Authors’ objectives
To review the eradication rates for Helicobacter pylori eradication therapy in the Netherlands.

Searching
The authors searched the MEDLINE and EMBASE electronic databases (1983 to May 1998). The authors also searched the bibliographies of retrieved articles and handsearched the abstracts from scientific meetings and the reference lists from pharmaceutical companies.

Study selection
Study designs of evaluations included in the review
Prospective and/or retrospective studies. Studies were excluded if an intention-to-treat (ITT) and/or per-protocol (PP) eradication percentage was required, or figures had to be present that allowed ITT and/or PP eradication percentages to be calculated per treatment arm.

Specific interventions included in the review
Triple or quadruple combination therapies using combinations of bismuth, amoxycillin, metronidazole, clarithromycin, tetracycline, omeprazole, pantoprazole, lansoprazole, ranitidine bismuth citrate, for 0, 1 or 2 weeks. One-week therapy was defined as the regimen as a whole lasting 4-9 days. Two-week therapy was defined as the regimen lasting more than 9 days. When a therapy lasted fewer than 4 days it was defined as a 0-week therapy. Mono- and dual-therapy trials were excluded, except for dual therapy trials with ranitidine bismuth citrate (RBC).

Participants included in the review
Patients diagnosed as Helicobacter pylori-positive.

Outcomes assessed in the review
Mean eradication rate.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
Two reviewers independently analysed each study arm and recorded the data on a form. The forms were compared and errors and disagreements were discussed and corrected. The final data were entered in a database. The database was automatically checked and also checked by hand by another investigator for errors.

Methods of synthesis
How were the studies combined?
Pooled N-weighted ITT and PP eradication rates with 95% confidence intervals (CIs) were calculated using an equal effects model (i.e. weighted by the number of participants).

How were differences between studies investigated?
Results of the review
Thirty papers with 38 study arms were included in the review with 2,197 participants.

Of the 38 study arms, 26 were published as full papers and 12 as abstracts only. A total of 20 were randomised study arms, 2 were double-blind, 2 were single-blind, and the rest were open-labelled studies.

Mean eradication rates for bismuth-based triple therapies was < 80%, except for bismuth-tetracycline-metronidazole therapy for 2 weeks which showed ITT and PP eradication rates of 94% (95% CI: 91%, 96%) and 96% (95% CI: 93%, 98%), respectively. Bismuth and metronidazole combined with tetracycline yielded superior cure rates (eradication rates of 78% and 94%) compared to the combination with amoxycillin (eradication rates of 35% and 78%). Patients with metronidazole-resistant strains, treated with bismuth-tetracycline-metronidazole for 1 or 2 weeks, showed significantly lower cure rates than patients with metronidazole-sensitive strains, with a mean drop in efficacy from 97% to 44%.

Proton pump inhibitor triple therapy eradication rates appeared to be lower in Dutch studies than those reported elsewhere, with a mean ITT cure rate of 84% for the 1 week PPI triple therapies. Omeprazole combined with clarithromycin and metronidazole for 2 weeks had the highest cure rate of 96%. Metronidazole-resistant strains show a trend toward lower mean eradication rates; however the 95% CIs overlap in all PPI triple therapy groups.

For quadruple therapy given for 1 or 2 days only (3 study arms) the mean eradication rate was < 60%. In 4 studies, quadruple therapy was given for 4 days with mean ITT and PP eradication rates of 89% and 91% respectively. All other quadruple therapies were given for 7 days, with ITT and PP eradication rates of 93% and 95% respectively. Omeprazole-bismuth-tetracycline-metronidazole for 1 week showed the highest mean eradication rate (93%). Metronidazole-resistance was found to be not statistically significantly different between groups. For ranitidine bismuth citrate (RBC) combinations (6 study arms) the mean ITT and PP eradication rates were 92% and 95% respectively. RBC in combination with clarithromycin and metronidazole for 1 week showed the highest cure rate of 96% on an ITT basis. No differences were found between patients with metronidazole-resistant or -sensitive strains.

The reported number of patients who stopped therapy because of side effects was < 1% in all pooled therapy groups.

Authors' conclusions
The authors state that a therapy should be tested in a defined population before becoming standard. Several eradication regimens studied in the Netherlands yield acceptable cure rates of 80% or more on an intention-to-treat basis.

CRD commentary
The authors have clearly stated their research question and some inclusion and exclusion criteria. While the literature search appears thorough the authors do not mention any language restrictions or the inclusion of unpublished data in the review. The quality of the included studies was not assessed and the authors have not reported on how the articles were selected. The authors have stated, however, how many of the reviewers were involved in the data extraction.

The data extraction is summarised by treatment groups in tables. Individual study details are not given; instead the treatment arms are combined and presented in groups by type of intervention. The statistical pooling summarised the mean eradication rates for individual treatment regimens but there were no tests reported for heterogeneity. The authors' conclusions appear to follow from the results but these should be viewed with caution because of the stated methodological limitations of the review.

Implications of the review for practice and research
Practice: The authors advise taking the local prevalence of metronidazole resistance into account when choosing a first-line eradication regimen.
Research: The authors do not state any implications for further research.

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