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Secular Changes in NSAID Use and Invasive Colorectal Cancer Incidence: An Ecological Study

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Background

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program has documented large secular changes in incidence of invasive colorectal cancer (CRC) between 1973 through the present day. Researchers have suggested several reasons for these changes including changes in CRC screening over this period [1–5] and increases in use, by the population, of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs have been shown in both observational studies and randomized control trials to prevent pre-cancerous colorectal polyps and subsequent invasive CRC.[6–14]

Objectives

In this exploratory ecological project, we sought to describe trends in NSAID use over time and trends in CRC incidence over time in order to inform the plausibility of the hypothesis that secular decreases in CRC incidence observed over the last 20 years are causally related to secular increases in NSAID use by the population. We hypothesized that an increase in NSAID use by the population would need to precede any fall in CRC incidence by six to ten years to be consistent with an NSAID mediated risk reduction as this was the induction period Chan et al found in their cohort studies of NSAID and/or aspirin use and subsequent CRC diagnoses. [15,16]

Methods

We used publicly available data from the National Center for Health Statistics' (NCHS) National Ambulatory Medical Care Survey (NAMCS) to estimate NSAID use over time.[17] The NAMCS is an annual, national sample survey of visits to office-based physicians that is designed to collect objective, reliable information about the provision and use of ambulatory medical care services in the United States. It utilizes a multistage probability design with the physician-patient office visit as the basic sampling unit. The information collected includes patient demographics, as well as information regarding patients' medical diagnoses and current medications, both over-the-counter and prescription.

We studied 518,590 visits over 15 years, between 1980–2001, to estimate secular changes in ambulatory NSAID use. We operationalized “NSAIDs” by evaluating the generic medication fields for the presence of one of 26 possible NSAIDs listed in the NAMCS codebooks over this period. We operationalized “ambulatory NSAID use” as the number of visits in which at

least one NSAID medication was mentioned/100 patient-physician visits. We calculated this figure for each year of available NAMCS drug data.

We used publicly available data from the SEER program to describe CRC incidence over time. The SEER program collects information regarding the diagnosis and treatment of patients with cancer from geographically diverse tumor registries in order to monitor trends in incidence and survival. It is estimated that approximately 14% of the American population with cancer is represented in these data.[18] Prior research has shown that, in the aggregate, patients in these registries are demographically representative of the general population.[19] The SEER program collects detailed information about initial diagnosis including date of diagnosis (i.e., month and year), site, histology, stage of tumor at diagnosis, and date of death as well as demographic information. We obtained estimates of secular changes in incidence of CRC between 1973 and 2001 from SEER through the use of SEER Stat.[20]

Findings

From NAMCS, we found a steady increase in the proportion of visits with an NSAID mentioned. Specifically, NSAID use nearly doubled within the observation period, going from 5.60/100 visits in 1980 to 9.67/100 visits in 2001. From SEER, we found that since its apogee in 1985, the incidence of CRC has fallen from 57.4/100,000 persons to 50/100,000 persons in 2001, or by 13%. Figure 1 describes these trends. With respect to induction time, we find that NSAID exposure precedes the decline in CRC incidence by seven years in these data. Because our observation period of the NSAID exposure begins in 1980, it may be that a longer period of induction occurred but is merely unobservable through these data. Nonetheless, because six years is the lower bound of the induction period described by Chan et al, we find that the seven year lag between an increase population NSAID use and CRC incident in our analyses support the plausibility of the hypothesis. That is, it may be that secular decreases in CRC incidence observed over the last 20 years are causally related to secular increases in NSAID use by the population. Clearly individual-level data that includes information on individual NSAID use and individual CRC risk are needed to further evaluate this hypothesis.

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Legend: This figure describes changes in the United States population incidence of invasive colorectal cancer over time according to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and documented use of prescription and over-the-counter non-steroidal anti-inflammatory drug (NSAID) by ambulatory patients according to the National Center for Health Statistics' (NCHS) National Ambulatory Medical Care Survey (NAMCS).

Figure 1.
Secular Changes in Rates of NSAID Visits (1980–2001) and Invasive CRC (1973–2001)