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THE THERAPEUTIC CONSEQUENCES OF THE WAR: WORLD WAR II AND THE 20TH-CENTURY EXPANSION OF BIOMEDICINE

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The Therapeutic Consequences of the War: World War II and the 20th-Century Expansion of Biomedicine

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ABSTRACT

During World War II, the U.S. Committee on Medical Research (CMR) undertook an integrated, cross-sectoral effort to develop medical science and technology for war, representing the U.S. government's first substantial investment in medical research. Using data on all CMR research contracts, we show that although it had mixed results during the war, it left a large imprint on the postwar U.S. biomedical innovation system. Research areas it supported experienced rapid growth in postwar science, especially in new subjects. It also stimulated the U.S. pharmaceutical industry's adoption of modern science-based drug discovery, fueled new postwar drug development, influenced medical practice, and shaped extramural research funding at the National Institutes of Health. Contemporary accounts of individual CMR programs point to specific ways these investments enabled old and new subjects to grow. The evidence documents the long-run effects coordinated, application-oriented biomedical research can have on science and technology and challenges the influential 'linear model' paradigm in research policy.

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1 Introduction

Improvements in human health rank among the most transformative developments of the twentieth century: Nordhaus (2003) estimates that the 30-year increase in U.S. life expectancy over the century was as valuable as measured economic growth in all other sectors combined. Although the reasons for these gains have been debated, a crucial contributor is widely thought to be advances in medical science, technology, and knowledge (e.g., Murphy and Topel 2003, Cutler and Kadiyala 2003, Cutler et al. 2006). The high social returns to medical research, coupled with difficulties in appropriating returns from private investments (Garber and Romer 1996), have prompted significant government funding for biomedical research worldwide.

For the past 75 years, biomedical research policy in the U.S. has primarily supported investigator-initiated scientific research (Azoulay and Li 2022), without imposing specific research priorities or playing a large role in how research is done, and without a commensurate emphasis on transitioning the science it funds into technology or practice, which is mainly left to the private sector.[1] Despite this, for decades there have been recurring calls for more "top-down" targeting of research toward development of specific technologies or in support of specific health objectives (e.g., Cook-Deegan 1996, Sampat 2012) and for broadening the scope of biomedical R&D policy to other stages of the R&D pipeline (Branscomb 1992, Nelson 1997)—from debates around the War on Cancer in the 1970s to the aftermath of Operation Warp Speed in the Covid-19 pandemic.[2] Although interest in applied or mission-oriented R&D policies with these features is growing (Mazzucato 2018, 2021, Azoulay et al. 2019a), there is limited evidence on what effects such a dramatically different approach might have and why (Bloom et al. 2019, Azoulay and Li 2022).

In this paper, we study the impact of the World War II medical research effort on the biomedical innovation system. Driven by military demand, between 1941 and 1945 the U.S. Office of Scientific Research and Development (OSRD) Committee on Medical Research (CMR) directed and funded a major effort to develop medical science and technology for war, including on problems as diverse as large-scale production of penicillin; antimalarials; vaccines; steroids; human hardships such as sleep and oxygen deprivation, freezing temperatures, nutrient deficiencies, and psychological stress; new methods of treating fractures, burns, and wounds; and many other techniques and therapies that helped win the war, while also guiding university-industry collaborations in the production of

[1] These choices reflect specific presumptions first articulated in Vannevar Bush's seminal report *Science, The Endless Frontier* (Bush 1945)—which has sometimes been described as a "blueprint" for postwar research policy (Mowery 1997)—including that basic research is particularly prone to market failures and thus most in need of public support, that practicing scientists know better than bureaucrats what research is worth pursuing, and that it is important to encourage a broad range of work because research has hard-to-predict benefits.

[2] The success of the similarly problem-oriented model of Operation Warp Speed in the Covid-19 pandemic has drawn substantial interest in whether it can be redeployed for other diseases (Gross and Sampat 2022, D'Souza et al. 2024). Independently, the recent creation of the U.S. Advanced Research Projects Agency for Health (ARPA-H) is also an explicit step towards increasing targeted medical research investments.

new drugs and devices—all for the cost of about four hours of World War II military operations. Despite its relatively low cost, CMR's scale was unprecedented for its time, and marked both the U.S. government's first extramural investment in biomedical research and one of its few pursuits (ever) of an actively-managed biomedical research policy—one which its leaders later described as a "novel experiment in American medicine," noting that "planned and coordinated medical research had never been essayed on such a scale" (Keefer 1969, p. 62).

Though most remembered for specific successes like penicillin, CMR's overall track record during the war was mixed. However, using newly-collected archival data on the universe of CMR research contracts, we show that it triggered a large postwar expansion of scientific research and drug development in the subjects it supported, with effects persisting into the 1960s and in some cases longer. CMR's impacts on biomedical science are especially pronounced in fields that were dormant or unexplored pre-1940 but which became a focal point of the war effort. Firms engaged in CMR-coordinated drug development projects, meanwhile, subsequently entered a two-decade period of prolific drug innovation, which was increasingly characterized by systematic approaches to drug discovery and closer links to science. Concurrent with these takeoffs, CMR also provided a foundation for the NIH extramural research funding program, which absorbed CMR's portfolio and several of its procedures after it was demobilized. With science, the pharmaceutical industry, and NIH forming the three pillars of the modern U.S. biomedical innovation system, World War II is now recognizable as a historical turning point that set in motion institutional development and growth in the postwar era which has continued to the present day.

Our first set of analyses examines science. To do so, we collect data on the universe of biomedical research publications between 1930 and 1970 and map both these and CMR contracts to Medical Subject Headings (the National Library of Medicine's controlled vocabulary for indexing research in the life sciences), as a measure of research space. Comparing the long-run growth trajectories of research subjects that were targets of CMR investment against those that were not, we find evidence of both continuity and change: less-developed (pre-1940) subjects that were a focus of CMR research (such as antibiotics or steroids) grew substantially during and after the war, while more established subjects which CMR supported continued their pre-1940 growth trajectory—in part through recombination with new subjects, as new subjects were integrated into old ones, such as the use of penicillin in treating specific infectious diseases—before tapering. Using journal-based proxies for basic and applied (clinical) publications, we also find that despite CMR's applied focus, its effects on basic research were large, and using the structure of the MeSH vocabulary, we show that CMR's spillovers across research space were substantial.

CMR's focus also engaged a number of firms in the chemical and pharmaceutical sectors to solve military medical problems. Our second set of analyses examines its impacts on the postwar phar-

maceutical industry. Using a list of new drugs introduced to the U.S. market between 1940 (when new drugs were first subjected to safety requirements and FDA review) and 1975, we show that drug categories where CMR was active yielded significantly more new drugs in the 1950s and 1960s, often on the back of new discoveries, capabilities, and technology platforms the war effort generated. There were also effects at the firm-level: CMR-contracted firms grew increasingly science-intensive, as measured by the frequency with which drug-related patents referenced academic science. Though scholars have previously linked CMR to the postwar antibiotic revolution (e.g., Bud 2007), the evidence in this paper points to its broader impact in modernizing the U.S. pharmaceutical industry (which prior to the war was heavily driven by trial-and-error empiricism rather than science) and shaping what is now recognized as a "golden age" for drug discovery.

Our third set of analyses examines the diffusion of CMR-funded research into medical training and practice. To do so, we draw on a leading medical textbook (Cecil's *Textbook of Medicine*) and popular clinical reference manual (the *Merck Manual of Diagnosis and Therapy*), motivated by research showing that textbooks were until recently a main source of information for clinicians (Catillon 2017) which "reflect the level of knowledge of the average medical practitioner and [can be used as] a consistent sampling device for measuring changing practice patterns" due to their regular revisions (Greene 2007, p. 294). Using successive editions of these texts spanning the pre- and postwar periods, we show that CMR-funded subjects were more likely to be added to postwar editions of these textbooks—reflecting the practical value of new medical knowledge which emerged from the war. Notably, these results show up with a several-year lag, reflecting the time it takes for new information to standardize and diffuse into practice.

Though CMR's impacts were broad and long-lasting, given that the war was short-lived a remaining question is why. Contemporary and historical accounts help shed light on this question while also pointing to a broader structural change. The historical evidence essentially reduces to one common theme: the creation of new R&D assets which firms and researchers continued using or building on after the war ended. In most cases, these fall into six categories: new research tools and techniques, new therapies and therapeutic candidates, new technology platforms, new research capabilities, new collaborations, and new fundamental knowledge produced in the course of efforts to address World War II medical problems. The breadth of new R&D assets CMR cultivated in turn appears to be a product of its use-orientation and integrative approach: solving urgent military medical problems required not only new technology, but also new understanding, equipment, and capabilities, and tighter links between science, technology, and manufacturing.

The paper's first contribution is in systematically evaluating the emergence of the modern U.S. biomedical innovation system and its links to the World War II research effort. As Figure 1 shows, the war marked a turning point in biomedicine visible in both publications and patents, which were

stagnant prior to 1945 but subsequently grew rapidly—bolstered by new discoveries in molecular biology, the growth of science-based drug discovery, and more. Though we do not argue this growth should be fully attributed to CMR alone, we show it left an indelible imprint on essentially every pillar of this system: investments made during the war enabled 20th century biomedical science to expand in new directions, modernized the U.S. pharmaceutical industry, triggered a golden era in drug discovery, and laid the foundation for the modern NIH.

[Figure 1 about here]

These results also add to the literature studying the effects of biomedical research funding. Though the NIH has been the subject of most previous empirical studies assessing the returns to medical research, its emphasis on funding undirected, investigator-initiated science at universities is specific and distinct from CMR's integrated research model in World War II, which set application-oriented priorities, coordinated the activity it funded, spanned sectors and disciplines, and linked science to technology, manufacturing, and diffusion—functions which modern innovation policy typically leaves to the private sector. This degree of integration across the R&D value chain is uncommon in scientific research today, but the evidence in this paper suggests these activities can be synergistic, raising questions of whether use-oriented science (Stokes 1997) may benefit from more connectivity and downstream collaboration, or possibly even vertical integration.

In addition to exemplifying a different kind of support, CMR was also a different type of shock: whereas NIH evolves incrementally, leading to causal analysis in this literature typically harnessing idiosyncratic variation in funding rules or comparing just-funded to just-unfunded grant applications (e.g., Jacob and Lefgren 2011, Li et al. 2017, Azoulay et al. 2019b), CMR was a larger, and broader, shock to the U.S. biomedical research system, with the potential for systemic effects. Crucially, the passage of time also allows us to evaluate long-run effects, and demonstrate lasting impacts of what was otherwise ostensibly a temporary intervention.

Beyond adding to our understanding of the origins of the U.S. biomedical innovation system and returns to medical research funding, the results provide broader insights on the economics of science and innovation. A large and interdisciplinary scholarship on innovation, and a significant share of innovation policy (including much of NIH), has developed around a "linear" view of innovation in which science flows downstream to technology, production, and implementation (e.g., Godin 2006, Balconi et al. 2010)—as reflected in a voluminous literature examining the impact of science on technology (see Rosenberg 1974 or Brooks 1994 for commentary), efforts to measure direct linkages from science to technology (e.g., Marx and Fuegi 2020, Bryan et al. 2020), and policies designed to encourage commercialization of university science (Mowery et al. 2001, 2004). With its integrative approach, CMR does not fit neatly into this model, and our evidence is a reminder that directionality

sometimes runs in reverse, as new lines of inquiry emerge from applications.[3] World War II medical research offers numerous examples of fundamental questions or knowledge that arose in the course of applied research, many of which we discuss in the paper and document in the appendix. This may be especially likely in a crisis like World War II if demand for technological solutions runs ahead of the science, or more generally when applied R&D runs into gaps in fundamental understanding, but it can just as well apply in other contexts (Balconi et al. 2010).

We proceed as follows. Section 2 provides institutional background, including on the importance of medicine in warfare, CMR and the World War II medical research effort, and CMR's influence on postwar research policy. Section 3 introduces our data and characterizes the CMR shock. Section 4 evaluates CMR's effects on postwar biomedical science; Section 5, on pharmaceutical innovation; and Section 6, on medical practice. Section 7 explores why CMR had such long-lived effects and what we can learn from it about the economics of science and science policy. Section 8 considers extensions and remaining questions and concludes.

2 World War II and Biomedicine

2.1 Military medicine: The battle against disease

Although nearly 70 countries participated in World War II, the U.S. military's greatest adversary was arguably disease: for most of history, infectious disease has killed more soldiers than battlefield wounds and incapacitated an even greater number (Hoyt 2006).[4] World War II also introduced a wider range of medical problems than the U.S. military had previously encountered—not only new diseases, but also new environmental conditions and traumatic injuries. In the early 1940s, there was thus an urgent need for knowledge and technologies that could address medical problems Allied soldiers faced, including prevention and treatment of bacterial and viral infections, malaria, wound and shock treatment, blood substitutes, mental health, and issues relating to aviation physiology, motion sickness, temperature, and nutrition, among many others.

When World War II began, there was no obvious office in the U.S. federal government to assign to this charge. Though the National Institute of Health was created in 1930, and with the addition of the National Cancer Institute became the National Institute*s* of Health (NIH) in 1937, it was small and had no serious extramural research funding capacity of the type that the war required. Private foundations had previously funded medical research through grants to individual researchers, but

[3] As Robert Sproull, a physicist and former DARPA Director, once observed while discussing DARPA's research portfolio, "In science, quite frequently, it happens that you're working on an applied problem and you suddenly discover that buried in it is a really very fundamental problem" (Sproull 2006).

[4] See Appendix A for further discussion. Appendix Table A.1 compares mortality from disease and injury in prior eight prior conflicts, based on reporting from the U.S. Army's Medical Department.

these too were insufficient for the demands the war presented, due to their relatively small scale and their focus on fundamental research rather than applications.

In 1941, the U.S. goverment's Committee on Medical Research (CMR) was created as a subsidiary to the Office of Scientific Research and Development (OSRD)—an agency established to coordinate and fund civilian R&D for war—to fill this void. For its time, this was an unprecedented move: before 1940, there was very little federal funding of research outside of agriculture, nor precedent or mechanism for funding extramural research. In the executive order creating OSRD, CMR was to support "the mobilization of medical and scientific personnel of the Nation" and advise and oversee contracts "with universities, hospitals, and other agencies conducting medical research activities ... related to the national defense" (Andrus 1948, p. xlii).

The R&D-funding apparatus that CMR ultimately developed to fulfill this charge was broad and multifaceted. General research priorities were determined in partnership with the military, which brought military medical problems to its attention. CMR then shared these priorities and solicited proposals from researchers widely, including from university scientists, firms, hospitals, and independent research institutes. Rather than reviewing these proposals directly, CMR forwarded proposals to the National Research Council's (NRC) Division of Medical Sciences (DMS), where over thirty committees—comprised of hundreds of elite medical researchers and officers from the Army and Navy—provided peer evaluations, in an early use of peer review. Based on these reviews, DMS gave each application a letter grade and returned a recommendation for funding, which CMR typically followed. Once funded, CMR provided active project management, including organizing meetings of investigators to promote information flows, collecting and circulating progress reports, and supplementing or terminating projects as their results, and CMR's priorities, evolved. For research directed at new treatments for diseases, CMR was also active in development, evaluation, and implementation, with many of its contracts supporting experimental interventions and/or clinical trials. Like OSRD in general, it was primarily a "results-oriented" program, and prioritized relevance and speed over fundamental, scientific value.

Beyond funding: coordination and brokerage

Beyond funding, CMR played an important role in creating connective tissue in the nascent U.S. biomedical innovation system. This connective role was particularly pronounced in specific projects, such as in the effort to mass produce penicillin. At the beginning of the war, the technology did not exist to produce enough penicillin to treat a single patient, let alone for clinical testing—yet by the end of the war, there was enough for all Allied troops and civilian use (Keefer 1969). Early in the war, CMR reportedly was crucial in persuading private firms to get involved, brokering information flows between these firms and the U.S. Department of Agriculture's Northern Regional

Research Laboratory (NRRL), organizing meetings, and refereeing conflicts among participants (Swann 1983, Neushul 1993). Once firms were able to produce enough penicillin for testing, CMR coordinated and funded clinical trials. After trials were complete, CMR worked with the Office of Production R&D of the War Production Board (WPB) to scale up production to the needed levels. The WPB provided needed material and equipment to firms, shared technical expertise, and provided some funding. WPB corresponded with 175 potential producers, and eventually worked with 20 in the program, chosen based on experience with penicillin, fermentation, and biologic production in general, as well as the quality of staff (Neushul 1993). Although CMR's primary role in the scale-up of natural penicillin was coordination and clinical testing rather than more upstream R&D funding for biochemistry or drug discovery, CMR did invest considerable research funds in a parallel synthetic penicillin development program—which, at the beginning of the war, it viewed as a more likely path to large-scale production (Swann 1983).

2.2 Results of CMR research

Between 1941 and 1945, CMR engaged researchers in roughly 570 contracts totaling around $400 million (2024 dollars). Though it comprised only 5% of OSRD's total spending, and is less than 1% of NIH's modern budget, CMR research funding was an order of magnitude larger than previous federal spending on medical research, much of it going into subjects that had not been a major focus of research prior to the war. As Stewart (1948, p. 102) describes:

> The shift in emphasis and even in direction was enormous. Many subjects of minor importance in peacetime become of controlling importance in war. Some subjects are born of war. Tropical medicine had been considered of rather academic interest to the health of the United States. Even the machine age had not adapted our younger generation to flying at 40,000 feet or diving at 400 miles an hour.

Though the performance of individual research programs it supported was mixed, CMR was successful enough during the war to impact its conduct. The mass production of penicillin is its most celebrated accomplishment: by 1944 the U.S. was able to produce enough natural penicillin to meet military demand, and so much by 1945 that it was made available for civilian use. In contrast, CMR's parallel effort to chemically synthesize penicillin—initially seen as more promising—was unsuccessful. Its research also extended to malaria. Though malaria had long been treatable with quinine, the Japanese invasion of Java and war in the South Pacific cut off supply routes. CMR's malaria program focused on finding quinine substitutes. It identified and synthesized over 14,000 compounds and tested promising candidates against animal models, in clinical trials, and on soldiers in the field (Keefer 1969). This effort struggled to find substitutes during the war, but when CMR established that an existing molecule, atarabine, could be used safely and effectively, it was adopted as the military's preferred preventative and treatment.[5]

[5]Chloroquine was also a subject of CMR research, though it came into focus too late to be useful during the war—and

There were numerous other successes and failures, most of which are detailed in Baxter (1946) and Andrus (1948). Hoyt (2006) finds that between CMR and other government agencies, wartime research helped develop new or improved vaccines for 10 of the 28 vaccine-preventable diseases identified in the 20th century. CMR had a crucial role in funding research and development on blood substitutes used to treat battlefield casualties (Creager 1999). CMR research also deepened understanding of human physiology under environmental hardships such as nutrient deficiencies, sleep or oxygen deprivation, and temperature exposure, as well as of stress disorders and mental health—all in response to wartime conditions.

The medical impacts of this work can be seen most clearly in military statistics (Appendix A). In short, World War II R&D essentially solved the military's problem of infectious disease. The ratio of U.S. military deaths from disease vs. injury fell from 1.02 in World War I to 0.07 in World War II (0.01 in the European theater). Hospital admission and death rates for many common infectious diseases—such as pneumonia, influenza, and typhoid fever—declined nearly 100% between the two conflicts. Appendix Figure A.1 extends these comparisons by plotting the time series of U.S. Army hospital admissions and death rates per capita between 1895 and 1955, which shows significant spikes in prior wars, but no such deviations in World War II.

2.3 CMR and postwar research policy

When CMR was disbanded in 1945, the Public Health Service took over its forty-odd open contracts, which became the kernel of NIH's extramural research program (Swain 1962, Fox 1987). Beyond providing a general model for using grants and contracts for funding extramural research, NIH adapted specific contracting approaches developed by CMR and OSRD during the war, including indirect cost recovery policies and elements of patent policy (Rosenzweig 1998, Sampat 2020). NIH's peer review approach was also based on CMR: "study sections" of external scientists providing initial scientific/technical review were modeled on the wartime NRC/DMS review system. In 1946, the NRC Penicillin Panel transitioned into the Syphilis Study Section, marking the inception of what has grown to encompass over 250 similar study sections within the NIH. The NIH budget has increased 1000-fold in real terms since the end of the war, and the agency is sometimes known as the "crown jewel" of the federal government (Sampat 2023).

Despite these continuities, NIH also made major and explicit departures from CMR, including by emphasizing fundamental research and providing flexibility for scientists to take their research in unplanned directions when opportunities emerged (Van Slyke 1946). In addition to this freedom of exploration, topic choice in the NIH program was also primarily investigator-initiated or "bottom up" rather than the "top down" priority setting of the wartime model. In a 1962 interview, Van

instead became a revolutionary malaria treatment in the years immediately after.

Slyke recounted that the targeting of biomedical research ("[T]hou shalt concern yourself with the making of anti-malarial. Thou shalt concern yourself with the survivor's suits.") was "justified by war time needs and exigencies" but was not the focus of the NIH.

Over time, and especially after Congressional investigations in the 1960s, NIH's original emphasis on scientific freedom eroded, with the growth of bureaucracy and reporting requirements (Sampat 2023). However, the NIH model continues to focus on "bottom up" investigator-initiated research with little of the explicit top-down project selection, active project management, and focus on application and diffusion that were core elements of the CMR model. NIH's approach has come under scrutiny, including during debates surrounding the War on Cancer in the 1970s, the Artificial Heart Program, concerns about NIH priority setting (Sampat 2012) and more recently in the initiative that led to ARPA-H (Sampat and Cook-Deegan 2021). Though nominally a mission agency, NIH (and its parent Department of Health and Human Services) also does not link up different aspects of its health mission (research, development, testing, diffusion into practice, procurement) as CMR's "integrated research model" (Hoyt 2006) did.

3 Data and Empirical Approach

To systematically examine the link between CMR and postwar biomedical innovation, we collected, transcribed, and harmonized a complete record of 590 CMR contracts (573 extramural, 17 intramural) from OSRD archival records.[6] For nearly all (588), we have a summary report that identifies the sponsoring CMR division and the research projects' subject, principal investigator(s) (PI) and other technical staff, institution(s), budget, and timing (see Appendix Figure B.1 for an example).[7] These summary reports also provide an extended abstract and list all resulting publications (e.g., journal articles, technical reports, progress updates). Collectively, this information provides the corpus we work with: titles and abstracts provide information on funded subject matter, publications on research output, and header data on the investigators and institutions involved. Through CMR records we identify 2,438 scientific publications produced by CMR-funded research, spanning a wide range of journals in medical science and related fields (e.g., public health, organic chemistry, entomology). We manually linked these publications to three external publication databases: Microsoft Academic Graph (MAG), Web of Science (WOS), and PubMed.

In parallel to information from CMR, we collect data on three categories of outcomes: science,

[6] See Appendix B for a detailed description of our data sources and data collection. We cross-validate and CMR contract and publication data against additional OSRD records, including separately-maintained CMR contract lists and publication lists (details in Appendix B). This cross-validation led to occasional minor corrections, usually attributable to minor typos in the source records. The 17 intramural contracts were entered into with other government agencies (primarily with the USDA, NIH, and FDA), which participated in a handful of CMR research programs (e.g., USDA's Bureau of Entomology in the malaria program).

[7] Extended abstracts are available for 441 (75%) of summary reports. The two contracts for which we do not have summary reports are CMR's first and last extramural contracts.

innovation, and medical practice. We measure scientific activity via research publications, which are attractive for their transparency and observability over long horizons, including both before and after the war. Our publication sample begins with the universe of publications between 1930 and 1970 in MAG. We filter this sample to the 5.5 million publications in the *Natural Sciences* and *Medical and Health Sciences* published over this period, as indicated by MAG topic labels (OECD field codes). Though other publication datasets (e.g., WOS) have been used in prior research, MAG has two main advantages over other sources: (i) it has comprehensive historical coverage dating to the late 1800s, and (ii) it is open access. MAG provides additional information about individual publications that are useful for our purposes, including titles, journals, authors, and cross-paper citation linkages, and enables us to use secondary data products produced from the MAG sample, such as patent citations to science (Marx and Fuegi 2020, 2022).

Measuring pharmaceutical innovation is harder: though drug development is often measured via FDA drug approvals, there are no electronic data on drug approvals from this era, and the FDA Orange Book begins only in 1985 (Durvasula et al. 2023). We fill this gap by locating and digitizing de Haen (1976)'s "Compilation of New Drugs, 1940-1975", which lists "new chemical entities or synthesized drugs not previously available in the United States" first marketed between 1940 and 1975 and serves as the basis for the FDA History Office's historical drug approval statistics.[8] The De Haen data document 1,010 drugs developed by 126 distinct firms over this period, along with their trademark name, generic name, and year introduced. Each drug is categorized into one of 42 therapeutic classes and over 150 subclasses, which we will use in our analyses below. In parts of the paper, we will also analyze drug-producing firms, for which we take two further steps. First, we link firms in de Haen (1976) to patent assignees and measure these firms' drug patents (which we define as those in NBER patent category 31, "Drugs"; Hall et al. 2001) and their characteristics.[9] Second, because some firms in our sample merged during the study period, we collect merger data from historical Federal Trade Commission tables (FTC 1980, covering 1947-1978) and dynamically assign firms to their contemporary parents after known mergers.

In examining the effects of wartime medical funding on science and pharmaceutical innovation, our analysis parallels previous work on the effects of NIH funding (e.g., Jacob and Lefgren 2011, Azoulay et al. 2019b, Myers 2020). Our third set of outcomes extends this line of work by studying diffusion. Though measuring the incorporation of publicly-funded research into medical practice is challenging, prior research points to medical reference books as a window into medical knowledge and practice. We focus on two series published both before and after the war: the *Cecil Textbook of Medicine* (henceforth CT), a staple textbook of medical training (Greene 2007), and the *Merck Manual of Diagnosis and Therapy* (MM), a popular clinical reference (Tomes 2021). For each of

[8] See https://www.fda.gov/about-fda/histories-product-regulation/summary-nda-approvals-receipts-1938-present.
[9] Patent data obtained from Google Patents and the Reliance on Science project (Marx and Fuegi 2020, 2022).

these book series, we digitize all editions with an index through approximately 1960 (1930 to 1959 for CT, 1940 to 1961 for MM) and compile a list of indexed subjects.

A final resource for this paper is postwar biomedical research funding. As Section 2 explains, CMR inspired and funded the creation of NIH extramural research funding, which increased sharply over the first two postwar decades. Postwar NIH funding in specific subjects may be another effect of the CMR shock. We digitize annual editions of the U.S. Public Health Service's *Research Grants and Fellowships Awarded by the National Institutes of Health* from 1948 to 1970 to collect information on all NIH grants over this period, complementing the CMR record.

3.1 Categorizing CMR contracts, publications, and other sources

We use the National Library of Medicine's (NLM) Medical Text Indexer (MTI) to map these data to a common domain: NLM's Medical Subject Headings (MeSH) vocabulary, which gives structure to biomedical research space. The MeSH vocabulary was developed as part of MEDLINE, NLM's database of biomedical journals, and consists of descriptors used to index MEDLINE articles for searching and retrieval. There were 29,915 unique MeSH descriptors ("MeSH terms") at our time of use (2021-2022).[10] MeSH has an accompanying hierarchical structure, and the underlying "MeSH space" is organized into 16 broad classes (Appendix Figure B.4 provides a list), each with subclasses, which have further subclasses, and so on.[11] For example, the "Diseases" branch (letter C) begins with Infections (C01), which in turn contains infections at various levels of specificity; each node in this tree we will refer to as a MeSH code (e.g., C01.221.250: Blood-Borne Infections). Individual MeSH terms can exist at multiple locations in the MeSH tree (e.g., "Blood" is listed under both Body Fluids and Hemic and Immune Systems)—a feature which shapes our preference for MeSH terms (which are unique) vs. codes as our unit of analysis.

MTI is a language processing tool that maps input text to MeSH terms and is used by NLM to provide initial indexing of MEDLINE articles based on titles and abstracts. It can also be used to categorize arbitrary biomedical text (NLM 2022). It does so in several ways, including (i) taking the words in provided text and finding similar concepts in NLM's UMLS Metathesaurus, then finding the closest MeSH headings, and (ii) by finding similar PubMed articles and extracting their MeSH terms (Mork et al. 2013). It also returns scores indicating confidence in each match. Prior research has used MTI in other applications, including to measure the breadth of scientific articles (Kolev et al. 2020) or determine the gender focus of patents (Koning et al. 2021). Here we use it to identify the subjects of contracts and grants, publications, and medical texts.

[10] The MeSH vocabulary is continuously revised and updated as new terms appear in the scientific literature.

[11] The MeSH tree is conceptually similar to hierarchical patent classification schemes such as the Cooperative Patent Classification (CPC), with top-level (lettered) MeSH codes conceptually analogous to top-level CPC sections, three-character MeSH codes (e.g., A01) analogous to CPC classes, and so on.

In practice, MTI requires choices over what input text to use, how to map text to terms, how to use confidence scores, and how to aggregate up to MeSH subjects or subject-years. Where possible, we use all available text: we index MAG publications on their titles, CMR contracts on their titles and abstracts, NIH grants on their titles, and medical textbooks on index entries. In using these data, we normalize the returned MeSH term confidence scores for each publication to sum to one, and drop all terms with a score below 10% to reduce noise.[12] Our analysis will at times make use of score-weighted totals at the MeSH term or term-year level, and at times binary indicators (e.g., of whether a given MeSH Term was a focus of CMR research). In addition to counting publications by MeSH term, we also measure co-occurring MeSH terms in publications as a proxy for recombinant science—especially focusing on the emergence of novel combinations.

For drugs we take a different approach, partly because we have less raw text to feed into MTI, and our preliminary probes indicated that MTI does not reliably return descriptors from drug names, active ingredients, or even drug categories as inputs. We instead create a manual crosswalk between de Haen (1976) drug categories and 12-digit MeSH codes on the *pharmacologic action* branch of the tree. We can then perform analysis at the level of these codes or their associated descriptors. The process we apply is also discussed in more detail in Appendix B.

3.2 Characteristics of the CMR shock

Table 1 describes the shape of CMR's research investment, showing the distribution of contracts, contractors, and research funding across CMR divisions. Two patterns stand out: one is the (relatively) even distribution of contracts and funding across divisions and the myriad problems they were solving. The other is the shockingly low total cost of the program, at roughly $21 million in the 1940s—equivalent to $400 million in 2024, or less than 1% of the current NIH research budget). The table also contextualizes CMR research in MeSH space, documenting the most common MeSH terms in each division: *Syphilis* (Medicine), *Burns* (Surgery), *Oxygen* (Aviation Medicine), *Shock* (Physiology), *DDT* (Chemistry), and *Antimalarials* (Malaria). The most common MeSH term across the CMR portfolio is *Penicillins*. Figure 2 extends the last row of this table, showing the top 10 MeSH terms for each of these divisions, by term share of division contracts. The results reveal a fuller list of focal subjects of CMR research, while also providing a check on the face validity of the MTI approach to categorizing contracts and publications.

[Table 1 and Figure 2 about here]

The raw data suggest that despite the specificity of the wartime problems CMR targeted, research it funded may have been more broadly impactful. One such indication is visible in publication

[12] We also drop check tags (MeSH descriptors that specify species, sex, or age, such as "Humans"), and supplementary concepts (terms outside of the MeSH thesaurus, many of which are chemical formulae).

counts alone. Table 2 lists the top five MeSH terms entering the publication record (based on titles in the complete MAG corpus) each year between 1939 and 1946. For each term, we also report the number of associated publications over the next 10 years and indicate whether the subject was a focus of CMR research. The final row of each panel shows averages for lower-ranked new subjects for comparison. Treatments and therapies that CMR cultivated were immensely more likely to be the most heavily studied new subjects of this period. Despite that CMR cost of only a few hundred million dollars (in 2024 dollars) and produced only around 2,500 scientific publications (out of roughly 280,000 published between 1939 and 1946), nearly half of the eventual top research subjects from this era were introduced or supported by CMR.

[Table 2 about here]

Other evidence comes from comparing CMR-funded research to contemporary work in the same subjects. In Table 3 we estimate differences in the characteristics of CMR and non-CMR publications, conditional on subject-year fixed effects.[13] We do so on three dimensions: novelty, breadth, and impact—measured by the introduction of a new MeSH term combination, the number of associated subjects, and forward citations, respectively. Column (1) reveals that CMR-funded publications are significantly more likely to introduce new combinations, with the difference a precisely estimated 25% increase on the mean rate. Columns (2) to (4) show that CMR-funded publications were also significantly broader, and a handful of its publications (e.g., surveys of antibiotics or malaria) were among the broadest of this era. Columns (5) to (8) show that CMR publications were also heavily cited, roughly twice as likely to be in the top 10% of cited articles in their year and nearly quadruple as likely to be in the top 1%, with relatively tight standard errors.

[Table 3 about here]

4 Effects on Biomedical Science

Our analysis begins by examining the impacts of CMR on science, where a closer look at a few examples can motivate our approach. As we discussed in Section 2, wartime medical research had several major thrusts, including research efforts in developing antibiotics, antimalarials, synthetic hormones, and vaccines, as well as developing new techniques and understanding for blood, blood preservation, and blood substitutes, or confronting physiological challenges the war presented (like human performance at high altitudes or in extreme temperatures). To understand the context in

[13] Concretely, we estimate the following specification: $Y_i = \beta \cdot \mathbb{1}(\text{CMR-funded})_i + \delta_{st} + \varepsilon_i$, where i indexes publications, δ_{st} are subject-year fixed effects, and standard errors are clustered by subject and year. For the purposes of these tests, publications' primary subjects are measured as their top MTI-scoring subject.

which CMR exists, we examine publication time series in specific MeSH subjects closely related to these efforts, which are shown in Appendix Figure C.1. Consistent with Stewart (1948)'s observation that "some subjects are born of war," we find that many of these research areas had little pre-war publication activity but took off after the war ended. *Penicillins*, for example, grew from 0 publications per year pre-war, to 450 at its wartime peak, and settled at roughly 150 publications per year afterwards, while *Anti-bacterial Agents* (often representing synthetics) was slower to grow but was the subject of roughly twice as many publications per year as natural penicillin after the war. Similar patterns are present for *Steroids* and *Blood Proteins*. Other subjects had pre-war research activity but grew significantly following the CMR shock (e.g., *Oxygen*). There are also exceptions: for example, research in *Antimalarials* temporarily spiked during World War II, but that intensity was not sustained in the postwar era.

This evidence motivates the empirical comparisons we make in the rest of this section, where we systematically compare publication activity over time in subjects with and without World War II investment. Our baseline estimating equation is as follows:

$$Y_{mt} = \sum_{t=1931}^{1970} \beta_t \cdot \mathbb{1}(\text{Any CMR contracts in MeSH term } m) + \alpha_m + \delta_t + \varepsilon_{mt} \tag{1}$$

where m and t index MeSH terms and years, and the sample runs from 1930 to 1970, with standard errors clustered by MeSH term. All β_t parameters will be estimated relative to 1930, which is the omitted (reference) year. Our preferred treatment measure is an indicator of whether a MeSH term was the subject of any CMR contracts. This choice is the product of two subsidiary choices—whether to measure inputs (research contracts) or outputs (e.g., publications), and whether to do so on the extensive versus intensive margin. We prefer inputs to outputs primarily because some CMR research may not have yielded output during the war but may have created longer-lived research assets (a theme we will return to in Section 7). We prefer the extensive to intensive margin for two reasons. The first is the potentially wide variation in the cost of research across subject areas (e.g., physiological studies vs. drug trials), which is difficult to adjust for. Second is that in a few areas (e.g., in natural penicillin), CMR primarily provided coordination rather than funding, and these contracts had only nominal legal consideration. This latter observation applies more broadly: CMR was both a research management organization and financier. For these reasons, the extensive margin is likely to be more meaningful than the intensive margin.

Our first dependent variable will measure the inverse hyperbolic sine (IHS) of publications in a given MeSH term, which generally approximates the log transformation but is defined at zero, and supports interpreting parameters as semi-elasticities.[14] A second dependent variable will be the

[14]Results are quantitatively similar with log transformations, and for most specifications statistically similar; where we

IHS of new MeSH term pairs in a given term-year, which we will use to examine the effects of CMR on new scientific combinations. Whereas publications reflect the level of research activity in a given subject, new combinations measure an expansion in its scope.

4.1 Identification

Though CMR produced the first significant U.S. government funding for medical research, a potential concern is the endogeneity of what it funded—especially the possibility that funding may have flowed to growing subjects or correlated with emerging scientific potential, which would result in upwardly-biased estimates of CMR's effects. On the one hand, this is less likely to be problematic if, notwithstanding the war, scientific activity would have concentrated in fundamental questions or in civilian health, and military medical needs that guided CMR investments were (exogenously) different. Conversely, Appendix A shows that civilian and military medicine sometimes coincide, such as in the prevention and treatment of certain infectious diseases, and CMR investments might have been directed to dual-use subjects with growing potential.

Whether this is the case is partly an empirical question, which pre-trends can help illuminate. But our understanding of the independence of the CMR shock is also informed by contemporary accounts. For example, the official history of CMR emphasizes that "War augments certain problems already existent in civilian life and engenders new ones" (Andrus 1948, p. 3). This observation is consistent with what we find in CMR's portfolio, and suggests both continuity and change. An implication is that among subjects with CMR support, perhaps only a subset were "treated" in the traditional sense of conditional independence. This is not necessarily problematic for our purposes: we seek to evaluate the relationship of CMR investment to research broadly. Motivated by these accounts, however, we will separately estimate the effects of CMR on subjects which were more vs. less heavily-developed by 1940, which we define as above or below the median number of publications in the 1930s (conditional on having any). In some cases, these underdeveloped subjects were even known subjects where research faced intractable challenges that CMR helped overcome: penicillin, for example, was known to have antibacterial properties with enormous therapeutic potential, yet at the dawn of the war no firm was making it, and there was no known means of producing it in sufficient quantities for research—nor therapeutic applications.

Evidence from pre-war biomedical research funding (however meager) reinforces a view that CMR was different, and many of its investments (and the research they funded) were unlikely to have taken place otherwise. In 1935, for example, the NIH received a then-windfall of $1 million (5% of CMR's future budget) for intramural research from social security legislation, and a published press release describing its research priorities emphasized problems and conditions as varied as cancer,

examine publication activity in "new" or "less-developed" subjects (defined below), results under logged outcomes remain quantitatively similar but grow noisier due to missing values.

heart disease, leprosy, and Rocky Mountain spotted fever (Minneapolis Journal 1935). Beyond the relatively low funds, the publicized list had few subjects that would become military priorities half a decade later, and no emphasis on drug development, clinical trials, or production techniques, which are all examples of work CMR coordinated and funded.

Collectively, this evidence thus suggests World War II presented a shock to the U.S. biomedical innovation system which was in many subjects independent of recent trends or scientific potential. Despite this, attributing these effects to CMR specifically could still be challenging, due to two concurrent changes. First, the CMR shock (a supply shock) coincided with war-driven demand for specific types of research, which could potentially produce similar effects (e.g., Clemens and Rogers 2023 show that prior U.S. wars attracted private R&D in prosthetic devices). Second, the postwar expansion of NIH may have correlated (in research space) with CMR investments and influenced postwar research trajectories (though as we have discussed, this is as much an effect of CMR as it is a potential confounder of other effects). Both possibilities can make it difficult to attribute changes to CMR specifically. We will consider (and rule out) these possibilities later in this section, by (i) evaluating research trajectories in World War I, when there was no directed funding for military medical research, and (ii) controlling for postwar NIH funding.

4.2 Baseline effects

Figure 3, Panel (A) presents our initial results, displaying the β_t estimates from Equation (1) for publication output, with 95% confidence intervals. Figure (A1) estimates effects among established subjects (those with above-median pre-war publications), which we find were growing steadily prior to the war, grew rapidly during it, but subsequently contracted slowly, returning to 1940 levels by 1970. Figure (A2) estimates effects among younger subjects (below-median pre-war publications). Here it appears that CMR had large effects: despite little growth pre-1940, these subjects grew even more quickly during the war (albeit off of a smaller base), and remained elevated through at least 1970, with 50-100% greater publications per year than they were producing before World War II. This first-line evidence immediately suggests that World War II marked an inflection point in biomedical science, as not only did total research volume take off (Appendix Figure 1), but new, CMR-borne subjects began to grow and old subjects stalled or declined.

[Figure 3 about here]

In Panel (B) we re-estimate Equation (1) for new combinations. This outcome does not mechanically rise as publications do, since scientific research regularly studies the same subjects (or bundles of subjects) as prior literature. It instead captures the tendency for researchers to expand the scope of inquiry around a given subject to encompass others. For a concrete example, consider the pairing

of known diseases with new treatments, or established treatments with new diseases—such as the postwar proliferation of studies on antibiotics and infectious disease. Figure (B1) shows that CMR triggered scope expansions in established subjects, with CMR-funded subjects producing 20-30% more new combinations per year in the 1940s than they did pre-1940; in Figure (B2), we find qualitatively similar but noisier effects in less-developed subjects. Panels (A) and (B) together suggest CMR cultivated new subjects and pushed existing subjects in new directions, where CMR-led combinations became subjects of sustained inquiry in existing fields.

4.3 Basic research vs. clinical medicine

Given the applied focus of CMR research, and presumptions that science flows downstream from fundamental investigation to applications, the finding that CMR affected postwar science is potentially surprising. Linear model intuition suggests these impacts would be concentrated in clinical medicine (e.g., research on the diagnosis and treatment of disease).

Whether or not this is the case is an empirical question—albeit a difficult one to answer directly, as there is no commonly agreed method of systematically distinguishing basic and clinical research in the biomedical sciences. Prior research has proposed several possibilities, including categorizations based on journals (Narin et al. 1976), titles (Lewison and Paraje 2004), and content (e.g., on model organisms; Li et al. 2017, Ke 2019), as well as machine learning methods (Boyack et al. 2014). We consider three ways of doing so. First, we rely on MAG subject headings that identify journals as basic medical research and clinical medicine. Second, we identify journals indexed by two historical publications, Current Contents: Life Sciences (CC:LS) and Current Contents: Clinical Practice (CC:CP), from a leading commercial indexing service (the Institute for Scientific Information, or ISI) that were intended to cover basic and clinical research, respectively (Garfield 1972, Cardoni 1973). Our third approach applies the term lists in Lewison and Paraje (2004) to identify articles as basic or clinical based on the presence of those terms in their titles.[15]

Our preferred approach is based on ISI journals, based on its simplicity, transparency, and apparent commercial value. We first obtained a list of 702 journals from CC:CP as of January 1973 (when it was first published, and shortly after our sample period ends), and over 1,000 journals from CC:LS

[15]The MAG-based basic and clinical subject headings are easy to use. However, because we do not have clarity on how they were assigned, we opt against using them in our main analysis—though the unique association of journals to these subjects in the data indicates that it is a journal-based classification. We consider the ISI data to be a preferred journal-based classification method, because (i) we better understand the data-generating process, (ii) the journal lists were produced around the period we study, and (iii) they are commercially validated. As Cardoni (1973) writes in a review of CC:CP: "Current Contents/Life Sciences provides tables of contents of over 1,000 medical science journals and includes broad coverage of basic science and medical specialty publications. Current Contents/Clinical Practice is a new service covering 700 journals and emphasizing clinical practice journals while providing minimal coverage of basic science journals." Cardoni goes on to explain that by his own reading, "An examination of this list [of journals covered by CC:LS but not CC:CP] indicates that the majority of journals falling into this category are basic science in nature and are not directly related to clinical topics."

in 1973 (for consistency). We hand-matched these journals to those in MAG, successfully linking 80% of the former to the latter. The linked journals are then categorized as basic, clinical, mixed, or neither based on whether they appear in CC:LS or CC:CP.

Using these measures, Figure 4 re-estimates Equation (1) to evaluate the effects of CMR on clinical and basic research, focusing our attention (and the sample) on initially less-developed subjects. Despite its applied and use-oriented focus, we find that the CMR shock appears to have produced sustained growth in both applied (clinical) and basic biomedical science in the subjects it funded. Panel (A) shows a long-run 25-30% increase in clinical research in these subjects, and Panel (B) a 40-50% increase in basic research. Appendix C.2 evaluates these effects using a wider range of measures of clinical and basic research. We find directionally similar results across all measures—though the precise magnitudes, and relative effects on clinical and basic science, vary somewhat depending on the specific measure chosen. Scientific activity in specific MeSH term combinations, which we show next, will reinforce this evidence of blended effects.

[Figure 4 about here]

4.4 Combinatoric spillovers

The analysis thus far has examined localized impacts of the CMR shock within treated subjects. We use our measurement of co-occurring MeSH terms to examine how CMR shocks in each subject area affected specific combinatoric pairings across MeSH space. To do so, we assign MeSH terms to branches of the MeSH tree based on their associated MeSH codes and examine the effects of CMR on publications in pairwise branch combinations—such as Diseases (C) and Drugs (D), Organisms (B) and Phenomena and Processes (G), and so on. To keep the presentation parsimonious, we focus on MeSH tree branches (A) to (G), which represent a large majority of research in medicine and the life sciences, excluding branches for ancillary subjects such as specific geographies or subpopulations, or research on the health care system or in social sciences.

The unit of analysis remains the same (MeSH terms, some of which are CMR-funded). Whereas we previously grouped these terms together, in each regression we now subsample terms on their membership in a given branch of the tree (A to G), and measure the number of associated publications where a co-occurring MeSH term is in each other branch of the tree. We re-estimate Equation (1) for each sample and outcome, plotting the estimates in Figure 5, where the focal branch is shown by row and the paired (combination) branch by column.

[Figure 5 about here]

We find spillovers across essentially all subjects, with varying magnitudes and in most cases little evidence of pre-trends. The figure offers several specific insights. First, we probe whether CMR's effects were greater in some fields than others—and we specifically find that the effects are similar across them all (column All, which estimates effects of CMR on all publications for terms in the row branch). Second, we can see in which areas spillovers were stronger, such as in anatomy (row A) and organisms (row B), where across columns, the estimated effects are larger in magnitude than those of other rows. We also see where spillovers were weaker: for example, the estimated effects for research that recombines with subjects in psychology and mental health (column F) are relatively small. Third, we get a more refined view of the pre-trends previously seen in Figure 3, which the figure indicates are driven by drug-related research (row D); in other subject areas, CMR appears to have funded research that was not otherwise growing.

Fourth, the results offer suggestive evidence of bidirectional, basic-to-clinical and clinical-to-basic research spillovers, challenging the linear model of innovation policy. Topics in MeSH branches B (Organisms) and G (Phenomena and Processes) are relatively basic in their nature—a pattern which we discern by our reading and which is also reflected in prior research. Consistent with the linear model, CMR-funded subjects in these branches (rows B and G) spur recombination with others. Conversely, CMR-funded subjects in more applied branches (e.g., D: Chemicals and Drugs or E: Techniques and Equipment) also appear to be increasingly recombined with subjects in the more basic branches of the MeSH tree in the postwar era.

4.5 Additional evidence

Appendix C presents several additional results. In Appendix C.3 we examine heterogeneity in these effects across CMR divisions, programs, and categories of research performers (firms, universities, hospitals, etc.). The effects of CMR tended to be lower for research in the specific diseases which it prioritized, and larger for research on drugs (like anti-infectives and hormones) and on physiology—an intriguing juxtaposition of applied and fundamental work with comparable impact. Contracts with firm and government performers also had a relatively higher impact. This result may implicitly reflect differences in subject matter, but likely also reflect differences in activities these performers undertook as well as how the research programs they participated in were run (e.g., the degree of coordination and active management). What these results do indicate, however, is that CMR's effects were not limited to any single research stage or subject.

Appendix Sections C.4 to C.6 provide additional robustness checks. In Appendix C.4, we estimate a variant of Equation (1) using intensive treatment measures—grouping subjects into quantiles of CMR funding—and find monotonically greater effects for more heavily-funded subjects. For the reasons enumerated above, we continue to prefer an extensive treatment measure, but we consider

these results reinforcing. In Appendix C.5 we re-estimate Equation (1) controlling for whether a given subject was funded by the postwar NIH (between 1948 and 1970), to test whether postwar funding might explain the persistent effects of CMR that prior results indicate, and we find these results unchanged—suggesting that the CMR effect is distinct from the postwar NIH. In Appendix C.6 we probe the possibility that the "CMR shock" may in fact be a war shock—particularly if war has a demand-pull effect that brings scientific attention and activity to new subjects (even without CMR-style funding or coordination), and that in turn triggers accumulative endogenous growth. To do so, we collected analogous data around World War I (WWI), including digitizing contemporary lists of WWI medical problems, and estimate Equation (1) around WWI in relation to these subjects. We find little evidence of a generic effect of war on science. Finally, in additional tests we have re-estimated our main results on a sample 12-digit MeSH codes (rather than MeSH terms), with quantitatively and statistically similar results. MeSH code-based results also remain similar when we cluster standard errors at higher levels of the MeSH tree to account for potential interdependency in error structures across related subjects.

5 The Postwar Pharmaceutical Industry

A second category of potential long-term impacts is on postwar technological innovation—especially drug development. Given the state of the pre-war pharmaceutical industry, that the war would have any impacts on pharmaceutical innovation—let alone that CMR's efforts might succeed during the war itself—is non-obvious. The U.S. pharmaceutical industry in the early 20th century was primitive and disorganized by modern standards: most drug manufacturers were chemical companies with incidental or subsidiary pharmaceutical businesses, and drug discovery was driven more by serendipity or trial-and-error empiricism than by science. Perhaps as a result, as Figure 1 shows, overall (patented) drug innovation was stagnant over this period.

The first two postwar decades, by contrast, produced an immediate and sustained take-off in U.S. pharmaceutical innovation in what is now recognized as a "golden age" of drug discovery, powered by growing use of synthetic chemistry, rational drug design, and systematic drug screens, and by the 1960s the U.S. pharmaceutical industry already looked much more similar to its current state than its pre-war condition. Several scholars have attributed these changes to wartime research in historical analysis: Landau et al. (1999, p. 63), for example, claims that "To a great extent the U.S. government's wartime policies led to the emergence of the American pharmaceutical industry as the undisputed worldwide leader," observing that "the federal war effort encouraged corporate research and development, widened and deepened the companies' cooperation with academic institutions, and catalyzed the diffusion of new technologies across the industry."[16]

[16] Also see, e.g., Temin (1979), Cockburn et al. (1999), and Pisano (2002).)

Perhaps no single firm exemplifies these changes better than Pfizer. Founded in 1849 by two German emigres, Pfizer was for most of its first 100 years a fine chemical manufacturer and commodity chemical supplier whose keystone product by the 1930s was citric acid, which it produced at scale through fermentation. Despite its lack of experience in drug development, Pfizer was brought into the wartime penicillin project for its expertise in fermentation, which was needed to produce natural penicillin from the *Penicillium notatum* mold at scale. Its success led it to become the U.S. Army's biggest penicillin supplier, and after the war ended, Pfizer pivoted around this experience and new R&D capability and entered the pharmaceutical industry, focusing first on developing a wider range of antibiotics and later expanding its R&D portfolio to other drug categories. As it did so, it grew increasingly scientifically oriented, employing a large staff of biologists, mycologists, and later organic chemists, and developing consulting relationships with leading academic scientists, and quickly became a leading drug developer (Daemmrich 2009).

In this section we aim to econometrically evaluate the links between CMR and the postwar U.S. pharmaceutical industry—first by examining the level of drug innovation, and then by more deeply probing how drug discovery itself might have changed as a result.

5.1 The "golden age" of drug discovery

To make systematic comparisons in relation to CMR, we harness the de Haen (1976) list of new drugs introduced between 1940 and 1975, which we manually link to 12-digit MeSH codes under the *therapeutic use* or *physiological effects* sub-branches of the *pharmacologic action* branch of the MeSH tree, and then through these links we retrieve associated MeSH terms. We use this crosswalk to produce a count annual new drugs associated with individual MeSH terms. Our analysis will examine changes in the rate of aggregate drug development across MeSH terms, comparing those which were a target of CMR-funded research vs. others. We then extend this analysis to the firm level, comparing the rate of new drug introductions by pharmaceutical firms (defined as firms in the De Haen sample) which were CMR contractors against those that were not. Here we will expand our treated set to include firms which were engaged in penicillin production under contract with WPB, most (but not all) of which were CMR contractors as well.

We continue using the same specification as in our analysis of CMR's effects on science, estimating time-varying differences across subjects or firms with vs. without CMR suport (Equation 1). Table 4 presents the results, estimating 5-year (rather than annual) parameters to simplify presentation. We first report estimates from our term-level analysis in Panel (A), where the unit of observation is a term-year. We estimate the impact of CMR on (i) the likelihood of any new drug introductions related to a given MeSH term in a given year, (ii) the number of new drugs, and (iii) the IHS number of new drugs. Even-numbered columns exclude anti-infectives, as a test of whether antibiotic drugs

were responsible for any overall effects. We do not find an effect of CMR on the extensive margin (Columns 1 and 2), in part because the many of the areas CMR emphasized already had relatively high propensity to produce at least one related drug per year in the aggregate. However, we find large effects on the intensive margin (Columns 3 to 6), with CMR-supported areas producing on average 1-2 more new drugs per year in the 1950s than others, and with similar-magnitude effects for both anti-infective drugs and in other drug categories.[17]

[Table 4 about here]

Table 4, Panel (B) reproduces this analysis at the firm level, with similar (if not stronger) patterns. Relative to other drug-producing firms, CMR contractors produced a differentially-large surge of new drugs over the next two decades. At its peak, these firms were an extra 25 p.p. more likely to introduce at least one new drug per year than other firms, and on average introduced one more new drug per year—in both cases doubling or tripling mean rates. As with total drug innovation (Panel A), these differences are largest during the pharmaceutical industry's golden age in the 1950s and early 1960s, and cannot be attributed solely to antibiotics.

5.2 Growth of science-based drug discovery

Beyond the sheer level of drug innovation, a closely-related question is whether CMR changed how firms approached drug discovery—i.e., the drug development process itself. One potential change was a growing application of science, including of some of the same science we found CMR research catalyzed in Section 4. Seeds of change were present during the war, where (for example) the effort to synthesize and test thousands of potential antimalarial drugs was shaped by basic understanding of Plasmodium parasites and quinoline biochemistry, in one of the early applications of rational drug design, which was pursued in tandem with traditional empirical trial-and-error. A corollary change was a deepening link between R&D and manufacturing, especially in biologics like penicillin and vaccines. Penicillin production, for example, used science in identifying productive mold strains and their optimal growing conditions, and linked science to engineering and manufacturing operations in designing and running industrial-scale fermentation systems.

The De Haen list of new drugs does not provide information on the underlying discovery process and its links to science. To evaluate this question we shift our analysis from drugs to drug-related patents, focusing on patents filed between 1930 and 1970 by firms in the De Haen sample. Through

[17] These differences are visible in the raw data (e.g., in binned scatterplots). We estimate count outcomes (Columns 3 and 4) by OLS in part to simplify interpretation of average cross-firm differences in drug counts, and in part because count models (including Poisson models) suffer from an incidental parameters problem with two-way fixed effects, due to the limited number of subjects in the sample: Table 4(A) includes 46 MeSH terms, only 25 of which have at least one associated drug in our data and would thus enter a PPML estimation sample.

patent data we can get more granular insight into changes in the nature of pharmaceutical R&D, and especially its use of published science (measured via in-text citations to science)—a hallmark of modern pharmaceutical innovation, which is extremely science-intensive. Appendix Figure C.7 shows that very little pre-war drug innovation had links to science, but World War II marked a phase shift in drug patents' scientific intensity, which subsequently grew rapidly. These patterns are consistent with known changes in R&D practices, such as the growing use of rational drug design anchored in physical, chemical, and biological understanding. Our question here is to what degree these changes might be causally linked to the CMR effort.

To evaluate this question we disaggregate the sample into CMR/WPB contractors vs. other firms and compare across them. Figure 6 counts non-science and science-citing drug patents in 5-year intervals, first for non-CMR/WPB firms (left panel) and then for CMR/WPB firms (right panel). Sheer patent counts suggest these changes were mainly driven by CMR/WPB firms. We formalize these comparisons in Figure 7, which estimates a triple-difference regression, comparing (i) science vs. non-science based patenting by (ii) CMR/WPB-contracted firms vs. other firms (iii) before vs. after the war. The estimating equation takes the following form:

$$Y_{ist} = \sum_{t=1931}^{1970} \beta_t \cdot \mathbb{1}(\text{CMR/WPB firm})_i \cdot \mathbb{1}(\text{Science-based})_s + \alpha_{is} + \delta_t + \varepsilon_{it} \tag{2}$$

where i, s, and t index firms, science- vs. non-science based innovation, and years, and the sample runs from 1930 to 1970, with standard errors clustered by firm. The unit of analysis is a firm-year-invention type, and the outcome (Y_{ist}) measures patenting by firm i in year t that is or is not based in science ($s \in \{0, 1\}$). Our preferred specification measures IHS patents, though results are similar for patent counts. In short, Figure 7 shows patenting by CMR/WPB firms significantly growing in its scientific intensity during and after World War II, with no pre-trend, and remaining permanently elevated (through 1970). In Appendix Table C.5 we extend this result by separately estimating a two-way fixed effects specification for science-based and non-science based patenting, finding that the former grows differentially larger at CMR/WPB firms on both the extensive and intensive margin after World War II, whereas the latter does not.

[Figures 6 and 7 about here]

6 Impacts on Medical Practice

The most significant potential impact of wartime research was improving human health. Appendix A.1 provides suggestive evidence of its short-run effects on military morbidity and mortality, with

hospitalizations and deaths from many common infectious diseases declining to near zero. These gains held large potential for postwar civilian health as well.

A crucial intermediate step for the adoption of new knowledge, techniques, and therapies in health care is getting frontier research findings to medical professionals (Phelps 1992, 2000). Historically, medical textbooks were used in both training and clinical practice (Greene 2007, Catillon 2017, Tomes 2021), especially before the academic publishing industry began to grow in the late 1960s and practitioner journals became more widely available. We therefore use historical textbook series to study the diffusion of CMR research into practice. As we described in Section 3, we digitized two textbook series that were published both before and after World War II: the *Cecil Textbook of Medicine* (CT) and the *Merck Manual of Diagnosis and Therapy* (MM). We obtained copies of each edition with an index between 1930 and ca. 1960 (comprising nine editions of CT spanning 1930-1959, and four editions of MM spanning 1940-1961), digitized each index, and mapped index entries to MeSH using MTI. For each MeSH term, we measure associated pages in each edition to assess coverage. Merging these data with MeSH term-level measures of the CMR shock, we use the specification in Equation (1) to estimate the differential growth of CMR-funded subjects' coverage in medical textbooks and manuals before versus after the war.

Table 5, Columns (1) to (3) present results for CT, where our data begin in 1930, and Columns (4) to (6) for MM, where our data begin in 1940—which are the omitted periods in each regression (respectively). We follow the structure of Section 4 in separately estimating effects for more vs. less heavily-developed subjects, using the same definitions.

[Table 5 about here]

We find that textbook coverage of CMR-funded subjects grew significantly in the postwar period, despite no differential pre-war growth, though it also took several years to realize these impacts. Although these subjects were slow to expand in the late 1940s, by the early 1950s their coverage had grown 20-30% more than other subjects in CT and 10-20% more in MM. These differences are similar for subjects that were more- and less-developed prior to the war, and relatively stable throughout the 1950s. To our knowledge, this table provides the first broad-based, systematic evidence of publicly-funded medical research entering the knowledge base of medical practice. In doing so, it offers a lens into how information about frontier research historically diffused to practitioners and the delayed horizons over which it reaches practitioners.

7 Discussion

7.1 Explaining CMR's Effects

Despite that World War II was a transient shock, the evidence across this paper indicates CMR's effects were large, broad, and long-lasting. A natural corollary question is why: what about CMR or its context led to it having such large and long-lasting effects? The empirical analysis provided clues, with evidence of newly-emergent fields, growing combinatoric science, and increasing scientific intensity of postwar pharmaceutical innovation. However, these findings are scattered snapshots of a broader structural change that appears to have taken place, which includes idiosyncrasies that are hard to summarize empirically. Contemporary and historical accounts help fill these gaps by pointing to several specific changes that were triggered by the CMR effort, which we describe in detail in Appendix D and more briefly summarize here.

In short, the principal mechanisms for CMR's long-run impacts appear to take the form of long-lived research assets which were a target or byproduct of R&D on specific World War II problems, and which researchers continued using or building upon after the war ended. We find these usually fell into one of six categories: (1) new therapies and therapeutic candidates, (2) new research tools and techniques, (3) new technology platforms, (4) new research capabilities, (5) new collaboration patterns, (6) new fundamental knowledge. CMR's specific contributions varied somewhat by program or subject, but in many cases spanned multiple of these categories, suggesting a potential added impact of complementary investments (e.g., in concurrently developing drug candidates and in deepening science on implicated biochemistry and cellular biology).

Continuity between World War II and the postwar era can be seen most clearly in the pharmaceutical industry, where most of these mechanisms were operative. The penicillin project is perhaps a canonical example, as it gave birth to a new class of drugs and spawned a new era for pharmaceutical innovation around it. One mechanism for impact was in establishing antibiotics as a subject for continued R&D; another was in developing methods of large-scale soil screening or fermentation. It also imbued firms (like Pfizer) with new capabilities and manufacturing capacity in biological drug development (Daemmrich 2009).[18] Even where CMR was unsuccessful during the war, such as in synthesizing penicillin, scholars have argued that the knowledge gained "paved the way for [the] general synthesis of penicillins in the 1950s" (Swann 1983, p. 189).

Similar dynamics applied to other drugs. On steroids, Achilladelis (1999, p. 62) writes "because the technology had diffused among participants of the OSRD [CMR] project, all of [the firms involved]

[18] These capabilities extended to new human capital: as (Daemmrich 2009, p. 242) writes, "Since people who understood both biology and engineering were not readily available, companies often had to assign both chemical engineers and microbiologists to their penicillin projects, [and] in this manner ... synthesized their own bioengineers, who would become instrumental in the invention and manufacture of subsequent antibiotics."

introduced corticosteroid drugs in the 1950s." Slater (2009) claims that research on chloroquine and other compounds identified by CMR's malaria program continued after the war, and its screening techniques were models for later research in cancer chemotherapy. Hoyt (2012, p. 74) explains that many companies involved in the wartime effort to produce new vaccines "found themselves at an advantage after the war, since they had been forced to adopt new production methods," several of which had become "state of the art" by the 1960s (Hoyt 2006, p. 47).

The mechanisms through which CMR impacted science were overlapping and distinct. New drugs opened up vast new possibilities for scientific research on how they worked and what diseases they could treat. But CMR also developed new research methods and produced fundamental discoveries that expanded the range of science that could be done. Here CMR's blood program is a canonical example. Creager (1999, p. 396) explains the techniques developed by CMR's blood research program "provided a technical framework for [a] productive research field" after the war on blood-related disorders and blood-derived therapeutics, echoing Cohn (1948, p. 436)'s observation shortly after the war that the separation of blood would enable further research into the function and therapeutic value "the function and the uses in therapy" of different components in blood fractions. CMR projects also produced new research inputs (e.g., bovine ribonuclease A, an important postwar model protein; Richards 1972), and spawned new collaborations, including cross-university and academic-industry partnerships. Elsewhere in CMR's portfolio, different programs developed new research instruments or basic understanding of new chemicals, organisms, and physiological phenomena, which created platforms for further postwar investigation.

The breadth of ways in which CMR impacted postwar science and technology appears to us to be a consequence of its integrated research approach: specific military medical problems required not only new technologies to address them, but also new basic science to understand the nature of each problem and what solutions (chemotherapeutic or otherwise) might work, new tools to perform this research, new techniques for accelerating drug development, and tighter links between science, technology, and manufacturing. This breadth and integrativeness seems to have created opportunities for high-value but hard-to-predict developments through new input combinations (e.g., the intersecting of fundamental knowledge and manufacturing expertise). It is telling that despite existing civilian demand for antibiotics, it took a collective effort to turn Fleming's discovery of penicillin into a mass-produced drug (as just one example among many). Prior research attributes these breakthroughs to a degree of coordination and knowledge sharing not ordinarily achieved in other contexts (e.g., Swann 1983, Neushul 1993, Daemmrich 2009).

7.2 Implications for research policy

CMR's research portfolio does not neatly fit into the "basic" versus "applied" dichotomy that typifies academic and policy understanding of the innovation process. Its focus on solving specific medical problems superseded this dichotomy and motivated an integrated effort spanning sectors, disciplines, and categories of R&D activity. Where it supported basic research, it was usually "use-oriented" basic research, a category that Stokes (1997) argued the one-dimensional basic-applied dichotomy obscures. Moreover, CMR also supported downstream activities, including production and implementation, connecting them to the laboratory science.[19]

This integrative approach does not map clearly to any specific funding model today, in biomedical research or in other fields. Though Mowery (2009) observed that a large share of U.S. government R&D is funded by "mission" agencies, they vary significantly in what the support (science vs. technology) and how they provide support. The Department of Defense and especially DARPA come closest to the CMR (and broader OSRD) paradigm, especially with respect to priority-setting, coordination, and their mix of upstream and downstream investments (Bonvillian et al. 2019). However, DARPA is a relatively small and distinctive part of the U.S. innovation policy apparatus. CMR is also different from DARPA and other ARPAs in its focus on applying science to solve specific problems quickly rather than pursuing high-risk research or fundamental breakthroughs towards long-term payoffs. At the other extreme, NIH—also, nominally, a mission-oriented agency—is quite distant from CMR in its bottom-up priority setting, passive management, and commitment to funding research without a tight link to application. CMR's example thus offers perspective on how an actively managed, top-down biomedical research might operate, and what its effects on science and technology might be, including beyond specific mission objectives.

More generally, research evaluating the impacts of innovation policy has a recognized gap around mission-oriented policies, and limited insight into potential effects of top-down, problem-oriented approaches (Bloom et al. 2019). As a result, calls for mission-oriented research often draw on a small set of historical (and successful) examples like the Manhattan or Apollo Projects as motivation, or otherwise articulate a rationale for relying on state capacity to solve problems that markets do not address (e.g., Mazzucato 2013, 2021). CMR provides an additional datapoint on the impacts of a coordinated, actively-managed, and application-oriented R&D policy. In contrast to these more common reference points, however, CMR had mixed results in the short term. Its long-term impacts were nevertheless broad and substantial. The evidence arguably strengthens the case for

[19] Scientific research occurred synchronously with clinical testing, engineering, and production. CMR's blood program, for example, had one research lab at Harvard Medical School evaluating the composition of blood fractions, testing their properties, running a plasma fractionation pilot plant, improving its efficiency, and more—enabling researchers to verify that bench results could be reproduced in the plant or to investigate questions on how production processes altered expected outputs, and facilitating transitions into large-scale production at partner industrial firms.

experimenting with more CMR-like approaches in biomedical research policy, which today mostly supports undirected, investigator-initiated basic or applied science.

Beyond the specific evaluation, our results also relate to broader questions on the dynamic relationship between science and technology. Near the end of the war, Vannevar Bush described basic research as "the pacemaker of technological progress" in making the case for postwar U.S. research policy (Bush 1945). This perspective has sometimes been called the "linear model" of innovation, with basic research stimulating applied research, followed by technology development, production, and diffusion (Godin 2006). There is a significant body of research documenting the links from publicly funded scientific publications to technology (Narin et al. 1997, Azoulay et al. 2019b, Marx and Fuegi 2020, 2022), broadly consistent with the linear model.

CMR, however, does not fit this model well. Its research portfolio merged science, technology, and manufacturing. Our results suggest (some of) its causal impacts ran in the opposite direction, as government investments in applications spurred science. This is consistent with the qualitative record. While historical accounts of CMR (especially those in Andrus 1948) often emphasize how CMR programs drew on existing knowledge in tackling wartime problems, they also show how CMR research brought attention to new fundamental questions, demanded new fundamental insights, or enabled new fundamental studies. Our evidence is consistent with prior challenges to the linear model of innovation (e.g., Balconi et al. 2010), particularly reinforcing that the relationship between scientific and technological progress can be bi-directional.

This may have implications for research funding. Together with claims about market failures in basic research—anticipating future arguments by Nelson (1959) and Arrow (1962)—the linear model of innovation shaped the Bush (1945) plan for postwar innovation policy, which advocated for government funding for science at universities, while relying on the private sector (incentivized by patents and tax policies) incorporating this science in applied R&D and new technology. This framing has been particularly influential in biomedical research policy. Although our evidence does not contradict this logic, the effects of CMR suggest there may be high social returns and market failures in "'downstream"' R&D activities as well (Nelson 1997).

8 Conclusion

The high returns to medical research for human health, coupled with market failures in R&D, have led to biomedical research becoming a major focus of innovation policy in the U.S. and around the world. In this paper, we study one of the largest shocks to biomedical research in history: World War II. Recognizing that disease and other ailments presented an even larger threat to America's military than enemy forces, in the 1940s the U.S. government created the Committee on Medical Research (CMR) to fund and coordinate civilian R&D into military medical problems. The CMR effort

was effectively the United States' first biomedical R&D policy, marking the U.S. government's first significant extramural funding for biomedical research. We show that the wartime effort triggered large, sustained growth in postwar scientific research, a surge of postwar pharmaceutical innovation, and postwar changes in medical practitioner knowledge in subjects it supported, while also laying the groundwork for postwar research policy and the growth of the NIH.

The paper's first contribution is in documenting CMR's role in shaping the modern biomedical innovation system. Beyond its specific setting, however, these results make several other contributions—most importantly in bringing systematic, large-scale evidence to bear on how applied research funding might affect the innovation system. Beyond program evaluation, the evidence that CMR catalyzed the emergence of new science by opening up new paths for research intriguingly points to limitations in two foundational frameworks for the economics of science. First, the linear model of innovation implies a division of labor, and a directional flow from science to applications, that CMR defied: much of its work was integrated and interdependent—connecting science, technology, manufacturing, and diffusion—and new science often emerged *from* applications. Second, the "burden of knowledge" thesis predicts that research productivity inexorably declines over time, as knowledge accumulates and the frontier gets increasingly hard to reach (Jones 2009). CMR, however catalyzed new research in an array of new problems and phenomena where postwar scientific and technological opportunities were apparently abundant.

Much as CMR did, our analyses raise new questions, fundamental and applied. Although we have specifically emphasized CMR's impacts, contemporary accounts from Bush (1945), Richards (1946), and others point to the importance of interwar science to the war effort, much of which was funded by foundations. Archival records from Rockefeller and other medical research funders of this era may help in assessing their impacts, as well as the dynamic relationships between fundamental and applied research and between science and technology. Second, we are cognizant that CMR is but one case of applied biomedical research policy. We anticipate that in the coming years, an analysis similar to ours on the post-crisis impacts of Operation Warp Speed or the broader Covid-19 pandemic response will be possible as well. Our results suggest that there may be long-lasting effects not just on technology, but on science itself. Finally, a natural policy question is whether a research funding organization similar to CMR would yield high social returns today, in a very different context and innovation system. While we cannot definitively speak to this question, our view is that the results from our analyses at least support calls for more experimentation with alternative funding models for biomedical research (Azoulay 2012, Myers 2023), including for late-stage research and commercialization (Ouellette 2023).

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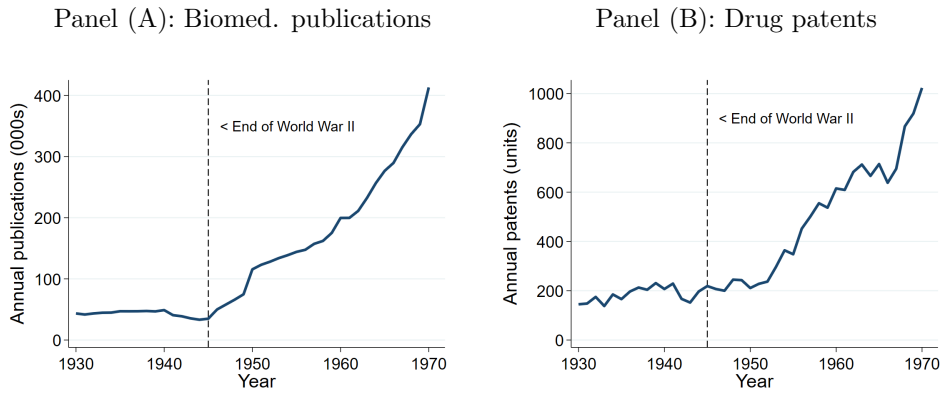
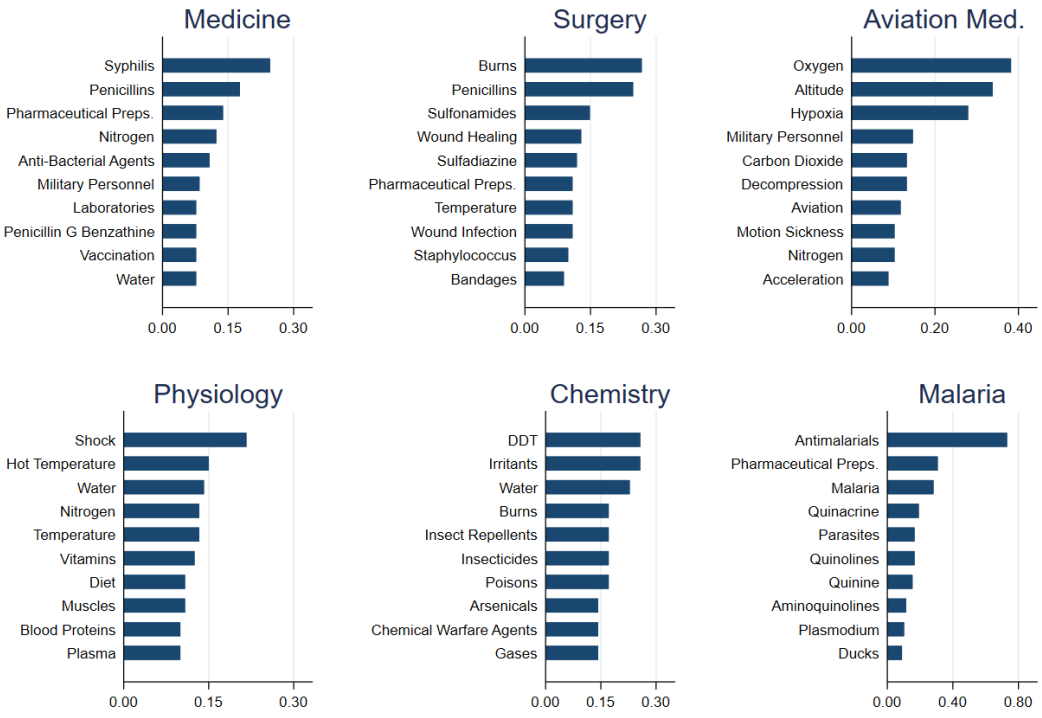
Figure 1: Biomedical research publications and USPTO drug patents, 1930-1970



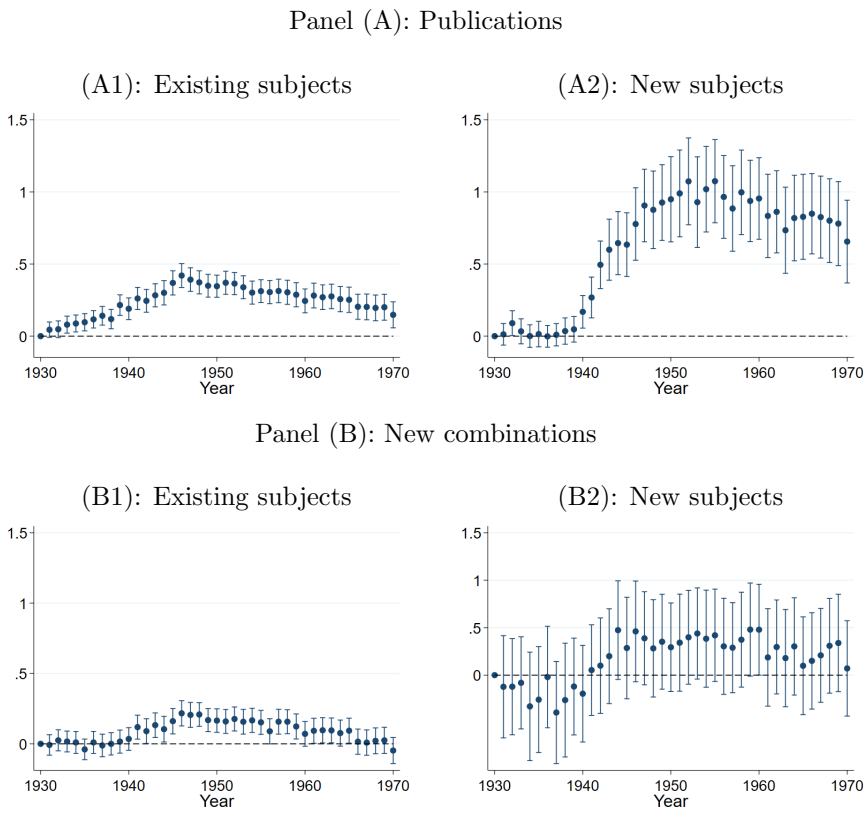
Notes: Left figure shows time series of total biomedical research publications in our core publication sample (Microsoft Academic Graph; see Appendix B). Sample consists of publications in the natural sciences and health sciences (OECD field codes 1 and 3) between 1930 and 1970. Right figure shows time series of total filings of drug patents in U.S. patent data, defined as patents in NBER category 31 ("Drugs"; Hall et al. 2001), corresponding to USPC 424 and 514. Dashed vertical line marks the end of World War II.

Figure 2: Top 10 MeSH terms by CMR division, as a fraction of division contracts



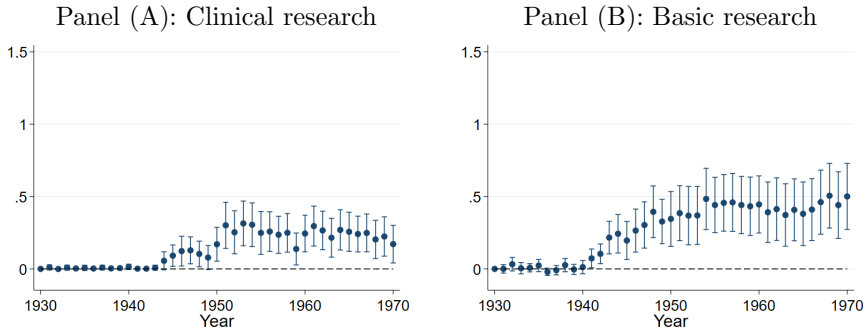
Notes: Figure lists the top 10 MeSH terms associated with CMR contracts in each of the six primary CMR divisions, showing what share of divisional contracts each term associates with. Individual contracts map to multiple MeSH terms.

Figure 3: Effects of CMR on research publications in treated subjects, 1930-1970



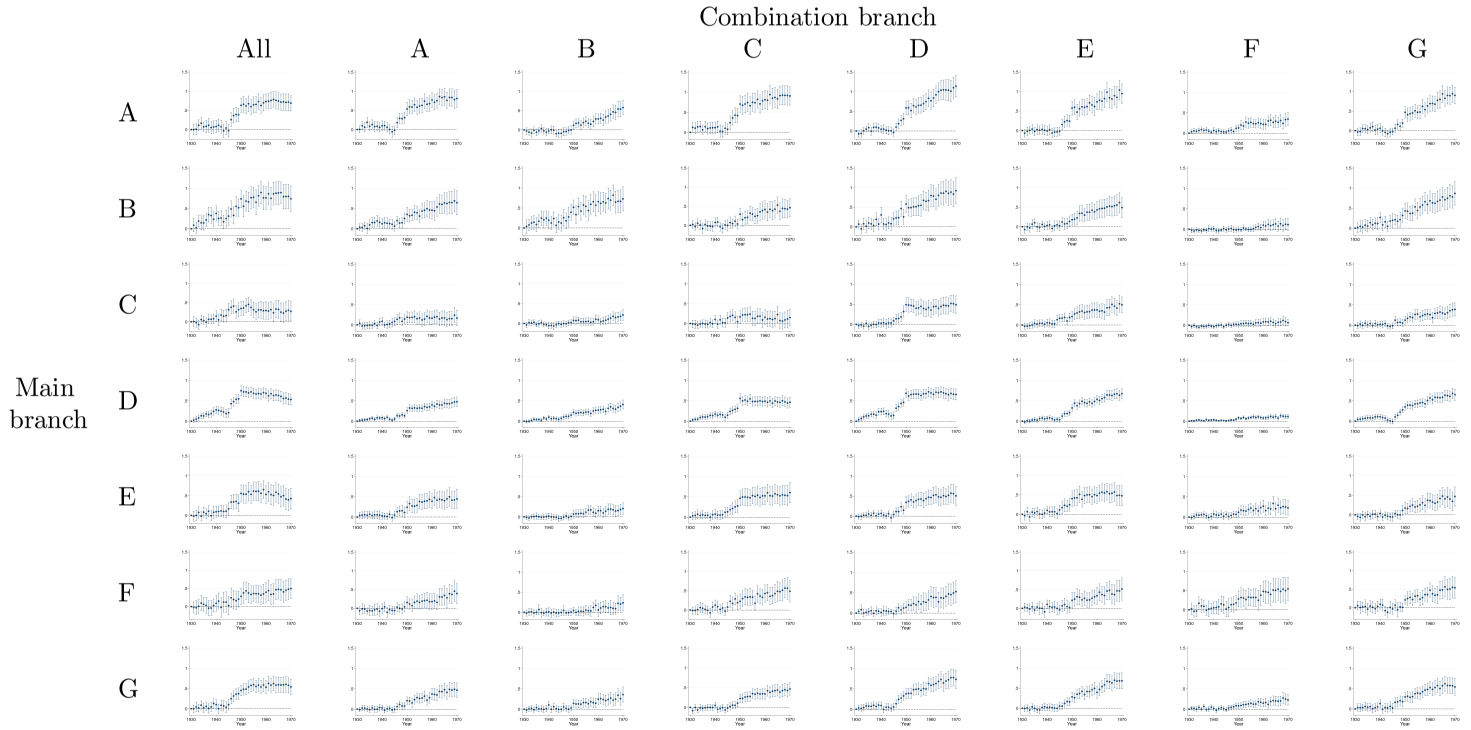
Notes: Figure shows annual estimates of the differential growth of scientific publications (Row A) and new combinations (Row B) in MeSH terms with CMR funding, relative to others. Columns (1) and (2) divide MeSH terms into subjects with greater than and less than the median number of pre-1940 publications, which we label "existing" and "new" subjects. New combinations are defined as new co-occuring MeSH terms in an article with the given MeSH term. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

Figure 4: Effects of CMR on clinical vs. basic research, 1930-1970



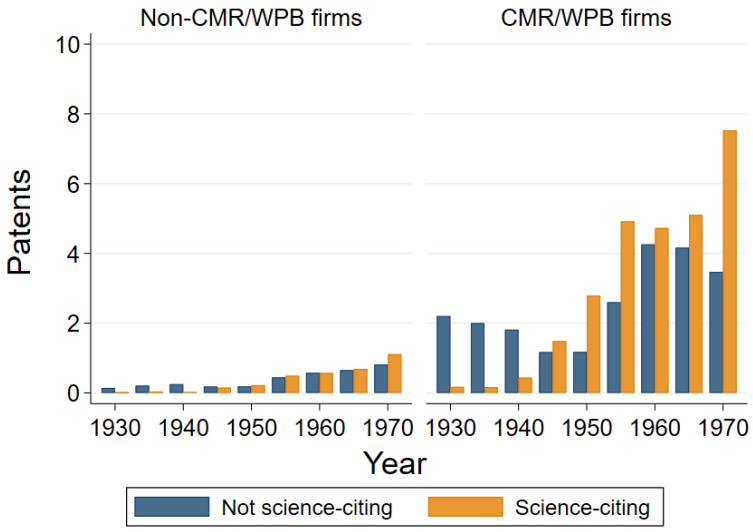
Notes: Figure shows annual estimates of the differential growth of scientific publications in MeSH terms with CMR funding, relative to others. The sample is restricted to "new" subjects (i.e., those with below-median pre-1940 publications) and the figure divides the sample into basic and clinical biomedical publications (see text for details). Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

Figure 5: Effects of CMR on research publications in treated subjects, by MeSH tree branch (row) and combo branch (column)



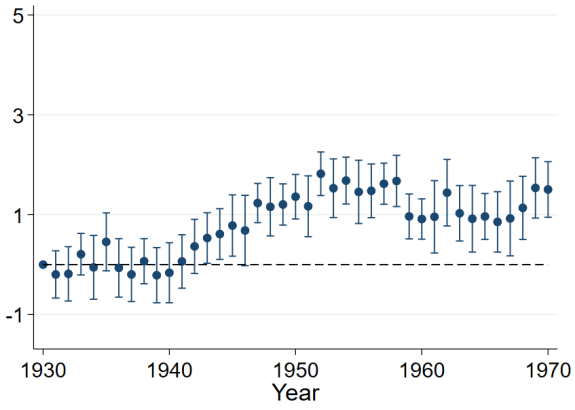
Notes: Figure shows annual estimates of the differential growth of scientific publications in MeSH terms from each branch of the MeSH tree (rows A to G) with a CMR shock. We provide results for all publications with the term (column All) and for publications that combine the term with another from other branches of the tree (columns A to G). The MeSH tree can be browsed at https://meshb.nlm.nih.gov/treeView. Branches are defined as follows. A: Anatomy. B: Organisms. C: Diseases. D: Chemicals & Drugs. E: Techniques & Equipment. F: Psychiatry & Psychology. G: Phenomena & Processes. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

Figure 6: Average annual drug patents by CMR/WPB-contracted firms vs. others



Notes: Figure shows the average annual number of drug patents filed by firms in de Haen (1976), separately reporting CMR/WPB-contracted firms and other firms, and science-citing and non-citing patents. Drug patents defined as those associated with NBER category 31 (Hall et al. 2001), and science-citing patents as those which cite non-patent literature (typically, scientific literature) in their text (Marx and Fuegi 2020, 2022).

Figure 7: Differential growth in science-citing vs. non-citing drug patents, by CMR/WPB-contracted firms vs. others, 1930-1970



Notes: Figure shows annual estimates of the differential growth of science-citing vs. non-citing patents at CMR/WPB-contracted firms vs. others. Error bars represent 95% confidence intervals, with SEs clustered at the firm level.

Table 1: Extramural research contracts, contractors, and modal research subjects by CMR division

		Division						
		(1)	(2)	(3)	(4)	(5)	(6)	
	All	Medicine	Surgery	Aviat. Med.	Physiology	Chemistry	Malaria	Miscellany
CMR contracts	571	130	101	68	120	36	78	38
Percent of total	100%	23%	18%	12%	21%	6%	14%	7%
Unique contractors	128	55	39	31	56	20	49	27
Percent of total	100%	43%	31%	24%	44%	16%	38%	21%
Contract value (MMs)	$21.3	$3.4	$2.2	$2.4	$3.7	$1.2	$4.8	$3.5
Percent of total	100%	16%	11%	12%	18%	6%	22%	17%
MeSH terms per contract	11.3	11.5	13.4	10	11.8	14.9	9.1	6.5
Modal MeSH term	Penicillins	Syphilis	Burns	Oxygen	Shock	DDT	Antimalarials	Penicillins

Notes: Table provides summary statistics for CMR, overall and by division. The table lists the number of contracts, contractors, and total contract value by division, and provides the modal MeSH term from contracts in each division, weighted by value. The overall modal subject across all of CMR is *Penicillins*.

Table 2: Top new MeSH terms entering the publication record, by year, 1939-1946

Rank	MeSH term	Pubs (10-yr)	CMR	Rank	MeSH term	Pubs (10-yr)	CMR
	1939				1943		
1	Sulfathiazole	407	1	1	Chromatography, Paper	367	0
2	Diphenhydramine	118	0	2	Penicillin G	244	1
3	Phenytoin	101	1	3	Angiocardiography	155	0
4	17-Ketosteroids	96	1	4	Coxsackievirus Infections	99	0
5	Fenestration, Labyrinth	87	0	5	Penicillin V	60	1
Average, lower rank		4.4	0.03	Average, lower rank		5.7	0.02
	1940				1944		
1	DDT	558	1	1	Streptomycin	4685	1
2	Thiouracil	425	0	2	Penicillin G Procaine	249	0
3	Sulfathiazoles	191	1	3	Parathion	212	0
4	Hyaluronoglucosaminidase	181	1	4	Disulfiram	179	0
5	Sulfaguanidine	94	1	5	Polyethylene	149	0
Average, lower rank		4.9	0.02	Average, lower rank		10.4	0.06
	1941				1945		
1	Histamine Antagonists	301	0	1	Nuclear Weapons	225	0
2	Tyrothricin	107	1	2	Dimercaprol	223	1
3	Radioactive Tracers	51	0	3	Methylthiouracil	200	0
4	Fontan Procedure	50	0	4	Nucleons	169	0
5	Folic Acid Deficiency	47	0	5	Histoplasmin	155	0
Average, lower rank		5.2	0.03	Average, lower rank		9.9	0.04
	1942				1946		
1	Dicumarol	371	1	1	Chloroquine	290	1
2	Newcastle Disease	116	1	2	Hypotension, Controlled	205	0
3	Sulfamerazine	84	1	3	Propylthiouracil	202	0
4	Penicillium chrysogenum	67	1	4	Tripelennamine	131	1
5	Stilbamidines	53	0	5	Promethazine	126	0
Average, lower rank		5.0	0.02	Average, lower rank		9.5	0.03

Notes: Table list the annual top 5 new MeSH terms in our publication data from 1939 to 1946, as determined by our indexing of publication titles. For each term we provide the number of associated publications over the next 10 years, and we indicate whether the subject was CMR-funded, measured as having an associated CMR contract or publication. The last row for each year provides averages for all lower-ranking terms. The evidence in the table suggests that many of the most important new biomedical research subjects and therapies emerging at this time were subjects of CMR research.

Table 3: Novelty, breadth, and impact of CMR-funded publications

	Novelty	Breadth (topics per publication)			Above given f. citation pctile.			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	New combo	# topics	≥3 topics	≥5 topics	75th pct.	90th pct.	95th pct.	99th pct.
CMR-funded	0.066***	0.114***	0.042***	0.006**	0.164***	0.103***	0.068***	0.024***
	(0.014)	(0.025)	(0.012)	(0.003)	(0.017)	(0.013)	(0.010)	(0.006)
N	493760	493760	493760	493760	230370	230370	230370	230370
R^2	0.20	0.23	0.19	0.14	0.25	0.23	0.21	0.19
Subj-Year FEs	Y	Y	Y	Y	Y	Y	Y	Y
Y mean	0.251	1.773	0.162	0.003	0.237	0.096	0.049	0.010

Notes: Table estimates differences between CMR-funded and contemporary publications in 20-year forward citations. Column (1) estimates differences in their propensity to include a new MeSH term combination (novelty); Columns (2) to (3), their number of associated MeSH topics (breadth); and Columns (5) to (8), their propensity to be top 25%, 10%, 5%, or 1% cited publications (impact). Sample is restricted to publications between 1940 and 1950. All specifications include fixed effects for publications' primary subject (highest-scoring MeSH term) and year. *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by subject and year in parentheses.

Table 4: Effects of CMR on new drug introductions, 1940-1970

Panel A: MeSH subject-year level

	1(Any new drugs)		# of new drugs		IHS(New drugs)	
	(1)	(2)	(3)	(4)	(5)	(6)
	All drugs	Excl. A-I	All drugs	Excl. A-I	All drugs	Excl. A-I
Any CMR * 1(1946-1950)	-0.011	-0.011	0.468	0.271	0.131	0.103
	(0.069)	(0.069)	(0.393)	(0.360)	(0.145)	(0.149)
Any CMR * 1(1951-1955)	0.141	0.141	1.420***	1.178**	0.469***	0.444**
	(0.087)	(0.087)	(0.518)	(0.487)	(0.163)	(0.170)
Any CMR * 1(1956-1960)	0.105	0.105	2.359**	2.078**	0.630***	0.612***
	(0.092)	(0.092)	(0.924)	(0.939)	(0.211)	(0.223)
Any CMR * 1(1961-1965)	0.146	0.146	0.543*	0.584*	0.267**	0.289**
	(0.100)	(0.100)	(0.301)	(0.317)	(0.127)	(0.132)
Any CMR * 1(1966-1970)	0.039	0.039	0.397	0.378	0.138	0.139
	(0.081)	(0.081)	(0.376)	(0.401)	(0.152)	(0.162)
N	1426	1426	1426	1395	1426	1395
R^2	0.57	0.57	0.62	0.57	0.67	0.63
Y mean	0.264	0.264	0.795	0.680	0.413	0.371

Panel B: Firm-year sample

	1(Any new drugs)		# of new drugs		IHS(New drugs)	
	(1)	(2)	(3)	(4)	(5)	(6)
	All drugs	Excl. A-I	All drugs	Excl. A-I	All drugs	Excl. A-I
CMR/WPB firm * 1(1946-1950)	0.205**	0.144**	0.446***	0.342***	0.295***	0.227***
	(0.080)	(0.065)	(0.140)	(0.121)	(0.097)	(0.083)
CMR/WPB firm * 1(1951-1955)	0.254***	0.303***	0.930***	0.768***	0.511***	0.475***
	(0.069)	(0.069)	(0.209)	(0.164)	(0.116)	(0.099)
CMR/WPB firm * 1(1956-1960)	0.222***	0.253***	0.977***	0.747***	0.514***	0.439***
	(0.072)	(0.076)	(0.246)	(0.210)	(0.127)	(0.119)
CMR/WPB firm * 1(1961-1965)	0.140**	0.123*	0.250**	0.261*	0.172**	0.172**
	(0.058)	(0.063)	(0.125)	(0.137)	(0.079)	(0.087)
CMR/WPB firm * 1(1966-1970)	0.111	0.089	0.079	0.090	0.074	0.077
	(0.074)	(0.059)	(0.111)	(0.072)	(0.080)	(0.055)
N	3686	3686	3686	3686	3686	3686
R^2	0.30	0.27	0.39	0.33	0.38	0.32
Y mean	0.183	0.157	0.274	0.220	0.204	0.169

Notes: Panel (A) estimates differences in the annual number of new commercially-marketed drugs associated with MeSH terms with CMR funding, relative to others, restricting the sample to terms in drug-related sub-branches of the *pharmacologic actions* branch of the MeSH tree (see text for details). Panel (B) estimates differences in the annual number of new drugs brought to market by firms engaged in the CMR (and WPB) medical research effort vs. others. Even-numbered columns (labeled "Excl. A-I") exclude anti-infective agents to examine the degree to which the results are driven by antibiotics. In preparing the firm sample in Panel (B), we dynamically reassign a small number of firms which merged or were acquired during the sample frame to their subsequent owners using data from FTC (1980). Results are estimated relative to the 1940-1945 period. *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by MeSH term (Panel A) or firm (Panel B) in parentheses.

Table 5: Cecil Textbook and Merck Manual coverage of subjects with CMR funding

	Cecil Textbook			Merck Manual		
	(1)	(2)	(3)	(4)	(5)	(6)
	All terms	Existing	New	All terms	Existing	New
Any CMR * 1933	-0.008	-0.019	-0.006			
	(0.018)	(0.021)	(0.033)			
Any CMR * 1937	0.058**	0.018	0.082			
	(0.026)	(0.029)	(0.064)			
Any CMR * 1940	-0.001	-0.018	0.017			
	(0.030)	(0.035)	(0.053)			
Any CMR * 1943	-0.014	-0.011	0.033			
	(0.032)	(0.037)	(0.058)			
Any CMR * 1947	0.055	0.010	0.129			
	(0.038)	(0.043)	(0.086)			
Any CMR * 1951	0.257***	0.179***	0.236***			
	(0.040)	(0.045)	(0.091)			
Any CMR * 1955	0.381***	0.223***	0.325***			
	(0.045)	(0.051)	(0.099)			
Any CMR * 1959	0.288***	0.185***	0.241***			
	(0.041)	(0.047)	(0.086)			
Any CMR * 1950				0.153***	0.093***	0.087***
				(0.019)	(0.022)	(0.032)
Any CMR * 1956				0.242***	0.155***	0.193***
				(0.023)	(0.026)	(0.045)
Any CMR * 1961				0.241***	0.152***	0.164***
				(0.024)	(0.027)	(0.045)
N	222885	73674	149211	99060	32744	66316
R^2	0.69	0.72	0.44	0.76	0.77	0.64
Y mean	0.207	0.485	0.070	0.080	0.202	0.020

Notes: Table estimates differences over time in whether the Cecil Textbook (Columns 1 to 3) and Merck Manual (Columns 4 to 6) cover individual MeSH terms with CMR funding, relative to others. The table divides the sample into MeSH terms above the below the median number of pre-1940 publications in Columns (2) to (3) and (5) to (6), respectively. Results are estimated relative to the 1930 edition of the Cecil Textbook (2nd ed., when the index is first observed) and the 1940 edition of the Merck Manual (7th ed.). *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by MeSH term in parentheses.

Online Appendix

The Therapeutic Consequences of the War: World War II and the 20th Century Expansion of Biomedicine

Daniel P. Gross and Bhaven N. Sampat

Table of Contents

A Historical Context

In this section we provide historical context for this paper, including on the motivations for medical research in World War II, the origins of OSRD's Committee on Medical Research (CMR), and the data we collect on CMR's World War II-era research investments.

A.1 The need for military medical research

As we note in the paper, disease killed more soldiers than battlefield injuries in nearly every major war prior to World War II. The top panel of Table A.1 shows statistics on deaths from disease versus injury in eight military conflicts in various regions between the Mexican-American War (1846-48) and World War I (1914-1918; U.S. at war 1917-1918), where the ratio of deaths from disease:injury varied from 0.9 to 12, and averaged 1.7—including a ratio >1 for the U.S. in World War I. In World War II, this ratio was 0.07 for the U.S. Army overall and 0.01 for the U.S. Army in Europe. In essence, disease was effectively eliminated as a cause of military mortality.

Table A.1: Deaths from disease versus battlefield injury in prior wars

		Deaths from...		
	Years	Disease	Injury	Ratio
Pre-World War II				
Mexican-American War (U.S.)	1846-48	11,155	1,721	6.48
Crimean War (France)	1854-56	70,000	7,500	9.33
U.S. Civil War (Union)	1861-65	199,720	138,154	1.45
Franco-Prussian War (Germany)	1870-71	14,904	17,225	0.87
Sino-Japanese War (Japan)	1894-95	15,850	1,311	12.09
Philippine-American War (U.S.)	1899-1902	4,356	1,061	4.11
Boer War (British)	1899-1901	11,377	6,425	1.77
World War I (U.S.)	1917-18	51,447	50,510	1.02
Weighted average				1.69
World War II				
U.S. Army, total	1941-45	15,779	234,874	0.07
U.S. Army in Europe	1941-45	1,779	135,576	0.01

Notes: Table reports deaths from disease and battlefield injuries, and the ratio of the former to the latter, for the U.S. Army and foreign armies in major wars of the late 19th century, World War I, and World War II. Data from Coates and Hoff (1958), page 21, Table 7.

Table A.2 puts these patterns in further context for the U.S. Army specifically, comparing per-capita, per-year hospital admissions and deaths from infectious diseases in the Civil War (1861-65), Spanish-American War (1898), World War I (1917-18), and World War II (1942-45). Hospital admissions declined from >1 per soldier-year in the Civil War to roughly 0.1 per soldier-year in World War II, and deaths from 0.03 to 0.0015—a 99.5% decline.

Table A.2: U.S. Army admissions and deaths from infectious diseases, by war

War	Years	Per 1,000 soldiers/year Admissions	Deaths
U.S. Civil War (Union)	1861-65	1,030.34	34.77
Spanish-American War	1898	986.89	20.81
World War I	1917-18	427.03	10.43
World War II	1942-45	112.46	0.15

Notes: Table reports U.S. Army hospital admissions and deaths from infectious diseases in four major wars of the 19th and 20th centuries, per 1,000 soldiers per year. Data from Coates and Hoff (1958), page 11, Table 2.

Tables A.3 and A.4 provide a more detailed accountings of (i) per-capita hospital admissions rates and (ii) death rates per hospital admission in World Wars I and II, in both cases drawing from military medical statistics published in the same U.S. Army Medical Department series. We present admissions and death rates for specific major infectious diseases (which were subjects of CMR medical research in World War II) and compare them to cancer (which was not). The right-most columns in each table compute percentage changes from World War I to II for the U.S. Army worldwide, in the U.S., and in Europe (geographies broadly shared across the conflicts, albeit with some residual differences, such as northern vs. southern Europe—where the latter was a theater of war in the second World War but not the first).

Despite the implicit association to the research effort, direct comparisons of admissions and death rates across the two wars is complicated by changing theater of war (e.g., World War II was fought in more tropical environments with higher incidence of mosquito-borne diseases like malaria or Japanese B encephalitis) and changes in diagnostics. Similarly, attribution to World War II medical research specifically is also complicated by the possibility of interwar progress in specific disease areas (e.g., malaria). The evidence is nevertheless provocative and potentially suggestive of causal effects. Hospital admissions rates for nearly all infectious diseases declined dramatically, albeit with a few exceptions, primarily malaria and encephalitis (Table A.3). Death rates (per admission) also declined dramatically for most infectious diseases (Table A.4). Mortality from influenza, for example, declined 100%, and mortality from pneumonia, meningitis, and encephalitis—among the most lethal diseases for hospital admits in World War I—declined nearly as much. Large declines were also observed for other diseases like tuberculosis, typhoid fever, and scarlet fever. Cancer death rates, by comparison, declined only incrementally.

Table A.3: Disease hospital admissions in World War II vs. World War I

			Per 1,000 average strength, per annum								
			World War I (1917-19) Admissions			World War II (1942-45) Admissions			Pct. change Admissions		
Disease category	Etiology	Disease	Global	USA	EUR	Global	USA	EUR	Global	USA	EUR
Infectious diseases	Bacterial	Diphtheria	2.670	2.630	2.920	0.190	0.040	0.530	-93%	-98%	-82%
Infectious diseases	Bacterial	Scarlet fever	2.850	4.040	1.420	1.120	1.710	0.510	-61%	-58%	-64%
Infectious diseases	Bacterial	Tuberculosis	9.300	13.520	4.290	1.110	1.430	0.620	-88%	-89%	-86%
Infectious diseases	Bacterial	Typhoid fever	0.370	0.240	0.530	0.020	0.010	0.010	-95%	-96%	-98%
Infectious diseases	Viral	Influenza	191.560	238.700	137.150	7.430	9.290	3.460	-96%	-96%	-97%
Infectious diseases	Viral	Measles	23.650	38.200	5.500	2.380	3.650		-90%	-90%	
Infectious diseases	Viral	Mumps	56.120	63.360	49.140	4.020	5.530		-93%	-91%	
Infectious diseases	Viral	Rubella	4.160	7.230	0.350	5.300	8.400		27%	16%	
Infectious diseases	Bacterial or viral	Encephalitis	0.020	0.020	0.020	0.070	0.070	0.010	250%	250%	-50%
Infectious diseases	Bacterial or viral	Meningitis	1.300	1.400	1.260	0.560	0.740	0.430	-57%	-47%	-66%
Infectious diseases	Bacterial or viral	Pneumonia	19.030	20.540	18.030	10.680	12.990	8.090	-44%	-37%	-55%
Infectious diseases	Venereal	Chancroid	9.470	9.650	7.990	3.710	1.370	3.750	-61%	-86%	-53%
Infectious diseases	Venereal	Gonococcus	61.300	94.670	18.730	33.350	30.460		-46%	-68%	
Infectious diseases	Venereal	Syphilis	16.250	23.050	7.610	11.750	14.390	0.150	-28%	-38%	-98%
Infectious diseases	Parasitic	Malaria	3.450	4.700	0.570	15.930	3.530	6.470	362%	-25%	1035%
Neoplastic diseases		Cancer	0.150	0.180	0.100	0.300	0.330	0.270	100%	83%	170%

Notes: Table compares U.S. Army hospital admissions per 1,000 soldiers per year from select infectious diseases in World War I and World War II, with an added comparison to cancer (final row). Data reported for global personnel, U.S.-based personnel, and the European theater. World War I data reported for 1917-1919 only and World War II data for 1942-1945. Data from Love (1925), Tables 47 and 49 and Reister (1975), Tables 29, 29a, 31a.

Table A.4: Disease death rates in World War II vs. World War I

			Per 1,000 average strength, per annum								
			World War I (1917-19) Deaths:Admissions			World War II (1942-45) Deaths:Admissions			Pct. change Deaths:Admissions		
Disease category	Etiology	Disease	Global	USA	EUR	Global	USA	EUR	Global	USA	EUR
Infectious diseases	Bacterial	Diphtheria	0.015	0.015	0.017	0.026	0.025	0.032	76%	64%	87%
Infectious diseases	Bacterial	Scarlet fever	0.032	0.030	0.028	0.002	0.002	0.002	-94%	-92%	-93%
Infectious diseases	Bacterial	Tuberculosis	0.072	0.048	0.172	0.029	0.018	0.074	-60%	-62%	-57%
Infectious diseases	Bacterial	Typhoid fever	0.162	0.125	0.170	0.050	0.000	0.100	-69%	-100%	-41%
Infectious diseases	Viral	Influenza	0.031	0.031	0.032	0.000	0.000	0.000	-100%	-100%	-100%
Infectious diseases	Viral	Measles	0.025	0.023	0.038	0.000	0.001		-98%	-98%	
Infectious diseases	Viral	Mumps	0.000	0.000	0.000	0.000	0.000				
Infectious diseases	Viral	Rubella	0.005	0.004	0.000	0.000	0.000		-100%	-100%	
Infectious diseases	Bacterial or viral	Encephalitis	0.500	0.500	0.500	0.057	0.057	0.300	-89%	-89%	-40%
Infectious diseases	Bacterial or viral	Meningitis	0.392	0.343	0.444	0.045	0.043	0.047	-89%	-87%	-90%
Infectious diseases	Bacterial or viral	Pneumonia	0.244	0.216	0.282	0.004	0.004	0.005	-98%	-98%	-98%
Neoplastic diseases		Cancer	0.200	0.222	0.200	0.183	0.182	0.167	-8%	-18%	-17%

Notes: Table compares U.S. Army death rates per hospital admission from select infectious diseases in World War I and World War II, with an added comparison to cancer (final row). Data reported for global personnel, U.S.-based personnel, and the European theater. World War I data reported for 1917-1919 only and World War II data for 1942-1945. Data from Love (1925), Tables 47 and 49 and Reister (1975), Tables 29, 29a, 31a.

The impact of war on military health, and the improvements achieved by or in World War II, can be seen most clearly in the time series. Figure A.1 plots U.S. Army annual hospital admissions and deaths from infectious disease per capita between 1895 and 1955. Both series show significant spikes in earlier wars but no such spike in World War II.

Figure A.1: Admission and death rates for infectious diseases, U.S. Army, 1895-1954
(measured as number of admissions or deaths per 1,000 soldiers per year)

Notes: Figure shows time series of U.S. Army admission and death rates from infectious diseases, per 1,000 soldiers per year. Reproduced from Coates and Hoff (1958), page 20, Chart 6.

A.2 Committee on Medical Research

As we recount in Section 2, the World War II research effort effectively began in June 1940, when U.S. President Franklin Roosevelt authorized and funded the creation of the National Defense Research Committee (NDRC) to coordinate civilian R&D in military science and technology. Based on its early successes, the NDRC was expanded into the Office of Scientific Research and Development (OSRD) in July 1941 by executive order and given formal appropriations. OSRD subsumed NDRC and created and added CMR as a second unit focused on coordinating and funding military medical research. In Gross and Sampat (2023b) we explain:

> [CMR] was charged with mobilizing medical researchers and identifying "the need for and character of contracts to be entered into with universities, hospitals, and other agencies conducting medical research activities," and was equally radical for its time.[1] Though the National Institute of Health (NIH) had existed since 1930, its budget was small and mostly spent in its own labs. Private foundations had previously funded medical research through block grants, and later (after the Depression made these financially infeasible) through grants to specific researchers. But as we discuss below, these were different in important ways from the CMR model, including their focus on fundamental research. CMR also drove a major shift in emphasis in medical research, away from peacetime problems to specific wartime medical needs ... Though there was some internal reorganization over the war, CMR's main divisions were General Medicine, Surgery, Aviation Medicine, Physiology, Chemistry, and Malaria.

In this prior work we explored more deeply how CMR operated. As a wartime research funding agency, CMR faced several basic questions which are characteristic of such efforts, including what to fund (priority-setting), whom to fund, and how to support it—including top-down vs. bottom-up priority-setting (whether to specify vs. solicit proposals), how large a role to play in managing and coordinating research efforts (vs. a more hands-off approach), and whether to invest in downstream activities like production and diffusion (vs. only R&D). Here we summarize CMR's general approach to these questions, drawing liberally from (Gross and Sampat 2023b), where we also observe that agency also accommodated exceptions when needed.

In contrast to NDRC, which identified specific R&D problems internally (based on the expertise of in-house staff and input from military representatives) and farmed out the work to suitable performers, CMR adopted a more bottom-up approach. It did so by circulating to the medical research community throughout the war bulletins identifying research priorities and soliciting "Proposals for Contract". Investigators submitting proposals were required to describe the subject of the proposed investigation, present the state of knowledge, explain its significance to national defense, and provide a research plan. These proposals were sent to a partner organization—the National Research

[1] Chester Keefer, the "penicillin czar", later described it as "a novel experiment in American medicine, for planned and coordinated medical research had never been essayed on such a scale" (Keefer 1969).

Council's Division of Medical Sciences (DMS), which has been created a year earlier in anticipation of war—where over thirty committees (with hundreds of elite medical researchers) reviewed applications for feasibility, in consultation with medical officers from the Army and Navy. Peer review was an "unprecedented approach" at the time, and CMR represented "the first sustained, large-scale exercise of the function in a biomedical context" (Mandel 1996). Based on the review feedback it received, the DMS gave each application a letter grade and submitted these reviews back to CMR, which screened them further for their possible impact on the war effort (in addition to feasibility) but typically funded what DMS recommended.

The executive order creating OSRD explicitly tasked it with coordinating wartime medical research, including across research performers and with the military. CMR undertook several activities towards this end. Several of the projects it funded or participated in were coordinated, multi-party or cross-sectoral attacks on specific problems, like blood separation and the preparation of blood substitutes. In these research programs, CMR actively managed the work it funded, including by organizing meetings of investigators to facilitate their cooperation, circulating technical reports, and continuously rebalancing its project portfolio (Stewart 1948).

CMR was also active in development, evaluation, and implementation. Even when there was initial evidence of the therapeutic benefits of new treatments from theory or animals, a key question was whether they worked in humans. Many of its contracts involved testing (e.g., of antimalarials, or an influenza vaccine). Members of the Army and Navy also helped arrange field trials on soldiers and reported back results. This user perspective helped facilitate bi-directional feedback, and ultimately utilization. In some cases, CMR supported manufacturing as well—most famously in the penicillin program, which we explore in depth in our prior work.

Further reading

Beyond our own work, several contemporary and historical accounts describe CMR's operation and the research it supported—many of which we have consulted in this and prior papers. Baxter (1946) and Stewart (1948) provide official histories of OSRD, and Andrus (1948) provides a recounting of OSRD medical research specifically. More recent writing has examined specific CMR-funded research efforts, such as in penicillin and antibiotics (e.g., Swann 1983, Neushul 1993), steroids (e.g., Achilladelis 1999), blood (e.g., Creager 1999), vaccines (e.g., Hoyt 2006), and malaria preventatives and treatments (e.g., Slater 2009), as well as links between CMR and postwar biomedical research policy (e.g., Strickland 1988, Mandel 1996, Sampat 2023).

The most comprehensive account of wartime medical research is, in our view, Andrus (1948), which is referenced heavily in Appendix D when we examine how features of specific CMR programs may explain their persistent effects. The data introduced in Appendix B are used to produce a more systematic accounting, complementing narrative histories.

B Data Appendix

B.1 OSRD/CMR data sources

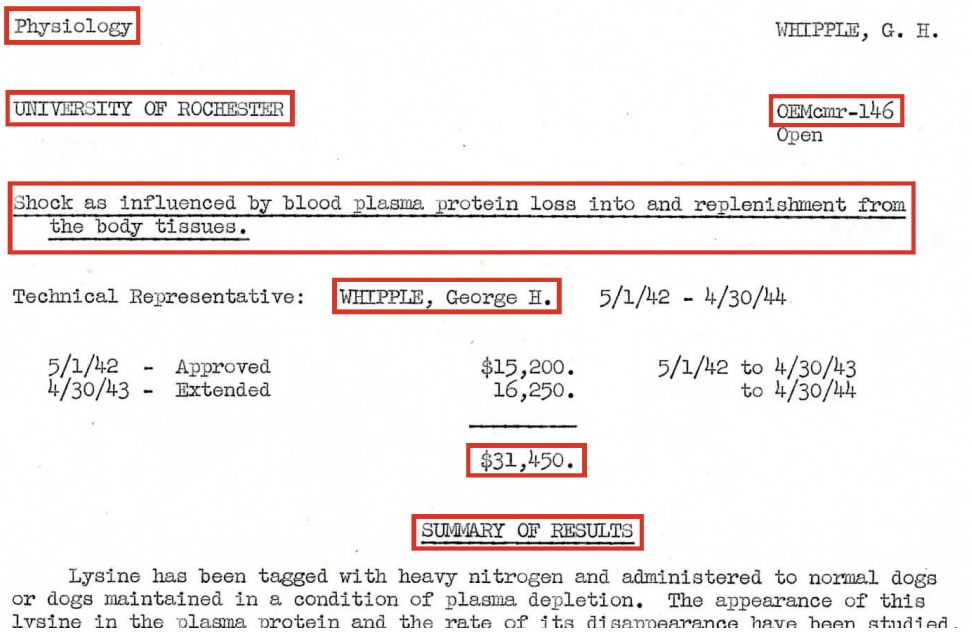
At the heart of this paper are new data on CMR-funded research obtained from OSRD archival records at the U.S. National Archives and Records Administration (NARA).[2] The principal data source for this paper is a set of CMR contract summaries, which identify the CMR division, contract number, principal investigator, institution, project title, value, award period, and a list of all technical reports, interim and final progress reports, and publications produced under the contract. For most contracts it also provided a summary of results. We cross-validate the information in these records against three other sources: (i) contract index in OSRD archival records, (ii) a contract list in the archival records, and (iii) a corresponding contract list in Andrus (1948). Figure B.1 provides a screenshot from an example CMR contract summary, highlighting key fields. Figure B.2 shows the corresponding index card from the OSRD contract index.

From the collective records we identify a total of 590 CMR research contracts: 573 extramural contracts to investigators at 128 universities, firms, hospitals, and institutes (identified in records as contracts OEMcmr-1 to OEMcmr-573), and 17 intramural contracts (primarily with the USDA, FDA, and NIH). The extramural contracts bore a total value of $21.3 million in 1940-45 dollars—around 5% of OSRD's total spending across all research contracts, most of which was comprised of NDRC developing physical war technologies like radar (see Gross and Sampat 2023a,b, Gross and Roche 2024)—equivalent to roughly $400 million in 2024.

We are also able to identify scientific publications produced under these contracts, using the union of (i) publications reported in contract summaries (like the one shown in Figure B.1), (ii) a "CMR bibliography" reported in Andrus (1948), and (iii) an independent CMR bibliography discovered in OSRD records which appears to have been the input for the Andrus list, though these sources mostly intersect. Figure B.3 provides excerpts from the archival and published bibliographies. We digitize and consolidate these bibliographies and link the results to Microsoft Academic Graph (MAG; 82% link rate), Web of Science (79% link rate), and PubMed (55% link rate, due to PubMed's limited coverage in this period). Though CMR publications provide insight into the shape of its research portfolio, throughout our analysis we prioritize contract-based measures over publication-based measures, as they indicate research inputs rather than output.

[2]See NARA Record Group 227, "Records of the Office of Scientific Research and Development". The key record set for this paper are the Committee on Medical Research *Contract Ledgers* (NC-138, Entry 164, Stack area 130, Row 22, Compartment 18, Shelf 2-3, Boxes 1-6). Also relevant were OSRD's *Index to Contracts* (NC-138, Entry 27, Stack area 130, Row 20, Compartment 11, Shelf 1, Boxes 1-5) and lists of CMR contracts and CMR-funded publications found in NARA records which we cross-validate against lists presented in Andrus (1948).

Figure B.1: Example medical research contract summary



Physiology

WHIPPLE, G. H.

UNIVERSITY OF ROCHESTER

OEMcmr-146
Open

Shock as influenced by blood plasma protein loss into and replenishment from the body tissues.

Technical Representative: WHIPPLE, George H. 5/1/42 - 4/30/44

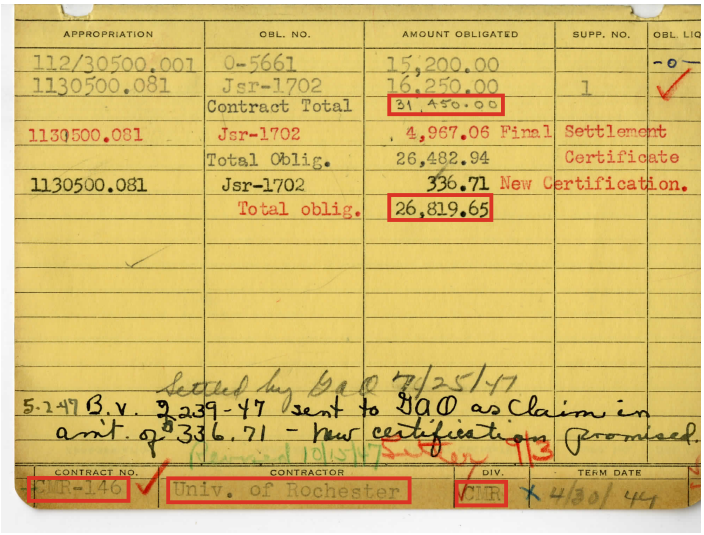
5/1/42 -	Approved	$15,200.	5/1/42 to 4/30/43
4/30/43 -	Extended	16,250.	to 4/30/44
		$31,450.	

SUMMARY OF RESULTS

Lysine has been tagged with heavy nitrogen and administered to normal dogs or dogs maintained in a condition of plasma depletion. The appearance of this lysine in the plasma protein and the rate of its disappearance have been studied.

Notes: Figure shows an excerpt from an example contract summary report from the CMR contract ledgers, for contract OEMcmr-146. The headings provide basic contract information, including the contract number, institution, subject, principal investigator, dates, and total obligated value. Also included in these reports were extended abstracts and publication lists.

Figure B.2: Corresponding contract index card



APPROPRIATION	OBL. NO.	AMOUNT OBLIGATED	SUPP. NO.	OBL. LIQ
112/30500.001	0-5661	15,200.00		-0-
1130500.081	Jsr-1702	16,250.00	1	✓
	Contract Total	31,450.00		
1130500.081	Jsr-1702	4,967.06 Final	Settlement	
	Total Oblig.	26,482.94	Certificate	
1130500.081	Jsr-1702	336.71 New	Certification.	
	Total oblig.	26,819.65		

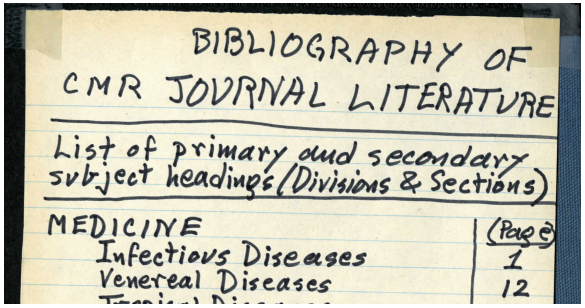
Settled by GAO 7/25/47
5-1-47 B.V. 9239-47 sent to GAO as claim in amt. of $336.71 - new certification promised.

CONTRACT NO.	CONTRACTOR	DIV.	TERM DATE
OEMcmr-146 ✓	Univ. of Rochester	CMR	X 4/30/44

Notes: Figure shows the corresponding index card from the OSRD contract index. The card identifies the contract number, contractor, OSRD division (in this case, "CMR"), and the total contracted and obligated value.

Figure B.3: CMR bibliography, archival and published copies

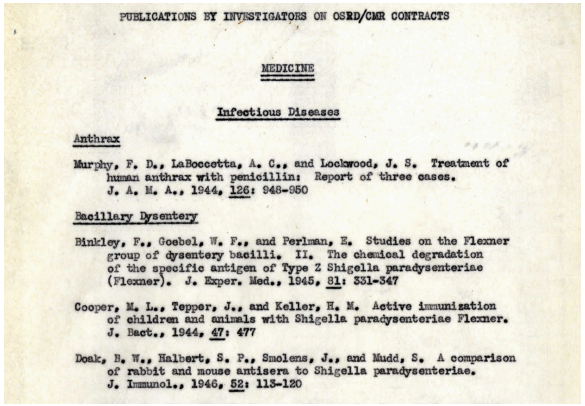
Archival records:



BIBLIOGRAPHY OF
CMR JOURNAL LITERATURE

List of primary and secondary subject headings (Divisions & Sections)

MEDICINE	(Page)
Infectious Diseases	1
Venereal Diseases	12
Tropical Diseases	



PUBLICATIONS BY INVESTIGATORS ON OSRD/CMR CONTRACTS

MEDICINE

Infectious Diseases

Anthrax

Murphy, F. D., LaBoccetta, A. C., and Lockwood, J. S. Treatment of human anthrax with penicillin: Report of three cases. J. A. M. A., 1944, 126: 948-950

Bacillary Dysentery

Binkley, F., Goebel, W. F., and Perlman, E. Studies on the Flexner group of dysentery bacilli. II. The chemical degradation of the specific antigen of Type Z Shigella paradysenteriae (Flexner). J. Exper. Med., 1945, 81: 331-347

Cooper, M. L., Tepper, J., and Keller, H. M. Active immunization of children and animals with Shigella paradysenteriae Flexner. J. Bact., 1944, 47: 477

Doak, B. W., Halbert, S. P., Smolens, J., and Mudd, S. A comparison of rabbit and mouse antisera to Shigella paradysenteriae. J. Immunol., 1946, 52: 113-120

Andrus (1948):

BIBLIOGRAPHY

Publications by Investigators on OSRD/CMR Contracts

MEDICINE

Infectious Diseases

Anthrax

Murphy, F. D., LaBoccetta, A. C., and Lockwood, J. S. Treatment of human anthrax with penicillin: Report of three cases. *J.A.M.A.*, 1944, *126:* 948–950.

Bacillary Dysentery

Binkley, F., Goebel, W. F., and Perlman, E. Studies on the Flexner group of dysentery bacilli. II. The chemical degradation of the specific antigen of Type Z Shigella paradysenteriae (Flexner). *J. Exper. Med.*, 1945, *81:* 331–347.

Cooper, M. L., Tepper, J., and Keller, H. M. Active immunization of children and animals with Shigella paradysenteriae Flexner. *J. Bact.*, 1944, *47:* 477.

Doak, B. W., Halbert, S. P., Smolens, J., and Mudd, S. A comparison of rabbit and mouse antisera to Shigella paradysenteriae. *J. Immunol.*, 1946, *52:* 113–120.

Dubos, R. J., Hoberman, H. D., and Pierce, C. Some factors affecting the toxicity of cultures of Shigella dysenteriae. *Proc. Nat. Acad. Sc.*, 1942, *28:* 453–458.

Dubos, R. J., Straus, J. H., and Pierce, C. The multiplication of bacteriophage in vivo and its protective effect against an experimental infection with Shigella dysenteriae. *J. Exper. Med.*, 1943, *78:* 161–168.

Ehrich, W. E., Halbert, S. P., Mertens, E., and Mudd, S. Mechanism of the augmenting acting of mineral oil on antibody production. Tissue reactions and antibody response to dysentery vaccine in saline, and in saline-lanolin-mineral oil emulsion. *J. Exper. Med.*, 1945, *82:* 343–360.

Goebel, W. F., Binkley, F., and Perlman, E. Studies on the Flexner group of dysentery bacilli. I. The specific antigens of Shigella paradysenteriae (Flexner). *J. Exper. Med.*, 1945, *81:* 315–330.

Goebel, W. F., Perlman, E., and Binkley, F. Antibody response in man to injection of the specific antigen of Type V Shigella paradysenteriae. *Science*, 1944, *99:* 412–413.

Notes: Figure shows excerpts from the CMR bibliography (publication list). On the left are archival records; on the right is the matching published version in Andrus (1948).

B.1.1 Linking CMR to the MeSH vocabulary

As we explain in Section 3 of the paper, we use the National Library of Medicine's (NLM) Medical Text Indexer (MTI) to connect CMR contracts to medical subjects, measured via MeSH descriptors (which we alternatively call "MeSH terms"). MeSH is the NLM's controlled and hierarchically-organized vocabulary used for indexing and cataloging biomedical and health-related research, and MTI is a natural language processing tool which identifies candidate MeSH terms for journal article indexing and serves as the first-line indexer for a large number of journals. We repurpose MTI to index CMR contracts in our setting, on the basis of their titles and contract summaries. The resulting output identifies associated medical subjects, a relevance score for each subject, and associated MeSH tree codes, identifying subjects' hierarchical relationship.[3]

MTI indexing of CMR contracts (and of MAG publications, as we discuss below) was performed between 2021 and 2022.[4] Figure B.4 provides a screenshot showing the structure of the MeSH tree; though most of our analysis occurs at the MeSH term level, in robustness checks we also make use of this hierarchical taxonomy for medical research space.

Figure B.4: Sample from Medical Subject Heading (MeSH) tree

Notes: Figure displays the MeSH tree, which assigns hierarchical structure to medical subject headings (see paper for a more complete discussion). Left image shows the main branches. Right image illustrates select subcategories of the 'A' branch.

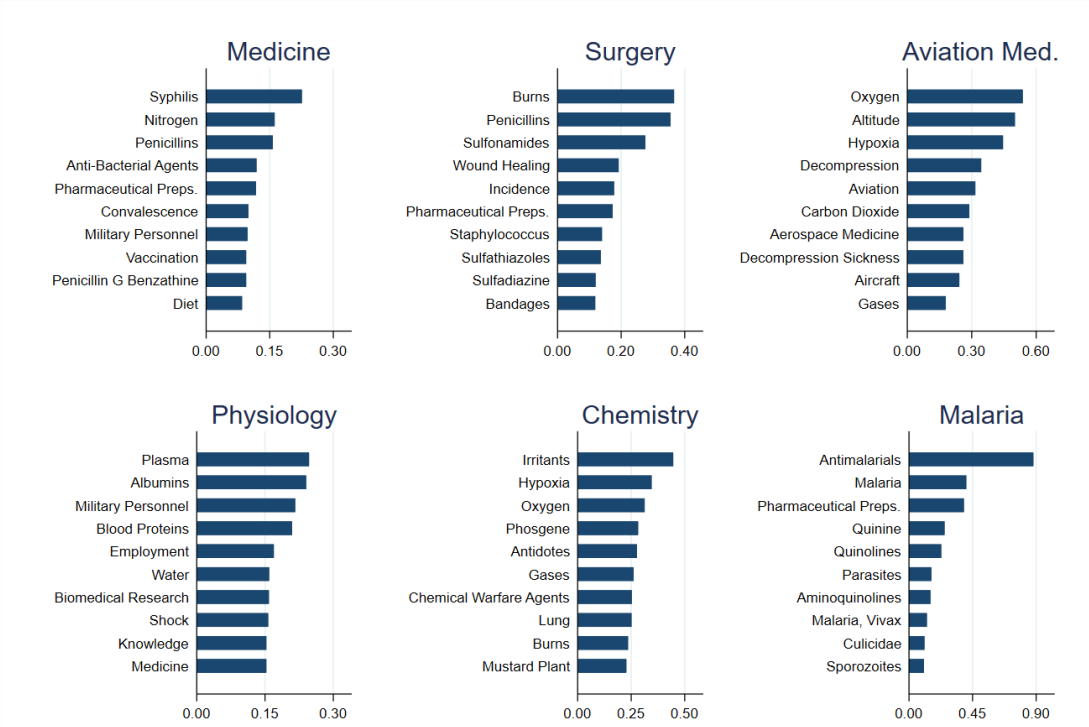
[3]The MeSH vocabulary has roughly 30,000 unique terms (descriptors) and 60,000 tree codes. Some terms link to multiple tree codes, reflecting relationships to distinct regions of biomedical idea space.

[4]Note that as of January 2025, MTI has been decommissioned, and is no longer available to the public. NLM has transitioned internal indexing to a "next-generation" replacement indexer named "MTIX" which uses neural network-based prediction methods, but MTIX is not currently available to the public. In an email exchange, NLM staff explained that there is no timeline for a public release.

B.1.2 What subjects did CMR support?

Figure 2 of the paper provides a lens into research subjects CMR funded, listing subjects in each CMR division with the most associated contracts. Here we provide two additional views of CMR's portfolio, empirical and qualitative. Figure B.5 reproduces Figure 2, showing the top subjects weighted by funding. Table B.1 presents the table of contents to Andrus (1948)—a collection of postwar summaries of CMR research programs—as a qualitative window into the research subjects CMR funded, including areas where it failed to make meaningful progress.

Figure B.5: Top 10 MeSH terms by CMR division, value-weighted



Notes: Figure lists the top 10 MeSH terms associated with CMR contracts in each of the six primary CMR divisions, showing what share of divisional contract value each term associates with. Individual contracts map to multiple MeSH terms.

Table B.1: Andrus (1948) Table of Contents

Section	Chapter
PART ONE—Medicine	
	Chapter 01 – Introduction
	Chapter 02 – Infectious Diseases
	Chapter 03 – Venereal Diseases
	Chapter 04 – Tropical Diseases
	Chapter 05 – Medical Problems of Convalescence
PART TWO—SURGERY	
	Chapter 06 – Introduction
	Chapter 07 – The Prevention of Infection in Accidental Wounds
	Chapter 08 – Experimental Wound Healing
	Chapter 09 – The Application of Penicillin to Surgical Problems
	Chapter 10 – Orthopedic Problems and Prosthetics
	Chapter 11 – The Problem of Gas Gangrene
	Chapter 12 – The Burn Problem
	Chapter 13 – The Repair of Peripheral Nerve Lesions
	Chapter 14 – Experimental Studies on Concusion
	Chapter 15 – Frostbite and Trench Foot
	Chapter 16 – New Surgical Plastics and Hemostatics
	Chapter 17 – Improvements in X–Ray Devices
	Chapter 18 – Studies on Wound Ballistics
PART THREE—AVIATION MEDICINE	
	Chapter 19 – Introduction
	Chapter 20 – The Study of Crash Injuries and Prevention of Aircraft Accidents
	Chapter 21 – The Effects of Acceleration and Their Amelioration
	Chapter 22 – Visual Problems
	Chapter 23 – Motion Sickness
	Chapter 24 – Anoxia and Oxygen Equipment
	Chapter 25 – Altitude Decompression Sickness
PART FOUR—PHYSIOLOGY	
	Chapter 26 – Introduction
	Chapter 27 – Shock
	Chapter 28 – The History of Plasma Fractionation
	Chapter 29 – Blood Substitutes
	Chapter 30 – Methods of Preservation of Whole Blood
	Chapter 31 – Problems of Nutrition
	Chapter 32 – Acclimatization to Heat and Cold
	Chapter 33 – Protective Clothing
	Chapter 34 – Water Disinfection and Allied Subjects
PART FIVE—CHEMICAL WARFARE AGENTS	
	Chapter 35 – Introduction
	Chapter 36 – Systemic Agents: Action and Treatment
	Chapter 37 – Recent Research on Respiratory Irritants
	Chapter 38 – Protection and Treatment of the Skin Exposed to Blister Gases
	Chapter 39 – The Effects of Toxic Chemical Agents on the Eye and Their Treatment
PART SIX—ANTI—PEST AGENTS	
	Chapter 40 – The Development of New Insecticides
	Chapter 41 – The Action of DDT on Invertebrates
	Chapter 42 – The Toxicology and Mechanism of Action of DDT in Mammals
	Chapter 43 – The Dispersal of Insecticides
	Chapter 44 – The Development of New Insect Repellents
	Chapter 45 – The Development of New Rodenticides
PART SEVEN—ADRENOCORTICOL STEROIDS	
	Chapter 46 – The Synthesis of Adrenocortical Steroids
PART EIGHT—MALARIA	
	Chapter 47 – Introduction
	Chapter 48 – The Synthesis of Antimalarial Drugs
	Chapter 49 – The Biology and Biochemistry of the Malarial Parasites
	Chapter 50 – The Screening Program
	Chapter 51 – The Clinical Testing of Antimalarial Drugs
PART NINE—PENICILLIN	
	Chapter 52 – Penicillin: A Wartime Achievement
	Chapter 53 – Research in the Development of Penicillin
PART TEN—SENSORY DEVICES	
	Chapter 54 – Sensory Devices

B.2 Scientific publication data

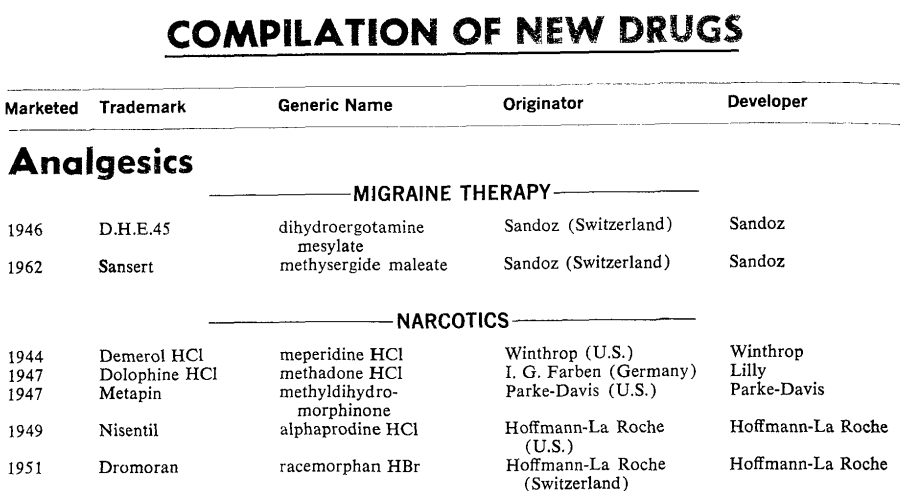
The core outcome data for this paper are biomedical publications, aggregated to the MeSH term-year level. Our base data consists of scientific publications from Microsoft Academic Graph (MAG) which we obtained from the Reliance on Science data repository (Marx and Fuegi 2020, 2022). We filter this sample to publications in the natural sciences and health sciences (OECD field codes 1 and 3) between 1930 and 1970. We then retrieved the titles of these publications and processed them through MTI to obtain MeSH subjects and associated weights. We then work with the MTI output. After dropping check tags (MeSH descriptors that specify species, sex, or age), supplementary concepts (terms outside of the MeSH thesaurus), low-scoring returned terms (specifically, those with less than 10% of a publications' remaining MeSH terms' total score) to reduce noise, we then aggregate to count score-weighted publications by subject and year. Using these data we also produce derivative measures, such as the number of unique other MeSH terms a given MeSH term co-publishes with in a given year, which we label "combinations". We measure the subset of these combinations which are new to the publication record in a given year as "new combinations", and count for each MeSH term-year its number of new combinations.

An important added step in our data collection is also to classify articles as basic or clinical (applied). As we explain in the body of the paper, there is no commonly agreed method of systematically distinguishing basic and clinical research in biomedicine. Prior research has proposed categorizations based on journal (Narin et al. 1976), title (Lewison and Paraje 2004), or content (Li et al. 2017, Ke 2019), or via machine learning (Boyack et al. 2014). We consider three ways of doing so. First, we rely on OECD subfield codes included in the MAG data which identify articles as basic medical research (3.01) and clinical medicine (3.02), via journals. Second, we identify journals indexed by two historical publications, Current Contents: Life Sciences (CC:LS) and Current Contents: Clinical Practice (CC:CP), from a leading commercial indexing service (the Institute for Scientific Information, or ISI) that were intended to cover basic and clinical research, respectively (Garfield 1972, Cardoni 1973). Concretely, we obtained a list of 702 journals from CC:CP as of January 1973 (when it was first published, and shortly after our sample period ends), and over 1,000 journals from CC:LS in 1973 (for consistency). We hand-matched these journals to those in MAG, successfully linking 80% of the former to the latter. Articles in the linked journals are then categorized as basic, clinical, mixed, or neither based on whether they appear in CC:LS or CC:CP. Our third approach applies the term lists in Lewison and Paraje (2004) to identify articles as basic or clinical based on the presence of those terms in their titles.

B.3 Pharmaceutical innovation

Our second set of outcomes measure drug development. We digitize de Haen (1976)'s "Compilation of New Drugs, 1940-1975" to produce a list of new drugs introduced over this period (see Figure B.6 for an excerpt), reporting 1,010 drugs developed by 126 distinct firms, including information on the drug class, trademark name, generic name, and year of introduction. We use these data in two ways. First, we manually crosswalk drug classes to 12-digit MeSH codes on the "therapeutic use" and "physiological effects" subbranches of the "pharmacologic action" branch of the MeSH tree (codes D27.505.954 and D27.505.696, respectively), obtain associated terms, aggregate up to the MeSH code-year of term-year level—in analogous format to our analysis of scientific publications. Second, we aggregate up by firm-year and study effects on firms.

Figure B.6: Sample from de Haen (1976) drugs list



COMPILATION OF NEW DRUGS

Marketed	Trademark	Generic Name	Originator	Developer
Analgesics				
		MIGRAINE THERAPY		
1946	D.H.E.45	dihydroergotamine mesylate	Sandoz (Switzerland)	Sandoz
1962	Sansert	methysergide maleate	Sandoz (Switzerland)	Sandoz
		NARCOTICS		
1944	Demerol HCl	meperidine HCl	Winthrop (U.S.)	Winthrop
1947	Dolophine HCl	methadone HCl	I. G. Farben (Germany)	Lilly
1947	Metapin	methyldihydro-morphinone	Parke-Davis (U.S.)	Parke-Davis
1949	Nisentil	alphaprodine HCl	Hoffmann-La Roche (U.S.)	Hoffmann-La Roche
1951	Dromoran	racemorphan HBr	Hoffmann-La Roche (Switzerland)	Hoffmann-La Roche

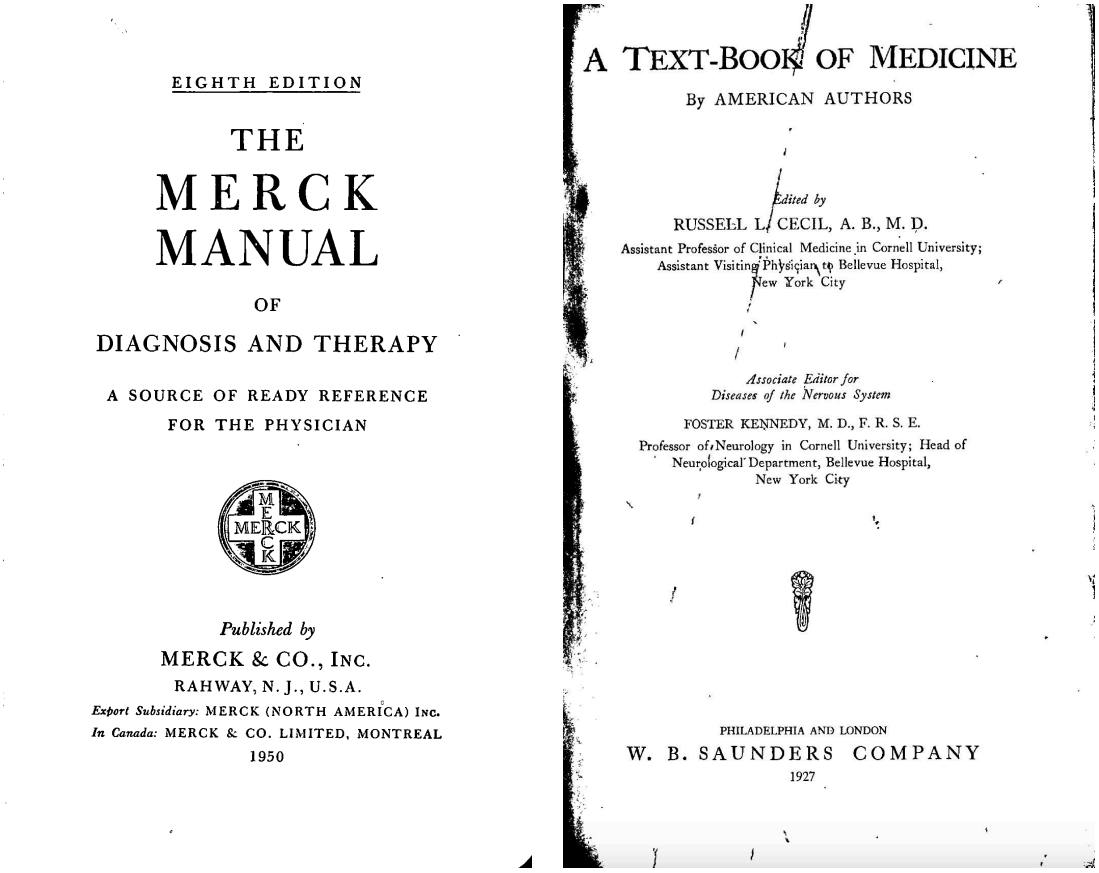
Notes: Figure provides an except from de Haen (1976)'s "Compilation of New Drugs, 1940-1975," which lists chemical entities and synthesized drugs available in the U.S.

Our firm analysis involves two further steps. Because some firms in our sample merged during our study period, we collect information on M&A from U.S. Federal Trade Commission (1980), which reports acquisitions of manufacturing firms with at least $10 million in assets between 1947 and 1978. We dynamically reassign firms to their contemporary parent in the years after a known merger. Second, we manually crosswalk these firms to assignees in patent data, which we obtain from Google Patents (through Google BigQuery). We then identify drug patents belonging to these firms filed between 1930 and 1970, measuring "drug patents" as patents in NBER patent category 31 (Hall et al. 2001), corresponding to USPC 424 and 514. We further measure whether these patents reference non-patent literature (generally, academic research) in the patent text using data from Marx and Fuegi (2020) and Marx and Fuegi (2022).

B.4 Mid-century medical textbooks

Our third set of outcomes studies knowledge diffusion. We use medical textbooks to measure the diffusion of biomedical research subjects into medical practice, focusing on two textbook series which were published both before and after the war: the *Merck Manual of Diagnosis and Therapy* (MM) and the *Cecil Textbook of Medicine* (CT).[5] Figure B.7 shows the covers of the Merck Manual and Cecil Textbook. We collect four editions of the Merck Manual covering 1940, 1950, 1956, and 1961 (editions 7 to 10) and nine editions of the Cecil Textbook covering 1930, 1933, 1937, 1940, 1943, 1947, 1951, 1955, and 1959 (editions 2 to 10). From each edition, we digitize the index and process it through MTI to identify covered subjects.

Figure B.7: Merck Manual and Cecil Textbook practitioner texts: sample volumes



Notes: Figure shows the cover of example editions of the textbooks used in our analysis.

[5]Our interpretation of textbooks as an indicator of medical knowledge is based on textbooks historically being a principal source of guidance for practicing physicians (Catillon 2017).

B.5 NIH extramural research grants

Our final set of outcomes measures postwar extramural NIH grants. We digitize annual editions of the U.S. Public Health Service's *Research Grants and Fellowships Awarded by the National Institutes of Health* from 1948 to 1970 to collect information on all NIH grants over this period, including the grant number, PI, institution, title, amount and funding institute (see Figure B.8 for an example). Similar to other data sources, we process grant titles through MTI to associate them to medical subjects and measure subject-level NIH support.

Figure B.8: NIH research grant listing: sample volume

Research Grants and Fellowships

Awarded by the National Institutes of Health
of the Public Health Service

From Fiscal Year **1951** *Funds*

by Ernest M. Allen, Chief, Division of Research Grants
National Institutes of Health

Public Health Service Research Grants approved for payment from fiscal year 1951 funds

DIVISION OF RESEARCH GRANTS

569 grants totaling $5,363,642

Research grant No.	Investigator and institution	Subject	Approved period of operation	Amount approved for payment
1254C2	Adams, W. E.—University of Chicago	Determination of pulmonary reserve	Mar. 1, 1951–Feb. 29, 1952	$7,938
1378C2	Adolph, E. F.—University of Rochester	Adaptation to cold and dehydration	Aug. 1, 1950–Jan. 31, 1952	12,960
2727	Albright, F.—Massachusetts General Hospital, Boston	ACTH and cortisone on growth	Sept. 1, 1950–Aug. 31, 1951	1,265
2301	Alexander, B.—Harvard University	Blood coagulation and hemorrhagic diseases	Nov. 1, 1950–Oct. 31, 1951	10,000
2301S	do	do	Feb. 2, 1951–Oct. 31, 1951	1,620
1350C3R	Alexander, H. E.—Columbia University	Treatment of tuberculous meningitis	Mar. 1, 1951–Feb. 29, 1952	7,711
2496	Allen, F. W.—University of California, Berkeley	Electrophoresis of nucleoproteins	Sept. 1, 1950–Aug. 31, 1951	11,232
H315C	Alving, A. S.—University of Chicago	Kidney function in normals and hypertensives	Sept. 16, 1950–Sept. 15, 1951	1,695
536C4	Amberson, J. B.—Columbia University	Combinations of therapy in pulmonary tuberculosis	Jan. 1, 1951–June 30, 1952	15,746
2063C	Amberson, W. R.—University of Maryland	Physico-chemical studies on muscle cells	Sept. 16, 1950–Sept. 15, 1951	6,973
81C3	Anderson, G. W.—University of Minnesota	Library research in global epidemiology	Nov. 1, 1950–Oct. 31, 1951	7,808
81C3S	do	do	Mar. 1, 1951–Oct. 31, 1951	4,725
58C4	Anderson, H.—University of California, Berkeley	Studies of mechanisms in analgesia	July 1, 1950–June 30, 1951	13,464
366C3	Anker, H. S.—University of Chicago	Mechanism of fatty acid synthesis	do	10,476
2695	Appel, K. E.—University of Pennsylvania	(See coinvestigator: Windle, W. F., 2695.)		
354C3	Armstrong, W.—University of Minnesota	Metabolism and composition of calcified tissue	do	14,192
2034C	Arnon, D. I.—University of California, Berkeley	Enzymes and photosynthesis in chloroplasts	Sept. 16, 1950–Sept. 15, 1951	2,916
3071	Astwood, E. B.—New England Medical Center, Boston	Mechanism of insulin action	Oct. 1, 1950–Sept. 30, 1951	540
1596C2	Atwood, K. C.—Columbia University	Biochemical aspects of mutations	Dec. 1, 1950–Nov. 30, 1951	4,860
3015	Badger, T. L.—Harvard University	Applied pulmonary physiology	Mar. 1, 1951–Feb. 29, 1952	10,156
2464C	Baehr, G.—Mount Sinai Hospital, New York	ACTH and cortisone on collagen diseases	July 1, 1950–Oct. 31, 1950	8,424
2964	Baer, H.—Tulane University	Immunochemistry of blood group O and H substances	Apr. 1, 1951–Mar. 31, 1952	6,858
3315	Bald, J. G.—University of California, Berkeley	Study of plant virus infection	June 1, 1951–May 31, 1952	540
607C3	Barker, H. A.—University of California, Berkeley	Bacterial synthesis and degradation of fatty acids	Aug. 1, 1950–July 31, 1951	9,072
3209	do	Mechanisms of microbial fermentations	Jan. 15, 1951–Jan. 14, 1952	540
160C4	Barnes, F. W.—Johns Hopkins University	Protein response to chemical stimulus	July 1, 1950—June 30, 1951	12,000
745C3	Barnett, H. L.—Cornell University	Kidney physiology in premature and newborn	do	12,327
2958	do	A study of the nephrotic syndrome in children	June 1, 1951—May 31, 1953	25,352
1465C2	Barron, D. H.—Yale University	The pregnant animal, fetal and maternal aspects	Jan. 1, 1951—Dec. 31, 1951	3,996

Notes: Figure shows the contents of an example issue of U.S. Public Health Service's publication *Research Grants and Fellowships Awarded by the National Institutes of Health*, from which we collect information on all NIH grants from 1948 to 1970.

C Supplementary Results

C.1 Evidence from the raw data

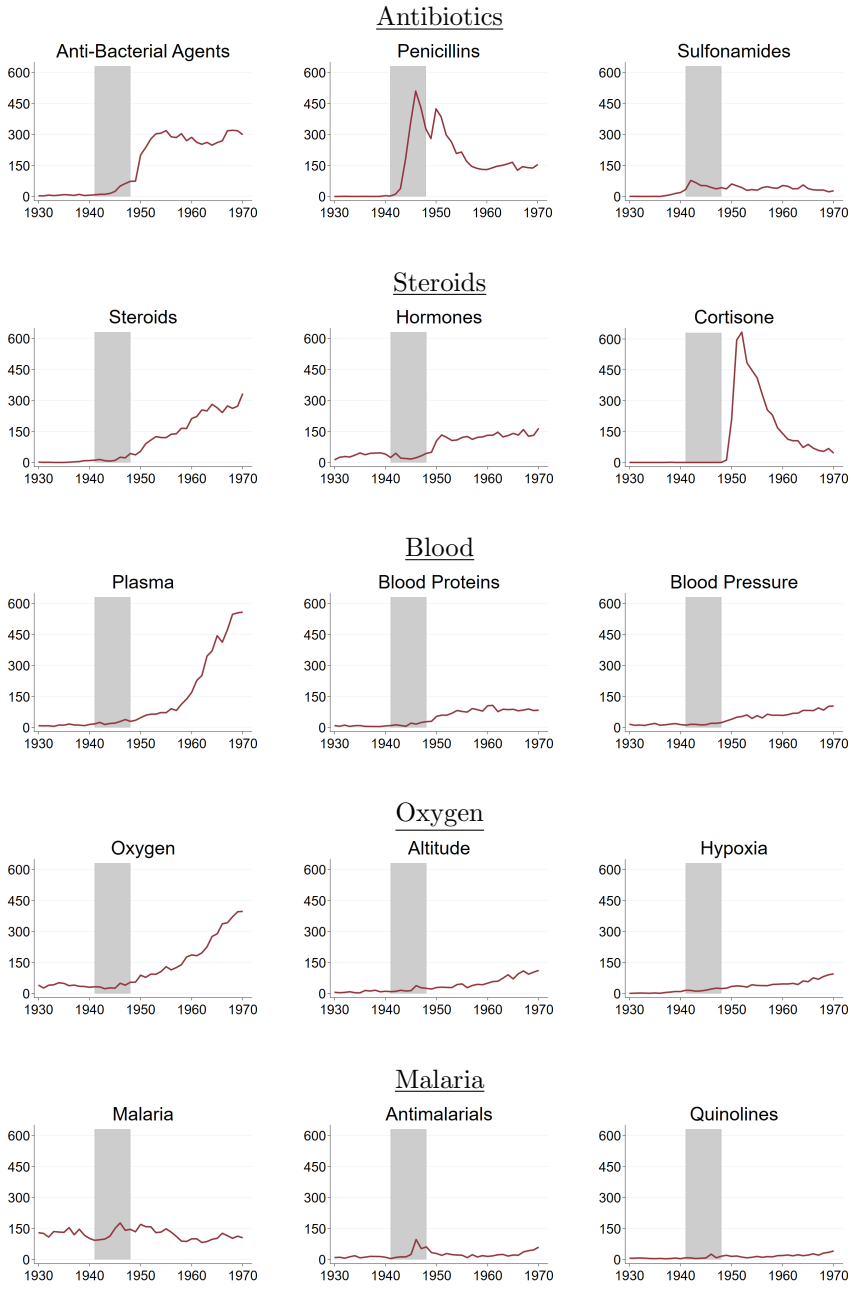
Our analysis of CMR effects on science (Section 4) effectively compares the postwar growth of CMR-funded research subjects against others. Even absent regressions, descriptive evidence from raw publication counts in individual subjects is revealing of the CMR effect, including of the utility in drawing distinctions between existing and new subjects.

Figure C.1 shows the time series of publication activity for example MeSH terms in five CMR-funded research areas—antibiotics, steroids, blood, oxygen and lung function, and malaria. Consistent with Stewart (1948)'s observation that "some subjects are born of war," several specific terms in these areas have little pre-war publication activity but take off after the war ends. Others had existing, pre-war research activity but nevertheless grew significantly after World War II (e.g., Oxygen).[6] As we discuss in Appendix D, historical accounts of specific CMR research programs at times point out pre-war knowledge they built on, but even more often remark on the subjects of wartime research having been essentially new and unexplored Andrus (1948). This was the case not only for a range of specific drugs discovered or developed during the war (like penicillin or new classes of antimalarials), but also for the many new physiological problems that World War II presented (like hypoxia or decompression sickness at 50,000-foot altitudes).

The data are also revealing of the importance of using inputs, rather than outputs, as a measure of the CMR shock (as we discuss in Appendix B)—especially when read in conjunction with history. Several CMR programs made failed to achieve breakthroughs during the war itself but nevertheless may have created a platform for postwar innovation. This was most notably the case for synthetic antibiotics, but also applied in other areas. CMR likewise funded efforts to synthesize cortisone which were unsuccessful during the war itself, but which supported a postwar explosion of research on cortisone and corticosteroids, visible in Figure C.1.

[6] An exception is malaria, which had roughly constant publication activity over time; though research in antimalarials temporarily spiked in World War II, that intensity was not sustained in the postwar era.

Figure C.1: Annual publications in example CMR research subjects around World War II

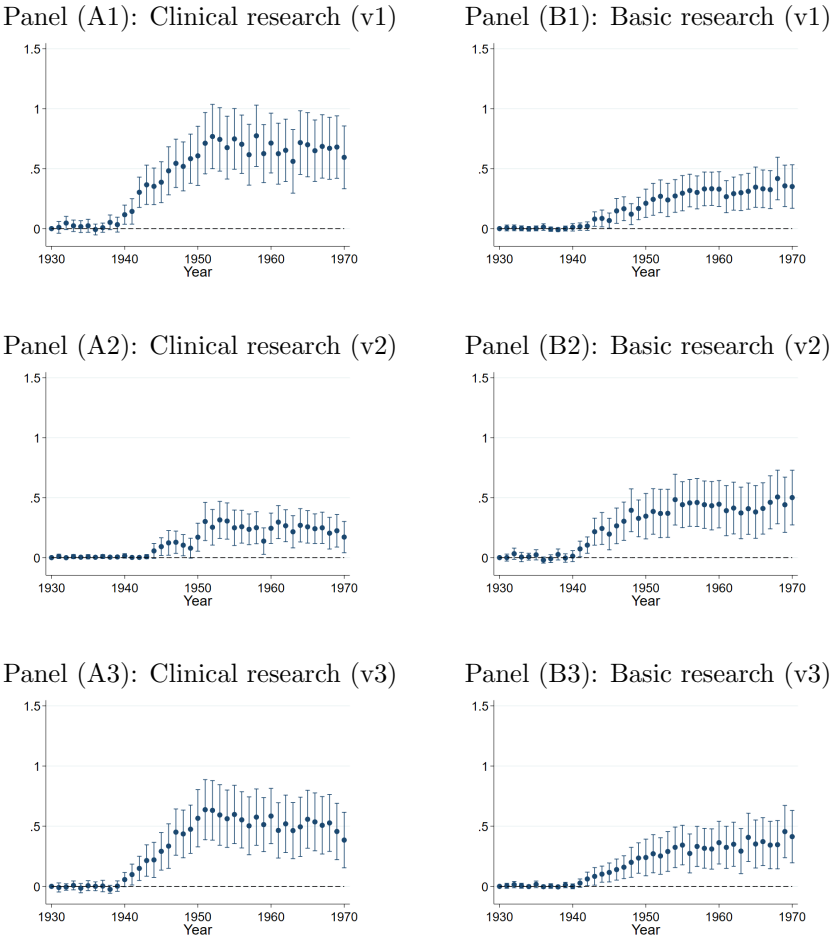


Notes: Figure shows the total publications for select MeSH terms which were major subjects of CMR research. Shaded region in each subfigure marks the war era (1941 to 1948, when most CMR articles were published).

C.2 Effects of CMR on basic versus clinical research: Results under different approaches to measuring basic and clinical research

Figure C.2 presents variants on Figure 4 from the body of the paper using different measures of basic and clinical research. "v1" refers to measures based on OECD subfields in the MAG data; "v2", measures based on historical commercial journal indexing services; "v3", measures based on publication titles. See Appendix B for detailed definitions.

Figure C.2: Effects of CMR on research publications in treated subjects, 1930-1970
Clinical vs. basic research



Notes: Figure shows annual estimates of the differential growth of scientific publications in MeSH terms with CMR funding, relative to others. The sample is restricted to "new" subjects (i.e., those with below-median pre-1940 publications) and the figure divides the sample into basic and clinical biomedical publications (see text for details). Each row uses a distinct approach to identifying basic and clinical research: the top row relies on MAG subject headings that identify journals as basic medical research and clinical medicine; the middle row distinguishes publications in journals indexed by two indexing lists, Current Contents: Life Sciences (CC:LS) and Current Contents: Clinical Practice (CC:CP); the bottom row applies the term lists in Lewison and Paraje (2004) to identify articles as basic or clinical biomedical research based on the presence of those terms in their titles. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

C.3 Heterogeneity by CMR division, program, and contractor

The following tables examine heterogeneity in CMR's effects on science. We re-estimate Equation (1) in Section 4) in several ways. Table C.1 estimates effects by CMR division (Medicine, Surgery, Aviation Medicine, Physiology, Chemistry, Malaria, and a residual "Miscellaneous" category we also observe in CMR records, which primarily funded R&D in synthetic antibiotics and hormones). Differences across divisions will reflect variation in subject matter and funding approaches, especially in the type of research supported (basic vs. applied—with, e.g., physiology on average more basic, medicine more applied, and the "miscellaneous" category largely reducing to drug development) and the relationship of CMR to the performance of the funded work.

To make these comparisons, we measure indicators for whether a MeSH subject had any associated CMR contracts from each division, and we run a single horserace regression of the effects of being funded by each division. The columns of Table C.1 represent division-specific effects from this horserace (i.e., with all parameters in the table estimated in one combined regression). Following the structure of our analysis in the paper, we also limit the sample to subjects which were less-developed at the dawn of World War II (i.e., those with below-median pre-1940 publications). We find substantial heterogeneity in the effects associated with each division. The largest effects (by far) are generated by contracts in the "Miscellaneous" category, where shocked subjects on average roughly quintupled scientific activity by the 1950s. The Physiology and Surgery divisions also had large and persistent effects. The Medicine and Chemistry divisions, by comparison, had shorter-lived effects on science, and Malaria effectively had none.

Table C.1: Heterogeneous effects of CMR on research publications, by CMR division (single horserace regression, presenting estimates for each division)

	Less-developed subjects						
	(1a)	(1b)	(1c)	(1d)	(1e)	(1f)	(1g)
Parameters for:	Medicine	Surgery	Aviat. Med.	Physiology	Chemistry	Malaria	Miscellaneous
Any CMR * Column division * 1(1935-1939)	0.014	-0.002	0.032	-0.005	-0.083	-0.143**	0.041
	(0.031)	(0.025)	(0.058)	(0.041)	(0.076)	(0.071)	(0.077)
Any CMR * Column division * 1(1940-1945)	0.607***	0.531***	0.222	0.354***	0.272	0.094	1.255
	(0.167)	(0.121)	(0.136)	(0.122)	(0.205)	(0.151)	(0.925)
Any CMR * Column division * 1(1946-1950)	0.829***	0.897***	0.307	0.770***	1.253**	-0.161	3.098***
	(0.216)	(0.174)	(0.204)	(0.221)	(0.564)	(0.125)	(1.043)
Any CMR * Column division * 1(1951-1955)	0.465*	0.898***	0.296	1.104***	1.376**	-0.379**	5.346***
	(0.258)	(0.215)	(0.247)	(0.244)	(0.693)	(0.148)	(0.768)
Any CMR * Column division * 1(1956-1960)	0.512**	0.783***	0.392*	1.107***	0.940	-0.388*	4.455***
	(0.247)	(0.218)	(0.238)	(0.250)	(0.657)	(0.218)	(0.666)
Any CMR * Column division * 1(1961-1965)	0.241	0.604**	0.293	1.221***	0.606	-0.236	4.037***
	(0.273)	(0.235)	(0.262)	(0.264)	(0.587)	(0.258)	(0.243)
Any CMR * Column division * 1(1966-1970)	0.249	0.495**	0.404	1.251***	0.440	-0.355	3.468***
	(0.264)	(0.221)	(0.304)	(0.262)	(0.473)	(0.292)	(0.154)

Notes: Table estimates differences in the annual number of scientific publications in MeSH terms with versus without CMR funding, estimating effects by CMR division. All estimates in the table are produced from a single horserace regression with CMR division-specific treatment indicators. A given MeSH term can be treated by multiple divisions. These division-specific coefficients are reported across columns. Estimation sample is restricted to "new" subjects (those with below-median pre-1940 publications). *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by MeSH term in parentheses.

CMR records also associate contracts to specific topics within its divisions, which by our reading roughly correspond to research programs. In Table C.2 we estimate a similar horserace regression by CMR program, which we organize into five categories: disease studies (infectious disease, tropical disease, malaria), injury studies (burns and wounds, gas casualties), research into therapeutic techniques (neurosurgery, convalescence), research on specific therapies (antibiotics, hormones), and physiology (blood, shock, nutrition and acclimatization). The columns in this table represent program-specific effects estimated from a single regression, with the top panel reporting estimated effects of disease- and injury-driven CMR research, and the bottom panel continuing this reporting with estimated effects of research in techniques, therapies, and physiology. The largest and most persistent effects appear to have been produced by CMR investments in specific therapies and in physiology. The categorical contrast between the two—studies of blood, shock, and nutrition were relatively more fundamental, and R&D in antibiotics and hormones very applied—speaks to not only the complex bundle that CMR as a whole represented (the agency does not fit neatly into the basic-applied dichotomy), but also the possibility that investments in both research and technology can propel science, eluding a traditional linear model of innovation.

Our final tests cut the CMR shock by research performer. Specifically, we examine the effects of a MeSH term being a subject of CMR research performed by investigators in each of five sectors: (i) universities, (ii) firms, (iii) hospitals, (iv) research institutes, or (v) government. Table C.3 presents the results, estimated via a single horserace regression (as in the prior tables). We find large effects for all sectors but research institutes, with particularly large effects for government-performed research, as well as large effects for industry-performed research. Due to subject differences across contractors, we cannot attribute differential effects to the contracting sector per se (i.e., to the quality or public value of industrial or government-performed research), but the differences are nevertheless revealing of the heterogeneity across CMR's portfolio.

Table C.2: Heterogeneous effects of CMR on research publications, by CMR program (single horserace regression, presenting estimates for each program)

	Less-developed subjects					
	Disease				Injury	
	(1a)	(1b)	(1c)	(1d)	(1e)	(1f)
Parameters for:	Infect. Disease	Malaria	Trop. Disease	Ven. Disease	Burns/Wounds	Gas Casualties
Any CMR * Column program * 1(1935-1939)	0.034	-0.152**	0.087	0.027	0.027	-0.157*
	(0.040)	(0.073)	(0.081)	(0.049)	(0.044)	(0.086)
Any CMR * Column program * 1(1940-1945)	1.245***	-0.019	0.194	0.286**	0.309**	0.193
	(0.252)	(0.110)	(0.118)	(0.127)	(0.123)	(0.277)
Any CMR * Column program * 1(1946-1950)	0.958***	-0.233	0.705***	1.128**	0.579**	1.424*
	(0.202)	(0.150)	(0.265)	(0.499)	(0.279)	(0.777)
Any CMR * Column program * 1(1951-1955)	0.254	-0.396**	0.403***	1.128*	0.547	1.822**
	(0.438)	(0.164)	(0.102)	(0.637)	(0.344)	(0.894)
Any CMR * Column program * 1(1956-1960)	0.168	-0.363*	0.278**	0.978	0.520	1.455*
	(0.476)	(0.199)	(0.127)	(0.668)	(0.337)	(0.812)
Any CMR * Column program * 1(1961-1965)	-0.343	-0.228	-0.407**	0.941	0.330	1.046
	(0.501)	(0.247)	(0.200)	(0.643)	(0.376)	(0.732)
Any CMR * Column program * 1(1966-1970)	-0.128	-0.349	-0.215	0.936*	0.312	0.921*
	(0.480)	(0.293)	(0.448)	(0.526)	(0.376)	(0.524)

	Less-developed subjects						
	Techniques		Therapies		Physiology		
	(1g)	(1h)	(1i)	(1j)	(1k)	(1l)	(1m)
Parameters for:	Neurosurgery	Convalescence	Antibiotics	Hormones	Blood	Shock	Nut. & Temp.
Any CMR * Column program * 1(1935-1939)	0.014	-0.023	-0.241**	0.147***	0.041	-0.055	-0.000
	(0.039)	(0.060)	(0.107)	(0.002)	(0.056)	(0.040)	(0.086)
Any CMR * Column program * 1(1940-1945)	0.395***	0.198	1.261***	-0.043***	0.341***	0.401**	0.331
	(0.126)	(0.210)	(0.286)	(0.003)	(0.129)	(0.179)	(0.216)
Any CMR * Column program * 1(1946-1950)	0.138	0.301	2.776***	1.636***	0.585**	0.820**	0.658
	(0.119)	(0.332)	(0.559)	(0.005)	(0.249)	(0.346)	(0.407)
Any CMR * Column program * 1(1951-1955)	0.099	0.298	3.214***	6.411***	1.042***	0.860*	0.799**
	(0.235)	(0.367)	(0.661)	(0.008)	(0.388)	(0.441)	(0.373)
Any CMR * Column program * 1(1956-1960)	-0.029	0.556*	2.916***	5.375***	1.011**	0.902*	0.779**
	(0.298)	(0.327)	(0.744)	(0.009)	(0.411)	(0.489)	(0.369)
Any CMR * Column program * 1(1961-1965)	0.187	0.333	3.913***	4.297***	1.244***	1.101**	0.654*
	(0.335)	(0.376)	(0.770)	(0.011)	(0.392)	(0.482)	(0.382)
Any CMR * Column program * 1(1966-1970)	-0.109	0.168	3.419***	3.464***	1.248***	1.004**	0.807**
	(0.297)	(0.421)	(0.795)	(0.012)	(0.385)	(0.487)	(0.401)

Notes: Table estimates differences in the annual number of scientific publications in MeSH terms with versus without CMR funding, estimating effects by CMR program. All estimates in the table are produced from a single horserace regression with CMR program-specific treatment indicators. A given MeSH term can be treated by multiple programs. These program-specific coefficients are reported across columns. Estimation sample is restricted to "new" subjects (those with below-median pre-1940 publications). *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by MeSH term in parentheses.

Table C.3: Heterogeneous effects of CMR on research publications, by contractor sector (horserace regression, presenting estimates for each sector)

	Less-developed subjects				
	(1a)	(1b)	(1c)	(1d)	(1e)
Parameters for:	University	Firm	Hospital	Institute	Government
Any CMR * Column sector * 1(1935-1939)	-0.005	-0.097	0.050	-0.061	-0.098**
	(0.021)	(0.111)	(0.043)	(0.076)	(0.046)
Any CMR * Column sector * 1(1940-1945)	0.355***	0.175	0.652***	0.554*	2.684***
	(0.062)	(0.165)	(0.233)	(0.334)	(0.249)
Any CMR * Column sector * 1(1946-1950)	0.763***	0.630	0.709***	0.492	4.814***
	(0.113)	(0.397)	(0.248)	(0.396)	(0.267)
Any CMR * Column sector * 1(1951-1955)	0.878***	1.026**	0.679**	0.501	4.087***
	(0.150)	(0.401)	(0.267)	(0.598)	(0.277)
Any CMR * Column sector * 1(1956-1960)	0.792***	1.048*	0.862***	0.484	3.178***
	(0.143)	(0.597)	(0.269)	(0.619)	(0.272)
Any CMR * Column sector * 1(1961-1965)	0.630***	1.422***	0.830**	0.492	3.161***
	(0.146)	(0.433)	(0.332)	(0.565)	(0.340)
Any CMR * Column sector * 1(1966-1970)	0.611***	1.433***	0.666*	0.590	2.939***
	(0.140)	(0.343)	(0.378)	(0.596)	(0.385)

Notes: Table estimates differences in the annual number of scientific publications in MeSH terms with versus without CMR funding, estimating effects by the sector(s) of associated contractor(s). All estimates in the table are produced from a single horserace regression with sector-specific treatment indicators. A given MeSH term can be treated by multiple sectors. These sector-specific coefficients are reported across columns. Estimation sample is restricted to "new" subjects (those with below-median pre-1940 publications). *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by MeSH term in parentheses.

C.4 Intensive margin: Value-weighted shock

Figures C.3 and C.4 below present robustness checks on Figure 3 in the paper, estimating the effects of value-weighted CMR shock (the intensive margin) rather than an indicator for whether a subject was the target of any CMR contracts (the extensive margin). We group subjects into three treatment quantiles, based on (MTI score-weighted) total funding: below-median, upper-middle quartile, and upper quartile. We then estimate the following regression:

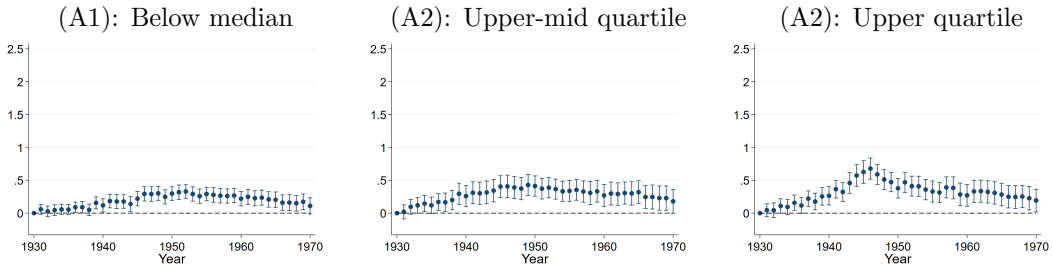
$$Y_{mt} = \sum_{q=1}^{3} \sum_{t=1931}^{1970} \beta_{qt} \cdot \mathbb{1}(\text{Term } m \text{ in treatment quantile } q) + \alpha_m + \delta_t + \varepsilon_{mt}$$

where q indexes treatment quantiles, and the omitted category consists of subjects with no CMR contracts. We essentially estimate heterogeneous effects in Equation (1) for three groups of subjects: those with the lowest, higher, and highest CMR funding level.

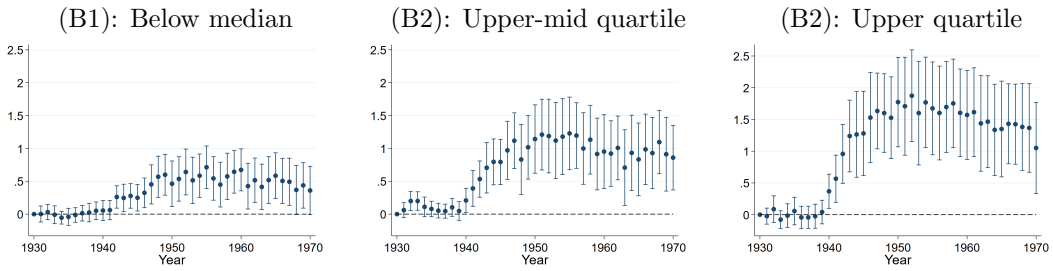
In both Figures C.3 and C.4, we find monotonically increasing effects across treatment quantiles. Our preferred treatment measure is nevertheless an extensive one, for reasons we describe in the paper (Section 4), as well as for its versatility in different analyses.

Figure C.3: Effects of CMR on research publications in treated subjects, 1930-1970, by quantile of CMR funding (0-50th, 50-75th, 75-100th percentiles)

Panel (A): Existing subjects (compare to Figure 3(A1))



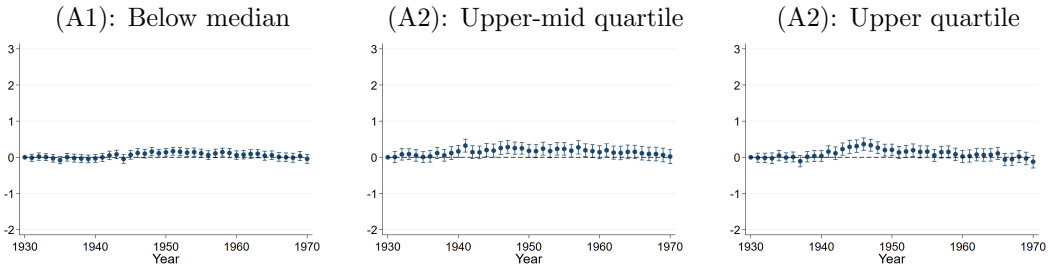
Panel (B): New subjects (compare to Figure 3(A2))



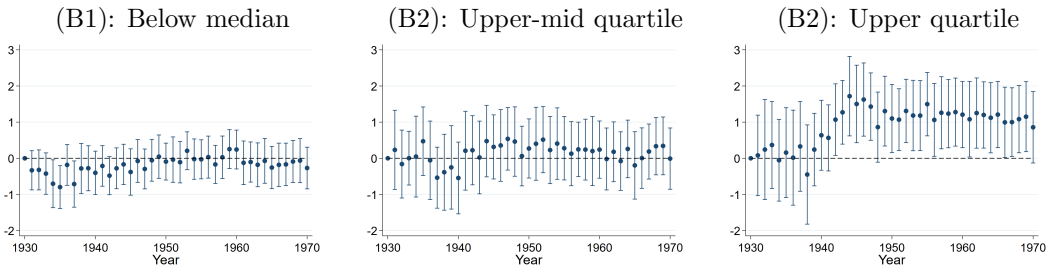
Notes: Figure shows annual estimates of the differential growth of scientific publications in MeSH terms with different levels of CMR funding, relative to others. Rows (A) and (B) divide MeSH terms into subjects with greater than and less than the median number of pre-1940 publications, which we label "existing" and "new" subjects. New combinations are defined as new co-occuring MeSH terms in an article with the given MeSH term. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

Figure C.4: Effects of CMR on new combinations in treated subjects, 1930-1970, by quantile of CMR funding (0-50th, 50-75th, 75-100th percentiles)

Panel (A): Existing subjects (compare to Figure 3(B1))



Panel (B): New subjects (compare to Figure 3(B2))



Notes: Figure shows annual estimates of the differential growth of new combinations in MeSH terms with different levels of CMR funding, relative to others. Rows (A) and (B) divide MeSH terms into subjects with greater than and less than the median number of pre-1940 publications, which we label "existing" and "new" subjects. New combinations are defined as new co-occuring MeSH terms in an article with the given MeSH term. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

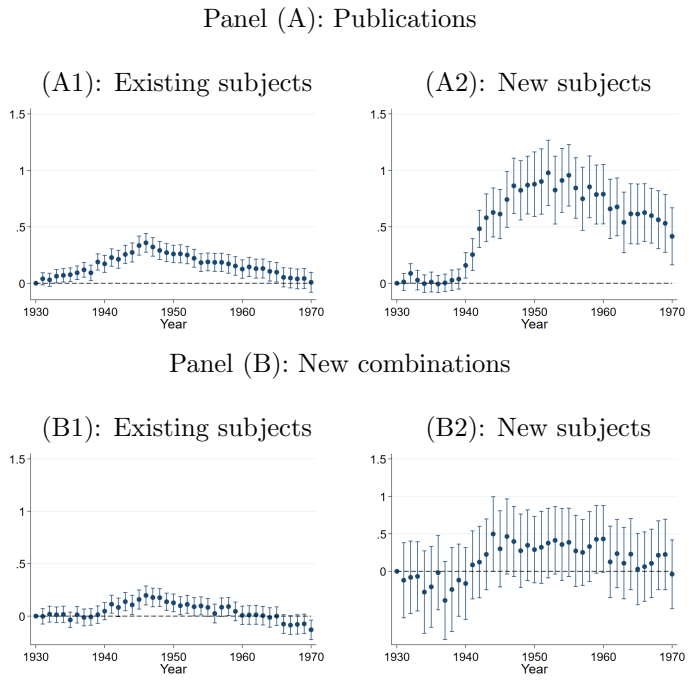
C.5 Controlling for postwar NIH funding

Figure C.5 below presents robustness checks on (i.e., re-estimations of) Figure 3 in the paper, controlling for indicators of whether a given MeSH term was funded by NIH interacted with observation year. Concretely, we estimate the following specification:

$$Y_{mt} = \sum_{t=1931}^{1970} [\beta_t \cdot \mathbb{1}(\text{Any CMR contracts in MeSH term } m) + \gamma_t \cdot \mathbb{1}(\text{Any postwar NIH grants in MeSH term } m)] + \alpha_m + \delta_t + \varepsilon_{mt}$$

The estimated CMR effect are quantitatively and statistically similar, suggesting the CMR effect is neither explained by nor confounded by postwar research funding.

Figure C.5: Effects of CMR on research publications in treated subjects, 1930-1970, controlling for postwar NIH funding (see text for discussion)



Notes: Figure shows annual estimates of the differential growth of scientific publications (Row A) and new combinations (Row B) in MeSH terms with CMR funding, relative to others. Columns (1) and (2) divide MeSH terms into subjects with greater than and less than the median number of pre-1940 publications, which we label "existing" and "new" subjects. New combinations are defined as new co-occuring MeSH terms in an article with the given MeSH term. All results are based on specifications which control for an indicator of whether the given MeSH term received postwar NIH funding (through 1970), interacted with years. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

C.6 Placebo test: World War I

Though World War II produced the first large-scale government funding of medical research, it potentially represents a bundle of two shocks: war (a demand shock for new science and technology) and medical R&D funding (a supply shock). Given their coincidence, the results in Section 4 may be difficult to attribute to CMR specifically, particularly if war has a demand-pull effect that brings research attention (and research activity) to subjects that were previously understudied, and that in turn triggers accumulative endogenous growth in science.

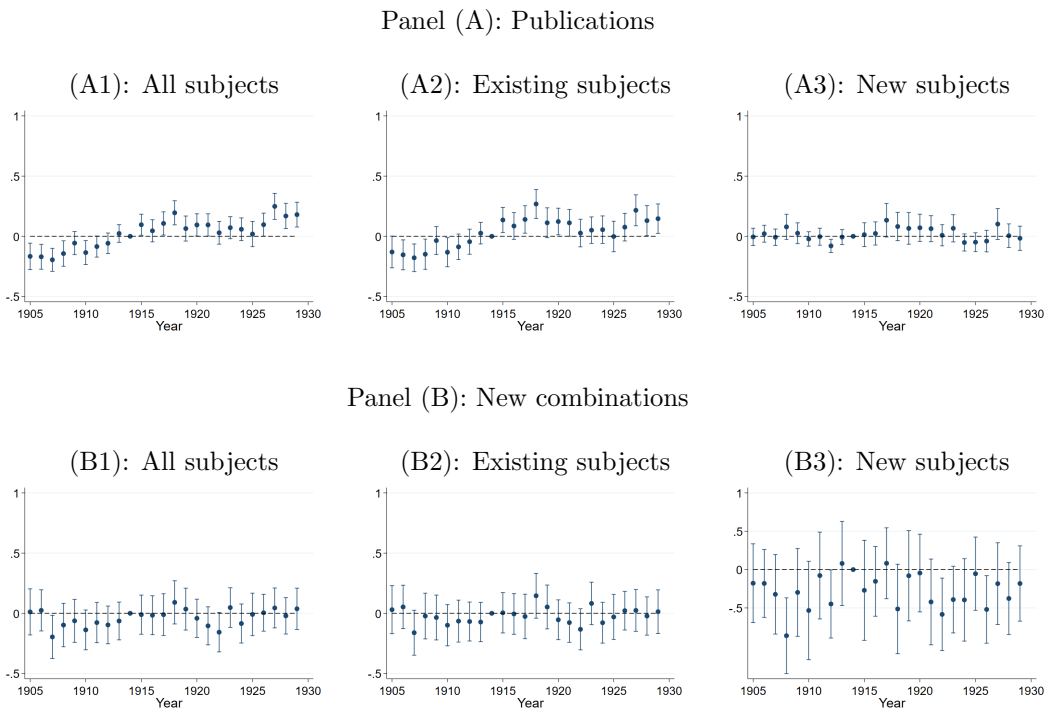
To separate CMR's effects from any general effects of war, we take our research strategy to World War I. We first identify medical subjects implicated in World War I by digitizing the index to American Red Cross (1918) titled *War Medicine*, a publication of the American Red Cross Society in France for medical officers of the U.S. Army presenting war-induced medical conditions, and processing it with MTI (see Appendix B) to link it to MeSH space. We then extend our MAG publication sample backwards to 1905 and run analogous regressions to those in Section 4 of the paper on a sample of MeSH terms between 1905 and 1929 (immediately preceding our World War II sample). Formally, we estimate the following specification:

$$Y_{mt} = \sum_{t=1906}^{1929} \beta_t \cdot \mathbb{1}(\text{MeSH term } m \text{ relevant to WWI}) + \alpha_m + \delta_t + \varepsilon_{mt} \tag{3}$$

where m and t index MeSH terms and years, and standard errors clustered by MeSH term. Following Section 4, we estimate this regression for two outcomes—publications and new combinations—and we do so separately for all terms, existing terms, and new terms, where terms are defined as existing or new based on whether they have above or below median pre-1914 publications (respectively). The resulting estimates are plotted in Figure C.6, and can be compared to the analogous World War II-era effects of CMR shown in Figure 3 in the paper.

In contrast to the effects of CMR estimated in Section 4, we find little evidence of a generic effect of war on science. Panel (A) suggests there may have been some modest pre-war growth in publications in existing war-related subjects, but this growth plateaus after World War I and appears (to our eyes) to be incidental. We find no evidence of growth in new subjects, with relatively tight standard errors small enough to rule out effects of the size found for CMR as well as more modest effects. Continuing the contrasts to the CMR effect we find in the paper, Panel (B) similarly finds no effects of World War I on the growth of new scientific combination.

Figure C.6: Pseudo-effects of "war shock" in World War I, 1905-1929



Notes: Figure shows annual estimates of the differential growth of scientific publications (Row A) and new combinations (Row B) around World War I (sample period: 1905-1929, with the war taking place in 1914-1918) in MeSH subjects implicated in World War I (according to American Red Cross publications). Columns (1) to (3) divide MeSH terms into subjects with greater than and less than the median number of pre-1914 publications, which we label "existing" and "new" subjects. Omitted (Reference) year in all figures is 1914. Error bars represent 95% confidence intervals, with SEs clustered at the MeSH term level.

C.7 Growth of the pharmaceutical industry

This appendix provides additional context, descriptive data, and results with respect to the postwar pharmaceutical industry and its relation to World War II. Section C.7.1 examines the growth of the industry, and Section C.7.2 changes in the nature of drug discovery.

C.7.1 The "golden age" of drug discovery

As we explain in the paper, several important changes to pharmaceutical science and drug innovation are understood to have taken place in the mid-20th century, such as the rise of synthetic chemistry and molecular biology, the growth of rational drug design and systematic drug screens, or advances in clinical testing. Many of these changes ostensibly have links to the war, including in efforts to synthesize new treatments for specific diseases or in large-scale testing, such as the first application of high-throughput screening in the search for new antimalarials.

The degree to which these changes were in fact triggered by the war is potentially an empirically-detectable question, and data on 20th century drug innovation (from de Haen 1976) may provide a window into the answer. Some initial indications are shown in Table C.4, which lists CMR- and WPB-contracted pharmaceutical firms in the De Haen data, along with their total number of drugs introduced in 5-year intervals from 1940 to 1970. By sheer counts, the late 1940s and 1950s was a revolutionary period for drug discovery, especially among CMR/WPB firms, whose average annual new drug introductions more than tripled to over 10 per firm every five years. Other firms increased their average 5-year drug introductions from 0.7 to 1.5 per firm.

Table C.4: Postwar new drugs developed by CMR- and WPB-contracted firms

	New drugs introduced in:					
Firm	1940-45	1946-50	1951-55	1956-60	1961-65	1966-70
Abbott	5	10	14	11	3	2
Bristol	0	0	2	6	4	1
Hoffmann-La Roche	7	7	15	10	7	4
Lilly	4	9	17	11	11	2
Merck, Sharp & Dohme	8	11	12	19	10	4
Parke-Davis	6	8	4	10	2	3
Pfizer	0	2	7	11	1	5
Squibb	0	6	9	7	2	3
Upjohn	1	6	10	12	4	4
Warner	0	2	5	5	5	1
Winthrop	3	3	7	6	2	3
Wyeth	2	5	7	18	6	6
CMR/WPB, Average	3.0	5.8	9.1	10.5	4.8	3.2
Others, Average	0.7	0.9	1.0	1.5	0.6	0.4

Notes: Table reports the number of new drugs developed and brought to market by CMR and WPB pharmaceutical contractors between 1940 and 1970, according to de Haen (1976), in five-year intervals. A small number of firms which merged during this period are combined throughout the sample (e.g., Merck and Sharpe & Dohme merged in 1953, and are reported as a single unit). The bottom row of the table compares these counts to the other-firm average.

Table 4 of the paper evaluates this growth econometrically in Panel (B), and formalizes this result: new drug development grew much more quickly in the first two postwar decades at CMR/WPB firms than others. By 1960, these firms were 20% more likely to introduce a new drug each year than non-CMR/WPB firms (Column 1), with similar effects for antibiotics and hormones (Column 2) and other drugs (Column 3). In percentage terms, the effect was to increase annual drug innovation by roughly 50% at these firms, relative to peers (Columns 4 to 6).

C.7.2 Growth of science-based drug discovery

Beyond its effects on postwar drug innovation, we can also explore whether CMR changed how firms approached drug discovery—i.e., the drug development process itself. To do so we shift our analytical unit from drugs to drug-related patents, focusing on patents filed between 1930 and 1970 by the firms in de Haen (1976). For the purposes of this analysis, we define "drug patents" as patents in the NBER patent category for drugs (Hall et al. 2001). This choice excludes other categories where pharmaceutical firms may have filed patents (such as organic or inorganic chemistry), in order to focus the sample on potential therapeutically-relevant inventions and exclude others—particularly because many drug-developing firms in this era (including the De Haen sample) were industrial chemical companies or had a parallel chemical business.

Through patent data we can get more granular insight into any potential changes in the nature pharmaceutical R&D. Our focus is on its relationship to science, for which we use existing data on patent citations to science (Marx and Fuegi 2020, 2022). For each patent in our sample, we measure whether it makes any in-text citations to scientific literature, limiting to in-text citations (rather than front-page) because (i) these are more likely to reflect intellectual inputs to the invention and (ii) front-page citations were only written into patents beginning in 1946. Patents which cite science we will call "science-citing" or "science-based".

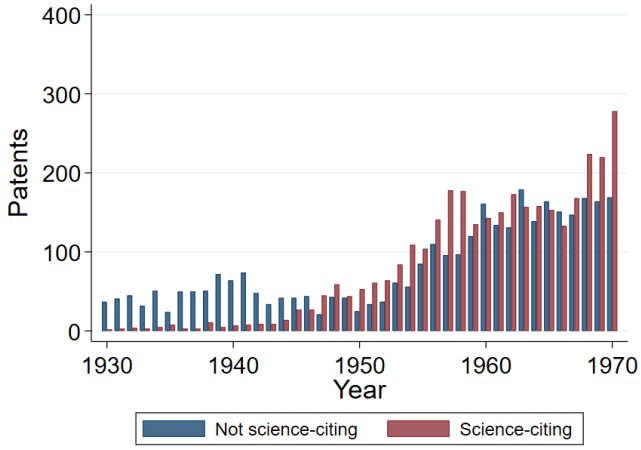
Figure C.7 plots annual counts of non-science and science-based patents in our sample. The figure provides two insights: first, prior to the late 1940s, total annual drug patenting by these firms was more or less constant; second, essentially none of these patents were based in science. Both patterns change after World War II: starting in the late 1940s, drug patenting begins to grow, powered by a rapid increase in science-based invention. Figure C.8 disaggregates this further, showing non-science and science-based patenting by non-CMR firms and CMR firms, respectively, where we see that these changes were mainly driven by CMR firms.

In Table C.5, we evaluate these differences econometrically. Specifically, for the De Haen (1976) firm sample, we estimate differences between CMR/WPB-contracted firms and other pharmaceutical firms in their (i) science-based patenting and (ii) non-science based patenting with parameters in 5-year intervals. We estimate a two-way fixed effects specification as follows:

$$Y_{it} = \sum_{t} \beta_t \cdot \mathbb{1}(\text{CMR/WPB firm})_i + \alpha_i + \delta_t + \varepsilon_{it}$$

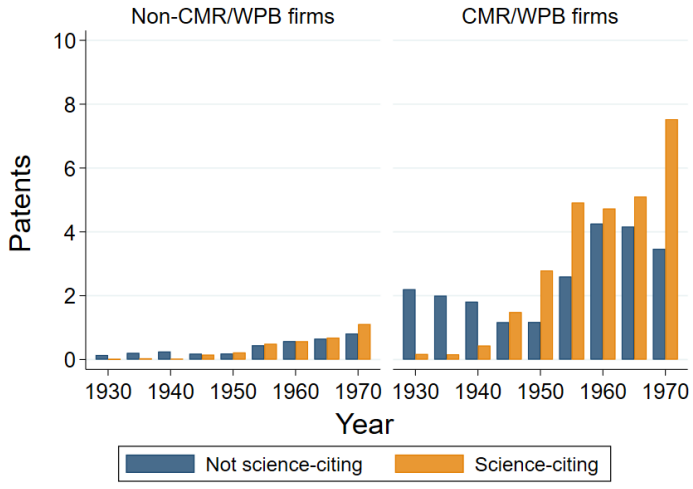
where i and t index firms and years, and the sample runs from 1930 to 1970, with parameters in 5-year intervals and standard errors clustered by firm. We limit the panel to years between each firm's first and last observed drug or patent, to ensure it only includes firm-years when the firm was known to be alive, though this restriction has limited impact in practice.

Figure C.7: Total annual drug patents, science-citing and non-citing, 1930-1970



Notes: Figure shows the number of drug patents filed by firms in de Haen (1976), separately reporting science-citing and non-citing patents. Drug patents defined as those associated with NBER category 31 (Hall et al. 2001), and science-citing patents as those which cite non-patent literature (typically, scientific literature) in their text (Marx and Fuegi 2020, 2022).

Figure C.8: Average annual drug patents by CMR/WPB-contracted firms vs. others



Notes: Figure shows the average annual number of drug patents filed by firms in de Haen (1976), separately reporting CMR/WPB-contracted firms and other firms, and science-citing and non-citing patents. Drug patents defined as those associated with NBER category 31 (Hall et al. 2001), and science-citing patents as those which cite non-patent literature (typically, scientific literature) in their text (Marx and Fuegi 2020, 2022).

We estimate this specification for three outcomes: (i) an indicator for whether the firm filed any science and non-science based patents (Columns 1 and 2, respectively), (ii) the number of such patents (Columns 3 and 4), and (iii) the inverse hyperbolic sine (IHS) number of such patents (Columns 5 and 6).[7] In all columns, time-varying parameters are estimated relative to the omitted 5-year interval of 1930-1934. The table shows two clear patterns. First, CMR/WPB firms rapidly increased their science-based patenting during and especially after World War II, with no discernable pre-trends pre-1940. Second, we find no such differences for non-science based patenting. Third, these results are present across all three outcomes: by the 1960s, CMR/WPB firms were roughly 50% more likely to file at least one drug-based patent in a given year, and these firms increased their drug-based patenting nearly 150% more than other firms. The combination of the results in Columns (5) and (6) in a triple-difference forms the basis for the finding in Figure 7 of the paper, which shows that the differences in the IHS number of science versus non-science drug patents between CMR/WPB and other firms was not changing before 1940, but subsequently doubled over the 1940s and remained higher through at least 1970.

Table C.5: Science-citing patents by CMR- and WPB-contracted firms

	Any patents?		Num. patents		IHS(Patents)	
	(1)	(2)	(3)	(4)	(5)	(6)
	PCS	No PCS	PCS	No PCS	PCS	No PCS
CMR/WPB firm * 1(1935-1939)	0.008	-0.041	0.037	-0.094	0.007	-0.054
	(0.080)	(0.085)	(0.154)	(0.426)	(0.083)	(0.160)
CMR/WPB firm * 1(1940-1945)	0.237**	-0.034	0.476**	-0.375	0.302***	-0.127
	(0.094)	(0.096)	(0.191)	(0.711)	(0.104)	(0.212)
CMR/WPB firm * 1(1946-1950)	0.399***	-0.167	1.339***	-1.088	0.662***	-0.416*
	(0.088)	(0.109)	(0.487)	(0.697)	(0.169)	(0.250)
CMR/WPB firm * 1(1951-1955)	0.539***	-0.126	2.855***	-0.692	1.215***	-0.257
	(0.085)	(0.127)	(0.582)	(0.753)	(0.198)	(0.274)
CMR/WPB firm * 1(1956-1960)	0.462***	0.036	4.314***	0.502	1.340***	0.132
	(0.094)	(0.101)	(1.184)	(1.072)	(0.254)	(0.293)
CMR/WPB firm * 1(1961-1965)	0.539***	0.071	4.343***	1.839	1.450***	0.459
	(0.082)	(0.104)	(0.979)	(1.150)	(0.216)	(0.300)
CMR/WPB firm * 1(1966-1970)	0.457***	0.030	4.564***	1.251	1.410***	0.304
	(0.093)	(0.108)	(1.127)	(1.044)	(0.263)	(0.295)
N	5172	5172	5172	5172	5172	5172
R^2	0.44	0.44	0.50	0.47	0.56	0.55
Y mean	0.208	0.225	0.649	0.645	0.320	0.334

Notes: Table estimates differences in pharmaceutical firms' annual science-based and other drug patenting, comparing CMR/WPB-contracted pharmaceutical firms to others. Sample consists of firms which introduced at least one new drug between 1940 and 1970, according to de Haen (1976). A small number of firms which merged or were acquired during the sample frame are dynamically reassigned to their subsequent owners using data from FTC (1980) (see text for details, including specific exceptions). The unit of analysis is a firm-year, and outcomes measure: (i) whether a firm filed any patents in drug classes (NBER category 31; Hall et al. 2001) in the given year (Columns 1 and 2), (ii) the number of such patents (Columns 3 and 4), and (iii) inverse hyperbolic sine (IHS) patents (Columns 5 and 6). Table separately estimates changes in patents that do vs. do not cite non-patent literature (typically, scientific literature) in their text (Marx and Fuegi 2020, 2022). Results are estimated relative to the 1930-1934 period. *, **, *** represent significance at the 0.1, 0.05, and 0.01 levels, respectively. SEs clustered by firm in parentheses.

[7]Despite that firm-year patenting is for most firms a low-count outcome, we estimate Columns (3) and (4) by OLS to simplify interpretation, as we are interested in the average cross-firm differences. Results are directionally and statistically similar under count models (e.g., two-way fixed effects Poisson), and the qualitative and statistical consistency across the reported columns in Table C.5 makes them mutually-reinforcing.

D Mechanisms of Action

The results of Sections 4 and 5 leave us with the deeper question of why CMR—an intrinsically temporary project, that started and ended with the war—had such large and long-lasting effects. Why was this limited research investment apparently so impactful? Though the mechanics of its research effort, and the specific links between wartime and postwar research and innovation, are difficult to measure empirically, the contemporary and historical accounts provide a range of clues as to what made CMR's approach distinctive and impactful.

Why were CMR's effects so long-lived?

New therapies and therapeutic candidates

Table 2 illustrates several subjects "born of war" (Stewart 1948): mass-produced penicillin, streptomycin, DDT, chloroquine, and dimercaprol each effectively launched research in new directions to understand their chemistry, physiological effects, mechanisms of action, applications to myriad organisms and diseases, and more. Geer et al. (1948, p. 636), for example, explain that the development of DDT as an insecticide "opened a new era in insect control," prompting a surge of new investigation. Similar observations could be made for penicillin and later other antibiotics, which drove an (even larger) surge in clinical studies on their effects. Much of this research had a combinatoric flavor: for example, Lockwood (1948, p. 92) observes "the proper combination of surgery and chemotherapy would permit the surgeon far greater latitude"—reflecting new opportunities for studying the interaction of old procedures and new therapies.

Even when CMR research was not successful during the war itself, but it may have opened up new lines of inquiry which postwar investigators continued: Carden Jr (1948, p. 670) anticipated that although "many of the most promising [antimalarial] compounds were developed too late in the program" to be useful during the war, these "unfollowed leads and current loose ends will undoubtedly be explored." Slater (2009) confirms that research on these "lead compounds" continued—one of which (chloroquine) became a revolutionary malaria treatment in the years after the war, and a major new subject of study (as Table 2 clearly illustrates).

New research tools and techniques

CMR also developed new research methods to meet the war's specific demands, many of which were useful in new problems after it ended. For example, CMR's massive drug screening efforts—including in the hunt for antimalarials, treatments for other tropical diseases, and insect repellents, which collectively screened nearly 20,000 compounds—later became a model for cancer chemotherapy research and other efforts at the NIH (Slater 2009). Techniques developed by the blood substitute research program "provided a technical framework for [a] productive research field" after the war (Creager 1999) on blood-related disorders and blood-derived therapeutics. Cohn (1948, p. 436) writes that the separation of blood "[made] possible the [further] discovery of the function and the uses in therapy" of different components in blood fractions.

Though malaria and blood were among CMR's largest programs, CMR developed new research tools and methods across its portfolio to address questions the war presented. For example, Windle (1948, p. 174) explains that "The introduction of methods of reproducing standard degrees of cerebral concussion and of measuring both the quantity of injury inflicted and the amount of effect produced have opened the possibility of measuring the relation of concussion to nervous metabolism, ... to shock, to fatigue, and to changes induced by anoxia, acidosis, electrical shock, and so forth." Millikan (1948, p. 317) writes of respiratory research that "The technics [sic] and instruments developed for aviation are already widely employed. Few researches on respiratory problems now fail to make use somewhere of a gas-analysis device, or of an instrument for measuring blood gases, or of a demand valve, developed by [OSRD] for war purposes."

New technology platforms

For several major drug categories, the CMR effort also introduced new techniques and platforms that supported continued development after the war ended. Chief among these was in the synthesis of new antibiotics: as Swann (1983, p. 189) points out, although CMR's synthetic penicillin program was a flop during the war, knowledge developed through this work "paved the way for [the] general synthesis of penicillins in the 1950s, [leading] to the development of the therapeutically invaluable semisynthetic penicillins," including dozens of antibiotics introduced in the 1950s (many of which form the basis for results in Section 5; also see de Haen 1976).

In vaccines, methods developed during the war (e.g., centrifugation techniques) subsequently became "state of the art" to the industry by the 1960s (Hoyt 2006, p. 47), contributing to the surge in new vaccines introduced in the 1950s and 1960s. Similar dynamics applied to steroids: the methods developed for producing the "miracle drug" cortisone (a general purpose steroid) during the war were used for developing other corticosteroids afterwards, and Achilladelis (1999, p. 62) writes that "because the technology had diffused among participants of the OSRD project, all of [the firms involved] introduced corticosteroid drugs in the 1950s."

New research capabilities

Beyond specific drugs, several scholars have argued that the war significantly expanded American pharmaceutical companies' general research capabilities, drawing them closer to science, and that this was an important catalyst for a more innovative and competitive U.S. pharmaceutical industry (e.g., Temin 1979, Cockburn et al. 1999, Pisano 2002). Landau et al. (1999), for example, claim that "To a great extent the U.S. government's wartime policies led to the emergence of the American pharmaceutical industry as the undisputed worldwide leader," observing that "the federal war effort encouraged corporate research and development, widened and deepened the companies' cooperation with academic institutions, and catalyzed the diffusion of new technologies across the industry." This was the case for both incumbent drug companies and new ones, as some non-pharmaceutical firms that became involved in drug development during the war continued in it afterwards—most notably Pfizer, which prior to the war was a chemical manufacturing company, became involved in

the natural penicillin program due to its experience with fermentation, and after the war pivoted to drug development, initially focusing on antibiotics.

New collaboration patterns

As we discussed in Section 2, CMR was more than a passive funding agency: it took an active role in organizing research to attack specific military needs. In many cases this required creating networks of academic researchers, hospitals, firms, and (at times) military partners around military medical problems, coordinating the acquisition of inputs, synthesis of drug candidates, fundamental research, clinical testing, and transitions to large-scale manufacturing.

This pattern can be seen across CMR's portfolio. For example, the American Red Cross' blood collection efforts supplied researchers with inputs for their investigation of blood plasma fractionation, the composition of blood fractions, and blood preservation—work which was centered at Harvard (in the laboratory of and under the direction of Edwin Cohn, a physical chemist at Harvard Medical School) but also distributed to and coordinated with researchers at the University of Wisconsin, Stanford University, Columbia University, and the Massachusetts Institute of Technology, with clinical testing units in cities across the country—while the Harvard team operated a pilot plant in conjunction with its laboratory research and worked with several pharmaceutical companies to transition plasma fractionation into production at scale. CMR's efforts to develop new insect repellents drew synthesized candidates from several universities, firms, and government laboratories, which were forwarded to the Department of Agriculture's Bureau of Entomology and Plant Quarantine's testing facilities in Orlando, whose results informed research on fundamental mechanisms at several other universities; here, Scholz (1948, p. 651) observed the "cooperation of government, private industry, and university groups," and noted that "although born of necessity during the war, the usefulness of such coordination of diverse interests for peacetime need is clearly evident." In aviation medicine, Bronk (1948, p. 209) describes how CMR organized a "cooperative scientific effort" which engaged "hundreds of medical scientists in more than a score of universities," and how it brought into "frequent conference groups of scientists working on related problems", and in nutrition Youmans and Guest (1948, p. 473) describe how CMR organized regular "conferences in which investigators and military liaison representatives met to discuss work in progress and practical applications of new information as it was gained."

The continuation of even a portion of these collaborative structures may have contributed to CMR's sustained effects. Although in many cases these fizzled, in some cases under pressures of competition—not only in the product market, but also for scientific talent, which was in high demand after the war and underdeveloped during it (Winternitz 1948)—in other cases collaborations persisted. In the study of blood, for example, relationships between Cohn's lab, blood banks, and firms with fractionation capabilities which Cohn established during the war endured after it ended, and supported Cohn's own postwar research (Creager 1999).

New fundamental knowledge

The most consistent pattern in contemporary accounts is that despite CMR's applied focus, its work produced fundamental understanding which could enable postwar research in new directions—for example, knowledge of the composition of separated blood fractions, the etiology of specific ailments like motion sickness, the epidemiology of diseases like streptoccal infections and rheumatic fever, and many insights into human, animal, and insect physiology.[8]

This anticipated postwar scientific opportunity is described in several contemporary accounts. For example, Youmans and Guest (1948, p. 487) write of nutrition: "The research program ... produced an enormous amount of new scientific information which, aside from its immediate practical value, forms a firm basis for advancing research to be continued in peacetime." Of aviation research, Millikan (1948, p. 316) writes: "As a result of the intensive study of the mechanism of respiratory processes stimulated by aviation's need, there is now a much wider understanding [of] these problems. The application of this knowledge to respiratory abnormalities of disease, in poliomyelitis, emphysema, tuberculosis, and pneumonia, is widespread." Hirshfeld (1948, p. 126) similarly observes of penicillin that "as [its] supply ... became more abundant and the knowledge concerning its action became available, it was possible to expand the categories of infections on which it could be tried" as well as the contexts where it could be applied.

These opportunities also emerged from unlikely topics like chemical warfare. Gilman and Cattell (1948, p. 546) explain that "[CMR's] approach has yielded unsuspected and fruitful byproducts ... not only have valuable research tools for the solution of many of the problems of cellular physiology and metabolism been uncovered, but also many potential therapeutic agents have appeared." With respect to the study of toxic chemicals on the eyes, Friedenwald and Hughes Jr (1948, p. 620) argue that "the net result ... has been to disclose that mustard and related compounds are useful tools in the study of a number of recondite fields of cellular and tissue physiology. In these fields more questions have been made accessible to study than have so far been answered." Regarding research on treatments for respiratory irritants, Gerard (1948, p. 566) explains: "Although the immediate practical results from the current studies have been few ... it has given us far deeper understanding ... and it has pointed the directions in which further research may be expected to yield profit." He later goes on to explain that "much knowledge on the physiology of respiration and circulation has accrued" that was valuable in attacking related medical problems.

Given CMR's heavy focus on developing new chemicals and drugs, a common theme emerges around opportunities to study mechanisms of action. This was especially the case with regards to malaria, parasites, and insect control. On insect repellents, Scholz (1948, p.651) writes: "It is only now becoming possible to correlate the chemical properties and physical characteristics of compounds with their insect-repellency effectiveness. Thousands of candidates remain to be

[8]Other examples (among many) include "fundamental knowledge related to clothing and climatic problems" Robinson and Belding (1948, p. 519), "the fundamental biochemistry of water disinfection" Fair (1948, p. 521), "fundamental studies [of] toxic chemicals in the chemistry and physiology of the cornea" Friedenwald and Hughes Jr (1948, p. 603) and "the fundamental mechanisms" of malaria Carden Jr (1948, p. 666).

analyzed in this light." Haller and Cristol (1948, p. 626) similarly explain of new insecticides: "No satisfactory correlations between chemical structure and toxicity to insects have yet been discovered ... [and] until the effect of various materials on biologic processes is fully understood, it will not be possible to systematize research in the chemistry of insecticides." Yeager (1948, p. 631) continues by explaining that "a generally acceptable theory of the lethal action of DDT must await the acquisition of more experimental data," but that "promising lines of attack ... have been opened up." Regarding the hunt for antimalarials, Carden Jr (1948, p. 670) notes that "intense efforts were made to coordinate the relation between the action of a compound and its chemical configuration, [and] although the complete answer was not found, interesting correlations of the accumulated data, which may bear fruit in the future, were brought to light. Likewise, intense efforts were made to understand the basic biochemical and biologic characteristics of the various malarial parasites, [and] much knowledge was gained that not only throws light on the basic biology of this disease but may also add to knowledge in other lines of investigation."

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