

**Background.** Meta-analyses are believed to represent the highest level of medical evidence (Grade A)

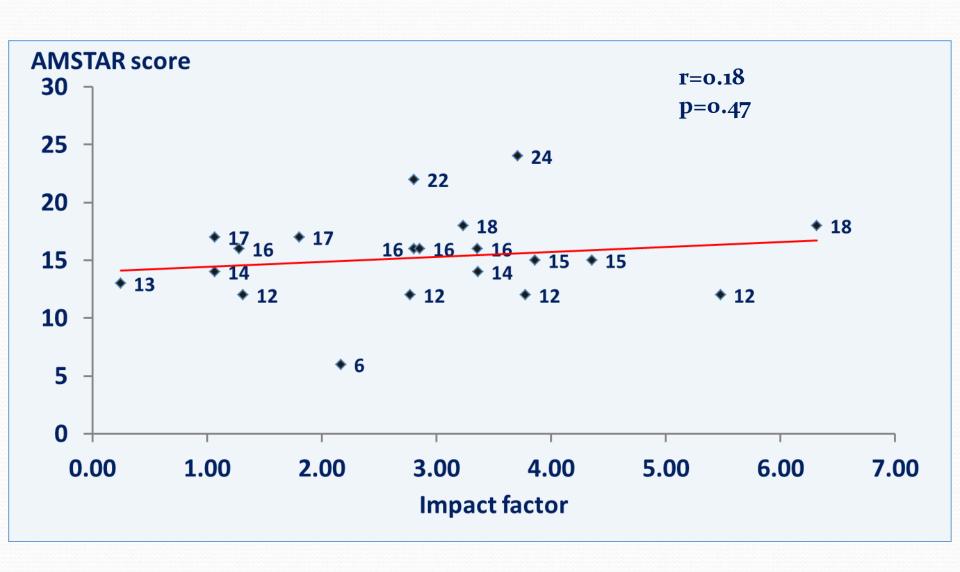
**Aim.** To assess the quality of meta-analyses published on the effect of adding probiotics to eradication regimens for *Helicobacter pylori* infection.

**Methods.** The full text of meta-analyses regarding the effect of probiotics on the eradication rates of regimens given for *Helicobacter pylori* infection were retrieved from MEDLINE and Google Scholar databases. The methodological and reporting quality were determined using the Assessment of Multiple Systematic Reviews-2 (AMSTAR 2) questionnaire. The correlation between the AMSTAR score as a dependent variable and the number of authors, number of databases used, impact factor and citation rate as independent variables was calculated. The rate of using the PRISMA checklist, PROSPERO registration and evidence grading was also noted.

### Results

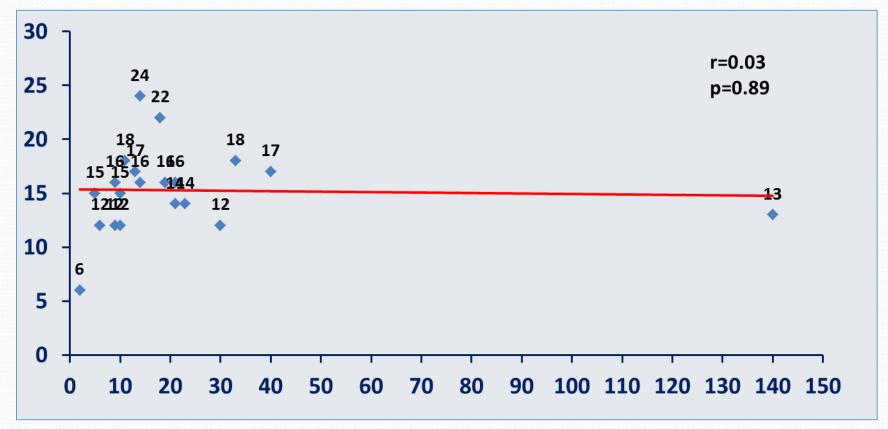
The literature search produced 20 meta-analyses published between 2007 and 2019. The mean AMSTAR score was 15.7±0.74 (95% CI: 14.1-17.3), corresponding to a moderate quality. The complete PRISMA checklist was used in 5 studies (25%), and no research protocol was registered in PROSPERO. The grading of evidence was explicitly stated only in 8 (40%) publications.

a) Correlation between the AMSTAR score and impact factor of the journals

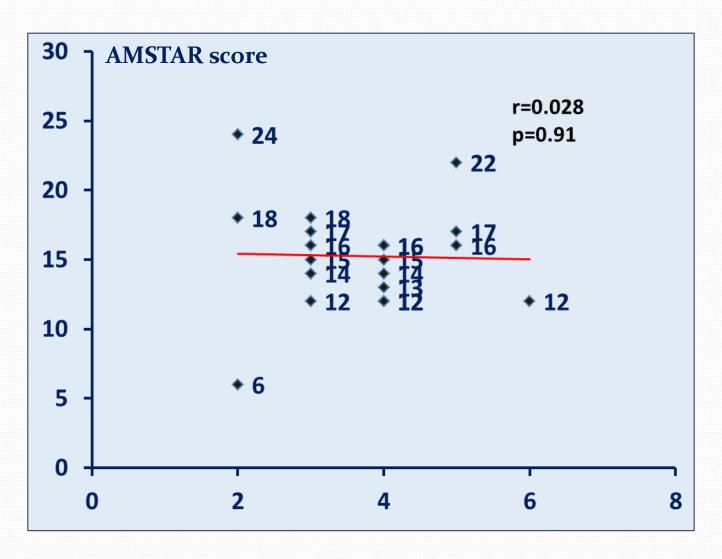


b) Correlation between the AMSTAR score and number of studies included

#### **AMSTAR** score

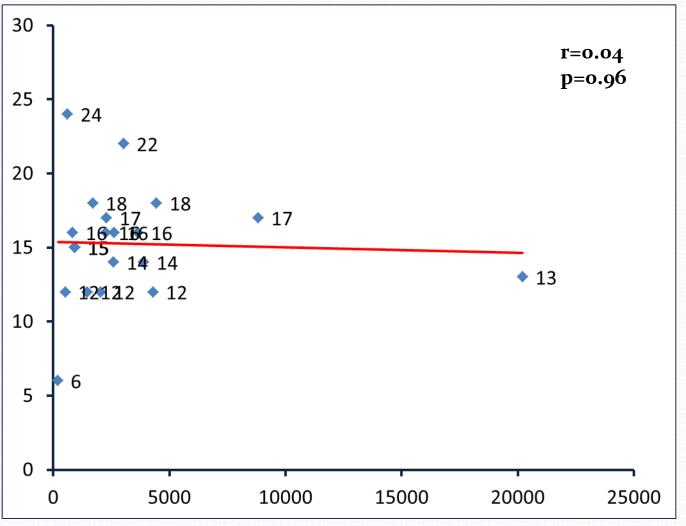


### c) Correlation between the AMSTAR score and number of databases studied



d) Correlation between the AMSTAR score and number of cases included

#### **AMSTAR** score



## Conclusions

Meta-analyses published so far on the proposed topic are of rather moderate quality. This resulted in divergent statements in the recent consensus meetings (see the Table below). Meta-analysis methodology must be improved to obtain more conclusive data on use of probiotics

# **Addendum:** Position statement of the guidelines: use of probiotics for eradication of Helicobacter pylori <sup>x</sup>

Year	Guideline	No. of ref.	Statement
2016	Toronto consensus	4 (2R, 2M)	In patients with H pylori infection, we recommend against adding probiotics to eradication therapy for the purpose of increasing eradication rates.
2016	Maastricht- Florence V	5(3R, 2M)	Certain multistrain probiotics can be used as add-on to reduce adverse effects on case by case basis
2016	IV Spanish consensus	14 (10M, 2 R, 2 RCT)	Recommendation 7. Probiotics should not be indiscrim-inately combined with eradication treatment.
2017	ACG guideline	2M	Although probiotic therapy for <i>H. pylori</i> infection seems promising, many important questions remain, including the optimal dose, the time of dosing (before, during, or aft er eradication therapy), and the duration of therapy.
2018	IV.Brazilian Consensus	6 (R2, RCT 2, M 2)	Probiotics use associated with ET is an attempt to optimize HP eradication and minimize adverse events, rebalancing the microbiota. Further studies are needed to better define the strain, amount, time, and period of supplementation
2018	V. Chinese Consensus	6 (3R, 3M)	Probiotics are useful in improving eradication rates and reducing the side effects of antibiotic therapies
2018	Bangkok (Asian)	6 (3R, 3M)	Probiotics can be used as adjunctive treatments to reduce adverse effects and increase tolerability. The use of probiotics plus standard therapy may be associated with a modest increase in eradication rate. However, the benefits have not been shown to be cost-effective.
2019	Reconcilliation (expert committee)	5 (2R, 3M)	Despite current uncertainities, probiotics may still offer significant potential and their influence on H pylori eradicationis worthy of further study
2020	Hellenic Consensus	7 (RCT:3, M:4)	Only certain probiotic strains, including <i>Lactobacillus</i> , <i>Bifidobacterium</i> and <i>Saccharomyces boulardii</i> , may be potentially useful in reducing gastrointestinal side effects (mainly diarrhea), associated with <i>H. pylori</i> eradication therapies.

Note: R: review; RCT: randomized controlled trial, M: meta-analysis x/ Some experts co-operated in several consensus meetings with divergent meeting statements