



Charles Darwin University

Treating onchocerciasis in regions in which *Loa loa* is endemic

Woolnough, Emily L.; Chmiel, Edward R.; Currie, Bart

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in our clinical-trial cohort, death from other causes would have reduced the 15-year risk of recurrence only slightly (from 13% to 12%) among women with stage T1 disease (tumor diameter, ≤ 2.0 cm) with no nodal involvement, with even smaller proportional changes among women with higher-stage disease.

We prefer to use Kaplan–Meier probabilities to describe our findings because they are more widely generalizable than probabilities that are reduced to allow for other causes of death, the risk of which varies according to age, concomitant disease, smoking, country, and period (past or future). We agree, though, that life expectancy

is an important consideration in clinical decision making about extending endocrine therapy.

Hongchao Pan, Ph.D.

Richard Gray, M.Sc.

Medical Research Council Population Health Research Unit
Oxford, United Kingdom

Daniel F. Hayes, M.D.

University of Michigan Comprehensive Cancer Center
Ann Arbor, MI

for the Early Breast Cancer Trialists'
Collaborative Group

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Treating Onchocerciasis in Regions in Which *Loa loa* Is Endemic

TO THE EDITOR: Kamgno et al. (Nov. 23 issue)¹ report an innovative use of the LoaScope to quantify microfilariae levels and facilitate the safe administration of ivermectin for the onchocerciasis elimination program. This LoaScope-based strategy provided a practical approach to the distribution of ivermectin in locations that were previously “off limits” because of potential serious adverse events among persons with higher *Loa loa* microfilarial densities. However, we suggest that Table 2 of their article (available at NEJM.org) does not appropriately present the data on adverse events. The percentages of total and specific adverse events were calculated with the total number of adverse events as the denominator, rather than with the number of participants in each group (those with detectable *L. loa* microfilariae vs. those with no detectable *L. loa* microfilariae). Although the number of participants with detectable microfilariae who received ivermectin was not provided, the overall prevalence of microfilaremia was 17.8% (Table 1 of the article). Therefore, the number of participants with detectable microfilariae must have been substantially lower than the number of participants with no detectable microfilariae. The use of these denominators would have shown higher percentages of total and specific adverse events among participants with detectable *L. loa* microfilariae. We believe that these aspects of the data need some clarification.

Emily L. Woolnough, F.R.A.C.P.

Edward R. Chmiel, B.Sc.

Bart J. Currie, F.R.A.C.P.

Royal Darwin Hospital
Darwin, NT, Australia
emily.woolnough@nt.gov.au

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1. Kamgno J, Pion SD, Chesnais CB, et al. A test-and-not-treat strategy for onchocerciasis in *Loa loa*-endemic areas. *N Engl J Med* 2017;377:2044-52.

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THE AUTHORS REPLY: Woolnough et al. highlight both the innovative and practical approach of the test-and-not-treat strategy described in our article, but they suggest that the information presented in Table 2 might be improved if the percentages of total adverse events and specific adverse events were calculated with the number of participants in each comparison group as the denominator rather than with the total number of adverse events. In Table 2, we focused on all study participants who had an adverse event and compared the percentages of each type of adverse event that occurred among the participants with and those without detectable *L. loa* microfilaremia. Among the 15,522 participants who received treatment with ivermectin, 2470 (15.9%) had detectable *L. loa* microfilaremia and 13,052 (84.1%) did not have detectable *L. loa* microfilaremia. Using these de-

nominators, the reader can make comparisons at the population level. However, we would like to point out that given the results of the multivariate analysis (Fig. 2 of our article), in which there was a significant association between the occurrence of any adverse event and the presence of anti-Ov16 IgG4 antibodies (a surrogate for infection with *Onchocerca volvulus*), focusing on the presence of *L. loa* microfilariae as the only or main cause of adverse events would be misleading.

Sébastien D. Pion, Ph.D.

Michel Boussinesq, M.D., Ph.D.

Institut de Recherche pour le Développement
Montpellier, France
sebastien.pion@ird.fr

Joseph Kamgno, M.D., Ph.D.

Center for Research on Filariasis and other Tropical Diseases
Yaounde, Cameroon

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Case 37-2017: A Man with Unintentional Opioid Overdose

TO THE EDITOR: The discussion of Case 37-2017 (Nov. 30 issue),¹ a 36-year-old man with unintentional opioid overdose, calls for rapidly removing barriers to buprenorphine (Suboxone) treatment for opioid addiction. As practitioners in a Suboxone clinic, we urge caution and are concerned that this approach might prove to have a dark side. History has repeatedly shown that all opiates are innately addicting and should be used sparingly, at small doses, and for short periods. A thriving black market for buprenorphine already exists (one 8-mg tablet sells for \$10 on the streets in Boston). Some addicts use this drug intravenously, in spite of naloxone being embedded in the product to prevent this. In Finland, where buprenorphine has been prescribed since 1997, it is now the most commonly abused intravenous drug.^{2,3}

There is a striking paucity of research into tapering and discontinuing buprenorphine.⁴ The lowest available dose is 2 mg, yet a lower amount is often effective in patients. Daily, we witness the efficacy of this drug, as well as the extreme difficulty that patients have discontinuing it.

Barbara Scolnick, M.D.

Linda Ploude, L.I.C.S.W.

500 Congress St.
Quincy, MA
scolnick@bu.edu

No potential conflict of interest relevant to this letter was reported.

1. Case Records of the Massachusetts General Hospital (Case 37-2017). *N Engl J Med* 2017;377:2181-8.

2. Yokell MA, Zaller ND, Green TC, Rich JD. Buprenorphine and buprenorphine/naloxone diversion, misuse, and illicit use: an international review. *Curr Drug Abuse Rev* 2011;4:28-41.

3. Aalto M, Halme J, Visapää JP, Salaspuro M. Buprenorphine misuse in Finland. *Subst Use Misuse* 2007;42:1027-8.

4. Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT,

O'Connor PG. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial. *JAMA Intern Med* 2014;174:1947-54.

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TO THE EDITOR: Raja and colleagues discuss a case that is common and that is central to the development of opioid-use disorder. This case shows how easily attempts to provide high-quality analgesia can result in addiction and accidental overdose. The discussants offer several potential solutions to manage accidental overdose, including the use of kits containing naloxone. An additional strategy may include the preferential use of buprenorphine for the management of acute pain.

Buprenorphine is well known for its unique safety profile, low potential for abuse, and efficacy in the management of opioid-use disorder. Only in recent years has it been recognized that buprenorphine has full agonist properties in terms of short-term analgesic efficacy.¹ A recent meta-analysis of 28 randomized, controlled trials studying acute pain has shown that buprenorphine provides analgesia that is equivalent to that of morphine, even within 1 hour after administration.² The high analgesic efficacy of buprenorphine, combined with the reduced potential for abuse, may help to strike a balance between high-quality analgesia and the risk of overdose and the development of opioid-use disorder.

Leigh White, M.B., B.S.

University of Wollongong
Wollongong, NSW, Australia
lw844@uowmail.edu.au