The 16-hour duty limit is the latest in a progression of changes aimed at reducing resident stress and fatigue, and potentially improving the quality of patient care. Our study highlights a potential balance between harmful and beneficial effects that in sum result in minimal overall impact when considering a wide-range of efficiency and quality outcomes.

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Adult Mortality in a Randomized Trial of Mass Azithromycin for Trachoma

Annual mass azithromycin treatments are provided to entire communities to clear the ocular strains of *Chlamydia trachomatis* that cause blinding trachoma. Mass treatments reduce the community burden of ocular chlamydia and have proven efficacious in community-randomized trials. Since 1999, more than 150 million doses of azithromycin have been distributed for trachoma worldwide.

Mass azithromycin distributions are directed at clearing ocular chlamydia but may have other effects. For example, in the Trachoma Amelioration in Northern Amhara (TANA) trial, we found that mass azithromycin distributions reduced childhood mortality. In contrast, a recent observational study suggested that azithromycin use may cause sudden death in adults. This finding could have major implications for trachoma elimination efforts. In our previous report, an intention-to-treat analysis found no evidence of increased mortality among individuals older than 9 years. However, in light of the recent observational study, we thought it worthwhile to reassess our data to determine the mortality rates and causes of death in an older subgroup of individuals and to compare mortality in individuals who received azithromycin with that in those who did not.

Methods. TANA was a National Institutes of Health–funded, cluster-randomized trial conducted in Ethiopia from 2006 through 2009 (clinicaltrials.gov Identifier: NCT00322972). The design and implementation of the trial, including the prespecified mortality outcome, have been described previously. Herein we report results from the following 4 study arms, each composed of 12 randomly selected “subkebeles” (government-defined units): (A) annual or (B) biannual directly observed mass distribution of azithromycin to persons 1 year or older, (C) quarterly mass distribution of azithromycin to children aged 1 to 9 years, and (D) no treatment. Mortality was defined as presence at the baseline census and absence at the 12-month census due to death. For each death, household members were asked about the cause of death.

In an intention-to-treat analysis, we compared communities where individuals aged at least 10 years received azithromycin (arms A and B) with communities where this age group did not receive treatment (arms C.
and D). We used negative binomial regression to calculate age-stratified mortality rates and mixed effects logistic regression to compare the 2 groups, with subkebele as a random effect. As a second independent analysis, we treated arms A and B as a cohort and compared mortality in persons who received any dose(s) of azithromycin relative to those who received no doses. This analysis could be biased if the baseline health status differed between participants and nonparticipants. Therefore, we performed a conditional logistic regression grouped on household, which removes all household-level confounding. We included sex and the interaction of age stratum and household, which removes all household-level confounding, and we report the odds ratio for the 30-years-and-older group. The TANA trial provided 80% power at the 0.05 level to detect a 0.7% reduction in the mortality rate of participants aged at least 30 years, assuming a mortality rate of 10 per 1000 person-years, 350 persons aged at least 30 years per subkebele, and a variance inflation factor of 2. Statistical analyses were performed with Stata software, version 10.1 (StataCorp).

Ethical approval for this study was obtained from the University of California, San Francisco Committee for Human Research, the Emory University Institutional Review Board, and the Ethiopian Science and Technology Commission.

Results. Baseline characteristics of the 4 treatment groups were similar (reported elsewhere). Of 8217 persons aged at least 30 years who were present at baseline in arms A and B, 7252 (88.3%) received azithromycin during the year. Of 8320 persons aged at least 30 years who were present at baseline in arms C and D, 109 (1.3%) mistakenly received azithromycin. By the 12-month census, 166 individuals aged 30 years or older had died. Although we were unable to detect a significant difference, mortality was lower in arms A and B than in arms C and D (odds ratio, 0.91 [95% CI, 0.63-1.30]). Causes of death were similar in the 2 groups (Table).

A separate analysis of arms A and B found no difference in mortality between individuals aged at least 30 years who received azithromycin and those who did not, although those who received azithromycin had a lower risk of mortality than did members of the same household who never received the drug (adjusted odds ratio, 0.59 [95% CI, 0.17-2.00], conditional logistic regression).

Comment. We were unable to detect an association between azithromycin use and increased risk of all-cause or cause-specific mortality among adults in this study; to the contrary, individuals treated with azithromycin had a lower rate of mortality compared with those who did not receive treatment. This lack of an association is in contradiction to a previous report that found an increased risk of sudden death in patients treated with azithromycin. The 2 studies are clearly different. Ours was a randomized clinical trial of healthy adults in Ethiopia, whereas theirs was a propensity score–adjusted observational study of hospitalized patients in Tennessee. Other studies have demonstrated that mass azithromycin distributions for trachoma have collateral benefits (eg, decrease in childhood respiratory infections, diarrhea, malaria, and mortality) and potential harms (eg, transient macrolide resistance). An argument could be made for trachoma programs to stop distributing azithromycin to adults, especially since the greatest burden of ocular chlamydial infection is found in children, and treatment of children provides some degree of indirect herd protection for adults. However, our findings provide no evidence to support discontinuation of mass distributions to entire communities for trachoma control, suggesting that if anything, benefit outweighs harm.
Overuse of Magnetic Resonance Imaging

Overuse of health care services such as magnetic resonance imaging (MRI) has become an increasingly recognized problem.\(^1\)\(^2\) We studied the appropriateness of requests for outpatient MRI of the lumbar spine and of the head for headache, as these are common indications and might be frequently inappropriate.

**Methods.** We used the RAND–University of California, Los Angeles, appropriateness method to define appropriate care, combining best evidence and expert opinion,\(^3\)\(^4\) to prospectively determine the appropriateness of requests for MRI studies of the lumbar spine and of the head for headache at the University of Alberta Hospital (UAH) in Edmonton, Alberta, Canada, and The Ottawa Hospital (TOH) in Ottawa, Ontario, Canada. As part of the process 2 expert panels, 1 each for headache and lumbar spine, were created, comprising specialists nominated by various Canadian specialty societies. The literature review and complete listing of scenarios were reviewed by the panels and then revised. The panels individually rated each scenario’s before and after group discussion on a 9-point scale, where 1 to 3 indicates an inappropriate indication for MRI; 4 to 6, uncertain indication; and 7 to 9, appropriate indication. For the final scenarios, we used the median rating for each scenario to determine the appropriateness of the intervention.

We prospectively identified outpatient requisitions for MRI scans at the UAH from May 2008 to September 2009 and TOH from September 2008 to March 2010. We collected data from 500 lumbar spine requisitions and 500 head for headache requisitions at each site. Each case was matched to a clinical scenario for which the appropriateness rating had been determined.

**Results.** The specialty of the referring physicians and indications for the studies can be found in the eTable (http://www.jamainternalmed.com).

**Lumbar Spine MRI.** Only 443 of 1000 requests were considered appropriate. The remainder were split between inappropriate (285 of 1000 [28.5%]) or of uncertain value (272 of 1000 [27.2%]) (Table).