Risk of Recurrent Helicobacter pylori Infection 1 Year After Initial Eradication Therapy in 7 Latin American Communities

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Importance The long-term effectiveness of Helicobacter pylori eradication programs for preventing gastric cancer will depend on recurrence risk and individual and community factors.

Objective To estimate risk of H pylori recurrence and assess factors associated with successful eradication 1 year after treatment.

Design, Setting, and Participants Cohort analysis of 1463 randomized trial participants aged 21 to 65 years from 7 Latin American communities, who were treated for H pylori and observed between September 2009 and July 2011.

Interventions Randomization to 1 of 3 treatment groups: 14-day lansoprazole, amoxicillin, and clarithromycin (triple therapy); 5-day lansoprazole and amoxicillin followed by 5-day lansoprazole, clarithromycin, and metronidazole (sequential); or 5-day lansoprazole, amoxicillin, clarithromycin, and metronidazole (concomitant). Participants with a positive 13C-urea breath test (UBT) 6 to 8 weeks posttreatment were offered voluntary re-treatment with 14-day bismuth-based quadruple therapy.

Measurements Recurrence after a negative posttreatment UBT and factors associated with successful eradication at 1-year follow-up.

Results Among participants with UBT-negative results who had a 1-year follow-up UBT (n=1091), 125 tested UBT positive, a recurrence risk of 11.5% (95% CI, 9.6%-13.5%). Recurrence was significantly associated with study site (adjusted odds ratio [AOR], 1.17; 95% CI, 1.01-1.35 per child; P=.03). Of the 281 with positive posttreatment UBT results, 138 completed re-treatment, of whom 93 tested UBT negative at 1 year. Among the 1340 who had a 1-year UBT, 80.4% (95% CI, 76.4%-83.9%), 79.8% (95% CI, 75.8%-83.5%), and 77.8% (95% CI, 73.6%-81.6%) had UBT-negative results in the triple, sequential, and concomitant groups, respectively (P=.61), with 79.3% overall effectiveness (95% CI, 77.1%-81.5%). In a single-treatment course analysis that ignored the effects of re-treatment, the percentage of UBT-negative results at 1 year was 72.4% (95% CI, 69.9%-74.8%) and was significantly associated with study site (P<.001), adherence to initial therapy (AOR, 0.26; 95% CI, 0.15-0.42; P<.001), male sex (AOR, 1.63; 95% CI, 1.25-2.13; P<.001), and age (AOR, 1.14; 95% CI, 1.02-1.27 per decade; P=.02). One-year effectiveness among all 1463 enrolled participants, considering all missing UBT results as positive, was 72.7% (95% CI, 70.3%-74.9%).

Conclusions and Relevance One year after treatment for H pylori infection, recurrence occurred in 11.5% of participants who had negative posttreatment UBT results. Recurrence determinants (ie, nonadherence and demographics) may be as important as specific antibiotic regimen in determining the long-term success of H pylori eradication interventions. Study findings are relevant to the feasibility of programs for the primary prevention of gastric cancer in high-incidence regions of Latin America.

Trial Registration clinicaltrials.gov Identifier: NCT01061437

In a randomized trial in Shandong, China, eradication of H pylori using amoxicillin and omeprazole reduced gastric cancer incidence by 39% over 20 years.

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significant illness (eg, active cancer, other
6 to 8 weeks following randomiza-
ported the results of eradication therapy
10,11

We observed a cohort of patients en-
rrolled in a randomized trial in 7 com-

METHODS

The trial sites and methods have been
previously reported15 and were coor-
dinated by SWOG, a federally funded cancer research cooperative group. In
brief, men and women aged 21 to 65
years were recruited and screened for
eligibility in 7 Latin American commu-
nities between September 2009 and
June 2010. Potential participants were
selected using a census of households
(Colombia, Costa Rica, Nicaragua), a
large public clinic registry (Chile), or
household recruitment (Honduras and
2 sites in Mexico). Eligibility require-
ments included having no prior treat-
ment for H pylori infection and no sig-
nificant illness (eg, active cancer, other
serious chronic illness).14 We ex-
plained the purpose and eligibility re-
quirements of the study to potential par-
ticipants and those who expressed an
interest provided signed informed con-
sent. The institutional review boards for
each center and the SWOG statistical
center approved the study protocol.19

H pylori infection was assessed using
the (13) C-urea breath test (UBT) with
a 75-mg oral dose of 13C-labeled urea,
analyzed with infrared mass spectro-
metry (IRIS, Wagner Analysen Tech-
nik). A change in 13C carbon dioxide,
relative to a baseline of 4.0% or greater,
was considered positive. Serologic mark-
ers for the H pylori CagA protein (cyto-
toxin-associated gene A) were assessed
by IgG antibodies in the study labora-
tory in Mexico (J.T.) by previously de-
scribed methods.13 Standard instru-
ments were used (including the Rome III
Diagnostic Questionnaire for the assess-
ment of baseline dyspepsia symptoms)
to assess demographic factors, house-
hold conditions, and health history.16,17

Individuals who had positive UBT re-
sults and met other eligibility criteria
were randomly assigned by a central
computer to 1 of 3 treatment groups
using a web-based dynamic randomiza-
tion procedure that assured balance of
sex, age, and study site across the 3 regi-
ments. The treatments were: (1) triple
therapy, given for 14 days of lanso-
prazole 30 mg, amoxicillin 1000 mg, and
clarithromycin 500 mg; (2) sequential
therapy, given for 5 days of lanso-
prazole 30 mg and amoxicillin 1000 mg,
followed by 5 days of lansoprazole 30 mg,
clarithromycin 500 mg, and metronida-

52 weeks following randomization for all
participants, included a UBT and final
examination, scheduled between 48 and
52 weeks following randomization for all
participants, included a UBT and final
examination, scheduled between 48 and
52 weeks following randomization for all
participants, included a UBT and final
examination, scheduled between 48 and
52 weeks following randomization for all
pa

Statistical Considerations

The trial sample size of 1470 partici-
pants was chosen to provide a greater
than 80% power to assess the first study
aim—which sequential therapy was
superior to triple therapy and whether
concomitant therapy was noninferior
to triple therapy in terms of eradica-
tion success (UBT negativity) at the 6-
to 8-week follow-up. This sample size
was determined to be sufficient to ad-

cide UBT results were considered as treat-
ment failures (UBT positive).

Participants as belonging to the treat-
ment group to which they were as-
signed, regardless of adherence to their
assigned regimens. Analyses of recur-
rence risk and treatment outcomes were
based on participants who had a con-
clusive (definite) UBT result at the 1-
year visit. Treatment outcome re-
results are also presented using 2 addi-
tional approaches: (1) a 1-year intent-
to-treat analysis in which participants
without a follow-up UBT were consid-
red as treatment failures (UBT posi-

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RECURRENT *HELICOBACTER PYLORI* INFECTION AFTER ERADICATION THERAPY

RECURRENT *HELICOBACTER PYLORI* INFECTION AFTER ERADICATION THERAPY

Figure. Latin America *Helicobacter pylori* Eradication Trial Profile

<table>
<thead>
<tr>
<th>1859 Individuals assessed for eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>1463 Randomized and treated</td>
</tr>
<tr>
<td>6 Excluded due to data entry error</td>
</tr>
<tr>
<td>1469 Participants randomized</td>
</tr>
<tr>
<td>390 Excluded</td>
</tr>
<tr>
<td>375 UBT negative, ineligible</td>
</tr>
<tr>
<td>7 Withdrew consent before UBT</td>
</tr>
<tr>
<td>1133 H pylori negative</td>
</tr>
<tr>
<td>6- to 8-wk Posttreatment status</td>
</tr>
<tr>
<td>281 H pylori positive</td>
</tr>
<tr>
<td>5 Had conclusive 1-y UBT</td>
</tr>
<tr>
<td>44 No 1-y UBT</td>
</tr>
<tr>
<td>4 Unable to contact</td>
</tr>
<tr>
<td>37 Other or unknown</td>
</tr>
<tr>
<td>10 Declined follow-up</td>
</tr>
<tr>
<td>1133 H pylori negative</td>
</tr>
<tr>
<td>1-y Follow-up</td>
</tr>
<tr>
<td>1091 Had conclusive 1-y UBT</td>
</tr>
<tr>
<td>20 Unable to contact</td>
</tr>
<tr>
<td>12 Other or unknown</td>
</tr>
<tr>
<td>10 Declined follow-up</td>
</tr>
<tr>
<td>47 No 1-y UBT</td>
</tr>
<tr>
<td>4 UBT inconclusive</td>
</tr>
<tr>
<td>10 Declined follow-up</td>
</tr>
<tr>
<td>1133 Included in analysis</td>
</tr>
<tr>
<td>1340 With conclusive 1-y UBT</td>
</tr>
<tr>
<td>123 Without 1-y UBT</td>
</tr>
<tr>
<td>61 Others or unknown</td>
</tr>
<tr>
<td>37 Unable to contact</td>
</tr>
<tr>
<td>25 Declined follow-up</td>
</tr>
<tr>
<td>1133 Included in analysis</td>
</tr>
<tr>
<td>1340 With conclusive 1-y UBT</td>
</tr>
<tr>
<td>123 Without 1-y UBT</td>
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<tr>
<td>61 Others or unknown</td>
</tr>
<tr>
<td>37 Unable to contact</td>
</tr>
<tr>
<td>25 Declined follow-up</td>
</tr>
<tr>
<td>6- to 8-wk Posttreatment status</td>
</tr>
<tr>
<td>49 H pylori status unknown</td>
</tr>
<tr>
<td>47 UBT performed</td>
</tr>
<tr>
<td>4 UBT inconclusive</td>
</tr>
<tr>
<td>12 Declined follow-up</td>
</tr>
<tr>
<td>1463 Included in 1-year analysis</td>
</tr>
<tr>
<td>1469 Participants randomized</td>
</tr>
<tr>
<td>281 H pylori positive</td>
</tr>
<tr>
<td>6- to 8-wk Posttreatment status</td>
</tr>
<tr>
<td>49 H pylori status unknown</td>
</tr>
<tr>
<td>47 UBT performed</td>
</tr>
<tr>
<td>4 UBT inconclusive</td>
</tr>
<tr>
<td>12 Declined follow-up</td>
</tr>
</tbody>
</table>

We identified 1859 adults who agreed to participate, of whom 1844 were potentially eligible with positive UBT results (FIGURE). Exclusions included 375 individuals (20.3%) because of negative UBT results, 7 withdrew consent, and 8 were ineligible on subsequent interviews. Six individuals with negative UBT results were incorrectly randomized due to data entry error and immediately withdrawn, leaving 1463 participants randomized to receive 1 of the 3 antibiotic regimens.

Table 1 shows participants’ characteristics according to their treatment assignment and follow-up status: 59% were women, 55% older than 40 years, 84% were *H pylori* CagA positive, and 26% had chronic dyspepsia symptoms. Reported use of alcohol (8%, ≥1 drink/week) and tobacco (16%, ≥1 cigarette/d) was relatively infrequent. We obtained a conclusive UBT result at the posttreatment (6- to 8-week) visit from 1414 participants (96.7%) and from 1340 (91.6%) at the 1-year follow-up visit.

Infection Recurrence

Of the 1133 participants who were UBT negative following initial treatment, 1091 had a 1-year UBT result, of whom 125
had become UBT positive, a recurrence risk of 11.5% (95% CI, 9.6%-13.5%). The recurrence risk ranged from 6.8% in Costa Rica to 18.1% in Colombia. Recurrence at 1 year was significantly associated with study site (P = .03), number of children in the household (odds ratio [OR], 1.17; [95% CI, 1.01-1.35 per child; P = .03), and nonadherence to therapy (OR, 2.94; 95% CI, 1.31-6.13; P = .01), but not with treatment assignment (P = .63) (Table 2).

1-Year Outcomes

In the primary analysis of treatment effectiveness based on the 1340 participants with definitive 1-year UBT results, the estimated 1-year eradication success rate was 80.4% (95% CI, 76.4%-83.9%) for triple therapy, 79.8% (95% CI, 75.8%-83.5%) for sequential therapy, and 77.8% (73.6%-81.6%) for concomitant therapy (P = .61). Overall effectiveness was 79.3% (95% CI, 77.1%-81.5%; Table 3). Outcome of treatment effectiveness among study sites ranged from a higher level (87%-90%) in Costa Rica and Honduras to a lower level (71%-76%) in Colombia, Nicaragua, and in Obregón and Tapanchula, Mexico. Women 21 to 44 years of age were significantly less likely to have eradication success at 1 year (72.3%; 95% CI, 68.0%-76.2%) when compared with women 45 to 65 years of age (82.8%; 95% CI, 78.2%-86.8%), and when compared with men who were both younger (82.1%; 95% CI, 77.3%-86.2%) and older (85.6%; 95% CI, 80.5%-89.9%).

Of participants with positive post-treatment UBT results, 244 of 281 returned for a 1-year examination. Of those who returned, 198 (81%) had accepted a prescription for re-treatment quadruple therapy but only 138 (57%) reported that they had completed the regimen; 37 (15%) refused re-
treatment. The UBT result had become negative for 38% overall (93/244) and also for 54% of those who reported completing re-treatment (74/138). Of the individuals with UBT-positive results who declined re-treatment, 4 of 46 had UBT-negative results at 1 year.

In a 1-year analysis that included all 1463 randomized participants, and that considered as treatment failures (UBT positive) the 123 individuals (8.4%) without a UBT result, treatment effectiveness estimates were 74.6% (95% CI, 70.9%-78.4%), 73.3% (95% CI, 69.1%-77.1%), and 70.1% (95% CI, 65.9%-74.2%) for the triple, sequential, and concomitant treatment groups, respectively, or about 7% lower than those in the analysis mentioned previously. (Table 3).

To explore the possible outcomes of a program without the retest and re-treatment component at 6 to 8 weeks, we conducted the single-treatment course analysis that considered as treatment failures the 93 participants whose negative 1-year UBT had been preceded by a positive UBT result at 6 to 8 weeks. Results of this analysis showed an overall effectiveness of 72.4% (95% CI, 69.9%-74.8%; Table 3). Voluntary re-treatment tended to dilute differences in effectiveness among the treatment groups, and removing these effects yielded estimates of 75.5% (95% CI, 71.3%-79.4%), 72.4% (95% CI, 68.0%-76.5%), and 69.2% (95% CI, 64.6%-73.4%) for the triple, sequential, and concomitant therapy groups, respectively (P = .11).

### Predictors of Treatment Success

In the logistic regression models of the posttreatment (6-8 weeks) and the

### Table 2. Helicobacter pylori Recurrence at 1 Year by Participant Characteristics and Treatment Regimen

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>1-year UBT Status</th>
<th>Adjusted</th>
<th>Value</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-d Triple</td>
<td>125/1091 (11.5)</td>
<td>.63</td>
<td></td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>10-d Sequential</td>
<td>36/356 (10.1)</td>
<td>.02</td>
<td></td>
<td>0.82 (0.51-1.30)</td>
<td></td>
</tr>
<tr>
<td>5-d Concomitant</td>
<td>42/346 (12.1)</td>
<td>.01</td>
<td></td>
<td>1.01 (0.64-1.58)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Helicobacter pylori Eradication Success at 1 Year by Treatment Regimen and Analytic Approach

<table>
<thead>
<tr>
<th>Analytic Approach</th>
<th>Negative No./ Total No.</th>
<th>% (95% CI)</th>
<th>Negative No./ Total No.</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitive UBT (n = 1340)</td>
<td>364/453</td>
<td>80.4 (76.4-83.9)</td>
<td>342/453</td>
<td>75.5 (71.3-79.4)</td>
</tr>
<tr>
<td>Single-Treatment Course (n = 1340)</td>
<td>356/456</td>
<td>79.8 (75.8-83.5)</td>
<td>323/456</td>
<td>72.4 (68.0-76.5)</td>
</tr>
<tr>
<td>1-y ITT (n = 1463)</td>
<td>343/441</td>
<td>77.8 (73.6-81.6)</td>
<td>305/441</td>
<td>69.2 (64.6-73.4)</td>
</tr>
</tbody>
</table>

### Abbreviations:
- OR: odds ratio
- UBT: (13) C-urea breath test
- CI: confidence interval
- ITT: intention to treat

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1-year (single-treatment course) outcomes (Table 4), significant associations were observed with study site, male sex, older age, and adherence to initial therapy. Having fewer children in the household was associated with the 1-year outcomes but not with 6- to 8-week outcome, while treatment assignment was significantly associated with 6- to 8-week outcome,14 but not with 1-year outcome. Other factors such as cigarette smoking, alcohol use, water source, sanitation, and baseline chronic dyspepsia were unrelated to outcome (eTable, available at http://www.jama.com).

**COMMENT**

In our 1-year follow-up study from this randomized trial in 7 community populations in Latin America, the risk of recurrent *H pylori* infection following apparently successful eradication was 11.5%. Although triple therapy in our initial analyses had appeared to be superior to sequential and concomitant therapies at 6 to 8 weeks, there were only modest and nonsignificant differences in 1-year outcomes among the 3 treatment groups. Triple therapy succeeded in eradicating *H pylori* infection in 84.4% of participants who had a UBT 6 to 8 weeks posttreatment15 but its observed efficacy at 1 year was 80.4%, and its success was estimated to be 75.5% if the effects of re-treating participants whose initial treatment had failed were ignored. Significant predictors of successful eradication of *H pylori* infection at 1 year were study site, male sex, older age, and adherence to initial therapy.

**Recurrent of Infection**

The 11.5% 1-year recurrence risk observed in our trial is consistent with prior reports from Latin America and other low- and middle-income regions.21,24,25 In a review by Gisbert21 of

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**Table 4. Characteristics Associated With Helicobacter pylori Eradication Success Posttreatment and at 1 Year by Single-Treatment Analysis**

<table>
<thead>
<tr>
<th>Posttreatment (6-8 Week) Success (n = 1414)a</th>
<th>1-Year Success Single-Treatment Course Analysis (n = 1340)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment regimen</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Study site</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Sex</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Age, y</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Children in the household</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adherence, pills returned</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Negative No./Total No. (%)</td>
<td>OR (95% CI)c</td>
</tr>
<tr>
<td>Adjusted Valuec</td>
<td>OR (95% CI)c</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; UBT, (13) C-urea breath test.

aAnalysis only includes participants with a conclusive UBT result at the 6- to 8-week visit after treatment initiation.

bAnalysis includes all participants with 1-year UBT results and assumes that those who were UBT positive at 6 to 8 weeks are still positive at 1 year, statistically eliminating the effect of retreatment.

cStatistically estimated from a logistic regression model that accounts for age (continuous), sex, and study center. CIs are based on the profile likelihood method. P values are based on the Wald test statistic. Statistics do not include missing values for children in the household (n = 12 at 6 to 8 weeks and n = 11 at 1 year) and adherence (n = 18 at 6 to 8 weeks and n = 16 at 1 year).

dIn the regression models, the variables age (per 10 y) and number of children in the household were considered as continuous variables.
more than 100 studies, the overall annual recurrence risk ranged from 3.4% (95% CI, 3.1%-3.7%) in high-income countries to 8.7% (95% CI, 8.8%-9.6%) in lower-income countries. In studies from Latin America with at least 50 person-years of follow-up,22,26-29 the 1-year recurrence risk ranged from 0% to 17.3%.28,29 In the largest prior study in Latin America, conducted in Colombia, the mean annual recurrence rate over 6 years of cohort follow-up was 5.4%.21 In our trial, the Colombia site had the highest recurrence risk (18.1%), and notably, the participants were recruited from the same region as in the aforementioned study. A high rate of recurrent infection was also seen in the eradication trial from Shandong,5 wherein UBT negativity in the group treated with amoxicillin-based treatment declined from 74% at 1 year to 47% by the seventh year.20 Nonetheless, participants randomized to eradication therapy in the Shandong trial had a statistically significant 39% decrease in gastric cancer incidence over a 14.7-year period of follow-up.5

H pylori recurrence in the first year following eradication seems likely to represent a mixture of recrudescent infection and reinfection, whereas reinfection dominates in subsequent years and the overall annual risk of recurrence tends to diminish.22,24,26 We found an association between recurrence with both medication nonadherence and study site (a possible marker of regional antibiotic resistance), suggesting that recrudescence was an important component of 1-year recurrence in the populations in this study.31 The borderline association between number of children in the household and recurrence suggests that an element of reinfection also occurred during the first year, consistent with previous reports wherein number of children was a risk factor for infection.32,33 Our finding that women who were between 21 and 44 years old were less likely to have successful 1-year eradication is also consistent with a risk of reinfection mediated through contact with young children. Differences in generic medications were unlikely to explain site differences because Honduras and Nicaragua used drugs from the same batch and manufacturer in Central America, yet they had disparate 1-year outcomes. Continued cohort follow-up should provide important insights.

**Implications of 1-Year Outcomes**

The observed 1-year outcomes of our study represent a mixture of the effects of initial eradication therapy, re-treatment, recurrence, and participant and community characteristics. Although H pylori eradication programs may be cost effective, particularly in high-incidence areas,34-36 retesting and re-treating individuals shortly after initial eradication therapy may not be cost effective, especially when the probability of successful eradication with initial therapy is relatively high and the efficacy of re-treatment is modest.31 To simulate a program that did not include an early retest and re-treatment stage, we conducted the single-treatment course analysis, which ignored the effects of voluntary re-treatment. Our estimated 75.5% success rate for triple therapy in this analysis was not remarkably better than that for the other 2 regimens tested and the success of all 3 regimens without re-treatment was comparable to what has been reported from prior eradication trials.5,7,10 Thus, while our data underscore the continued use of 14-day triple therapy in Latin America, from a program perspective they also point to the possible acceptability of a lower-cost regimen (eg, sequential therapy). Assessment of program effectiveness must also consider potential adverse outcomes such as adverse effects of treatment, rare serious events,37 and the potential contribution to community antimicrobial resistance.38 In low- and middle-income nations, the incremental effects of an eradication program on resistance are difficult to gauge given the prevalence of unsanitary conditions that facilitate spread of resistant bacteria and the common practice of self-prescription with over-the-counter antibiotics.39

In our current study, adherence, study site, sex, and age were significantly associated with the probability of a successful 1-year outcome. From the public health perspective, a “one size fits all” intervention strategy may not be optimal. For example, the fact that age-specific rates of gastric cancer incidence in women lag those of men by 10 to 15 years,1 coupled with the higher risk of recurrent infection in younger women, suggests that an eradication program could enroll men beginning at age 30 years but delay enrolling women until they reach 40 or 50 years of age. In general, programs will be more effective if tailored to the demographics and community ecology of their target populations.40

The feasibility and success of an H pylori eradication strategy for preventing gastric cancer focused on specific populations in high-risk regions will depend on the cancer risk in the target population, the prevalence of virulent H pylori strains, the probability of success of initial treatment, the risk of recurrent infection, and the per-person program cost of screening and eradication. Eradication programs seem likely to be cost effective if they prevent at least 10% of cancer deaths,41,42 a threshold that was exceeded in the Shangdong Intervention Trial3 and in a trial from Japan that randomized patients with resected gastric cancer to antibiotics or placebo and observed a statistically significant 64% decrease in risk of metachronous cancers over 3 years of follow-up.9 A combined analysis of the effects of 5 randomized trials of H pylori eradication on gastric cancer incidence3 reported a pooled relative risk of 0.58 (95% CI, 0.42-0.81).5

**Study Strengths and Limitations**

Our trial was designed as a public health intervention with a vision toward future programs of H pylori eradication in high-risk areas of Latin America. The trial incorporated data from 7 heterogeneous community populations in 6 countries, noninvasive H pylori testing with UBT, generic medications purchased locally, and standard anti-
croebial regimens. However, this public health approach had inherent limitations. Participants were recruited from the community and the results may not be generalizable to symptomatic patients requiring clinical evaluation. We also did not assess antibiotic resistance or gastric histology. Additionally, re-treatment of UBT-positive participants was voluntary, and thus, efficacy estimates with quadruple therapy are qualified.

**CONCLUSIONS**

In this large study in diverse community populations in Latin America, our results indicate that geographic site, demographic factors, adherence to initial therapy, and infection recurrence may be as important as the choice of antibiotic regimen in H pylori eradication interventions. Ongoing research initiatives are needed, given the expected increase in the gastric cancer burden in Latin America over the next 2 decades, evidence that H pylori infection is the dominant risk factor, and evidence that eradication reduces gastric cancer risk.

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