Leontien C. M. Kremer, MD, PhD
Mathilde C. Cardous-Ubbink, MSc
Department of Pediatric Oncology
Emma Children's Hospital/Academic Medical Center
Amsterdam, the Netherlands

Maud M. Geenen, MD
Department of Medical Oncology
Academic Medical Center
Amsterdam

Flora E. van Leeuwen, PhD
Netherlands Cancer Institute
Amsterdam

Huib N. Caron, MD, PhD
h.n.caron@amc.uva.nl
Department of Pediatric Oncology
Emma Children's Hospital/Academic Medical Center

Financial Disclosures: None reported.

1. Speechley KN, Barrera M, Shaw AK, Morrison HI, Maunsell E. Health-related quality of life among child and adolescent survivors of childhood cancer. *J Clin Oncol*. 2006;24(16):2536-2543.
2. Recklitis CJ, Lockwood RA, Rothwell MA, Diller LR. Suicidal ideation and attempts in adult survivors of childhood cancer. *J Clin Oncol*. 2006;24(24):3852-3857.
3. Hobbie WL, Stuber M, Meeske K, et al. Symptoms of posttraumatic stress in young adult survivors of childhood cancer. *J Clin Oncol*. 2000;18(24):4060-4066.
4. Langeveld NE, Grootenhuis MA, Voûte PA, de Haan RJ, van den Bos C. Quality of life, self-esteem and worries in young adult survivors of childhood cancer. *Psychooncology*. 2004;13(12):867-881.
5. Zebrack BJ, Zeltzer LK. Quality of life issues and cancer survivorship. *Curr Probl Cancer*. 2003;27(4):198-211.

Definitions of Chronic Health Conditions in Childhood

To the Editor: In their Review, Dr van der Lee and colleagues[1] found wide variability in the reported prevalence of chronic health conditions in childhood, largely a result of different definitions. Only 1 of the 64 articles included in the Review reported the percentage of children with more than 1 condition.[2] Multimorbidity, the co-occurrence of multiple chronic conditions in 1 individual, is increasingly recognized as having a major effect on patient outcomes and health care costs, posing a significant challenge to current models of health care.[3]

Certain features of multimorbidity in children make it a very promising field for investigation. First, although the proportion of children and adolescents with more than 1 disease is lower than in adults and older patients, the number of those with 3 or more different diseases is also greater than would be expected due to chance alone, more so than for any other age group.[4] Second, the mix of comorbid conditions in children and adolescents is very different from that of adults, more commonly including asthma and different types of allergic conditions.[2] The natural history of these conditions includes recurrence or complete resolution; they therefore require a different management approach than diseases typically clustering in the elderly population. Third, multimorbidity in children and adolescents has the potential to predict subsequent multimorbidity in older ages, but this has not yet been investigated.

To better understand the life course of illness and to determine the utility of different concepts of "chronic," more study of the natural history epidemiology of common diseases and their co-occurrence is needed. The article by van der Lee et al did not include definitions used by systems that characterize morbidity based on types of illnesses (eg, chronic, acute self-limited, acute but likely to recur). Such systems may become useful in characterizing morbidity burdens in both adults and children.[5]

Jose M. Valderas, MD, PhD, MPH
jose.valderas@manchester.ac.uk
National Primary Care Research and Development Centre
University of Manchester
Manchester, England

Barbara Starfield, MD, MPH
Johns Hopkins Bloomberg School of Public Health
Baltimore, Maryland

Chris Salisbury, MD, MBChB, MSc, FRCGP
School of Primary Care Research
University of Bristol
Bristol, England

Financial Disclosures: None reported.

1. van der Lee JH, Mokkink LB, Grootenhuis MA, Heymans HS, Offringa M. Definitions and measurement of chronic health conditions in childhood: a systematic review. *JAMA*. 2007;297(24):2741-2751.
2. Newacheck PW, Stoddard J. Prevalence and impact of multiple childhood chronic illnesses. *J Pediatr*. 1994;124(1):40-48.
3. Fortin M, Soubhi H, Hudon C, Bayliss EA, van den Akker M. Multimorbidity's many challenges. *BMJ*. 2007;334(7602):1016-1017.
4. van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol*. 1998;51(5):367-375.
5. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med*. 2002;162(20):2269-2276.

In Reply: In response to the comments of Dr Valderas and colleagues, the measurement of multimorbidity indeed poses a methodological challenge. Because the goal of our Review was to find definitions of chronic conditions in childhood, we restricted our search to the literature concerning "children" (aged 0-18 years). Thus, we did not include potentially important articles on this subject from the adult literature. Their comments, coming from a primary care research and development center, emphasize that there is a need for consensus on the definition of chronic health conditions in children and that the associated measurement methods should involve all relevant disciplines including general practice, internal medicine, rehabilitation medicine, and public health.

Johanna H. van der Lee, MD, PhD
j.h.vanderlee@amc.uva.nl
Department of Pediatric Clinical Epidemiology
Emma Children's Hospital
Academic Medical Center
University of Amsterdam
Amsterdam, the Netherlands

Lidwine B. Mokkink, MSc
Pediatric Psychosocial Department
EMGO Research Institute
VU University Medical Center
Amsterdam, the Netherlands
Hugo S. Heymans, MD, PhD
Department of Pediatrics
Martin Offringa, MD, PhD
Department of Pediatric Clinical Epidemiology
Emma Children's Hospital
Academic Medical Center
University of Amsterdam
Amsterdam, the Netherlands

Financial Disclosures: None reported.

Genetic Associations With Age-Related Macular Degeneration

To the Editor: In their study of the Age-Related Eye Disease Study (AREDS) participants,[1] Dr Seddon and colleagues investigated whether genetic variants were associated with progression of age-related macular degeneration. In the article, they did not present the main results stratified by treatment assignment. Results for the antioxidants-plus-zinc group and the placebo group would have been a useful addition to Table 6 in the article. The authors did note that genotype and treatment had no significant interaction, but interaction tests may have very low statistical power.

Providing these specific results would also help interpret the corrected abstract conclusion: "Presence of these polymorphisms plus smoking and body mass index of 25 or higher, controlling for AREDS vitamin-mineral treatment, identifies patients who are highly susceptible to developing advanced stages of this visually disabling disease."[1] The treatment used in AREDS appears to be one of the few options to help manage this public health problem,[2] but high doses of vitamin E (an essential component of AREDS treatment) can be harmful,[3] making this additional information important.

Javier Damián, MD, MPH
jdamian@isciii.es
National Centre for Epidemiology
Carlos III Health Institute
Madrid, Spain

Financial Disclosures: Dr Damián reports having received research support from Pfizer.

1. Seddon JM, Francis PJ, George S, Schultz DW, Rosner B, Klein ML. Association of *CFH Y402H* and *LOC387715 A69S* with progression of age-related macular degeneration [published correction appears in *JAMA*. 2007;297(23):2585]. *JAMA*. 2007;297(16):1793-1800.
2. Bressler NM, Bressler SB, Congdon NG, et al; Age-Related Eye Disease Study Research Group. Potential public health impact of Age-Related Eye Disease Study results: AREDS report No. 11. *Arch Ophthalmol*. 2003;121(11):1621-1624.
3. Miller ER, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med*. 2005;142(1):37-46.

In Reply: In response to Dr Damián, we had considered including details of the treatment analysis. However, it would have been necessary to analyze both the interactions with treatment components considered separately (antioxidants vs placebo, zinc vs placebo) as well as in combination (antioxidants with zinc vs placebo). Furthermore, it is important to consider both quantitative interactions (when the direction of the effect is the same in 2 treatment groups, but the magnitude is different) and qualitative interactions (when the direction of the effect is different in different treatment groups). However, these analyses are complex, and we believed that to do justice to the treatment data and not make this article too cumbersome to interpret, the genotype-treatment data would be best presented in a separate publication.

Johanna M. Seddon, MD, ScM
jseddon@tufts-nemc.org
Tufts-New England Medical Center
Boston, Massachusetts
Peter J. Francis, MD, PhD
Michael L. Klein, MD
Casey Eye Institute
Portland, Oregon
Bernard Rosner, PhD
Harvard School of Public Health
Boston, Massachusetts

Financial Disclosures: Dr Seddon reports that she is named as an inventor on a patent application (US Patent Application No. 11/066,641, filed by Massachusetts Eye and Ear Infirmary on February 25, 2005, and published as US-2005-0250745-A1 on November 10, 2005) regarding biomarkers for age-related macular degeneration.

Clinical Revenue Investment in Biomedical Research

To the Editor: In their Commentary, Drs Bowman, Rubinstein and Levine[1] discussed clinical revenue investment in biomedical research at the University of Pennsylvania and the University of Pittsburgh. The authors characterized the University of Pittsburgh Medical Center as "the only academic health system in western Pennsylvania"; this is not accurate.

The West Penn Allegheny Health System serves as campuses for the training of undergraduate medical students from the Temple University School of Medicine and the Drexel University College of Medicine. It has a large number of accredited residencies and fellowships, well-published faculty, and significant external funding.

J. Christopher Post, MD, PhD
cpost@wpahs.org
Allegheny-Singer Research Institute
Pittsburgh, Pennsylvania

Financial Disclosures: Dr Post is president and scientific director of the Allegheny-Singer Research Institute.

1. Bowman MA, Rubenstein AH, Levine AS. Clinical revenue investment in biomedical research: lessons from two academic medical centers. *JAMA*. 2007;297(22):2521-2524.

In Reply: I agree with Dr Post that the West Penn Allegheny Health System has academic interests and characteristics, for which I have great respect. However, a com-