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ORIGINAL ARTICLE

Photographic grading for trachoma diagnosis within trachoma impact surveys in Amhara region, Ethiopia

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Background: As countries reach the trachoma elimination threshold and cases of trachomatous inflammation follicular (TF) become rare, it becomes difficult to train survey graders to recognize clinical signs. We assess the use of photography as a grading tool, the efficiency of an in-country grading center and the comparability of field and photographic grading.

Methods: During January–February 2017 surveys in Amhara, Ethiopia, field graders assessed TF, trachomatous inflammation intense (TI) and trachomatous scarring (TS). Photographs were taken from each conjunctiva and later graded at the Gondar Grading Center (GGC) at the University of Gondar in Amhara. Two trained ophthalmology residents graded each set of photographs and a third grader provided an adjudicating grade when needed.

Results: A total of 4953 photographs of 2477 conjunctivae from 1241 participants in 10 communities were graded over 5 d at the GGC. Six examined participants were not photographed. Agreement between field and photographic grades were for TF: percent agreement (PA) 96.7%, κ=0.70 (95% confidence interval [CI] 0.64 to 0.77; for TI: PA 94.7%, κ=0.32 (95% CI 0.20 to 0.43); and for TS: PA 83.5%, κ=0.22 (95% CI 0.15 to 0.29).

Conclusions: Conjunctival photography may be a solution for programs near the elimination threshold where there are few available community cases for training field graders.

Keywords: conjunctiva, Ethiopia, photography, survey, trachoma

Introduction

Trachoma is caused by the bacterium *Chlamydia trachomatis* and is the leading infectious cause of blindness worldwide.[1] Trachoma prevalence is currently determined through in-person conjunctival examinations within population-based surveys. Typically, trained and certified trachoma graders examine individuals using the World Health Organization's (WHO) simplified trachoma system, including trachomatous inflammation follicular (TF) among children ages 1–9 y.[2] The prevalence of TF in this age group determines whether and how many years of mass drug administration (MDA) with antibiotics are needed for a given area or district.

Grader training currently includes both photograph review tests and field reliability examinations, where graders can observe TF and other signs of trachoma among children living in trachoma-endemic communities. Frequent standardization of trachoma graders prior to surveys is important as disagreements exist in grading, even among experienced graders, including for TF and trachomatous inflammation intense (TI) signs.[3] Training graders to recognize these clinical signs will be more difficult as countries reach the threshold (<5% TF) for trachoma elimination as a public health problem and available community-based TF cases from which to certify graders become scarce. Conjunctival photography could be a solution for grader training and possibly a substitute for field grading in these settings.

Conjunctival photographs have been increasingly utilized as part of trachoma research to validate the quality of field grading assessments and to train field graders.[4–6] However, more data are needed on the feasibility of including photographic grading in large-scale trachoma surveys as part of programmatic monitoring. This study aimed to assess the feasibility of taking photographs alongside field grading, the effectiveness of an in-country grading center and the comparability of field and photographic grading within standard programmatic trachoma surveys in the Amhara region of Ethiopia.

Methods

Ethical considerations

Survey methods conformed to the tenets of the Declaration of Helsinki. Ethical approval for the study was obtained from the Institutional Review Boards of Emory University (Atlanta, GA, USA; protocol number 079-2006) and the Amhara Regional Health Bureau (Amhara, Ethiopia). Verbal informed consent in Amharic was obtained before any grading or photography. Because of the high illiteracy rate, special permission was granted by review boards for verbal informed consent and assent among study participants.

Surveys and field grading

Photographic grading occurred alongside trachoma impact surveys, which were conducted following 1–5 y of the surgery, antibiotics, facial cleanliness, and environmental improvements (SAFE) strategy for trachoma control.[7] Data for this study were taken from the surveys conducted in January and February 2017. The methodology for these district-level surveys have been published previously. Briefly, a multistage cluster random sampling methodology was used, whereby villages were selected as clusters.[7,8] Upon arrival in the village, community leaders assisted with the second selection stage by randomly choosing segments of households to be surveyed. Individuals in all households in selected segments were eligible for trachoma examination. Upon receiving consent, conjunctival examinations were conducted for each eye of each present household member and results were recorded electronically as the field grade.[7,8]

All field graders were certified through comprehensive training, consisting of a photographic slide examination using a standardized 50 slide set and a field grade reliability examination.[7] When compared with a consensus grade of three expert graders, only those trainees who achieved a $\kappa > 0.7$ for TF were eligible to participate as survey team graders. Field graders examined participants with the WHO simplified trachoma grading system using 2.5× binocular magnification loupes with illumination.[2] Of the four certified field graders selected for the photography study, two had previous experience working on trachoma surveys and two were first-time graders.

Photography

A single photographer worked alongside the four graders over the course of the study, with the goal of collecting conjunctival photographs of all individuals within 10 selected clusters. The photographer was deployed with each grader based on daily and weekly survey logistics and therefore cluster selection could be considered unbiased with respect to the cluster-level trachoma burden. The field photographer was trained in conjunctival photography by an experienced photographer who participated in previous trachoma clinical trials.[9] Training consisted of instruction and field practice. A minimum of 1000 practice conjunctival photographs were taken before the surveys began.

Photographs were taken using a Canon EOS 60D in M mode (manual exposure) and a Canon EF 100 mm f/2.8 macro USM lens. The aperture was f/18, shutter speed was 1/100 s and ISO was 400.

Conjunctival photographs were taken of both eyes of all individuals in selected clusters. Following field grading, the grader kept the conjunctiva everted for photography and provided light on the conjunctiva if needed. The photographer took a minimum of two photographs of each eye, beginning with the right. If photographs were deemed to be of poor or ungradable quality at the time, more photographs were taken.

Grading center and photographic grading

Conjunctival photographs were graded in the newly established Gondar Grading Center (GGC) at the University of Gondar, Gondar, Amhara, Ethiopia. Two Hewlett-Packard ProBook computers with external monitors (27-in. Quad HD 2560×1440) were used at the GGC to assess photographs. Images were viewed on full-brightness settings; no other changes were made to the display settings. Windows were shaded and the lights turned off to reduce glare and other impediments to photograph viewing. The software used for grading was adapted from a previous randomized controlled trial.[10] A custom-built database was used to manage photographs and data and a custom data entry form was developed for graders to record conjunctivae grades.

The six individuals who took part in the photograph grader training were ophthalmology residents at the University of Gondar with background knowledge of trachoma. A 3-d training was conducted at the GGC and included lectures and exercises and concluded with a photographic grading certification exam conducted by an ophthalmologist (J.D.K.). To be included as a photograph grader for this study, trainees were required to complete the workshop and pass with a κ of 0.6 relative to the consensus grade of a panel of three expert graders who were ophthalmologists with significant experience in trachoma studies.[11] Trainees graded 400 practice conjunctival photographs before grading study photographs. All six graders passed the exam.

During 1–5 November 2019, five trachoma graders assessed photographs for the presence of TF, TI or trachomatous scarring (TS) using the WHO simplified grading system. Three photograph graders were assigned to one grading computer and two were assigned to another. Each computer was loaded with every pair of conjunctival photographs in random order, which were then graded by one of that computer's graders. Pairs of photographs for each eye were displayed together and magnified 2.5× for grading. Graders were masked to both the field grade as well as the photographic grades of the second eye belonging to the participant in the photograph.

After the initial grading by two graders was complete for each individual eye photograph pair on both computer stations, photograph pairings that were discordantly graded for any one trachoma grade were loaded again onto one computer along with any photographs determined to be ungradable due to corrupted file transfer. For an adjudicating grade, a third grader (the sixth trained grader) then assessed these photographs from 6 to 9 December 2019. The third grader's input was only considered for those trachoma signs that were graded discordantly. All final photographic grades were determined as those that had been agreed upon by at least two of the three graders.

All conjunctival photographs that were graded discordantly for TF between field graders and the final photographic grade was graded by an ophthalmologist, along with a random 5% of the photographs that were concordantly graded. Photographs were randomly sorted before grading by the ophthalmologist. The ophthalmologist grades were intended to provide additional context and characterization of TF grades.

Analysis

We assessed pair-wise grade concordance by calculating the percentage agreement (PA) and Cohen's κ between the initial two photographic grades as well as between the field grade and the final photographic grade for each eye. Analysis was conducted in R (R Foundation for Statistical Computing, Vienna, Austria) using the irr and rel packages. Confidence intervals (CIs) were calculated by bootstrapping Conger's generalization of Cohen's κ with 10 000 replicates. TF prevalence at the district and cluster levels was defined as the presence of TF in either eye. District-level estimates accounted for the clustered nature of the survey data using svy procedures in Stata 15 (StataCorp, College Station, TX, USA). Cluster-level estimates produced by final photographic grades were tested for statistical similarity with estimates resulting from the field grades using a Student's t-test.

Results

The field-graded TF prevalence among children ages 1–9 y ranged from 3.0 to 55.3% among study districts (Supplemental Figure 1) and the TF prevalence of the 10 clusters where photographs were taken ranged from 0.0 to 48.0%. A total of 1247 participants of all ages were examined for trachoma in the 10 selected clusters (Table 1). Of these participants, field grade data was captured for 1231 participants and 1241 participants contributed a total of 4953 photographs of 2477 conjunctivae. Six participants were examined but were not photographed and 16 participants were photographed but were missing field grades due to a software malfunction.

Interrater agreement between the two initial photographic grades was high for TF (PA 96.5%, κ=0.69, CI 0.62 to 0.75) and TS (PA 85.2%, κ=0.53, CI 0.49 to 0.58) but moderate for TI (PA 94.6%, κ=0.40, CI 0.30 to 0.50). After initial photograph grading by two graders, 87/2477 (3.5%) conjunctivae were discordantly graded for TF, 134/2477 (5.4%) were discordant for TI and 365/2477 (14.7%) were discordant for TS (Table 2). After the adjudication stage, only 1 of the 2477 conjunctivae was unable to be given a final TF grade, as both initial grades were classified as ungradable.

Agreement between the field and final photographic grades was good for TF (PA 96.7%, κ=0.70, CI 0.64 to 0.77) but lower for both TI (PA 94.7%, κ=0.32, CI 0.20 to 0.43) and TS (PA 83.5%, κ=0.22, CI 0.15 to 0.29) (Table 3). For each clinical sign individually, the final photographic grades achieved higher agreement and κ scores when compared with grades provided by experienced field graders as compared with grades provided by first-time field graders, although the κ confidence limits overlapped for each sign (Table 4).

Table 1. Sample size among individuals providing field grades and conjunctival photographs, Amhara, Ethiopia, 2017

Characteristics	Field grading, n	Photographic grading, n
Sex		
Male	487	490
Female	739	739
Missing	5	12
Age range (years)		
1–9	413	413
10–19	177	176
20–29	133	134
30–39	152	152
40–49	134	134
50–59	86	87
≥60	136	141
Missing	0	4
Total	1231	1241

Table 2. Comparison between two initial photographic grades and final photographic grade for three trachoma clinical signs, Amhara, Ethiopia, 2017

Final photographic grade		Initial two photographic grades: Concordant, n	Discordant, n
TF	+	105	51
	−	2277	36
	Total	2382	87
TI	+	50	16
	−	2283	118
	Total	2333	134
TS	+	305	179
	−	1801	186
	Total	2106	365

+, positive; −, negative.
Total numbers for each sign are different due to instances where no consensus grade (i.e. at least two 'votes' for the same sign for a given eye) could be determined for that sign.

Table 3. Comparison between field grade and final photographic grade, Amhara, Ethiopia, 2017

Field grade		Final photographic grade +	Final photographic grade −	PA	κ (95% CI)
TF	+	102	26	96.7	0.70 (0.64 to 0.77)
	−	54	2262		
TI	+	34	98	94.7	0.32 (0.20 to 0.43)
	−	32	2279		
TS	+	72	4	83.5	0.22 (0.15 to 0.29)
	−	399	1967		

+, positive; −, negative.

Among the 80 conjunctivae where the field TF grade differed from the final photographic grade, the ophthalmologist agreed with the photographic grade 38.8% (31/80) of the time and the field grade 61.3% (49/80) of the time. Among the 31 discordant grades between ophthalmologist and field grade, the ophthalmologist frequently noted the TF-positive conjunctivae to be 'borderline TF' and as having 'buried follicles', while TF-negative conjunctivae were most often described as having 'mild scarring' or 'too few follicles'. The ophthalmologist disagreed with the concordant field and final photographic grade in 15.5% (64/414) of the reviewed photographs, often noting 'too small' or 'too few follicles' among those graded as negative by the ophthalmologist but positive by both the field and final photograph grader.

Using the final photographic grade, cluster prevalence of TF ranged from 1.7 to 70.0%. These estimates showed no statistically significant difference from the cluster prevalence estimates determined using field grades (p=0.62) (Figure 1). Furthermore, cluster prevalence estimates determined by field grading were not statistically significantly different than estimates based on photographic grading for experienced graders (p=0.69) or first-time graders (p=0.78).

Discussion

Within programmatic trachoma surveys conducted in rural communities in the Amhara region, high-quality gradable photographs were collected from participants with a high response rate. Further, large numbers of photographs were graded and adjudicated in a short period of time at a grading center within this trachoma-endemic region. Agreement between field and photographic grades was good for TF, the programmatic indicator for trachoma. The results of this study add to the body of evidence that conjunctival photography may be a feasible and reliable research, training and program monitoring tool.

It was possible to integrate photography into routine trachoma impact surveys under programmatic conditions. While photography has often been used as part of randomized controlled trials and in trachoma research generally, data are scarce on the reliability of conjunctival photography within various programmatic surveys.[6] The photographer in this study traveled house-to-house alongside field graders and achieved a high response rate. Within the 10 selected communities, which were scattered across a large geographic area, the team photographed nearly all participants examined for a field grade. For each participant, a minimum of two photographs from each eye were captured for nearly all individuals across a wide age range, suggesting that tolerance for this activity was high among participants. Upon grading at the GGC, only one photograph was found to be ungradable. These findings suggest that with proper training, equipment and planning, quality images of participants examined within programmatic trachoma surveys are possible.

The development of a novel in-country trachoma photographic grading center demonstrated how partnering with in-country institutions can strengthen programmatic impact, and this was a good example of successful local research capacity building by the Trachoma Control Program in Amhara. Trainees demonstrated the ability to learn grading protocols and pass reliability exams, although in this case trainees were highly trained ophthalmology residents. Further work is needed to determine if less highly trained professionals can achieve similarly strong results within grading centers. The GGC was able to grade many photographs (4953) in a short amount of time (9 d, including adjudication). Speed and volume are key components of a grading program such as this since control programs may need results in time to make MDA decisions. Furthermore, graders at the GGC were masked to the field grade of the participant, as well as the grades of family or community members, a strength of photographic grading. This should allow for a reduction in grader bias. Agreement between photographic graders was high for TF (κ=0.69) on initial grading and comparable to past studies, with only 87 photographs needing adjudication.[6] This study used a third adjudication grader, not as a gold standard grader, but as a way to come to a consensus on discordant photographs. The adjudication step at the GGC took approximately 4 extra days, but a consensus grade is likely an important step for grading borderline cases, which may be more common in low-prevalence settings near elimination thresholds where greater reliability is required.[3] While this study used the consensus grade of three graders, any number of graders could be used to potentially improve the reliability of the final grade.

Agreement between field and final photographic grades for TF was high (κ=0.70) and comparable to other research studies assessing photographic grading for trachoma.[6] Communities in this study were selected from a population-based sample and thus represented the range of trachoma severity, including borderline cases. Borderline trachoma cases would normally be observed in hypo- and meso-endemic communities by programmatic surveys. In this study, while TF cluster-level prevalence estimates were not statistically significantly different between field and final photographic grading, there were two clusters where the photograph estimate was ≥5% and the field estimate was <5%. Programmatically, if all children in all clusters were photographed in a district-level survey, results around treatment or surveillance cut-points, such as observed here, could be reviewed by outside experts to aid in decision making. The agreement between field and photographic grades improved when compared against experienced field graders,

Table 4. Comparison between field grade and final photographic grade, stratified by grader experience, Amhara, Ethiopia, 2017

Field grade		Final photographic grade		PA	κ (95% CI)
		+	−		
Experienced field graders TF	+	54	10	97.1	0.73 (0.65 to 0.82)
	−	26	1136		
First-time field graders TF	+	48	16	96.4	0.67 (0.57 to 0.76)
	−	28	1126		
Experienced field graders TI	+	11	10	97.9	0.45 (0.24 to 0.66)
	−	16	1189		
First-time field graders TI	+	23	88	91.5	0.27 (0.14 to 0.41)
	−	16	1090		
Experienced field graders TS	+	45	3	87.6	0.33 (0.23 to 0.43)
	−	149	1028		
First-time field graders TS	+	27	1	79.4	0.14 (0.05 to 0.24)
	−	250	939		

+, positive; −, negative.

although the first-time graders' agreement with photographic graders was not statistically significantly different from that of experienced graders. The standard 5-d grader training appears to be successful in producing field graders of comparable quality regardless of experience level. Agreements between field and photographic grading for TI and TS were lower than agreements for TF. It is possible that these signs are more difficult to diagnose from a two-dimensional photograph compared with a three-dimensional conjunctiva. While grader trainees do learn the signs of TI and TS via slide exams and field training, the grader reliability certification is for the TF sign only. A higher agreement may be possible if greater emphasis is placed on certifying graders on TI and TS during field-grader training.[8,12]

Comparisons between field and photographic grading can be difficult, as there is no gold standard for comparison, and misclassification with both types of grading are expected. To better understand observed discrepancies between field and photographic grading for TF, nearly 500 photographs were regraded by an ophthalmologist. Among these were 80 conjunctive that likely represent harder-to-grade or borderline cases, as they were discordant between field and photographic grading. Despite the use of a consensus for the photographic grades, the ophthalmologist agreed with the field grade (61%) more often than with the photographic grade (39%), when there was discordance for that conjunctiva. This suggests that increased training may be warranted for photographic graders, particularly for conjunctivae with borderline TF. When the ophthalmologist disagreed with the field grade, the conjunctiva was often characterized as having follicles with the size and number to classify as a borderline case. When the number of follicles is close to the definitional cut-point (five or more follicles at least 0.5 mm in diameter), it is likely that even experts would disagree on the diagnosis.[4] The increased grading variability around programmatic thresholds and the reliance on a subjective clinical sign as a key programmatic indicator may contribute to the increased number of pre-validation surveillance surveys that return unfavorable results above the 5% threshold.[7]

There were several limitations specific to this study. The study photographer used an SLR camera which, because of the expense and weight, may not be a scalable option for use in programmatic settings. However, with the increasing advances in mobile phone photography, field photography will likely require less training and will become more cost effective. Cell phone cameras have been shown to produce similar sensitivities and specificities for active trachoma and better sensitivity for TI when compared with SLR cameras.[13] Recent developments, including the use of cellphone attachments with lights and magnification, should make programmatic use of photography by field graders feasible soon.[11,14,15] Photographic sets were double graded by certified photographic graders rotating on two different computer stations. Therefore it was not possible to calculate agreement by individual graders. Instead of using all individually graded photographic grades in the comparisons with field grades, this study used a single 'grading center' consensus grade for each photograph. Because this method reduced the number of photographic grades in the comparison, particularly for harder-to-grade, adjudicated photographs, it may have underestimated the overall agreement with field grading. However, future programmatic use of grading centers is likely to require a consensus to be reached for each eye to calculate a district prevalence. Various methods for arriving at final decisions on difficult photographs should be further evaluated prior to programmatic use.

Some important research questions remain to be answered before photographic grading is ready for programmatic use. This study assessed programmatic feasibility through the response rate and gradeability of the photographs taken but did not capture costs associated with this approach. Future operational studies should compare the total costs associated with traditional field-graded surveys vs photograph-graded surveys. While cost estimates have been calculated for traditional surveys in

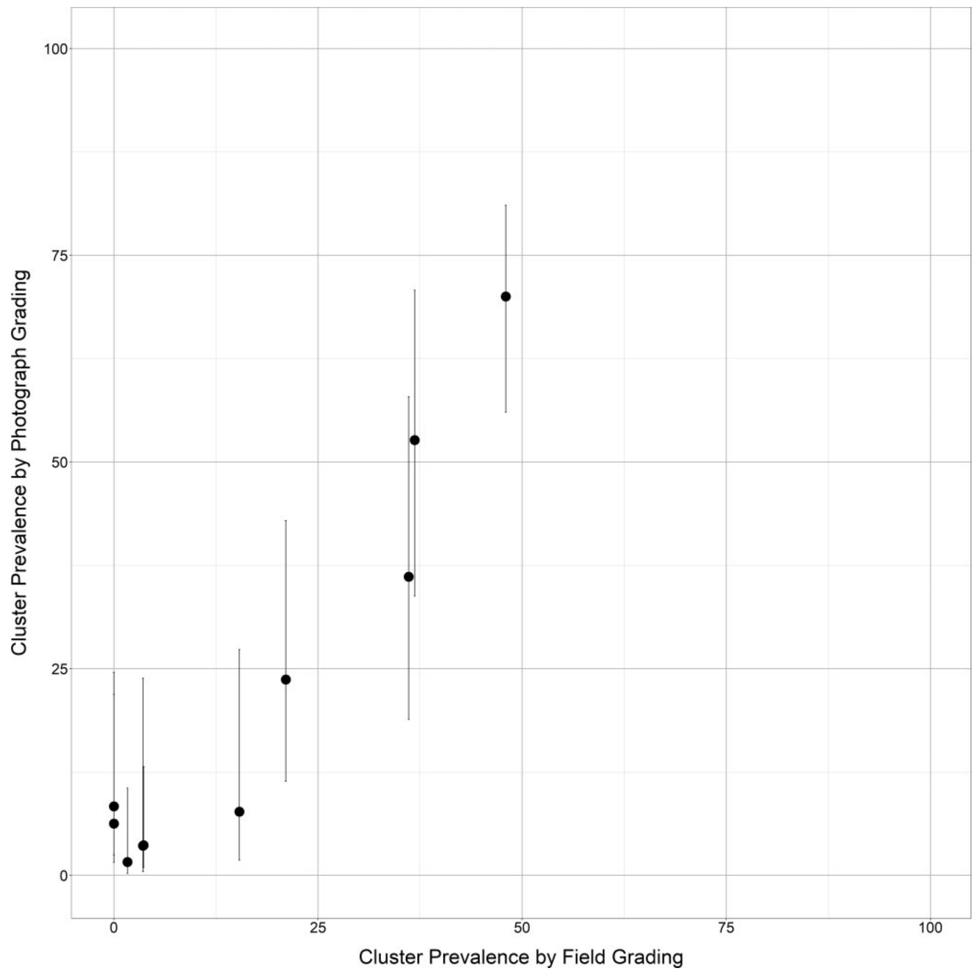

Figure 1. Cluster TF prevalence determined by field grading vs photographic grading, Amhara, Ethiopia, 2017.

this region,[16] new categories for assessment would include the training of the photographer, the per-person time to collect photographs and the costs associated with running a grading center, including training photograph graders and management of the photographs and associated data. Costs may be reduced by this grading center approach; however, so far, photographic grading still requires having a two-person team: a 'lid-everter' and a photographer/data recorder. While this approach would not reduce the number of individuals on a team, it could reduce the costs associated with training and certification as well as the need to have community cases of TF available to certify the graders.

This study demonstrated that it was possible to embed a photographer within routine programmatic activities and that photographs could be graded quickly in-country by trained trachoma photograph graders. Under a programmatic setting, good agreement between field and photograph grades for TF was achieved. Work is needed to improve agreement for the other signs of trachoma. Conjunctival photography may be a possible solution to providing quality trachoma monitoring as the prevalence of community cases decreases and trachoma elimination as a public health problem nears.

Supplementary data

Supplementary data are available at *Transactions* online.

Authors' contributions: TA, ES, EKC, FA and SDN conceived the study. TA, ZA, DG, ES, MZ, BM, FA, and SDN designed the study. BH, TA, ZA, DG, ES, MZ, BM, MH, TZ and ZT supervised the clinical assessments. BG, BW, EK, HG, MS, SB, SA, DMW, JDK and FA supervised the photography assessment. CCW, AWN, ARD, DMW, JDK and SDN conducted the analysis and interpretation of data. CCW, AWN, BH, ARD and SDN drafted the manuscript. CCW, AWN, BH, ARD, TA, ZA, DG, ES, MZ, BM, MH, TZ, BG, BW, EK, HG, MS, SB, SA, DMW, ZT, EKC and JDK critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. CCW, AWN and SDN are guarantors of the paper.

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Data availability: The data underlying this article are available in the article and in its online supplementary material.

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