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DIAGNOSIS OF URINARY SCHISTOSOMIASIS: A NOVEL APPROACH TO COMPARE BLADDER PATHOLOGY MEASURED BY ULTRASOUND AND THREE METHODS FOR HEMATURIA DETECTION

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Abstract. We aggregated published data from field studies documenting prevalence of *Schistosoma haematobium* infection and bladder pathology determined by ultrasonography or hematuria detected by reagent strip, questionnaire, or visual examination. A mathematical expression was used to describe the associations between prevalence of pathology/morbidity and infection. This allows for indirect comparison of these methods, which are rarely used simultaneously. All four methods showed a similar, marked association with infection. Surprisingly, ultrasound revealed higher prevalences of pathology in schools than in communities with the same prevalence of infection, implying a need for age-related cut-off values. Reagent strip testing yielded a higher prevalence than questionnaire, which in turn was higher than by visual examination. After correction for morbidity due to other causes, a consistent ratio in prevalence of hematuria of 3:2:1 resulted for the three respective methods. The simple questionnaire approach is not markedly inferior to the other techniques, making it the best option for field use.

INTRODUCTION

Identification of cases or communities for treatment of infection with *Schistosoma haematobium* is usually based on microscopic detection of eggs in urine. Detection of hematuria, the main symptom of urinary schistosomiasis due to *S. haematobium* infection, may be a simpler and cheaper alternative for identifying communities in need of treatment.[1,2] Microhematuria can be detected by reagent strip testing. Macrohematuria can be detected with the help of a questionnaire (i.e., asking individuals if they have experienced blood in urine in a given period) or by visual examination of a urine sample.[3] Since 1970, ultrasonography has been applied to visualize lesions in the bladder wall caused by trapped *S. haematobium* eggs.[4–6] This method is not suitable for large-scale use in control, but it is accepted as a relatively simple noninvasive method in hospital or research settings.[7]

Many epidemiologic studies have been conducted to investigate the characteristics of the above methods to measure urinary schistosomiasis. This usually involved comparing the outcomes with infection. The four methods enumerated above have rarely been directly compared. Moreover, most studies concerned a single school or community or neighboring schools/communities in a defined area (district).

In this study, we aimed at evaluating four techniques for detecting pathology or morbidity due to *S. haematobium* infection: bladder pathology by ultrasound, microhematuria by reagent strip, and macrohematuria by questionnaire or visual examination. We aggregated all field studies reporting prevalence of infection and prevalence of pathology/morbidity. We explored the association of each of these methods with infection over different endemicity levels. Using these associations, we were able to make an indirect comparison of the performance of each of these four methods.

METHODS

Data collection. We searched PubMed (United States National Library of Medicine) to identify all articles published up to the year 2002 reporting on the prevalence of ultrasonographically detectable bladder pathology, reagent strip–detected microhematuria or macrohematuria determined by questionnaire or by visual examination in unselected study populations (schools or whole communities) with known prevalence of *S. haematobium* infection. The references of the collected articles were checked for additional articles and quantitative information was extracted. Only pretreatment data were included. Prevalence data from each community or school were included as independent observations, i.e., one study could contribute multiple observations to the analysis.

Data on bladder pathology were included if the pathology had been detected by ultrasound and was defined using the international standards,[8,9] i.e., the presence of an irregular bladder wall, a bladder wall thickness > 5 mm, the presence of masses or presence of pseudo polyps. For microhematuria determined by reagent strip, we used the data reported for the 1+ positive limit. Data on macrohematuria obtained by means of the questionnaire method were included if measured by asking participants to respond to a question such as "Have you urinated blood during the past period" (the period varied between studies and a maximum of four weeks was chosen). We used the results reported for the longest period in analyzing the one study that used two recall periods (1 day and 1 week).[10] Prevalence studies on visibly detected macrohematuria (inspection of urine samples by health workers) were included if they scored clearly red urine as positive. Only studies with prevalence of infection based on standard filtration of 10 mL of urine or a method with comparable sensitivity were included: namely, filtration, centrifugation, or sedimentation of 5–20-mL urine samples.[11]

Relating pathology or morbidity to infection. A mathematical expression was used to describe the associations between prevalence of pathology/morbidity and prevalence of infection (Appendix 1). The lines representing the expression start in the origin or a point higher on the *y*-axis (baseline level). This is because morbidity can also be due to other causes (e.g., microhematuria from bacterial urinary tract infection) or misclassification (e.g., brown concentrated urine can be reported as hematuria). Positive hematuria testing in the absence of *S. haematobium* infection (i.e., prevalence of infection close to zero) was considered to be a false-positive test result. The lines are assumed to remain horizontal at low prevalence of infection because only few or no cases have an infection intensity high enough to cause morbidity. For higher

prevalences, the lines rise with increasing speed as the proportion with high intensity, associated with morbidity will increase faster than the corresponding prevalence.[12] The lines eventually reach their maximum level somewhere below 100%. This is because morbidity can be intermittent, or some of the infected individuals may not be susceptible for developing morbidity. Further details of the mathematical equation and its three parameters can be found in Appendix 1.

Using this methodology, we assessed the associations between prevalence of *S. haematobium* infection and the prevalence of the four diagnostic methods: ultrasonographic detection of bladder pathology, microhematuria determined by reagent strip testing, and macrohematuria determined by questionnaire or by visual examination. We examined the impact of two determinants on these associations: study setting (school or community survey) and geographic area (west Africa: Benin, Burkina Faso, Gambia, Ghana, Côte d'Ivoire, Mali, Niger, Nigeria, Senegal, Chad; east Africa: Kenya, Madagascar, Mozambique, Tanzania, Zambia, Zimbabwe; and north Africa: Egypt, Ethiopia, Sudan). The fitted expressions corrected for the baseline level (i.e., not taking into account morbidity due to other causes) were used to study the pathology or morbidity caused by *S. haematobium* infection. We used the derived associations to compare the performance of the different diagnostic methods. Finally, we predicted the consequences for community diagnosis if it were based on detecting hematuria instead of infection. This was done by comparing the proportions of schools and communities correctly categorized according to the World Health Organization (WHO) recommendations for mass treatment using the three methods to detect hematuria (Appendix 2).

RESULTS

We were able to make use of data from 19 studies containing information from 16 schools and 16 communities to estimate the association between prevalence of *S. haematobium* infection and bladder pathology by ultrasound.[13–31] The prevalence of bladder pathology was clearly found to increase with the prevalence of infection (Figure 1a). Prevalences from school surveys were generally higher than from community surveys with a comparable prevalence of infection, as demonstrated by both a difference in baseline prevalence and a stronger association with infection. The calculated baseline prevalence was 13% for schools and 3% for community surveys. Apparently, school children have more bladder pathology due to other causes or are more often misclassified by ultrasound. The lines finally reached 79% for school children and 59% for communities. Pathology prevalences were somewhat higher in west Africa compared with north Africa, but this is partly explained by the fact that the latter mainly concerned community studies.

Data from 45 studies comprising 74 schools and 28 communities was available to evaluate the prevalence of microhematuria detected by reagent strip testing.[10,15,19,22–25,28,30–66] Again, the prevalence of hematuria increased markedly with the prevalence of infection (Figure 1b). Separate analysis for schools and communities showed a slightly lower baseline prevalence of microhematuria (reagent strip) for schools (24% versus 16%); however, the lines largely overlapped and both ultimately reached 77% for higher endemicity levels. The lower baseline prevalence for schools was mainly caused by one study contributing 25 observations to the analysis. The same study was also responsible for a slightly lower baseline prevalence rate in east Africa.

Twenty-one studies, comprising 117 schools and 14 communities, presented information on macrohematuria that had been obtained by questionnaire.[1,2,10,15,17,19,20,23–25,28,30,35,38,50,54,58,59,65,67–69] Schools and communities showed virtually identical associations of self-reported macrohematuria rates with the prevalence of infection (Figure 1c). The fitted associations started at a baseline prevalence of approximately 12% and finally reached 60%. The majority of data points (80%) came from two studies in Tanzania.[1,2] These studies did not unduly influence the results because associations separately fitted for each study did not markedly differ from each other, nor from that of the other 19 studies.

The association between prevalence of infection and macrohematuria detected by visual examination was derived from 14 articles concerning 16 schools and 31 communities.[28,31,33,38,50,59,60,65,70–75] School surveys and community surveys with a low prevalence of *S. haematobium* infection reported no cases of macrohematuria, yielding a baseline prevalence of 0.0% (Figure 1d). Overall, the prevalence of macrohematuria by visual examination was markedly lower than for the other diagnostic methods. The lines for schools and communities initially overlapped and slightly diverged for higher prevalences. Geographic area nor study setting influenced the association between infection and visibly detected macrohematuria.

The associations in Figure 1 between prevalence of infection and bladder pathology and hematuria were summarized (Figure 2a). Since no significant difference was found between the associations for hematuria in school children and communities, these were combined ($P > 0.20$ by covariance analysis for all three methods). At all levels of infection, the prevalences estimated by each of the three methods did not vary in terms of order: microhematuria (detected by reagent strip screening) showed the highest prevalence, followed by macrohematuria determined by questionnaire, and lastly, macrohematuria detected by visual examination. After correcting for baseline, i.e., morbidity due to other causes (false-positive results), a proportional hematuria detection rate was found, corresponding with a ratio of approximately 3:2:1 for these three methods over all prevalence of infection levels (Figure 2b). For example, at a 50% level of infection, the corresponding prevalence of hematuria due to *S. haematobium* infection was 38% for detection by reagent strip testing, 24% when using the questionnaire approach, and 12% using the visual examination method. The associations of infection and bladder pathology for schools and communities were also proportional to those of hematuria, with bladder pathology in schoolchildren 15% above and bladder pathology in communities 25% below microhematuria. Thus, studies in communities showed approximately 35% less bladder pathology due to *S. haematobium* than studies in school children with the same prevalence of infection (Figure 2b).

DISCUSSION

It is reassuring to have been able to demonstrate that the four methods used to detect pathology or morbidity due to *S. haematobium* all showed a clear and consistent association with prevalence of infection. Also, in line with expectations,

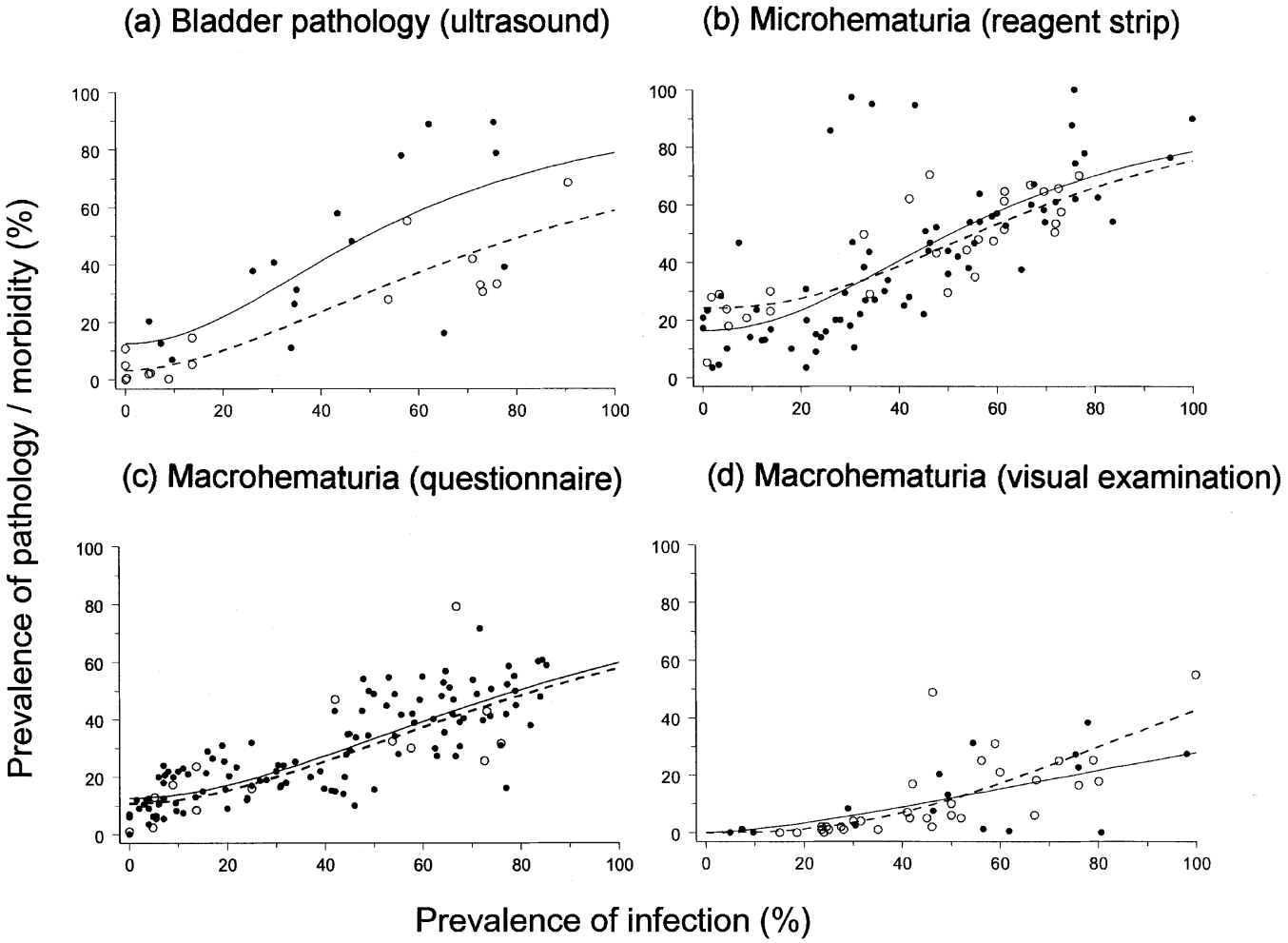

FIGURE 1. Observed associations between *Schistosoma haematobium* infection and clinical consequences. Prevalence of **a**, bladder pathology by ultrasound; **b**, microhematuria by reagent strip; **c**, macrohematuria by questionnaire; and **d**, macrohematuria by visual examination as a function of prevalence of *S. haematobium* infection. Observations come from published studies and concern schools (**dots**) or whole communities (**circles**). The lines are based on equation 1 and represent schools (**continuous lines**) or communities (**dashed lines**). Parameters for bladder pathology are $a = 0.13$, $b = 3.13$, and $c = 2.04$ (schools) and $a = 0.033$, $b = 1.35$, and $c = 1.78$ (communities). Parameters for microhematuria detected by reagent strip testing are $a = 0.16$, $b = 2.90$, and $c = 2.14$ (schools) and $a = 0.24$, $b = 2.09$, and $c = 2.37$ (communities). Parameters for macrohematuria detected by the questionnaire approach are $a = 0.13$, $b = 1.17$, and $c = 1.91$ (schools) and $a = 0.11$, $b = 1.12$, and $c = 1.88$ (communities). Parameters for macrohematuria detected by visual examination are $a = 0.00$, $b = 0.38$, and $c = 1.50$ (schools) and $a = 0.00$, $b = 0.75$, and $c = 2.50$ (communities). The interpretation of parameter values is given in Appendix 1.

the prevalence of microhematuria determined by reagent strip testing was higher than that of macrohematuria reported by questionnaire, which in turn was higher than the prevalence of visibly detected macrohematuria. Furthermore, the fact that previous studies that explored associations between prevalence of infection and hematuria measured by reagent strip,[60,76] questionnaire,[1,77] or visual examination[75] found patterns similar to the current study, in which all available observations from the different field studies and geographic areas were aggregated.

Our methodology offers a closer look at the test characteristics of the different diagnostic techniques and their (biologic) relationships (Figure 2). The baseline levels (parameter *a* in the equation) of the estimated associations correspond to a universal proportion of false-positive results, i.e., those showing positive test results due to misclassification or other diseases/infections than *S. haematobium*. In our methodology, this proportion resulted from studies in populations not infected with *S. haematobium* or with low endemicity. We believe this approach to be superior to the common method of using the presence or absence of detected infection in individuals as a gold standard. In such studies, only a limited amount of urine (1–3 repeated standard 10-mL urine filtrations[2,28,45,48,52,55,68,78]) is usually used, so that many cases tend to go undiagnosed. This results in an overestimation of false-positive test results and thus also in an underestimation of the specificity of the test.[79] In our study, the specificity of the different diagnostic techniques simply follows from a 100% baseline prevalence: e.g., for hematuria, the specificity is 82% for screening by reagent strip, 88% for the questionnaire method, and 100% for the visual examination method. The sensitivity is unable to be directly determined by our methodology because the number of individuals with blood in their urine due to *S. haematobium* infection that goes undetected is unknown (false-negative results). However, the proportional differences between the associations in Figure 2b provide

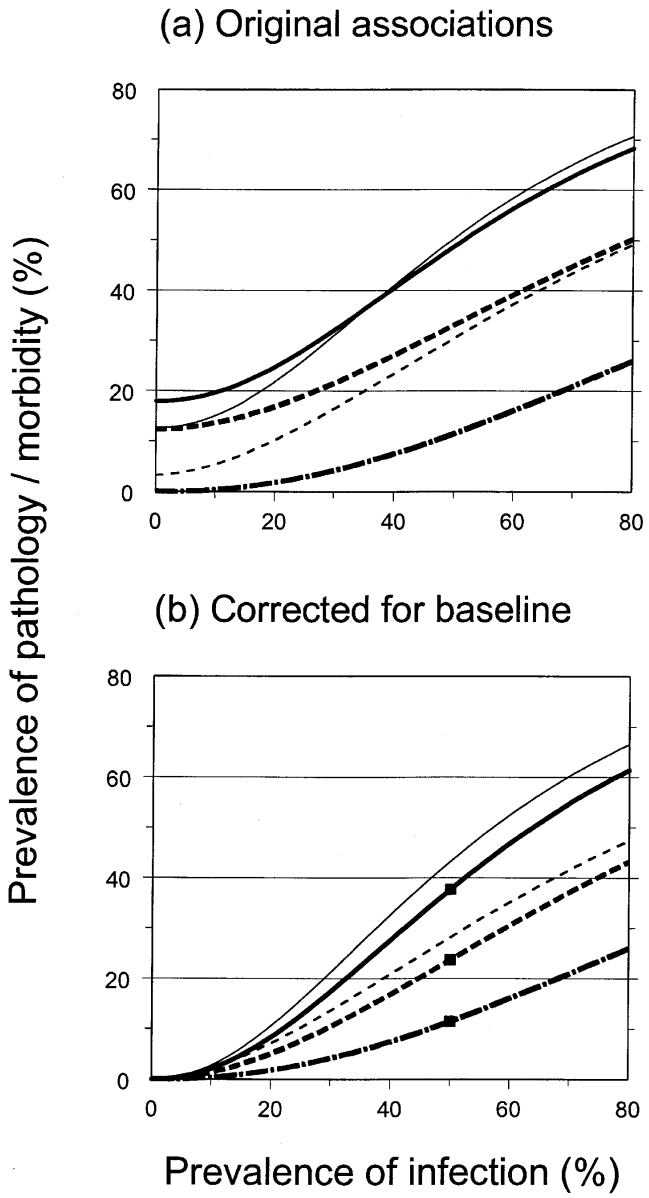

FIGURE 2. Predicted associations between *Schistosoma haematobium* infection and prevalences of bladder pathology (**thin lines**), microhematuria by reagent strip (**thick continuous lines**), and macrohematuria by questionnaire (**thick evenly dashed lines**), or visual examination of a urine sample (**thick long-short dashed lines**) using the original lines from Figure 1 (**a**) and after correction for baseline prevalence of morbidity or pathology due to other causes or misclassification (**b**). Separate associations are given for bladder pathology in schoolchildren (**thin continuous line**) and whole communities (**thin dashed line**) (see Figure 1 for parameter values). Combined lines are given for hematuria, with parameters $a = 0.18$, $b = 2.53$, and $c = 2.07$ (reagent strip), $a = 0.12$, $b = 1.17$, and $c = 1.90$ (questionnaire), and $a = 0.00$, $b = 0.56$, and $c = 2.11$ (visual examination). At a 50% prevalence of infection, the corresponding prevalences of hematuria corrected for baseline morbidity are indicated by the **squares**.

some indication of how many cases are at least missed by the respective techniques.

We assumed that the baseline prevalences do not depend on endemicity. This may be an oversimplification because infectious diseases tend to cluster.[80] For example, the risk of both schistosomiasis and urinary tract infection (also responsible for hematuria) will probably be higher in environments with no sanitary facilities available. Also, individuals living in the poorest rural areas are likely to have nutritional deficiencies, making them more susceptible to any disease. While the clustering of disease may have resulted in somewhat steeper lines, the relationship between the different associations will not have been seriously affected. The proportion of false-positive test results due to misclassification is not likely to be associated with the prevalence of schistosome infection.

After correcting for false-positive results, the prevalence of ultrasound-detected pathology in school children appeared to be largely parallel (always about 10% lower) to that of infection. As stated earlier, many infected cases are missed by standard parasitologic screening and are not included in the prevalence of infection. Therefore, more than a fixed 10% of the children will be infected with *S. haematobium* infection, but will have no ultrasound-detectable pathology. Nevertheless, a 10% prevalence of (detected) infection means that hardly any cases with an infection intensity high enough to show *S. haematobium*-related pathology will occur, whereas an 80% prevalence of infection (and a probable 100% infection rate) causes this percentage to increase to 70%. This clearly demonstrates the impact of increasing intensity of infection (and risk of developing disease) with increasing prevalence of infection.

Surprisingly, the prevalence of bladder pathology measured by ultrasonography was considerably lower in communities than in school children with the same prevalence of infection. Children showed both more false-positive results (higher baseline prevalence in Figure 2a) and a stronger association with infection (Figure 2b). The difference between adults and children are in actual fact likely to be even larger because community observations also include children. Assuming that children make up 50% of a community, the line for communities is expected to be located somewhere halfway between schoolchildren and adults. The large difference in baseline prevalence for schoolchildren (13%) and communities (3%) would appear to suggest that false-positive ultrasound results do not occur in adults. However, the baseline level for communities was disproportionately determined by six observations from a series of publications from one study in Egypt.[23–27,30] This extensive study, which reported relatively low prevalences of bladder pathology in situations of low endemicity, may have resulted in some underestimation of the rate of false-positive results, but it could only account for half of the difference between studies on children and communities. Thus, misclassification or false-positive results due to other diseases such as urinary tract infections and urethral stenosis seem to be substantially more prevalent in children than adults. It is not clear why this should be the case.

Our finding that approximately 35% less *S. haematobium*-related bladder pathology was found in community studies than in studies in school children, given the same prevalence of infection, may also have been subject to bias, in particular because the number of observations was rather low. However, in areas of moderate to high endemicity, almost consistently lower prevalences were seen in community studies than in studies of school children (Figure 1a). Other studies corroborate the finding that lower rates of ultrasonographically detected bladder pathology are seen in adults than in children. In the four studies where observations for children and adults were reported separately,[13,14,17,19] prevalences of pa-

thology in children were always considerably higher than in adults, even after correction for false-positive results and the difference in prevalence of infection. Moreover, the study by Heurtier and others,[13] which was the only one that presented prevalences of bladder pathology for different ages and egg count groups, reported a prevalence of 77% in 70 children with 1–99 eggs/10 mL of urine versus 62% in 68 adults of the same egg count group ($P = 0.05$). The difference in presence of (ultrasound detected) bladder pathology between children and adults could be explained by a more potent immune response in children. However, our results on hematuria were very consistent in showing equal levels of morbidity for children and communities (and thus adults). Since hematuria results from the same mechanism, i.e., bladder lesions from eggs that get trapped in the bladder mucosa,[34,69] we would expect equal levels of pathology for children and adults with the same prevalence of infection. Thus, the most plausible explanation is that ultrasound leaves a considerable number of adults with bladder pathology undetected. Apart from those with *S. haematobium*-related bladder pathology, this could also concern cases with pathology from other diseases (false-positive results). One explanation would be that the internationally agreed standards to define bladder pathology by ultrasound[8,9] cannot simply be used irrespective of age. It may be better to have criteria for children and adults separately.

In accordance with the general characteristics of the three methods used to detect hematuria, reagent strip testing had a higher baseline prevalence and stronger association with infection compared with macrohematuria established by the questionnaire approach, and by visual examination. First, occult blood in urine can be detected with the help of reagent strips (high sensitivity for detection of hematuria, i.e., >5 erythrocytes/μL[81,82]), yet it will not be reported nor detected by visual examination. The latter methods are thought to select cases with relatively heavy infection and more severe pathology.[60] Second, hematuria due to *S. haematobium* infection is transitory,[83,84] implying that macrohematuria has a higher chance of being detected via the questionnaire method than after visual examination of a single urine sample. Given a detection ratio of 2:1 (Figure 2b), at least 50% of macrohematuria cases will be missed when relying solely on a visual examination. All cases with macrohematuria detected by either visual examination or questionnaires that are truly attributable to *S. haematobium* infection will in all likelihood yield a positive reagent strip test result. It is therefore not likely that questionnaires or visual examination of a urine sample will add to the information derived from the reagent strip results. The one study that presented individual results by reagent strip and questionnaire showed that only 10 of 133 individuals who had negative reagent strip test results reported having hematuria.[58] This small proportion (7.5%) can easily be explained by the rate of false-positive results observed in our study. False reports of blood in urine easily result, especially when brown, concentrated urine is mistaken for blood, a mistake that is far less likely to occur during visual examination of a urine sample, a procedure that is normally performed by a trained health worker. Conversely, the questionnaire method may also underdiagnose hematuria because individuals may consider blood in urine as a venereal disease and feel ashamed,[85] or forget recent episodes of hematuria, especially in areas where blood in urine is not considered a problem.[86,87] However, in the light of the fact that 50% more truly positive cases are detected by reagent strip screening (given the ratio of 3:2 in Figure 2b), most of whom will not have gross hematuria, this underdiagnosis is not expected to pose problems. Regarding the possibility of recall bias, it is also interesting to note that length of the recall period used in the studies included (usually two or four weeks) proved to be of no importance.[88] The proportion of positive reagent strips not attributable to *S. haematobium* is even higher than the proportion of false-positive results by questionnaire. This is because other (medical) causes such as urinary tract infections, sexually transmitted diseases, and menstruation mainly result in very small quantities of blood in the urine, usually not visible to the eye. These causes may be more prevalent in adults than in children,[89,90] thereby explaining the difference in baseline levels between communities and schoolchildren (24% versus 16%). However, this difference is not significant and disappears at higher endemicity levels (prevalence of infection >20%). Ultimately, in choosing between the three methods for detecting hematuria, the objectives of the research or control program and the resources available are decisive. Many false-positive results will lead to unnecessary treatment of cases with no (or low) infections and consequently high drug cost, whereas many false-negative results will limit the effect of the intervention. The questionnaire method may sometimes be favorable because it requires fewer materials and personnel training than does the use of reagent strips or the visual examination approach.

We were also able to evaluate the performance of the three hematuria detection techniques for categorizing communities in the WHO recommended treatment strategies[91] with the help of our database. The probability of identifying communities below or above the cut-off values of 20% and 50% prevalence of infection with *S. haematobium* was comparable between the three hematuria detection methods (Appendix 2). Approximately 50–80% of communities and schools would remain in the same category as when using the WHO recommended cut-off values based on infection. Only three schools would be seriously misclassified by visual examination of a urine sample, i.e., no treatment instead of mass treatment of the entire population. Given the practical advantages of the questionnaire method, we consider it the best alternative to infection for cheap and simple identification of communities in need of treatment.

In conclusion, 1) the detection methods for clinical pathology and morbidity show marked associations with prevalence of *S. haematobium* infection; 2) ultrasound detects fewer cases with bladder pathology in adults compared with children with the same degree of pathology; 3) after correction for false-positive results, prevalences of hematuria due to *S. haematobium* are almost proportional, with a ratio of reagent strip:questionnaire:visual examination of 3:2:1; 4) since the questionnaire method does not have test characteristics markedly inferior to the other diagnostic techniques, its advantage in terms of required cost, time, and personnel will usually make it the method of choice for both individual and community diagnosis; and 5) our methodology can also be applied for other infectious diseases, particularly those in which development of disease depends on the intensity of infection.

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APPENDIX 1

For a given school or community, we assume a prevalence (%) of pathology or morbidity Y to be a function of prevalence (%) of infection X according to

$$Y/100 = (a + b\,(X/100)^c)/(1 + b\,(X/100)^c) \qquad (1)$$

with baseline parameter a ($0 \leq a < 1$) and shape parameters b ($b > 0$) and c ($c > 1$). The equation has a first derivative that equals zero at $X = 0\%$ and $Y = a \cdot 100\%$. This guarantees that at very low prevalences of infection, no or only limited detectable morbidity is assumed to be due to *Schistosoma haematobium*. $Y = a \cdot 100\%$ is the baseline prevalence of pathology or morbidity, i.e., pathology or morbidity caused by misclassification or other diseases (false positives). Thereafter, the line rises monotonously and finally reaches a prevalence of morbidity below $Y = 100\%$. The shape of the line is determined by parameters b and c in combination. By taking parameter $a = 0$ (no baseline), the equation represents morbidity due to *S. haematobium* infection corrected for morbidity due to other causes. Further details are described in Van der Werf and others.[92,93]

We used Systat version 3.0 (Systat Software, Inc., Richmond, CA) to estimate the values of parameters a, b, and c by fitting the equation to all n observations. The fit was determined by assuming a binomial distribution for each observation i ($i = 1, \ldots, n$), without assigning weight according to size of the population. The latter assumption can easily be made since the vertical location is determined by many more phenomena (e.g., the community base-line morbidity) than the size of the population alone. The number of individuals comprising one observation was usually about 100, with a minimum of 32. To explore potential bias due to overrepresentation of large studies (contributing many observations), we have re-analyzed all associations with attributing weight to observations according to the reciprocal of the square root of the number of observations coming from each study. For instance, observations from a study contributing 16 schools or communities had a weight of 1/4 compared with observations from studies contributing one school or community. This approach did not lead to significantly different results and we therefore only reported the standard procedure based on associations without attributing weight according to study size.

Some adjustments were necessary to apply our methodology. For micro-hematuria detected by reagent strip (association for community) and macro-hematuria detected by questionnaire, fitting Equation 1 yielded a biologically unrealistic trend indicated by a sharp increase of morbidity at low prevalence of infection and a point of inflexion at prevalence of infection $X < 25\%$. For both situations, we reduced the number of parameters by pre-setting the point of inflection at prevalence of infection $X = 50\%$, which corresponds to $b = [(c - 1) / (c + 1)]\, 2^c$. One study [94] with many outlier observations and one outlier observation from the study by Lengeler and others[1] (prevalence of *S. haematobium* infection = 23% and prevalence of macro-hematuria by questionnaire = 64%) were excluded from the analysis.

APPENDIX 2

The World Health Organization recommends no treatment (apart from those found positive at the screening) if the prevalence of *Schistosoma haematobium* infection is ≤20%, mass treatment of the 5–19-year-old age group (20–50%), and mass treatment of the whole community (>50%).[91] The prevalence of hematuria may provide a better (rapid, simple, and cheap) method for community diagnosis.[95] Some have used the same cut-off levels of 20% and 50% for hematuria by reagent strip.[96] It may be better to use cut-off prevalences corresponding to the values for infection. From Figure 2a, it follows that these prevalences are 25% and 49% for reagent strip, 17% and 33% for questionnaire, and 2% and 12% for visual examination.

TABLE 1

Recommended treatment strategy based on prevalence of hematuria*

Hematuria test	No treatment	Mass treatment of 5–19-year old age group	Mass treatment of whole community
Reagent strips	78 (61–95)	46 (30–63)	79 (66–92)
Questionnaire	64 (50–78)	47 (32–62)	78 (66–90)
Visual examination	100 (48–100)	61 (41–81)	74 (54–94)

* Values indicate the percentage (%) of schools and communities that would be correctly categorized using cut-off prevalences for hematuria instead of the World Health Organization recommended prevalence categories for *Schistosoma haematobium* infection. Shown are no treatment (apart from those found positive at the screening) if the prevalence of infection was ≤20%, mass treatment of the 5–19-year old age group (20–50%), and mass treatment of the whole community (> 50%).[91] Cut-off prevalences for hematuria corresponding to 20% and 50% infection from Figure 2a were 25% and 49% for reagent strips, 17% and 33% for questionnaires, and 2% and 12% for visual examination, respectively. Values in parentheses are the 95% confidence intervals.

For each data point (community or school) in our database, we assessed whether the same treatment strategy would follow from using cut-off levels for hematuria compared with infection. To prevent dependency, the cut-off levels for hematuria for each data point were determined after re-fitting the associations of Figure 2a excluding this data point. Table 1 shows the proportion of schools and communities correctly categorized for all three methods detecting hematuria. The overall performance of the three methods did not significantly differ ($P > 0.3$, by chi-square test). Only for visual examination of a urine sample, a number of schools (3) would be seriously misclassified, i.e., receiving no treatment instead of mass treatment of the whole community.