Such research is hampered, however, by difficulties in locating teenage and adult survivors and by their reluctance to return to pediatric hospitals [4]. Studies that actively follow participants by repeated contact are subject to drop-out that may differentially affect particular subgroups, e.g., underprivileged minorities [5]. Although statistical methods adjust for such loss in estimating population mortality rates, serious bias may result if subjects who drop out differ in health status from those who remain on study [6,7]. Studies that maintain passive follow-up by linkage of clinical records to disease or mortality registries are likewise subject to bias from failure of matching algorithms or events that occur outside the jurisdiction of the registry [8].

The National Death Index (NDI) is a centralized registry maintained by the National Center for Health Statistics of all deaths that occurred in the United States, Puerto Rico, and the Virgin Islands since 1979 [9]. Record linkage through the NDI has been well tested in adult populations [8] and is now commonly used to study death rates in adult cohorts [10-14]. The NDI has also been used to ascertain mortality in cohorts of children and young adults [15-17] but a literature search revealed no systematic evaluation of its use in these populations. In addition, no previous work was found evaluating the NDI as a means of augmenting follow-up in a study that attempts to maintain active contact with all participants.

Our study compared mortality ascertainment via active follow-up of a large cohort of subjects with childhood kidney cancer to mortality ascertainment using record linkage to the NDI. There were two specific aims: first, to identify which factors best predicted an NDI match among known decedents; and second, to determine how well information from the NDI search might substitute for missing follow-up data for those alive at last contact, but lost to follow-up before the closing date, in an attempt to improve the accuracy of mortality estimates.

Analysis

Study population

Between 1969 and 1995, medical institutions in the US and Canada enrolled 6,618 children with renal neoplasms on one of four randomized clinical trials conducted by the National Wilms Tumor Study (NWTS) Group [18-21]. Nearly 95 percent of enrollees had Wilms tumor while the remainder had clear cell sarcoma (CCSK), rhabdoid tumor of the kidney (RTK) or other rare histologic variants [22]. From the outset the NWTS emphasized continued follow-up of surviving participants as part of a late effects study to increase understanding of the long-term effects of diagnosis and treatment on development of second malignant neoplasms, congestive heart failure, renal failure and adverse pregnancy outcomes [23-26].

Follow-up is rigorously pursued for all on-study participants. Data requests are sent annually to the institution where the subject received treatment, for subjects still returning there, or otherwise directly to participants or a designated family member. When the most recent record for any subject is more than two years out-of-date, the computer system flags the case for immediate action. If the subject is not returning to the institution for follow-up, the NWTS requests authorization to track the participant in order to reestablish annual contact directly. If the NWTS discovers that a participant already in direct contact has moved, aggressive tracking is initiated to locate and renew contact with the participant.

The cohort for the present investigation comprised the 6,217 subjects enrolled from US institutions. By June, 2003, 198 were known to have died prior to January 1, 1979; 786 were known to have died after 1978 but prior to January 1, 2002, the closing date of the study; 1,827 were known to be alive on the closing date; and 3,406 had vital status unknown. Available identifying information for the 984 known decedents and for the 3,406 with vital status unknown was submitted to the NDI, which at the time of submission in June 2003 had collected data on deaths occurring in the US from 1979 through 2001.

The NWTS clinical trial protocols were approved by the Institutional Review Board (IRB) of the Fred Hutchinson Cancer Research Center and by the IRB of each participating institution. Each subject, or in the vast majority of cases their parent/guardian, provided informed consent at the time of enrollment. At age 18 each subject was contacted and asked to provide their own informed consent for continued participation as an adult.

National death index search

Details of the NDI matching procedure have been discussed in detail elsewhere [9,27]. Multiple potential NDI record matches are frequently identified for a single submitted user record. It is the investigator's responsibility to assess match quality and to make the final determination of match status. Briefly, in the cohort of known decedents all exact matches, where the NDI and NWTS records matched on all available identifiers, were accepted. For the remaining decedents and for subjects with vital status unknown potential matches assigned a suitably high score by the NDI [27] or which we determined to be of interest were assessed manually. This involved searching the subject's chart for information bearing on the validity of the potential match. For example, we compared the NDI recorded state of death with the state(s) where the subject