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## Carrier screening for CF unmasks newborn screening deficiencies

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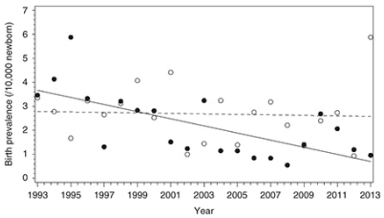


In a study that spanned 21 years, a group of Italian researchers found that carrier screening for cystic fibrosis (CF) significantly reduced the number of children born with the disease. However, carrier screening unmasked deficiencies in the newborn screening (NBS) programs in regions with carrier screening. In those regions, the ratio of false-positive or uncertain CF diagnoses to confirmed cases identified through NBS also increased, suggesting deficiencies in NBS test accuracy. In Italy, structured carrier screening differs by region. The researchers compared two regions: the eastern region, which routinely offered carrier screening, and the western region, which did not. Over the study period, the research team tallied 150 carrier couples and 259 newborns with a positive CF diagnosis. Over the study period, the number of children born with CF decreased 15%—from 1 in 2,730 to 1 in 14,200 in the region with carrier screening—whereas no significant change occurred in the region without carrier screening. The researchers noted that the study provides no information about reproductive choices that carrier couples made because preimplantation genetic diagnosis and in vitro fertilization were illegal in Italy for most of the study period. However, they did note that only two infants with CF were born to carrier couples detected through screening. The researchers also noted that the low number of CF births might, in the long term, influence whether NBS for CF continues to be offered, since infants are identified and evaluated, only to have false-positive results or inconclusive diagnoses. *—Karyn Hede, News Editor*

## A call for better rare disease therapies in real-world clinical settings

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The current focus on development of interventions and treatments for rare diseases is producing new options for patients, but getting those treatments to patients in real-world clinical settings remains challenging. In this issue, Potter et al. argue that future research must "focus on appropriate patient-oriented outcomes, include robust study designs that can accommodate real-world decision priorities, and involve effective stakeholder-engagement strategies." They point to the documented gap between treatment outcomes observed in highly controlled trials and those experienced by patients in community-based health-care settings as a rationale for investment in research to address translation of biomedical discoveries into improved population health. Because most new treatments are likely to be considered incremental improvements, they argue, care must be taken in any study design to ensure that interventions can be effectively embedded in real-world systems of care. The authors suggest that study designs take into account the expected range of therapies and health services available to patients, such as diet therapy, physiotherapy, family support and counseling, and telehealth. In addition, they suggest study designs that evaluate long-term impacts of care, including potential adverse effects, and determine how patient variation and disease characteristics influence treatment effectiveness. *—Karyn Hede, News Editor*

# NEWS BRIEFS

## Tiny, durable tardigrades take up a mishmash of genes from plants, bacteria

Turns out tardigrades, the nearly microscopic animals known for their ability to survive in extreme environments, have been promiscuous in their borrowing of genes obtained directly from other species, making them the only animals known to have undergone extensive horizontal gene transfer. Sequencing of the tardigrade genome, as reported in *Proceedings of the National Academy of Sciences* in November 2015, reveals that


a stunning 17% consists of genes from a wide variety of sources, including bacteria, fungi, viruses, and plants. The foreign genetic material is not clustered together, but spread fairly uniformly throughout the animal's genome. Assimilated genes have since acquired properties characteristic of animal genes, such as intron regulatory elements, the research team found. Further analysis revealed that the most abundant acquired genes encode catalases, antioxidant enzymes involved in neutralizing oxidative conditions that might damage cells under environmental stress. Tardigrades also acquire DNA-repair genes and other genes known to mitigate damage to cells caused by extreme environmental conditions. The authors suggest that tardigrades may be more prone to picking up genes from their environment during the transition

## NEWS BRIEFS *(continued)*

from desiccation to rehydration, when cell membranes become transiently leaky. When combined with desiccation-induced breaks in double-stranded DNA, the newly introduced foreign DNA may be more likely, they suggest, to become a permanent resident of the tardigrade genome. *—Karyn Hede, News Editor*

### More kids genetically predisposed to cancer than previously understood

At least 8% of children with cancer have heritable genetic alterations that may have predisposed them to the disease, according to a large genomic study published in the *New England Journal of Medicine*. The surprising results, which may change clinical practice, suggest that comprehensive genomic screening may be warranted for all pediatric cancer patients, not just those with a family history of cancer. The study of 1,120 pediatric cancer patients, led by investigators from

St. Jude Children's Research Hospital/Seth Dixon

the Pediatric Cancer Genome Project at St. Jude Children's Research Hospital, Memphis, TN, and Washington University School of Medicine, St. Louis, MO, overturns the idea that germ-line mutations in pediatric cancer patients are rare and occur only in children with a family history of cancer. More than half of the 95 children with germ-line mutations in genes associated with autosomal dominant hereditary cancer predisposition syndromes had no family history of cancer. Perhaps most surprising, eight patients harbored mutations in *BRCA1*, *BRCA2*, or *PALB2*—genes thought to predispose adults, not children, to cancer. The findings suggest that mutations in *BRCA1* and *BRCA2* are more common in pediatric cancers than is currently understood and have clearly important implications for management of children and their extended families. Additionally, 109 children (9.7%) had germline mutations in other cancer-associated genes. In comparison, only 1% of 966 adult controls from the 1000 Genomes Project had alterations in these same genes. The study "lays the groundwork to understand the spectrum of cancers and age-specific cancer risks associated with germline mutations in predisposition genes and how best to monitor at-risk patients and families," stated investigator Kim Nichols, director of the St. Jude Hereditary Cancer Predisposition Clinic. St. Jude has now launched Genomes for Kids (G4K), to sequence the genomes of eligible pediatric cancer patients who enter the hospital for treatment. *—Karyn Hede, News Editor*