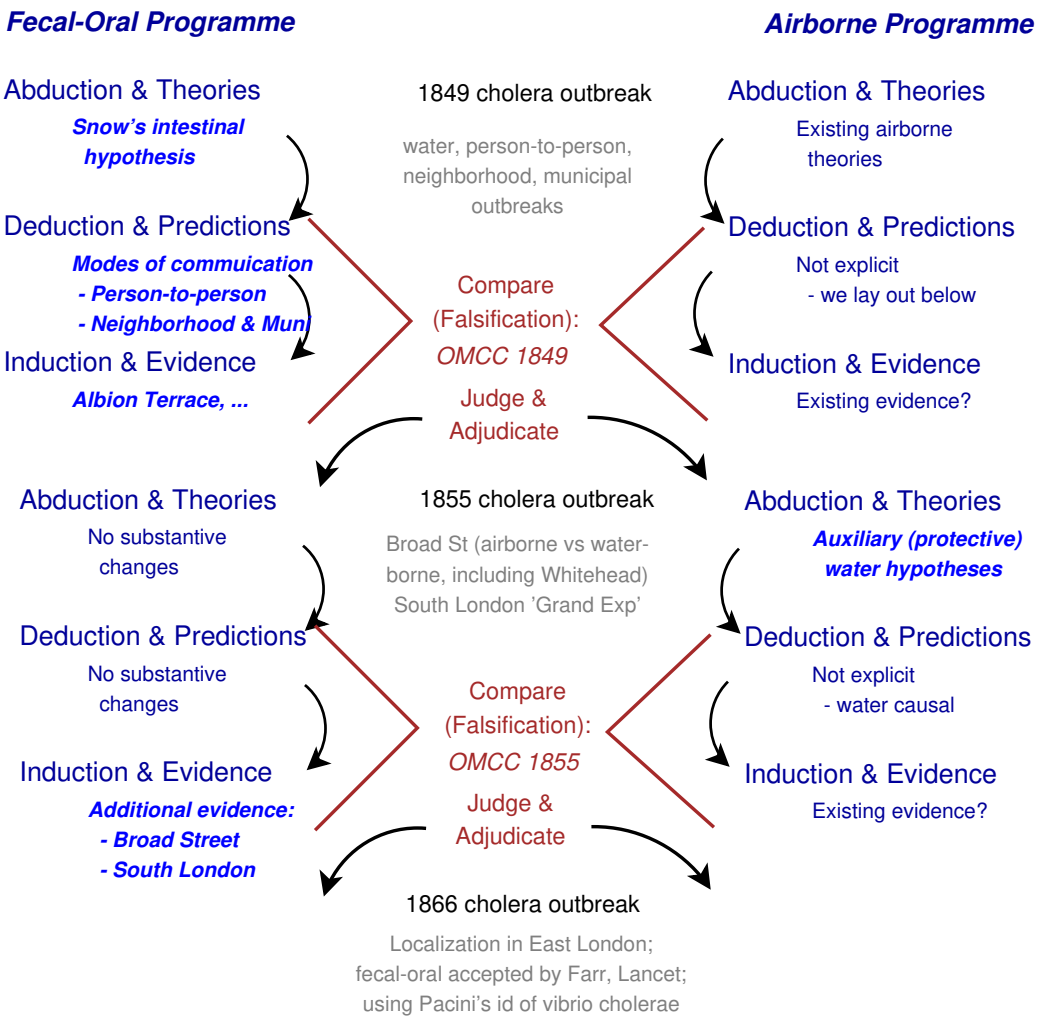
Some time in 1849 Snow seems to have made a mental leap, an abductive leap, to recognize that airborne transmission was not necessary: "There is, however, no reason to conclude, *a priori*, that this [contagion via inhalation] must be the mode of communication of cholera" Snow (1849a, 6). Having broken from inhalation, and calling upon both his medical experience in treating patients and widespread observations of the symptoms of cholera ("it has always appeared, from what the writer could observe, that in cholera the alimentary canal is first affected" Snow 1849a, 7), Snow hypothesized that cholera was a disease of the intestines (the alimentary canal) and transmitted person-to-person via ingesting contaminated fecal matter because, unintentionally, "a portion of the ejections or dejections [from a patient with cholera] must often be swallowed by healthy persons" (Snow, 1849a, 9). Snow proceeded to develop a variety of implications or predictions for observed mortality and transmission of cholera, as discussed in Section 2 and Appendixes A and B.

Figure 3 provides a schematic of the overall scientific inquiry process. In 1849 Snow made the abductive leap to arrive at the intestinal oral-fecal hypothesis, represented schematically under "Abduction & Theories" in the upper left. Snow combined the fact of long-standing evidence contradictory to inhalation (evidence refuting those theories), observations and evidence concerning cholera, and intuition and knowledge of medicine to develop his theory. But this was only the first step in an on-going process of inquiry that went back-and-forth between data and theory. To supplant existing and widely-accepted theories, more was required than a good idea and some scattered evidence, as Snow himself recognized: "The opinions now made known [in late 1849] have been entertained by the author since the latter part of last year ... but he [the author, Snow] hesitated to publish them, thinking the evidence in their favour of so scattered and general a nature as not to be likely to make a ready and easy impression" Snow (1849a, 12).

Snow had to move to the next stages of the process, deduction of predictions and induction versus evidence. The was the first attempt at falsification of alternatives, the attempt to use evidence to refute alternative theories while showing that the evidence supported his theory – corroborating his predictions and showing that his theory had "higher corroborated content". Snow had to collect and examine evidence, both existing and new. He had to marshal facts, logic, and explanation to make a case for his theory versus alternatives. We know that Snow found additional evidence in late 1849: "Within the last few days, however, some occurrences have come within his [the author, Snow's] knowledge which seem to offer more direct proof [of the theory], and have induced him [Snow] to take the present course [publishing]" (Snow, 1849a, 12).

The new evidence Snow discovered were the neighborhood outbreaks in Thomas Street (Horsley-down), and Albion Terrace (Wandsworth Road). Snow spent roughly 10 pages providing a detailed description of the two sets of buildings and specifically the way in which faulty plumbing allowed sewage-contaminated water to be shared among the residences. Snow was undertaking the falsification or comparison part of the inquiry process, comparing predictions against evidence to sort

Figure 3: Schematic of Abductive Scientific Process for Cholera 1849-1855



The "Fecal-Oral" column represents the development and progression of the fecal-oral theory, from Snow's original abductive leap in 1849 (upper left), the publication of *On the mode of communication of cholera* in 1849, the outbreak in 1854, and the publication of the 2^{nd} edition of *OMCC* in 1855. The "Airborne" column represents the progression of the airborne theories. Predictions were not explicitly stated and comparison versus evidence was implicit; we try to reconstruct predictions and comparisons in the Appendix and Section 5. In each column we have highlighted new hypotheses and evidence by ***bold and italic***

among alternative theories. For now we only outline the falsification effort, returning in Section 5 to use Snow (1855) and related publications to examine it in detail. Here we highlight that Snow (1849a) 1) developed predictions (deduction) – particularly how cholera would be transmitted via hand-to-hand contact and via contaminated water; 2) provided evidence (induction) – particularly on the importance of water in cholera transmission and mortality; 3) compared predictions versus evidence for his theory and (rather cursorily) for alternatives (falsification).

For present purposes the important result is that Snow provided strong evidence that sewage-contaminated water was an important factor in cholera mortality. Contemporaries acknowledged the importance of water, due to Snow's work and also evidence from others. William Farr of the General Registrar Office concluded that "Dr. Snow is unfortunately able to show that this excremental distribution ... is possible to a very considerable extent.... The experience of ... many of our own towns lends some countenance to Dr. Snow's theory" (General Register Office, 1852, lxxviii). During and shortly after the 1849 epidemic, local officials throughout England and Wales submitted reports to London that detailed similar associations between water quality and cholera mortality. In its final report, the General Board of Health noted that "much additional evidence has been elicited proving the influence of the use of impure water in predisposing to the disease" (General Board of Health, 1850, 50). John Sutherland, a supervising inspector, noted that "in nearly every city and town affected, ... a number of most severe and fatal outbursts of cholera were referable to no other cause except the state of the water supply" (Sutherland, 1851, 14). Richard Grainger, who summarized reports received from local inspectors in the London metropolis after the 1848-49 epidemic, cited "unquestionable evidence" of water "contaminated in various ways by decomposed organic and noxious matter" and then "taken up ... by the blood vessels of the alimentary canal ... as noxious aerial agents do by way of the respiratory apparatus" (Grainger, 1851, 91)

Remember that prior to Snow cholera was assumed to be airborne and propagated by inhalation. And yet by 1851 impure water – broadly defined as water containing decomposing organic matter – was widely recognized as at least a contributing cause for cholera; for some, water was elevated to "perhaps the most fatal of all" predisposing causes (Sutherland, 1851, 14). It is natural for a modern reader to assume that evidence for water as a causal factor would serve to refute airborne theories and confirm the ingested fecal-oral theory, and furthermore that falsification of inhalation would be widely recognized. This was not the case and instead water was incorporated into the existing theories, making them in effect hybrid theories of inhalation with water as a secondary mechanism. Even though this was an incorrect and truly unfortunate scientific response, it was a reasonable response.

The research programme framework tells us that any prediction is a combination of core and protective hypotheses. Evidence refuting a prediction refutes the joint hypotheses, not the core theories alone. It is perfectly appropriate to maintain the core and reject (and then adjust) the auxiliary hypotheses. A single anomaly, even an accumulation of contrary evidence, does not of necessity refute the core theories.

For pre-1849 inhalation theories the core would be that cholera is a disease of the blood with individuals inhaling a choleric poison which entered through the lungs, into the blood, and thus caused disease (by some unknown mechanism). The protective belt of hypotheses would detail how the choleric poison was produced and transmitted and thus the observed patterns of disease and

mortality. One hypothesis would be that cholera is contagious with the choleric poison created in an individual and passed person-to-person via inhalation. If this hypothesis were contradicted by evidence, this would not (of necessity) contradict the core of an inhaled blood disease, but simply require adjustment of the auxiliary contagion hypothesis – adjusting by hypothesizing that cholera is non-contagious.

Now we come to evidence that water is strongly associated with cholera mortality. Rather than taking such evidence as refuting the underlying core of an inhaled blood disease, such observations could be interpreted as positive evidence that the cholera poison was produced or transmitted through water and that a source of the cholera poison had been previously overlooked. Possibly water and general dampness contributes to organic decomposition that amplifies production of airborne cholera poison that is then inhaled, thereby producing a strong (and causal) association between contaminated water and cholera mortality. Contemporary writers explicitly proposed such mechanisms, with Grainger (1851, 34) as one example:

> when the numerous sewers of a city reach the stream [rivers], ... [this] presents a physical condition favourable to its subsequent escape into the atmosphere in the form of mephetic gases

Another mechanism, possibly acting in parallel, is that the airborne cholera poison can be dissolved into water, ingested, and then make its way to the bloodstream. Exactly this mechanism was laid out by Grainger (1851, 91):

> water ... is contaminated in various ways by decomposed organic and other noxious matter; as by the absorption of deleterious gases ... these injurious substances get into the blood ... the most poisonous being soaked up by the blood-vessels of the alimentary canal as readily as the most harmless. Thus a second great inlet is established by which injurious substances in a liquid form as certainly find their way into the circulating blood, as noxious aerial agents do by the way of the respiratory apparatus.

Today we know these proposals are mistaken but they were not contrary to either medical knowledge or scientific method – they are *not* examples of smart people clinging to outlandishly incorrect ideas. They are examples of an unfortunate but still rational response to contrary evidence or anomalies, adjusting the protective belt of hypotheses that translate from the core theories (inhaled blood disease) to the world of observations (cholera mortality). Schematically, the response is shown in the middle of the right column of Figure 3 – auxiliary water hypotheses are introduced. Yes, strong evidence of the causal effect of water supports Snow's fecal-oral theory. And yes, the evidence is contrary to a simple (non-water) version of inhaled blood diseases. But instead of throwing out the existing theory, new auxiliary hypotheses were introduced concerning the role of water in the production and transmission of the cholera poison, and thus the previously contradictory evidence incorporated into the inhaled blood-disease theory (or research programme).

These new auxiliary hypotheses were not unscientific – they produced testable predictions and were thus scientific in Popper's terms. Nonetheless they were in Lakatos's terms signs of a degenerative theory: "It is always easy for a scientist to deal with a given anomaly by making suitable adjustments

to his programme (e.g. by adding a new [auxiliary hypothesis]). Such manoeuvres are *ad hoc*, and the programme is *degenerating*, unless they not only explain the given facts they were intended to explain but also predict some new fact as well" (Lakatos, 1980, 179). Today we recognize how wrong they were, and in the next section we show that there was sufficient contemporary evidence to argue against both the auxiliary hypotheses and the core inhaled blood disease theories. These auxiliary hypotheses remain as examples of the process of actual scientific method.

Simplifying somewhat, the outcome of the Snow's scientific inquiry and abductive efforts from the 1849 outbreak, culminating in the publication of the 1849 first edition of *On the mode of communication of cholera*, was a productive stand-off: (1) the causal importance of water was widely (although not universally) recognized; (2) water as a causal factor was incorporated into inhaled blood disease theories through expansion of the protective belt of auxiliary hypotheses; (3) water was removed as a crucial distinguishing factor between theories, with inhaled blood diseases now "protected" against evidence of water as a causal factor; and most importantly (4) the fecal-oral theory was recognized although not widely adopted. In the following years both Snow and skeptics were impelled to collect new evidence, re-examine existing evidence, and refine predictions to compare against that evidence.

Cholera struck again in 1854, bringing new hardship but providing substantial new evidence on cholera. The Broad Street outbreak in Soho in early September 1854 is probably the most widely-known episode in the history of epidemiology. The case of South London, which closely approximated a randomized trial with treatment by clean and contaminated water, provided quantitative evidence from a population of over 450,000. Snow published the 2^{nd} edition of *OMCC* in 1855 (Snow, 1855), and also papers in learned journals (e.g. Snow, 1856b) in a renewed attempt at falsification in Section 5, which we discuss in Section 5. The fecal-oral theory gained marginally wider acceptance but was not generally accepted.

In 1866 cholera arrived in London for the fourth (and final) time. In the years since 1855 (and Snow's death at the age of 45) the fecal-oral theory had gained wider although not universal acceptance. Reports to the Privy Council, to Parliament, and by the *Lancet* all recognized the fecal-oral theory, and Filippo Pacini's identification of the "germs of vibrions" (Farr, 1868, xv), as the correct theory for the cause of cholera.

4 Potential Outcome & Testing for Specific Causal Effect: Causal Water 1850s

After outlining and illustrating the overall process of scientific inquiry, we now zoom into one aspect of this process – the testing of a single hypothesis within the potential outcome framework. Figure 2 shows that such hypothesis tests (1, 2, ...) form one component of the larger abductive process of scientific inquiry – crucial but only a component. Single hypothesis testing is the most commonly applied statistical framework in causal inference research and the purpose of this section is to show that, while single hypothesis tests are crucial, they cannot *on their own* differentiate between (refute) research programmes. We first outline the potential outcome framework, then illustrates its application for testing the causal effect of water in the 1850s, showing how the demonstration of

"causal water" did not differentiate between research programmes – all theories had incorporated "causal water".

4.1 Potential Outcome Framework

Testing for specific causal effects within a Neyman-Rubin potential outcome framework (Neyman, 1923; Cox, 1958; Rubin, 1974; Holland, 1986) forms the central focus for causal analysis in social, behavioral, and medical sciences. The approach has been and continues to be extremely fruitful. It is simple but powerful, providing a conceptual and statistical framework for separating correlation from causation, a framework for the empirical evaluation of causal policy interventions and treatments. The basic question for any treatment, say consuming clean water in the case of cholera, is whether the outcome (mortality) is different when the treatment is applied (clean water) versus when it is not (contaminated water). This is asking a hypothetical or counterfactual question – would an individual's chance of dying from cholera be lower when drinking clean water? This counterfactual is the important question but impossible to measure empirically, because the individual drinks either clean water (treated) or contaminated (control). One cannot measure the same person both treated and not.

The idea is simple, to explicitly introduce the counterfactual world (potential outcome) where the individual *does* consume clean water and we *do* observe the mortality outcome, contrary to the real world:

$$mortality\,rate = Y = \begin{cases} Y_1\,if\,treated\,(clean) & counter\text{-}factual \\ Y_0\,if\,control\,(contaminated) & observed \end{cases}$$

We cannot measure that counterfactual and thus the effect of treatment for any individual, but we can hope to measure some average treatment effect across a population: $ate = E\left[Y_1 - Y_0\right]$. The potential outcome approach focuses our attention on the statistics and mechanics of correctly estimating the effect of treatment (most basically an average treatment effect). The primary challenge is confounding by observable or unobservable factors – spurious association (correlation). The goal is to control for (eliminate the effect of) those confounding factors.

Tools for controlling for confounders are available. Regression and matching on observables control for observable characteristics. The real challenge is unobservable factors. Instrumental variables, of which randomization is the most intuitive and commonly used, controls for unobservable confounders. Experimental design, such as difference-in-differences (DiD), provide another set of tools.

4.2 Single Tests of 'Causal Water' in 1855

Many components of Snow's cholera analysis fall squarely within this framework, as illustrated in this section. Snow and his contemporaries did not have the statistical tools to conclusively demonstrate that water has a causal effect. They nonetheless had an understanding of many of the issues, and they did provide strong evidence to support the claim that water had a causal effect on cholera mortality.

Snow's analysis of the large (400,000+) population in South London (Snow, 1855) exploited two research designs which are in widespread use today – randomization as an instrumental variable and difference-in-differences (DiD). First, for randomization, Snow compared mortality for customers of two water-supply companies, one of which supplied contaminated water (the Southwark & Vauxhall Company or S&V) and the other clean water (the Lambeth Company). Snow argued, plausibly, that the choice of water company (and thus treatment with contaminated versus clean water) was effectively random, and that customers were well-mixed on all characteristics (such as location, age, sex, income, housing). These circumstances allowed comparison of those treated with contaminated versus dirty water in a natural experiment (an *experimentum crucis* following Farr 1853, 401) that well-approximated a randomized control trial. Snow's comparison of the mixed South London population in Snow (1855, Table IX) is cited as the first use of randomization as an instrumental variable – see (Greene, 2018, 228), which also quotes (Deaton, 1997; Grootendorst, 2007); see also (Deaton, 2013, 95-96).

The second, nascent DiD analysis (Snow, 1855, 89), exploited the fact that the Lambeth company, which supplied clean water in 1854, had supplied contaminated water in the 1849 outbreak. By comparing in 1849 (when all customer were exposed to contaminated water) subdistricts (regions) supplied jointly by the two companies versus subdistricts supplied only by S&V, Snow could difference out subdistrict or regional effects. Comparing those same subdistricts in 1854 (when jointly-supplied subdistricts had some customers with clean water) allowed comparison of the water effect and controlling for subdistrict (regional) effects. The result was "a considerable diminution of mortality in the sub-districts partly supplied by the Lambeth Company" (Snow, 1855, 89). This is cited as the first use of difference-in-differences; see (Angrist and Pischke, 2014, 205), (Angrist and Pischke, 2008, 227).

In fact, both of Snow's analyses suffer from flaws. The issue with the randomization, recognized at the time by, for example, Parkes (1855, 461), was that Snow combined disparate subdistricts (regions). Lacking detailed population data by supplier, Snow was only able to compare at the *aggregate* or regional level, and not the subdistrict level where customers were well- (quasi-randomly) mixed. For the DiD, the across-subdistrict variation in mortality rates is high enough that the observed treatment effect observed in the raw DiD is not statistically significant (see Coleman, 2020). Neither of these flaws is fatal, however. For the randomization, there was evidence in 1855 (from the DiD) that subdistricts did not differ greatly in 1849 when all customers were supplied with contaminated water, and so combining subdistricts would be unlikely to cause problems with randomization. For the DiD, Snow recognized that the treatment effect was stronger for subdistricts with more Lambeth customers[10] and this effect is statistically significant. Re-analysis using modern statistical tools (in Coleman, 2020) confirms that these issues are not significant, and that there is considerable evidence for water as a causal factor in cholera mortality.

There was other, arguably stronger, evidence provided in the 1850s which showed the causal effect of water; we highlight two instances. Sutherland (1851, 15-16) reports an outbreak in Hope Street, Manchester, in 1849. Ninety houses were on the street, 30 using water from a particular pump-well and 60 not. Twenty-five persons died, all in houses drinking from the pump and none from houses

[10]"In certain sub-districts, where I know that the supply of the Lambeth Water Company is more general than elsewhere, as Christchurch, London Road, Waterloo Road 1st, and Lambeth Church 1st, the decrease of mortality in 1854 as compared with 1849 is greatest" Snow (1855, 89).

with other water sources. People were well-mixed with regard to location, and presumably with regards to other characteristics – mixing (quasi-randomization) almost as good as Snow's but here in a small and concentrated locale. In the second instance, Simon (1856) discussed at some length the same 1854 South London outbreak and population that Snow analyzed, but with the benefit of population-by-supplier detailed by subdistricts (which was not available when Snow published in 1855). Simon concludes, justifiably, that "The above conclusions [that higher mortality was caused by drinking contaminated water] rest on so large a basis of facts, that I venture to believe they will be accepted as the final solution of any existing uncertainty as to the dangerousness of purefiable drinking-water during visitations of epidemic cholera" Simon (1856, 9). Among other evidence, in Table I Simon provides a difference-in-differences analysis recognizable to a modern reader, one that arguably serves as a better case of first use than Snow's.[11]

The evidence available in 1855 strongly supported water as a causal factor in cholera mortality, even by today's standards. But in the end this result contributed little to deciding between theories, for two reasons. First, existing airborne theories were modified so that water was incorporated as a causal factor, thus protecting them from refutation by "causal water". This extension or modification was not contrary to either medical knowledge or scientific logic. Modification of a theory by auxiliary hypotheses is common practice in science and (building on Lakatos 1980) we discuss the case of water and cholera in Section 3.

The second, more general, reason the single test of "causal water" was not crucial is that testing for and demonstrating an isolated causal effect is rarely sufficient to refute a theory within the overall process of scientific inquiry – Lakatos argues there are no "crucial experiments". In Section 5 we expand on this theme and show that "causal water" was only one piece of the overall evidence for comparing between theories. We argue that the broad range of evidence should have been sufficient to justify replacing existing theories with the fecal-oral theory, but water alone was not sufficient.

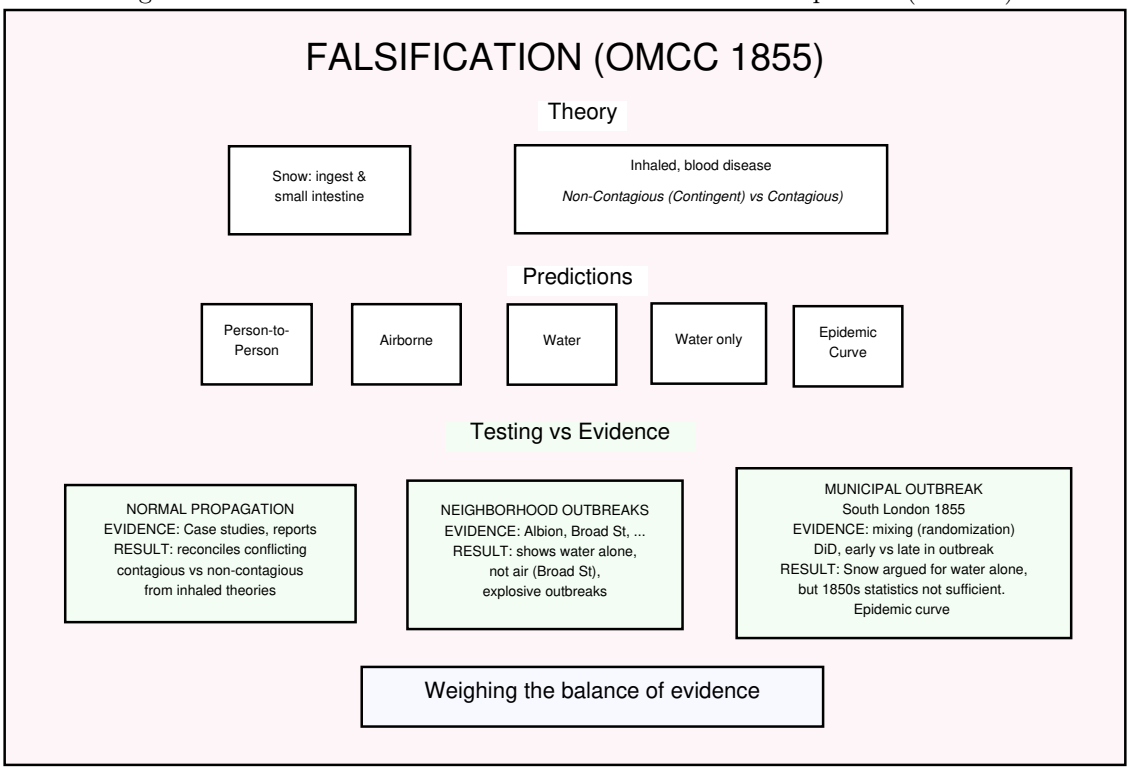
5 Appraisal & Falsification of Research Programmes: Comparing Theories 1855

Snow (particularly Snow, 1849a, 1855, 1856b) fits well within Lakatos' broader perspective of falsification and competition between rival programmes. In this section we examine how Snow employed multiple strands of evidence and a wide range of predicted phenomena in the attempt to demonstrate his theory and refute alternatives. We fit this within Lakatos's framework of sophisticated falsification and progressive versus degenerating programmes.

We show that Snow's fecal-oral theory was both theoretically and empirically progressive. The theory had new predictions: regarding person-to-person transmission; water as a casual factor but other factors not affecting mortality in a municipal outbreak; and the time-pattern (often called the *epidemic curve*) for neighborhood and municipal outbreaks. All of these predictions were corroborated, so the theory was also empirically progressive. Alternative – airborne – theories accommodated otherwise-recalcitrant observations, particularly water-borne transmission and contradictory

[11] Snow (1856b) highlights problems with both the number of reported deaths assigned to water companies (pp 248-249) which form the numerator for mortality rates and the number of houses (pp 245-246) which form the denominator. The conclusion is that Simon's underlying data is not as reliable as Snow's.

Figure 4: Schematic of Contradiction & Corroboration Comparison (1855-56)



evidence on person-to-person transmission, by additional auxiliary hypotheses. These hypotheses did not, however, predict new facts, and there is a strong argument that these theories were degenerating. A formal comparison of the fecal-oral theory versus the alternative airborne theories, following Lakatos's falsification criterion, argues for the supremacy of the fecal-oral theory, even using only evidence available in the 1850s.

Figure 4 shows schematically how we aim to formalize the process of falsification (and corroboration), through four steps: (1) laying out the theories, being honest about both the preferred theory *and* alternatives; (2) developing predictions for all theories; (3) comparing predictions against evidence, comparisons that may involve both formal statistical testing and less formal comparisons; and (4) weighing the balance of evidence for and against the alternatives.

5.1 Comparing Predictions versus Evidence

Choosing among competing theories is not easily formalized and does not neatly fit in a statistical testing framework – the process is qualitative, fuzzy, and somewhat ambiguous. It is nonetheless crucial, and it can be organized and structured. The process produces neither the "instant rationality" of Popper's falsification (Popper, 1985) nor the "sudden, irrational changes in vision" of Kuhn (1962) (quoting in both instances Lakatos 1980, 6).

We rely on Lakatos (1980, 32) definition of sophisticated falsification, the superseding of one theory by another with higher corroborated content. Snow's efforts in 1855 and 1856 are an ideal exemplar and test-case because the wide range of predictions and evidence demonstrates that such an effort

requires multiple strands of evidence and comparisons that are sometimes qualitative rather than quantitative or statistical.

Appendix C, Table 4, lays out details for the comparison of predictions versus evidence. Table 4 is dense because we are trying to synthesize disparate information across multiple theories and a wide range of evidence: predictions of alternate theories concerning cholera mortality; evidence and observations on cholera; concordance between the various theories' predictions and evidence; the quality of evidence and relevance to separating between theories.

Here, in Table 1, we focus on a subset of the predictions and observations: (2 a&b) – person-to-person transmission; (4) – airborne transmission; (5b) and (5c-f) – water and other factors; and (8) and (9) – the time-pattern of mortality or the "epidemic curve". These are predictions that are particularly valuable for discriminating between theories (2 a&b, 5c-f, 8, 9), or highlight the consequence of introducing the water-based auxiliary hypotheses (4 and 5b), showing why the airborne theories are degenerating according to Lakatos's criterion.

Regarding person-to-person transmission, since cholera first appeared there was debate whether it was contagious or not. The airborne theories can broadly be categorized as contagious or non-contagious. Evidence was presented on both sides (for early evidence on both sides see (Blane and Corbyn, 1821, 143, 148-150, 152-153)). Both were contradicted by the evidence, but this was based on the (maintained) hypothesis that transmission was by air. In the 1830s a protective auxiliary hypothesis (*contingent contagion*) was introduced to the non-contagious airborne theory to make it consistent with contrary observations. Snow's breakthrough in 1849 was to recognize that cholera did not *have* to be airborne, and that the extant evidence would be implied by a disease that was intestinal and transmitted via inadvertent ingestion of contaminated fecal matter – an abductive leap (to use Peirce's meaning of the term).

Summarizing person-to-person transmission we can conclude the following: 1) the fecal-oral theory is corroborated by the evidence; 2) evidence contradicts the airborne contagious theory; 3) the airborne non-contagious theory is protected by the auxiliary contingent contagious hypothesis, but the hypothesis produces no new predictions or facts – it is theoretically and empirically degenerating. The consistency of the fecal-oral theory and observed person-to-person transmission could be considered a new "fact" – the fecal-oral theory changes the interpretation and understanding of the evidence.

Regarding other factors (prediction 5c-f) airborne theories list many predisposing causes and susceptibilities: for example overcrowding, poor ventilation, filth. In terms of observations, mortality should vary with some (or all) of these. The fecal-oral theory, on the other hand, predicts that in a municipal outbreak such as South London (contaminated water supplied by the Southwark & Vauxhall Company) mortality should vary with exposure to contaminated water with no (or minimal) effect from other factors – the evidence should contradict or refute the airborne hypothesis of other factors. Snow recognized that this difference in predictions – in contrast with predictions on causality of water (5b) discussed shortly – would provide a sharp separation between alternate theories. Snow (1856b), in Table VI, compares actual versus predicted mortality across subdistricts, with predicted mortality based on the fraction of the population exposed to contaminated (Southwark & Vauxhall) water. Snow claimed that after accounting for water exposure other factors were

Table 1: Highlights of Comparing Predictions versus Evidence

	Prediction	Evidence / Observation	Value	Contradict? Fecal	Air
	PERSON-TO-PERSON CONTAGION				
2a & 2b	***Airborne theories*** predict that when contagion occurs it is between those sharing airspace in close proximity ***Fecal-oral theory*** predicts contagion occurs for those in close proximity, via sharing food, clothing	Evidence is good quality (Anecdotes, reports, and case studies. See Blane and Corbyn (1821, 143, 148-150, 152-153), Snow (1855, 2-9)). **CONTRADICTORY** for Airborne theories since some reports show those sharing airspace get sick, others not. Evidence is *Agree*=**YES** for fecal-oral since reports are consistent with transmission via food, clothing, hand-to-hand contact.	**High**	N	Y
	GENERAL CHARACTERISTICS				
4	***Transmission by Air – Airborne theories*** predict transmission by air: Sharing same air (different water) ⇒ similar mortality; sharing different air (same water) ⇒ different mortality	Broad Street provides good quality data showing that transmission is *not* by air – evidence on those sharing air but not water, and water but not air (Snow 1855, 42, 44-45; Whitehead, Cholera Inquiry Committee, 1855, 128 ff). The airborne theories are protected from contradiction by the auxiliary hypotheses concerning water as a predisposing cause and as a mode of transmission.	Medium	N	P
5b	***Water – Airborne and fecal-oral*** theories (post-1849) all predict water is a causal factor for cholera mortality	This is supported by multiple strands of high-quality evidence (narrative of neighborhood outbreaks (Albion Terr, Broad St, etc. Snow 1849a, 12 ff, 15 ff; Snow 1855, 23-56); quantitative analysis of municipal & neighborhood outbreaks (Snow 1855, 89, Table IX ; Sutherland 1851, 14 ff; Simon 1856, 9 & 13-14; Whitehead, Cholera Inquiry Committee, 1855, 128 ff)). The airborne theories are protected from contradiction by the auxiliary hypotheses concerning water as a predisposing cause and as a mode of transmission.	Low	N	P
5c, d, e, f	***Other Factors – Airborne theories*** predict cholera is associated with variety of factors, independent of water ***Fecal-oral theory*** predicts water will be the overriding factor in a neighborhood or municipal outbreak and other factors will have no or very small effect	Snow (1856b) attempts to show the "overwhelming influence" of water – doing so would be strong evidence contradicting airborne theories; without statistical tools of regression Snow was only modestly successful. Re-analyzing the data using modern statistical tools strongly contradicts the airborne hypothesis – in the 1854 outbreak in South London other factors had no significant effect.	Medium	N	Y
	EPIDEMIC CURVE				
8	***Fecal-oral theory*** predicts explosive neighborhood outbreaks: Mortality grows quickly initially then falls off	*Quality*: **High**; *Agree*: **YES** – Narratives of neighborhood outbreaks (Snow 1849a, 12 ff, 15 ff; Snow 1855, 23-56) showing explosive growth from low background rates	**High**	N	Y
9	***Fecal-oral theory*** predicts municipal outbreak mortality will differ early vs late: Early: high mortality for those exposed to contaminated water; Later: difference remains but diminishes as normal and neighborhood propagation contribute	*Quality*: **High**; *Agree*: **1855 YES**: Snow highlighted in multiple instances, (Snow 1855, 82, 86, 88; 1856b; 1856a, 243; 1857) *Quality*: **High**; *Agree*: **2021 YES**: DiD combined plus mixed population (quasi-randomization) split into first 4 vs next 3 vs final 8 weeks	**High**	N	Y

not important, but he did not have the tools to support his contention. This evidence only weakly refuted the airborne hypothesis, although his method was sound and he was, in fact, correct.[12]

Turning to the time-pattern of outbreaks, the fecal-oral theory predicts that neighborhood outbreaks (due to a localized contaminated water or food source) should have explosive (but localized) growth and then tail off quickly, assuming the localized source is either removed or avoided by local residents. It also predicts that municipal outbreaks, where a water-source such as a river or water company intake is contaminated, will exhibit a large difference in mortality rates at the beginning of an outbreak, which is moderated as time progresses. At the start of the outbreak, exposure will be predominantly due to consumption of contaminated municipal-source water and the difference in mortality rates for those supplied by contaminated versus clear water will be large. As time progresses, normal person-to-person – within and between households – will increase and so the disease will spread, but with lower mortality, to those supplied with clean water.

Both of these predictions were well-corroborated by evidence. For neighborhood outbreaks, Hope Street (Sutherland, 1851, 15-16), Horsleydown and Albion Terrace (Snow 1849a, 15ff; Snow 1855, 30ff) are three examples. For municipal outbreaks, Snow emphasized the time pattern in multiple instances (Snow 1855, 82, 86, 88; 1856b; 1856a, 243; 1857). The time pattern for municipal outbreaks qualifies as a "new fact" uncovered by the theory, in the sense that Snow looked for the fact based on the prediction. Airborne theories had no such predictions, and thus were contradicted by these observations.

To summarize so far, predictions (2 a&b) concerning contagion, and predictions (8 &9) concerning the time-pattern of mortality, all strongly refuted the airborne theories. Prediction (5c-f) concerning other factors weakly refuted the airborne theories – weakly because Snow could not demonstrate (as we can today) that in fact the actual versus predicted mortality across subdistricts depended only on water and not other factors.

The two remaining predictions – (4) concerning airborne transmission and (5b) concerning water – demonstrate how auxiliary hypotheses can protect a theory from recalcitrant facts. If cholera is airborne, then those sharing the same air should suffer similar mortality, while those not sharing the same air may not. Snow discusses counterexamples to both. The St. James workhouse at 50 Poland Street and the Lion Brewery at 50 Broad Street both had lower mortality rates despite sharing the same air as those around them (Snow, 1855, 42). The widow Susannah Eley in Hampstead, far from Broad Street and clearly not sharing the same air, died after drinking water from the Broad Street pump (Snow, 1855, 44-45). The Reverend Henry Whitehead collected data for those on Broad Street who drank and did not drink from the pump, data that clearly showed dramatically different mortality those who shared the same air, depending specifically on whether they drank from the pump (see Whitehead, Cholera Inquiry Committee, 1855, 128 ff; and Coleman 2018, Section 5.1.4 for a presentation in a modern contingency table format).

The evidence shows that transmission was *not* airborne but waterborne. And yet this does not contradict the airborne theories, because they had incorporated water as both a predisposing cause and as a mode of transmission. A quote from the General Board of Health's *Committee for Scientific Inquiries* is quite explicit:

[12]See Coleman (2020) for details of Snow's method and a re-analysis with modern statistical tools showing that other factors do not contribute to cross-subdistrict variantion.

> There is mentioned, however, a remarkable instance [Susannah Eley (Snow, 1855, 44-45)] in which it seems probably that the water of this well did really act as a vehicle of choleraic infection; but (assuming the absence of fallacy in the case) this probability might easily be admitted, without its therefrom resulting that infection depended on the specific material alleged. (General Board of Health, 1855, 52)

The airborne theories were protected from contradiction by the auxiliary hypotheses concerning water, and for this prediction we have entered "P" into the final column of Table 1 to denote that the airborne theories are protected from refutation by this prediction. Nonetheless, this prediction does have some value for discriminating between theories. First, airborne cholera requires some *positive* evidence of airborne transmission, and we know of none. Second, this case is grounds for claiming the airborne theories are degenerating – the auxiliary hypotheses indeed protects against the observations of waterborne transmission but *without* any increase in theoretical or empirical content, and with no new facts within the airborne programme.

Finally, we turn to the prediction of water as a causal effect for cholera mortality (5b in Tables 4 and 1), often considered the signature evidence for Snow's theory. In fact, this prediction and evidence did little to discriminate between theories, because by 1855 all theories predicted that water would be causal – at least in some if not all cases. We rate the value of this prediction as low for discriminating between theories, although as with the case of airborne transmission, the adoption of the auxiliary hypotheses within the airborne programme without any increase in content or new facts is an indication of a degenerating programme.

5.2 Weighing the Balance of Evidence

There are two levels on which we consider whether the airborne theories were "falsified" by the evidence in 1855-56. First, naive falsification, whether the evidence refutes or contradicts the airborne theories. We might be tempted to answer "yes" but close examination of Tables 4 and 1 shows why this is a vain hope. The final two columns of Table 4 *do* show that the airborne theories are (naively) contradicted by some but only some of the evidence – the theories are protected on two crucial predictions regarding airborne and waterborne transmission (4 and 5b). For those predictions which *are* contradicted, suitable adjustments to the theories could be no doubt be made: "It is always easy for a scientist to deal with a given anomaly by making suitable adjustments to his programme" Lakatos (1980, 179). And indeed, the evidence for other factors not affecting mortality (5c-f) was rather weak. The fecal-oral theory is without doubt better supported by the evidence, but there is no single observation to which we can point as definitively refuting the alternatives.

Turning to Lakato's three-part criterion for sophisticated falsification (Lakatos 1980, 32 and Section 5 above), the fecal-oral theory satisfies all three conditions:

1. the fecal-oral theory has excess empirical content, predicting new patterns of person-to-person transmission different from airborne theories (2b); the absence of factors other than water affecting mortality (5c-f); time-patterns of mortality (epidemic curve, 8 & 9)
2. the fecal-oral theory explains the previous success, regarding geographic spread, transmission by water, and other observations

3. new predictions (2b, 5c-f, 8 & 9) are corroborated

Existing airborne theories could be adjusted to accommodate the evidence and in some respects were, thus avoiding naive falsification. They could not escape in the same way sophisticated falsification; there is a strong argument that those theories were degenerating (in Lakatos's terms) and the fecal-oral theory progressive. In summary, while continued adherence to the airborne theories was not irrational or illogical, we can conclude there was sufficient evidence for the fecal-oral theory to supersede the alternatives.

6 Conclusion: The Ultimate Success of the Fecal-Oral Theory

We entered into this project with the notion that John Snow was the lone voice of cholera-knowledge in a wilderness of miasma ignorance – only to find a richer and more nuanced reality. The causes of cholera were actively debated in the 1850s and following. Accumulation and analysis of data was an active undertaking, contributed to by many in addition to Snow. Most importantly, while it may be true that Snow's work in the early 1850s did not lead to the over-night conversion of the medical and public health establishment, by 1866 the fecal-oral theory was accepted by many.

Snow, and particularly the two editions of *On the mode of communication of cholera*, were given prominent credit, but many contributed to the accumulation and analysis of evidence on cholera. Two particular examples regarding water as a causal factor are Sutherland (1851, see p 15 ff) and Simon (1856). Neither mentioned Snow or his work, but we interpret this as a reflection of the wide-ranging analysis of water and cholera mortality, not as any slight or ignoring of Snow's contributions. William Farr cited the importance of water following the 1848-1849 outbreak (although he did, at the time, advocate elevation as a more important factor):

> there is often a way open for it [cholera] to extend itself more widely, and that is by the mixture of the cholera evacuations with the water used for drinking and culinary purposes (General Register Office, 1852, lxxvii)
>
> through nearly the whole of this Table the impurity of the waters with which the inhabitants of the several districts are supplied is in nearly a direct proportion to the mortality from cholera (Farr, 1853, 406))

The Reverand Henry Whitehead made crucial contributions to the Broad Street investigation, publishing in Cholera Inquiry Committee (1855) and elsewhere – see also Johnson (2007, 173 ff) and Coleman (2018, Section 5.1.4) – and later contributions to the 1866 investigation.

By the time cholera struck London for the last time in 1866, the fecal-oral theory, and particularly the importance of water in wide-spread municipal transmissions, had been accepted by one part of the medical establishment. Snow's careful analysis, his attempt at falsification of alternative theories through accumulation of evidence and careful analysis – a template for good scientific inquiry – had indeed won converts. William Farr, in the report to Parliament from the Registrar-General, (Farr, 1868, 99), states the fecal-oral theory and water propagation as a seeming accepted matter:

> That cholera stuff can be distributed through the river waters of London was demonstrated in 1854, in the weekly returns of 1849 and 1854, from the experiment in South London on a large scale of the two qualities of Thames water, one containing much sewage (the Southwark), the other containing little sewage (the Lambeth). Dr. Snow first propounded distinctly the theory that cholera is propagated exclusively by cholera discharges, and that water is the chief medium of diffusion.

The *Lancet*, in reviewing Farr's report, agrees on the importance of the water supply:

> We apprehend that, to an unbiased mind, the elaborate array of facts which Dr. FARR has set forth with so much skill, as the result of great labour and research, will render irresistible the conclusions at which he has arrived in regard to the influence of the watersupply in the causation of the epidemic (Lancet, 1868a).

The report to the Privy Council by J. Netten Radcliffe (Radcliffe, 1867) also identified waterborne transmission as the primary cause of the high and localized mortality (see also the review in the Lancet 1867).

Farr, the Lancet, and Radcliffe advocated a germ theory that we can recognize today:

> if the cholera germs are living molecules or organisms, the uniformity of their distribution in water would depend on a variety of conditions. Only one in ten or more persons may actually swallow these germs ; and even if the whole ten did swallow them, it by no means follows that they would all be affected in an equal degree. (Lancet, 1867, 559, describing Radcliffe's views)

Farr used the work of Fillippo Pacini on the discovery and identification in 1854 of the cholera bacterium, what Farr called *cholera corpuscles*. Farr (also quoted in the Lancet 1868b) used estimates from Pacini of the volume of diarrhoea (dejections) and concentration of bacteria to account for how a single individual could contaminate a river (Farr, 1868):

> Pacini, an excellent microscopic observer, has found that the germs of vibrions (molecule vibrionali are less the 1/25000 of an inch in diameter (footnote: Appendix to the 9th Report of Medical Officer of Privy Council, page 519; Pacini, Sulla Causa Specifica del Col. Asiatic, 1865; and the work Della Natura del Col. As., 1866.) (1868, xv)
>
> Applying Pacini's data to the fatal cases of different durations, it is found that the average volume of the dejections in a cholera case is equivalent to 8.24 litres. How many cholera corpuscles this quantity contains cannot be calculated. They are exceedingly minute. By Pacini's estimate 1000 millions would not occupy more space than a cubic millimetre ; and there are a million cubic millimetres in a litre of water. ... It is certain that the flux finding its way down the sewers would not be equally distributed in the river Lea for instance, but in the water would be in irregular masses like clouds in the sky; and that at some points a quart of the waters might contain hundreds or thousands of corpuscles capable of propagating their numbers by millions in the mucus membranes

> of the stomach and intestines. Whether the cholera corpuscle can propagate itself in sewage water at a high temperature is not yet known, but its diffusion is adequately accounted for on the hypothesis that it is only propagated in the living organism. (1868, lxiii)

Nonetheless, the fecal-oral or water-only theory was not yet ascendant. Luckin (1977) provides some of the answers for why, discussing the commercial and political forces that shaped the social and medical environment. One crucial piece that was missing from the fecal-oral, germ-based theory, was a method for testing (and identifying) the cholera "poison" in contaminated water. Without such a means of clearly identifying the causal agent, skeptics could always cast doubt on the conclusions. Luckin (1977, 34) highlights the issue during the 1866 outbreak, with an attempt to chemically test the water:

> Farr asked the assistant [to Frankland] to undertake rigorous analyses of water ... . Predictably, the chemical analysis revealed nothing and the repercussions ... were to prove of exceptional methodological significance in the controversy which ensued.

Given the fact that Pacini had identified the bacteria, and this was known and used by Farr and others, it seems to us but a small step to identify the bacteria in the contaminated water supplied by the East London Water Company. But doing so requires culturing and isolating the bacteria from the contaminated water. In 1866 this was not easy or even possible. Louis Pasteur first cultured bacteria in 1860, and Robert Koch first isolated *vibrio cholerae* in pure culture in 1883. Advocates of the fecal-oral theory had to rely on primarily epidemiological and statistical (circumstantial) evidence until the end of the 19th century.

Appendices

A Theories of Cholera in Mid-Century Britain

Theories of cholera in the 1850s can be categorized along three dimensions. These do not exactly correspond with modern understanding of medicine and physiology, but are close enough to be both understandable and useful. First, the mode of transmission, being (for cholera) either inhaled or ingested. Second, whether contagious or non-contagious. Third, the "seat of the disease", being the nervous system, the blood, or the gastrointestinal tract.

Figure 1 shows a timeline and Table 2 lists the alternative theories under consideration during the 1850s. The first detailed reports to medical practitioners in Britain (Blane and Corbyn, 1821) presumed cholera was a disease of the nervous system, although by the 1830s it was more widely thought to be a blood disease. For present purposes the distinction between nervous system versus blood disease is not important, because the mode of transmission for both was inhaled and through the lungs. Up until Snow's 1849 *On the mode of communication of cholera* (Snow, 1849a) inhalation was almost universally accepted.[13]

The major point of contention and debate prior to 1849 was whether cholera was contagious (infectious) or non-contagious. (The debate over contagion continued after ingestion was introduced as a method of communication.) For contagionists a cholera poison was produced in the bodies of the sick and communicated through the disease process known at the time as infection, what we would now call inhalation or respiratory infection. Non-contagionists considered that cholera was generated by the interaction of an imperceptible atmospheric influence and local concentrations of decomposing organic matter (filth). They classified cholera as a typical epidemic disease, but we need to recognize that in 1850 'epidemic' had a somewhat different meaning than today, meaning a localized outbreak of non-contagious nature.

In the 1830s a hybrid termed *contingent-contagion* was introduced to non-contagious theories to allow for cholera to become temporarily contagious under certain conditions, say overcrowding (see Wakley, 1832, 124-125). The hypothesis was necessary to account for conflicting evidence. Two instances from early in the period suffice to demonstrate the issue: Pro-contagious was a episode from Mauritius where cholera seemed to be imported by the frigate Topaz from Cylon (Blane and Corbyn, 1821, 148-150, 152-153); anti-contagious was a case of three Sepoys in Seroor hospital who escaped disease despite being in close proximity to patients (Blane and Corbyn, 1821, 143).

The contingent-contagion hypothesis is noteworthy for a number of reasons. First, it is an example of what Lakatos termed a protective auxiliary hypothesis introduced to protect a core theory, non-contagion in this case (Lakatos, 1980, particularly section 1.3). It made non-contagious theories immune from contradiction by evidence of contagion, a sign of a degenerative research programme in Lakatos's terms. Second, as a result the hypothesis weakened non-contagion relative to any alternative that could account for apparently conflicting evidence within the core theory. We will see that Snow's ingested fecal-oral theory could account for the evidence that appeared contradictory

[13] Parkin (1832) suggests that an airborne cholera poison can be diffused into water and then ingested, but ingestion and gastrointestinal disease were not widely considered prior to 1849.

Table 2: Cholera Theories in Mid-Nineteenth Century England

Theory		Comment
Blood Disease, Airborne (inhaled, + water post-1849)	**Infection** (contagious, airborne): Airborne morbid poison produced in victims' bodies. Transmitted via inhalation, with water possible post-1849.	Current in 1850s. **Predisposing Causes**: close proximity to victims; overcrowding, poor ventilation; Post-1849: impure water/food a major predisposing cause; **Susceptibility**: constitutional depression of vital powers; previous or current pulmonary diseases.
	General Atmospheric (generally non-contagious, airborne): An active morbid poison in atmosphere. Transmitted via inhalation, with water possible post-1849.	Less in favor after 1850. **Predisposing Causes**: Environmental: hot, moist, stagnant atmosphere. Associated with decomposing vegetation, and/or soil contamination. **Susceptibility**: constitutional depression of vital powers; poverty; unhealthy, moist living conditions
		Contingent-contagion – protective "auxiliary hypothesis" aligns theory with evidence of contagion
	Localization (generally non-contagious, airborne): Concentrations of the "cholera poison" from localized sources of organic decomposition (including sewer gases and "privy atmospheres"). Transmitted via inhalation, with water possible post-1849.	**Predisposing Causes**: Environmental: overcrowding, dampness, filth, poor ventilation, proximity to graveyards, bad water, bad sanitation; Post-1849: impure water/food a major predisposing cause; **Susceptibility**: living in unhealthy situations, constitutional weaknesses
		Contingent-contagion – protective "auxiliary hypothesis" aligns theory with evidence of contagion
	Elevation / Zymotic: A refinement of localization (above).	Evaporation & inhalation: sewage & organic matter in rivers evaporates, those at higher elevation (further distance) inhale less
Gastrointestinal tract, Ingested	**Alimentary Canal** (contagious, now termed fecal-oral transmission): "excretions of the sick ... being accidentally swallowed" Snow (1849a, 8)	**Normal (Ordinary) Propagation**: close communication with infected individual leading to inadvertently swallowing fecal matter. Predominant mode of transmission. **Neighborhood Propagation**: Choleraic contamination of a common food or (more frequently) water source **Municipal Propagation**: water contaminated by sewage containing cholera dejections is distributed through municipal water supply (either rivers or water supply companies)
	Intestinal Canal (non-contagious)	Introduced around 1850 to account for strong association with water

under inhaled non-contagious (or contagious) theory and thus had some support relative to theories that relied on contingent-contagion.

All these theories invoked predisposing causes or conditions, and susceptibility. Predisposing causes were environment factors that caused or contributed to cholera. For airborne contagious, overcrowding would be a predisposing cause since more people in close proximity would lead to more transmission and more disease. For non-contagious (localization in particular) local sources of decomposing organic matter, say pigsties or open sewers, would activate or amplify the airborne cholera poison. Susceptibility was invoked to explain why some but not all those exposed fell ill with cholera, and might include exposure to other diseases, poor food, or poor living conditions.

In 1849 John Snow published the first edition of his monograph *On the mode of communication of cholera*, where he proposed that cholera was gastrointestinal and transmitted by the inadvertent ingestion of contaminated fecal matter, either through food, water, or hand-mouth contact: "excretions of the sick ... being accidentally swallowed" Snow (1849a, 8). The fecal-oral theory predicts three modes of communication or propagation, all of which Snow described more or less explicitly: (1) ordinary or normal propagation, person-to-person transmission through contamination of food or water, or hand-mouth contact: "evacuations ... become attached unobserved to the hands of the person nursing the patient, and are unconsciously swallowed" (Snow, 1849a, 9-10); (2) neighborhood propagation, the contamination of a local water (or food) source accessed by multiple households in a neighborhood(Snow, 1855, 22-23); and (3) municipal propagation where sewage was mixed with municipal water supply: "the emptying of sewers into the drinking water of the community" (Snow, 1849a, 11)

Snow's was a contagionist theory, but broke from most others by proposing that cholera was not airborne, and affected the intestines rather than the blood. William Budd, a doctor from Bristol, independently proposed a non-contagious fecal-oral theory. Writing just a few weeks after the publication of Snow's pamphlet in early September, Budd concluded that morbid cholera matter must be "taken by the act of swallowing into the intestinal canal ... [and] develop[s] only in the human intestine ..." (Budd, 1849, 5). In other words, airborne cholera matter was only morbid if it settled on something that was subsequently swallowed. As such, Budd agreed with Snow that the sole mode of cholera communication was via the fecal-oral route.

B Predictions

Repeating from above, Snow's core theory posited cholera as a disease of the intestine, transmitted by some unknown material that passed out of one individual (vomit or more commonly diarrhea) and was then inadvertently ingested by others. The three modes of communication (person-to-person or normal, neighborhood, and municipal transmission) together predicted the

The core of the alternative theory (or theories) posited cholera as an airborne poison causing a blood disease.[14] For predictions the important characteristic is that the cholera poison was airborne. various There were many and various factors that could produce or amplify the airborne

[14]Today, we would say "an airborne poison infecting the blood" but in the 1850s the word "infection" had a different meaning, reserved for contagious epidemic diseases, and we will try to avoid its use.

poison ("predisposing causes"), or increase individuals' susceptibility – factors such as crowded hosing conditions, dampness, filth, bad sanitation. Prior to 1849 transmission was generally considered via inhalation. After 1849 auxiliary hypotheses added water as a mode of transmission – the airborne poison could diffuse into water and enter through the stomach – and also added water as a cause – contaminated water could produce or amplify the airborne poison that could be inhaled (predisposing cause), or could increase an individuals' susceptibility. Note that these water-borne auxiliary hypotheses are not prima facie contrary to logic or the science of the 1850s (or even science today). Today we know they are wrong, but they were not and are not silly.

Table 3 details predictions from the alternative theories. Each row is a specific predicted observation – matching with evidence. The second column ("Predicted Observation") shows the prediction about the pattern of observed mortality. The third column indicates the theory and specific hypothesis generating that prediction. The third, fourth, and fifth columns show whether the listed theory generates the predicted observation or not.

For example, prediction (2a) concerns person-to-person transmission for those sharing airspace – the prediction is that increased cholera mortality occurs for those in close proximity via sharing airspace. The airborne contagious blood disease theory produces this prediction because it hypothesizes that transmission is person-to-person via inhalation, and so the cell in the fifth column is "Yes". The airborne non-contagious theory does not generate this prediction (so "No"), but the auxiliary contingent-contagious hypothesis specifies that cholera can become contagious under certain circumstances. The entry is therefore "No/Yes" – the theory predicts both airborne contagion and non-contagion. The fecal-oral theory predicts "No" because the theory predicts fecal-oral transmission, and thus sometimes those sharing airspace will become infected, sometimes not.

The table is valuable because it allows us to identify predictions and evidence (patterns of mortality) that distinguishing between theories. A row with mixed "Yes" and "No" distinguishes between theories, while a row with all "Yes" does not. A row is particularly valuable when predictions separate between theories *and* the quality of evidence is good. On this basis, the most important predictions are: (2a) and (2b) person-to-person contagion; (5) transmission via air; (6c-f) association with water versus other factors; (9) and (10) concerning the time-pattern of mortality, what is now termed the epidemic curve. The final column ("Overall Value") summarizes the overall value of the prediction for separating between theories.

Some predictions distinguish between theories (for example predictions (1), (4), or (7)) but the evidence is not good quality. Other predictions have strong evidence but do not allow one to distinguish between theories. Prediction (5a) – water as a causal factor for cholera mortality – is particularly notable, and helps us understand some puzzles about the competition among theories in the 1850s. There was strong evidence for water as a causal factor in cholera mortality – Snow (1855) is well-known and widely cited, but Simon (1856) provided even stronger evidence – and today we are puzzled that such evidence did not lead to the acceptance of Snow's theory (remember the comments of Johnson (2007, 125) about "smart people cling[ing] to an outlandishly incorrect idea despite substantial evidence to the contrary"). The fact, reflected in row (5a), is that all theories predicted water as a causal factor, so that evidence did not distinguish between them. Simon (1856) clearly states the case, first providing strong evidence for water as causal ("The above conclusions [that fecalized water causes cholera mortality] rest on so large a basis of facts, that

Table 3: Predictions for Alternative Theories as of 1855

	Predicted Observation	**Theory**: Hypothesis	Fecal-Oral, Intestinal (Snow)	Airborne, Blood Disease		Quality of Evidence	Overall Value
				Non-Contagious / Contingent	Contagious		
	PERSON-TO-PERSON CONTAGION						
1	***Geographic Spread***: Cholera occurs along trade routes, at the speed of travel	**Airborne and Fecal-oral**: Person-to-person transmission	YES	NO / neutral	YES	Moderate, anecdote	Low
2a	***Person-to-Person airborne contagion***: occurs between those sharing airspace in close proximity	**Airborne**: person-to-person transmission	NO	YES/NO	YES	Good, case studies	**High**
2b	***Person-to-Person non-airborne contagion***: Cholera occurs for those in close proximity, via sharing food, clothing	**Fecal-oral**: person-to-person transmission	YES	NO	NO	Good, case studies	
3	***Winds***: Cholera follows winds (not contagious)	**Airborne**: but no person-to-person transmission	NO	YES	NO	Poor	Low
	GENERAL CHARACTERISTICS						
4	***General transmission by air***: Sharing same air (different water) ⇒ similar mortality; sharing different air (same water) ⇒ different mortality	**Airborne**: transmitted via air	NO	YES	YES	Good, case studies	Medium
5a	***Water is causal***: pre-1849, cholera not associated with water (NB – prediction from airborne is reversed)	**Airborne** pre-1849: water not a predisposing cause or method of transmission	–	NO	NO	High	Low
5b	***Water is causal***: post-1849, cholera associated with water – post-1849	**Airborne** post-1849: water *is* a predisposing cause or method of transmission **Fecal-oral**: water is a cause through neighborhood and municipal transmission	YES	YES	YES	High, quantitative (statistical)	
5c, d, e, f	***Other factors***: Cholera associated with variety of factors, independent of water: 5c) Overcrowding & poor ventilation; 5d) Hot weather & decomposing refuse; 5e) Poverty & unhealthy living conditions; 5f) Dampness, filth, bad sanitation	**Airborne**: many other factors are predisposing causes and susceptibilities **Fecal-oral**: other factors may have some influence but will be negligible relative to water in a municipal outbreak	NO	YES	YES	1856: Good; 2022: High, quantitative (statistical)	Medium
6	***General characteristics***: Cholera erupts simultaneously in non-contiguous locations; Visits same areas in subsequent outbreaks	**Airborne non-contagious** (localized): dependent on local predisposing conditions **Fecal-oral**: dependent on local conditions that favor municipal outbreaks (e.g. water from the Thames)	YES	YES	NO	Moderate, anecdotal	Low
7	***Elevation***: Mortality falls with higher elevation and further from river	**Zymotic** (subset of airborne non-contagious): Mortality falls with higher elevation and further from river	YES - but confounding	YES	NO	Good, quantitative	Low
	EPIDEMIC CURVE						
8	***Explosive neighborhood outbreaks***: Mortality grows quickly initially then falls off	**Fecal-oral**, Neighborhood propagation: contamination of a point source, usually water	YES	NO	NO	High, quantitative	**High**
9	***Municipal outbreaks early vs late***: Early: high mortality for those exposed to contaminated water; Later: difference remains but diminishes as normal and neighborhood propagation contribute	**Fecal-oral**, Municipal propagation: contamination of a municipal water supply, usually a river	YES	NO	NO	High, quantitative	**High**

Each row presents a prediction about observed patterns of mortality. "Yes" or "No" in a column (and color) indicates whether the theory in the column predicts the observation, or the opposite. This table does not compare predictions versus evidence.

I venture to believe they will be accepted as the final solution of any existing uncertainty as to the dangerousness of putrefiable drinking-water during visitations of epidemic cholera" Simon 1856, 9), but then explicitly states that this does not rule out other causes ("The present contribution therefore aims only at giving a more exact knowledge of one cause, not at gainsaying the existence of other causes" Simon 1856, 13).

We can also use Table 3 to understand why Snow turned from demonstrating water as *a* causal factor (Snow, 1855) to trying to demonstrate water as the *only* causal factor (Snow, 1856b). Snow (1855, Table IX) compared across quasi-randomized water customers to try and demonstrate a large difference in mortality between contaminated-water customers (served by the Southwark & Vauxhall Company) versus clean-water customers (served by the Lambeth Company) – to demonstrate water as causal. Due to data limitations, Snow could only compare across a large area, which included subdistricts served by both companies (where customers were mixed and quasi-randomized) *and* subdistricts served by Southwark & Vauxhall only. Snow recognized, and Edmund Parkes emphasized, that combining all regions left the comparison open to problems of confounding: "the Lambeth Company supplies, to a considerable extent, a good neighbourhood on elevated ground (including the healthy districts of Streatham, Foresthill, and Syndenham); while the Southwark and Vauxhall Company supplies the greater part of the poorest, lowest, and marshiest district in London" (Parkes, 1855, 461).

With the publication of detailed by-supplier population statistics in Simon (1856), Snow now had access to data to re-analyze the quasi-randomized data, but he did not. Instead, in Snow (1856b), he turned to demonstrating that variation across subdistricts was due to water alone, and not other factors. Such a shift in focus, however, is understandable when we recognize that prediction (5b) – water as causal – does not separate theories, but evidence *against* predictions (5c-f) – other factors causal – would separate theories. Showing that water was the only causal factor, and other factors did not affect cholera mortality, would sharply separate Snow's theory from alternatives.

Laying out the predictions for alternate theories, as in Table 3, provides guidance for experimental design and interpretation. In the present circumstances, when all experiments were completed over 150 years ago, it provides guidance for understanding the competition between theories. In the 1850s, such a table could have been used to direct research towards particular predictions, and collection of data, that could help separate between theories.

C Comparing Predictions versus Evidence

Although choosing among competing theories is not easily formalized and does not easily fit in a statistical testing framework, it can be organized and structured. Table 4 expands on the predictions in Table 3 to include evidence, and specifically whether the prediction agrees with the evidence.

The content of Table 4 is rather dense – we are summarizing a wide range of predictions and evidence that varies substantially in form and quality. The first column shows "Prediction & Observation" – each row a particular prediction about cholera and observed mortality. The sixth or penultimate column contains a description of the evidence – the observation itself. First, the quality or reliability

of the evidence, whether *moderate*, *good*, or *high*. Second, whether that evidence agrees with the prediction or not. Finally, a brief summary of the evidence.

Columns two, three, and four now shows two pieces of information. First, whether the theory of that column agrees with (generates) the predictions shown in the first column – indicated by a "yes" or "no". Second, whether the theory's prediction is supported (shown in teal) or contradicted (shown in red) by the evidence in the sixth column.

Consider prediction (5b), "water is causal". The prediction (column one) is that water is a causal factor – consuming contaminated water causes higher mortality. Column six summarizes evidence that water *is* causal, so column six is labeled "Agree: Yes". The fecal-oral theory (column three) agrees with the predictions so the cell is labeled "yes". The prediction of the fecal-oral theory ("yes water is causal") matches the evidence ("evidence indicates water is causal"), so the cell is labeled "Support".

The case of airborne theories is more nuanced. The primary mode of transmission is airborne, so one might presume they would *not* predict water is causal. Such a presumption might have been correct prior to 1849, but by 1855 water had been, by means of auxiliary "protective" hypotheses, broadly incorporated as both a predisposing cause and as a mode of transmission.[15] These auxiliary hypotheses were degenerating in Lakatos's terms because they protected the theories from recalcitrant observations but did not increase the empirical content of the theories by predicting *new* facts, simply explaining the existing old facts. Nonetheless, the airborne theories by 1855 *did* predict water as causal, so that in Table 4, columns three and four of row (5b) is labeled "yes". To record that the theory is protected from contradiction by adoption of (*ad hod*) auxiliary hypotheses, however, the cells are labeled protected.

The fecal-oral theory's predictions and observations summarized in Table 4 fits the description of a progressive programme: new predictions (2b, 5c-f, 8, and 9) all of which were corroborated. The airborne theory fits the description of a degenerative programme: water as a predisposing cause explained given facts but did not predict new ones. Furthermore, predictions of the airborne theory were contradicted by the new facts: the fecal-oral theory exhibited higher corroborated content.

It is important to recognize that, among the wide range of predictions and evidence available in the mid-1850s bearing on alternative theories shown in Table 4, there is no single crucial prediction or experiment that did serve, or even should have served, to convince skeptics of the primacy of the fecal-oral theory. What Table 4 does show is that, although airborne theories were not uniformly refuted by the evidence (largely due to the auxiliary hypotheses concerning water as a predisposing cause or method of transmission – see predictions 5a and 5b), the preponderance of evidence was in favor of the fecal-oral theory *and* the airborne theories were refuted in many instances; the fecal-oral theory was a theory that exhibited higher corroborated content.

In summary, one might suspect that if the predictions and evidence were presented in a comprehensive and transparent manner as Table 4, more skeptics might have been convinced in the 1850s.

[15]Regarding water as a cause: "a number of most severe and fatal outbursts of cholera were referable.to no other cause except the state of the water-supply" Sutherland (1851, 15). Regarding water as a mode of transmission: "Thus a second great inlet is established by which injurious substances in a liquid form as certainly find their way into the circulating blood, as noxious aerial agents do by the way of the respiratory apparatus" Grainger (1851, 91).

Table 4: Comparison of Predictions versus Evidence

	Prediction & Observation	Fecal-Oral, Intestinal (Snow)	Airborne, Blood Disease: Non-Cont Contingent	Airborne, Blood Disease: Contagious	Evidence / Observation	Value	Contradict? Fecal	Contradict? Air
	PERSON-TO-PERSON CONTAGION							
1	***Geographic Spread***: Cholera occurs along trade routes, at the speed of travel	yes Support	no Weak contradict	yes Support	*Quality*: **Moderate**; *Agree*: **YES** – Anecdotes and general observations that it spreads along trade routes – not specific or detailed	Low	N	M
2a	***Person-to-Person airborne contagion***: occurs between those sharing airspace in close proximity	na	yes/no Protected	yes Contradict	*Quality*: **Good**; *Agree*: **CONTRADICTORY** for Airborne – in some cases those sharing the same airspace are infected, sometimes not*Quality*: **Good**; *Agree*: **YES** for fecal-oral Anecdotes, reports, and case studies. See Blane and Corbyn (1821, 143, 148-150, 152-153), Snow (1855, 2-9)	**High**	na	M
2b	***Person-to-Person non-airborne contagion***: occurs for those in close proximity, via sharing food, clothing	yes SUPPORT	na	na			N	na
3	***Winds***: Cholera follows winds (not contagious)	no Weak support	no Weak support	yes Weak contradict	*Quality*: **Poor**; *Agree*: **NO** – Anecdotes and general observations that it does not follow winds – not specific or detailed	Low	N	M
	GENERAL CHARACTERISTICS							
4	***General transmission by air***: Sharing same air (different water) ⇒ similar mortality; sharing different air (same water) ⇒ different mortality	no SUPPORT	yes Protected	yes Protected	*Quality*: **Good**; *Agree*: **NO** – Broad Street provides events and data on those sharing air but not water, and water but not air (Snow 1855, 42, 44-45; Whitehead, Cholera Inquiry Committee, 1855, 128 ff)	Medium	N	P
5a	***Water is causal***: pre-1849, cholera not associated with water (NB – prediction from airborne is reversed)	na	no Contradict	no Contradict	*Quality*: **High**; *Agree*: **YES** – Multiple strands: narrative of neighborhood outbreaks (Albion Terr, Broad St, etc. Snow 1849a, 12 ff, 15 ff; Snow 1855, 23-56); quantitative analysis of municipal & neighborhood outbreaks (Snow 1855, 89, Table IX ; Sutherland 1851, 14 ff; Simon 1856, 9 & 13-14; Whitehead, Cholera Inquiry Committee, 1855, 128 ff)	Low	na	Y
5b	***Water is causal***: post-1849, cholera associated with water – post-1849	yes SUPPORT	yes Protected	yes Protected			N	P
5c, d, e, f	***Other factors***: Cholera associated with variety of factors, independent of water: 5c) Overcrowding & poor ventilation; 5d) Hot weather & decomposing refuse; 5e) Poverty & unhealthy living conditions; 5f) Dampness, filth, bad sanitation	no 1856: weak 2021: strong support	yes 1856: Weak 2021: strong contradict	yes 1856: Weak 2021: strong contradict	*Quality*: **High**; 1856 *Agree*: **Weak NO**: Snow (1856b) attempts to show the "overwhelming influence" of water but without statistical tools of regression only modestly successful 2022 *Agree*: **Strong NO**: Strong evidence that other observed correlations are spurious	Medium	N	Y
6	***General characteristics***: Cholera erupts simultaneously in non-contiguous locations; Visits same areas in subsequent outbreaks	yes Support	yes Support	no Contradict	*Quality*: **Moderate**; *Agree*: **YES** – Anecdotes and general observations – not specific or detailed	Low	N	M
7	***Elevation***: Mortality falls with higher elevation and further from river	no 1856: weak 2021: strong support	yes 1856: Support 2021: Contradict	no Neutral	*Quality*: **Good**; *Agree*: **YES but spurious** – Quantitative analysis (Farr, General Register Office, 1852, lxi ff) but Farr recognized association with water and crowding. 2021 re-analysis shows relation is spurious due to association with water supply.	Low	N	M
	EPIDEMIC CURVE							
8	***Explosive neighborhood outbreaks***: Mortality grows quickly initially then falls off	yes SUPPORT	no Contradict	no Contradict	*Quality*: **High**; *Agree*: **YES** – Narratives of neighborhood outbreaks (Snow 1849a, 12 ff, 15 ff; Snow 1855, 23-56) showing explosive growth from low background rates	**High**	N	Y
9	***Municipal outbreaks early vs late***: Early: high mortality for those exposed to contaminated water; Later: difference remains but diminishes as normal and neighborhood propagation contribute	yes SUPPORT	no Contradict	no Contradict	*Quality*: **High**; *Agree*: **1855 YES**: Snow highlighted in multiple instances, (Snow 1855, 82, 86, 88; 1856b; 1856a, 243; 1857) *Quality*: **High**; *Agree*: **2021 YES**: DiD combined plus mixed population (quasi-randomization) split into first 4 vs next 3 vs final 8 weeks	**High**	N	Y

Each row presents a prediction about observed patterns of mortality, as in Table 3. The sixth column indicates the evidence regarding the prediction. In columns 3-5 the "yes" or "no" indicates whether the theory and evidence agree with the prediction, or the opposite. The color of each cell indicates whether the evidence supports (teal), contradicts (red), or weakly supports / contradicts (orange) the theory in the column. Protected (violet) indicates the theory is protected from refutation by adoption of a protective auxiliary hypothesis. The seventh column is a subjective assessment of the value of the prediction in separating between theories, and may be "Low" because either the predictions do not separate, or the evidence is low quality. The final two columns indicate whether the indicated theory is contradicted by the evidence: "Y"=yes, "N"=no, "M"'=mixed.

C.1 Discussion of Detailed Predictions

Prediction (2) – Person-to-Person Contagion A central controversy and puzzle over cholera, going back to the earliest publications (Blane and Corbyn, 1821), was whether it was contagious (transmitted person-to-person). Airborne contagious theory produced a set of predictions that those in close proximity and sharing airspace (breathing the same air) should become sick (prediction 2a). Evidence for this set of predictions was contradictory, with some showing direct transmission person-to-person and others seeming to show no direct transmission. A major insight in Snow (1849a, 6) was that the predictions of the theory and the bearing of evidence on the theory depended crucially on *how* cholera was transmitted. For predictions of airborne inhaled cholera (prediction 2a) the evidence was conflicting, some evidence supporting and some contradicting contagion. A fecal-oral theory, where the material causing cholera is ingested, leads to an alternate set of predictions that those in close contact will transmit cholera through hand-to-mouth contact or sharing food, but *not* by sharing airspace (prediction 2b). For this set of predictions, the evidence was consistent with the prediction.

The fact that the fecal-oral theory was able to account for observations that posed a substantive puzzle for alternative theories should be viewed as the major accomplishment that it was. According to Lakatos (1980, 69) "an objective reason [to reject a research programme] is provided by a rival research programme which explains the previous success of its rival and supersedes it by a further display of heuristic power."

Prediction 4 – General Transmission by Air In the simplest case, with no auxiliary hypotheses about water as a predisposing cause or as a method of transmission, the prediction "cholera is transmitted via air" means that those sharing the same airspace should have similar mortality and illness outcomes, while those not sharing the same airspace could have different mortality outcomes. Snow recognized these predictions and provided evidence that refuted them. (The Reverend Henry Whitehead collected evidence strongly refuting the first.) Nonetheless, auxiliary hypotheses for the airborne theories served to protect them from contradiction by the evidence.

There are three pieces of evidence from the 1854 Broad Street cholera outbreak bearing on airborne transmission. The first is mortality rates that are unusually low among particular residents near the Broad Street pump. The St. James workhouse at 50 Poland Street had 535 residents but only five died of cholera. The Lion Brewery at 50 Broad Street had more than 70 workers and none died of cholera. Snow explains that both institutions had an independent water supply, residents did not drink from the Broad Street pump, and thus were not exposed to contaminated pump water (Snow, 1855, 42). But all these people were, presumably, exposed to the same air as those nearby ("The Workhouse in Poland Street is more than three-fourths surrounded by houses in which deaths from cholera occurred" (Snow, 1855, 42)); in other words the evidence contradicts the prediction that those sharing the same air will have similar mortality.

The second piece of evidence was data collected by the Reverend Whitehead, data on the number of residents of Broad Street who drank or did not drink from the pump, and then fell ill or not (Cholera Inquiry Committee, 1855, 128 ff). Importantly Whitehead collected data both for the number who drank and those who did not drink pump water, thus avoiding the survivorship bias that could arise

from only sampling those who were sick or died.[16] The data show that those who did not drink did not get sick (low mortality rate), and those who did drink got sick (high mortality rate).[17] Again, this contradicts any prediction that those breathing the same air should suffer similar mortality rates.

The third piece of evidence was the death of the widow Susannah Eley in Hampstead, far from Broad Street (Snow, 1855, 44-45). She had lived in Soho near the pump (her husband had owned the percussion-cap factory at 37 Broad Street) and her sons (the current owners) regularly sent her water from the Broad Street pump. She clearly did not share in the air of the Broad Street pump, instead breathing the (seemingly clean) air of Hampstead where few others died. She consumed water from the Broad Street pump, as did her niece, and both died. This contradicts the prediction that those breathing different air should suffer different mortality outcomes, and corroborates that those drinking the same water should suffer similar mortality.

Stating the prediction and evidence in this detail clarifies how and why this is valuable for separating the alternative theories – a value sometimes not fully recognized. Evidence contradicted the simple airborne predictions (with water not a predisposing cause). Nonetheless the refutation did little to convince those skeptical of Snow's theory. After 1849 water was incorporated as both a predisposing cause, and a potential vehicle for transmission. As a predisposing cause, it could be that contaminated air would only cause disease in those also exposed to contaminated water. And as a vehicle for transporting (possibly dissolved) airborne cholera poison, it could cause disease in someone exposed to clean air but drinking contaminated water. This is, in fact, exactly the justification used by the *Committee for Scientific Inquiries* in defending airborne theories:

> [the case of the widow] might easily be admitted, without its therefrom resulting that infection depended on the specific material alleged [fecal matter or *choleraic excrements*]. The water was undeniably impure with organic contamination; and ... if, at the times of epidemic invasion there was operating in the air some influence which converts putrefiable impurities into a specific poison, the water of the locality ... would probably be liable to similar poisonous conversion. Thus, if the Broad Street pump did actually become a source of disease to persons dwelling at a distance ... this ... may have arisen, not in its containing choleraic excrements, but simply in the fact of its impure waters having participated in the atmospheric infection of the district.

These auxiliary hypotheses meant that breathing the same air or not no longer determined mortality outcomes – water was now a causal factor. These auxiliary hypotheses were not themselves irrational, but they did serve to protect the airborne theory from refutation by the evidence that mortality was not associated with breathing air.

Although the airborne theory is protected from refutation by these particular pieces of evidence, it does not relieve advocates of the airborne theory of responsibility for both explaining why the airborne theory is a better explanation than the fecal-oral theory, and producing *positive* evidence

[16] As highlighted, for example, by Johnson (2007, 173, 175)

[17] See Coleman (2018, 23 ff) for a discussion of the underlying data and the presentation as a modern contingency table analysis. The probability that not drinking vs drinking and healthy vs sick are statistically independent is exceedingly small – the p-value for a Fisher exact test is far less that 0.01%

of airborne transmission instead of simply avoiding contradiction by contrary evidence. On both counts the airborne theory falls short. As Snow (1849a, 6) states, there is no a priori reason to conclude that airborne must be the mode of communication, and ingestion of contaminated fecal matter provides a direct explanation for the observations of *both* person-to-person transmission *and* these instances of non-airborne transmission. Further, we know of no evidence produced during the 1850s that demonstrated airborne transmission directly. In other words, even though this evidence was prevented from directly refuting the airborne theories, it does argue against airborne theories.

5b – Water is Causal As already discussed, all theories predicted that water is a causal factor for cholera mortality; evidence may have been important for other reasons (determining public health policies to mitigate cholera in particular and limited circumstances, for example) but were not definitive for separating between theories.

5c-f – Other Factors Than Water as Causal The fecal-oral theory predicted that, particularly in a municipal outbreak such as South London in 1854, factors other than water would have no or only minimal influence. Airborne theories predicted many other predisposing conditions – overcrowding and poor ventilation, poverty and unhealthy living conditions, dampness and filth – would all contribute substantially to mortality. Failure to find any influence of any other factors apart from water would be a corroboration of the fecal-oral theory and contradiction of alternative airborne theories.

Snow's nascent difference-in-differences and randomized comparison (Snow, 1855, 89 and Table IX) and more definitively Simon's re-analysis with population data by supplier (Simon, 1856, 6-7) was evidence that water was causal. But none of these addressed or ruled out the possibility that other factors also contributed to cholera mortality. Comparison between clean and dirty water for a mixed (quasi-randomized) population would average out effects of, say, overcrowding, and provide estimates of a water effect purged of confounding by crowding. But this does *not* rule out crowding as a separate causal factor, it simply rules out that an association between water and crowding causes a spurious association between water and mortality.[18]

Snow may have recognized this, but in any case in Snow (1856b) he turned from trying to demonstrate water as *a* factor to water as the *primary* factor, attempting to "prove the overwhelming influence which the nature of the water supply exerted over the mortality" (Snow, 1856b, 248). He did so by a useful and ingenious idea. South London consisted of some 30 subdistricts, with varying proportions of the population supplied by the Southwark & Vauxhall Company (contaminated water) versus the Lambeth Company (clean water). He assumed mortality for S&V customers was constant across the whole region, and the same for Lambeth customers. He then predicted mortality in each subdistrict based solely on the proportion of customers by company, under the hypothesis that only water (no other factors) mattered, and compared the predicted versus actual mortality (Snow, 1856b, Table VI). At this point, however, Snow was hamstrung by the lack of statistical and quantitative tools available in 1856. He states "it will be observed that the calculated mortality bears a very close relation to the real mortality in each subdistrict ... and proves the overwhelming influence which the

[18]Coleman (2020) discusses the Snow's use of the South London municipal outbreak of 1854 and issues of randomization and determining water as *a* causal factor versus the *primary* causal factor.

nature of the water supply exerted over the mortality, overbearing every other circumstance which could be expected to affect the progress of the epidemic" (Snow, 1856b, 248).

Snow's argument is correct but weak, relying as it does on comparing two sets of 30 mortality rates by eye. Today we can use regression analysis and apply formal measures for the goodness of fit and testing for the significance of other factors and confirm that Snow's claim is correct (see Coleman, 2020). Considering this question within a Neyman-Rubin causal effects framework (as discussed in the next section) allows us to say with confidence that water is causal but other factors are not, i.e. to corroborate Snow's fecal-oral theory and refute the alternatives. Even with a definitive result for this single prediction, however, it would be reasonable to argue that the alternatives do not need to be abandoned. The analysis here is limited to South London, and possibly there is not the necessary variation in alternative factors. For example, it would be possible that an experiment comparing a relatively low-lying area near the Thames (South London) with a higher-elevation area further from the Thames (Hampstead) would produce a different result. The fact that a single negative result rarely leads to abandonment of a theory echos Lakatos's contention that "[o]ne of the most important points one learns from studying research programmes is that relatively few experiments are really important" (Lakatos, 1980, 65). Consideration of the range of predictions and multiple strands of evidence is required for any firm conclusion in sorting between theories.

Predictions 8 & 9 – Epidemic Curve (Timing) for Neighborhood & Municipal Outbreaks The fecal-oral theory predicts the time-pattern of outbreaks. For neighborhood outbreaks due to contamination of a point source such as the Broad Street pump, the outbreak will be explosive: "In the cases in which the cholera poison gains access to a limited supply of drinking water, such as a tank or pump-well, the outbreak it occasions is always sudden, violent, and limited" (Snow, 1856b, 250). For municipal outbreaks the outbreak will be more moderate: "when a river is the medium of the propagation of the disease, its progress is more gradual and extended" (Snow, 1856b, 250). But a municipal outbreak will also show important variation in the relative mortality of those supplied with contaminated versus clear water. Early in the outbreak, when most cases are from exposure to the contaminated municipal source, the mortality will be much higher for those drinking contaminated water. As the outbreak progresses and normal (person-to-person and within-household) propagation increases, the relative mortality will fall (but never one-to-one): "In the beginning of the epidemic the cases appear to have been almost altogether produced through the agency of the Thames water obtained amongst the sewers and the small number of cases; occurring in houses not so supplied, might be accounted for by the fact of persons not keeping always at home and taking all their meals in the houses in which they live but as the epidemic advanced it would necessarily spread amongst the customers of the Lambeth Company, as in parts of London where the water was not in fault, by all the usual means of its communication" (Snow, 1855, 82).

Airborne theories will not predict these patterns, and therefore these predictions provide a good means of separating between the alternatives.

The evidence for explosive neighborhood outbreaks is in the form of case studies (rather than statistical) but is pretty clear. Broad Street, Albion Terrace, Horsleydown are all instances of point-source neighborhood outbreaks. The fecal-oral theory has a good explanation for the pattern of those outbreaks: sudden onset and explosive growth in mortality from an otherwise low background rate.

Airborne theories do not.

Regarding the time pattern for municipal propagation, Snow argued that the influence of the water supply should be highest at the start of an outbreak – the ratio of mortality for those supplied by contaminated versus clean water highest at the beginning. As the outbreak progressed the disparity would diminish: "as the epidemic advanced [cholera] would necessarily spread amongst the customers of the Lambeth Company [those with clean water] ... by all the usual means of its communication" Snow (1855, 82). Snow presented evidence for this (Snow, 1855, 80, 86-88) but most clearly in Snow (1856b, 243-245):

> the influence of the water supply was found to diminish in relative intensity as the epidemic progressed. In the first four weeks ... the disease was between thirteen and fourteen times as fatal to the population having the impure water [supplied by the Southwark and Vauxhall Company] as to that having the improved supply [the Lambeth Company]. ... In the next three weeks ... the mortality [rate] was ... nearly eight times as great in that supplied by the Southwark and Vauxhall Company as in that supplied by the Lambeth Company. During the last ten weeks ... the mortality [rate] was still more than five times as great amongst the population supplied by the former company as amongst that supplied by the latter.

Snow repeated these observations in Snow (1856a, 1857).[19]

Predictions about the time pattern or epidemic curve for mortality rates, for both neighborhood and municipal outbreaks, are unique to the fecal-oral theory – airborne theories make no such predictions. The prediction and the evidence supporting the prediction are a strong corroboration of the fecal-oral theory and strong contradiction of airborne theories.

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[19]Using modern statistical tools the observations on the time pattern of mortality rates can be reproduced and strengthened – see Coleman (2020).

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