

## Early deaths from childhood cancer up to 4 times more common than previously reported

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Treatments for childhood cancers have improved to the point that 5-year survival rates are over 80 percent. However, one group has failed to benefit from these improvements, namely children who die so soon after diagnosis that they are not able to receive treatment, or who receive treatment so late in the course of their disease that it is destined to fail. A study published today in the *Journal of Clinical Oncology* explores this challenging population, finding that death within a month of diagnosis is more likely in very young children and those from minority racial and ethnic groups even independent of low socioeconomic status. The study uses a large national database to find that the rate of deaths within one month of diagnosis has been previously under-reported in clinical trial data, with early deaths from some pediatric cancer subtypes up to four times as common as had been implied by clinical trial reports.

"During my pediatric residency a teenager came in with leukemia, but had so much cancer when he presented that he had multi-organ failure and died within about 24 hours of coming to our attention, before we could even start treatment. I wanted to find out who these kids are in hopes that as a system we could learn to spot them earlier, when treatment still has a chance of success," says Adam Green, MD, investigator at the University of Colorado Cancer Center and pediatric oncologist at Children's Hospital Colorado. Green originated this study during his clinical fellowship at Dana Farber Cancer Institute, working with Carlos Rodriguez Galindo, MD.

Green and colleagues used data from the Surveillance, Epidemiology and



End Results (SEER) database, finding 36,337 cases of pediatric cancer between the years 1992 and 2011. Of these young patients, 555 or 1.5 percent died within one month of cancer diagnosis. Overall, the strongest predictor of patients who would die soon after diagnosis was age below one year.

"In general, babies are just challenging, clinically, because they can't tell you what they're feeling. Parents and physicians have to pick the ones with cancer from the ones with a cold, without the patient being able to tell you about symptoms that could be diagnostic. Babies tend to get aggressive cancers, it's hard to tell when they're getting sick, and some are even born with cancers that have already progressed. These factors combine to make very young age the strongest predictor of early death in our study," Green says.

Additionally, black race and Hispanic ethnicity predicted early death, even beyond the influence of <u>socioeconomic status</u>. Green hopes that future studies will be able to discover whether biologic or cultural factors may be responsible for these disparities, or if higher rates of early death in minority populations could be due to factors built into insurance and health care systems.

He also points out that the rate of early deaths due to pediatric cancers is higher than previously reported.

"Most of what we know about outcomes for cancer patients come from clinical trials, which have much more thorough reporting rules than cancer treated outside trials. However, these kids in our study aren't surviving long enough to join <u>clinical trials</u>," Green says.

For example, the paper shows that a clinical trial against childhood Acute Myeloid Leukemia (AML) reported early death in 16 of 1,022 young patients, or 1.6 percent of these cases. In contrast, the SEER



database, which collects about 15 percent of all cancer outcomes across the United States (representing a geographic and socioeconomic cross-section), shows 106 early deaths in 1,698 diagnoses, or 6.2 percent of all cases, almost four times as high as previously reported. When comparing the rates of early deaths seen in the SEER database to rates of early deaths reported in clinical trial data, early death was higher for all cancer subtypes (0.7 versus 1.3 percent in non-infant ALL; 2.0 versus 5.4 percent in infant ALL; 1.4 versus 3.8 percent in hepatoblastoma; 0.04 versus 0.5 percent in Wilms tumor).

"I had a hunch this was a bigger problem than we thought. Now we see that is indeed the case," says Green.

Now that Green has shown the fact of early death in this population, he hopes to work with CU Cancer Center colleagues to design a national prospective study that could more closely examine the factors associated with this outcome. "So that whenever a family has a child who dies of cancer within a month of diagnosis, we could contact the family to gather information about timing of symptoms and their experience accessing care. We can already act on our findings in this current study to improve early identification of these patients. But with prospective, patient-level data, we can move from understanding the scope and risk factors for <u>early death</u> to identifying problems in the diagnostic process we can fix," Green explains.

The overall goal of this ongoing line of research is to change potential early deaths to long-term survivors.

"This is a population that deserves our attention," Green says.

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