Austin Bradford Hill (1897-1991) [1]

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During the twentieth century, Austin Bradford Hill researched diseases and their causes in England and developed the Bradford Hill criteria, which comprise the minimal requirements that must be met for a causal relationship to be established between a factor and a disease. Hill also suggested that researchers should randomize clinical trials to evaluate the effects of a drug or treatment by monitoring large groups of people. In addition, Hill advocated for case-control studies, in which researchers compare a group of people with a medical condition to a group without that condition to investigate the condition's possible causes. Hill's own work with clinical trials and case-control studies helped him prove that smoking caused lung cancer. The Bradford Hill criteria have also been used to establish causal links between factors and cancer, including reproductive cancers such as human papillomavirus that causes cervical cancer.

Hill was born on 8 July 1897 as the third of six children to Janet Alexander and Leonard Erskine Hill in London, England. Hill's father worked as a professor of physiology at the London Hospital [3] Medical College in London, England. The previous four generations of the Hill family featured at least one member noted in the *Oxford Dictionary of National Biography*, an ongoing collection of notable figures in British history. Hill's father also received the title of Fellow of the Royal Society for his research on the circulation of blood in the brain.

In 1902, Hill's family moved to Loughton, England, a town in the countryside. From 1908 to 1916, Hill attended Chigwell School in Chigwell, England, where he also participated in different sports including cricket, soccer, and track. A close colleague of Hill's and later research partner, Richard Doll, noted that though Hill did well in sports, he did not excel in his school work, which covered English, mathematics, Latin, and Greek. During his final year of school, on a visit to a friend's school, Hill crashed a British military plane onto a cricket field. After graduating from Chigwell School and despite his previous flying accident, Hill joined the air arm of the British navy, the Royal Naval Air Service, to serve during World War I [4].

Once he completed his pilot training, during which he crashed another plane, Hill served first on the northeast coast of England patrolling for German submarines, and then in Greece to support an attack on a strait in Turkey. In 1917, Hill caught tuberculosis, a bacterial infection that primarily affects the lungs. He coughed up blood and suffered from fever, chest pain, and fatigue. The Royal Naval Air Service dismissed Hill in November of 1917 so he could die of tuberculosis away from the war, but after nine months at home, Hill recovered. He underwent the most common treatment for tuberculosis at the time, which consisted of collapsing one lung to allow it to rest and then alternating that procedure between the two lungs until they recovered. Because of his health, Hill could not pursue a career in medicine like his father, nor could he attend the laboratory sessions required to attain a degree in science. Instead, Hill pursued an economics degree as a correspondence student at the University of London in London, England, meaning that he studied at home and corresponded with instructors. He graduated with a Bachelor of Science degree in economics in 1922.

At that point, Hill shifted his focus away from economics and began to work in epidemiology, the study of the distribution and causes of disease. With help from Major Greenwood, an established epidemiologist and medical officer in charge of statistics at the Ministry of Health in the United Kingdom, Hill applied for a grant from the Medical Research Council [5]. The Council funded and coordinated medical research in England, and Hill obtained funding to study mortality rates of a specific age group in the countryside. During his investigation, Hill attended a statistics course at University College London [6] in London, England, that introduced him to many of the concepts in epidemiology. Hill worked for the Medical Research Council for ten years, researching diseases that arose in certain occupations. In one of his cases in 1930, he investigated respiratory diseases common among workers in cotton spinning mills. He found that poor conditions in the mills twenty years prior caused the development of respiratory diseases in the workers in 1930.

In 1933, Hill left his position at the Medical Research Council [5] to join Greenwood at the London School of Hygiene and Tropical Medicine in London, England, where he taught epidemiology and statistics. Hill taught statistics to medical students and postgraduates, and in 1937, published his lectures in the English medical journal *The Lancet* and then as a book titled *Principles of Medical Statistics*. In his publications Hill used plain language to convey information and used equations and symbols sparingly. That method proved effective enough that within ten years, Hill's book underwent three reprints and an expansion, followed by translations into several languages. By the 1990s, Bradford Hill's *Principles of Medical Statistics* was in its twelfth edition. When World War II began in 1939, the English government assigned Hill to the Research and Experimental Department of the Ministry of Home Security, and later the Medical Directorate of the Royal Air Force, both in the United Kingdom. After the war, Hill remained an honorary civilian consultant in medical statistics for the Royal Air Force until 1978.

Once the war ended, Hill returned to his own research and began to focus on implementing randomization in controlled trials. Hill's randomization method included randomly assigning patients to receive either the new treatment, or the old treatment, or nothing at all. Hill's style of research based conclusions off of unmistakable events such as death, used unbiased judges with no stake in the research when evaluating subjective measurements, and masked which patient received a particular treatment from doctors and patients alike. Those standards in clinical trials helped researchers avoid bias in their results, and identify variation in their results due to differences among patients. In 1945, Hill became the chair of medical statistics at the London School of Hygiene and Tropical Medicine and the honorary director of the Medical Research Council's statistics research unit. A year later in 1946, Hill persuaded a group of researchers to use his randomization techniques in their trial. That trial investigated the effectiveness of a vaccine for whooping cough, or pertussis, a bacterial infection that causes cold-like symptoms followed by a prolonged cough with a distinctive whooping sound. He also convinced researchers conducting a clinical trial studying a treatment for pulmonary tuberculosis to use his randomized method.

In 1951, the Medical Research Council [5] asked Hill to investigate the increase in the number of deaths due to lung cancer in England. Assisted by his colleague and old college friend Doll, Hill designed one of the earliest formal case-control studies. A case-control study allows researchers to compare a group of people with a medical condition to a group without that condition to investigate the condition's possible causes. In their study, Hill and Doll selected participants who already had lung cancer and interviewed them to see if they had something in common that could have caused their cancer. For the second group in the study, Hill and Doll interviewed participants with stomach and bowel cancer as well as patients with no cancer, which allowed them to identify the causes of lung cancer specifically. After conducting the study, Hill came to the conclusion that smoking was the most likely explanation for the participants' lung cancer. According to Doll, however, the medical community was skeptical of Hill's conclusion.

To ensure the validity of the relationship between smoking and lung cancer, Hill conducted another study with Doll in 1964. Their 1964 study focused on doctors who smoked or who had previously smoked because they were easily tracked through a national registry. The study followed the participants for twelve years and found high rates of lung cancer. Based off of that finding and other supporting evidence, Hill and Doll more conclusively deemed smoking a prominent cause of lung cancer.

Continuing his work with establishing causes of diseases, Hill gave an address to the Royal Society of Medicine in 1965 that outlined the Bradford Hill criteria, a group of nine conditions used to determine whether a causal relationship exists between two variables. Some of the criteria include the strength of the relationship between two variables, the consistency of observing that relationship, and how likely it is that those two variables biologically relate to each other.

After Hill presented his criteria, researchers used them in their analyses on the causes of cervical cancer as well as on the exposure to human papilloma virus, and on the causes of cardiovascular disease as measured by levels of certain molecules in the blood. The transcription of the address has been cited over six thousand times.

Hill earned many distinctions over the course of his career. He won five medals from various societies, including the Royal Statistical Society in 1953 and the Royal Institute of Public Health & Hygiene in 1961. In 1962, the Royal Society of Medicine named him an honorary fellow, as did the Royal College of Physicians in 1963.

Hill retired in 1961 and lessened his involvement in research to care for his wife, who had developed Alzheimer's disease. They lived in their home in Little Kingshill, England, until her death in 1980, at which point Hill moved in with his married daughter. Hill suffered from inadequate supply of blood to his organs, resulting in a weak left leg and eventually his placement in a nursing home, where he died on 18 April 1991.

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