DISCUSSION II

Question: **There are a number of methods available for measuring quality of life. Why can we not have one method to analyse quality of life that is used worldwide?**

Dr Veldhuyzen van Zanten: That would be ideal but unlikely to happen as several different methodologies can be used. In functional dyspepsia, a lot of progress has been made. I am aware that several groups are further refining their outcome measures, and I believe that improvement over the current symptom scores is still possible. The questionnaires are not very lengthy to administer, so we could look at a whole battery of tests and see which one performs best. Compared with five years ago, investigators now have a choice of instruments to use, but there is no consensus at the moment on which ones are the best.

Question: **Is six or 12 months a sufficient period of observation? Suppose that when you inflame the mucosa, you induce a prolonged neuropathophysiological change. It might then take years for abnormalities to return to normal. Should we not follow up these patients for much longer to assess the final outcome?**

Professor Bazzoli: Assessing patients for one year is, I believe, an achievement. Until recently, results were assessed usually after only four weeks. The new studies suggest that there is probably a role for inflammation. Most scientists would say that gastritis can heal within a year, but the mechanism is not known, so we can also argue that it will take more time to heal the gastritis than it does to improve the symptoms. We therefore need to identify the pathophysiological mechanisms.

Professor Tytgat: I would suggest that we continue to look at the data long term, as it is an important area.

Dr Veldhuyzen van Zanten: In my opinion, if you do not see an effect at 12 months then any effect is unlikely to be clinically meaningful. Also, practically, it is very difficult to maintain blinding beyond one year.

Question: **One week omeprazole triple therapy produced an *H pylori* eradication rate of 82% in the ORCHID and OCAY studies.[1 2] Should we be giving eradication therapy for 10–14 days in patients with functional dyspepsia in an attempt to achieve at least 90% eradication?**

Professor Tytgat: I would suggest that in patients with functional dyspepsia, for whom the *H pylori* eradication rates are definitely somewhat lower than in patients with peptic ulcer disease, we should seriously consider 10 day therapy, if you use a combination of omeprazole, amoxycillin, and clarithromycin, in an attempt to obtain an eradication rate of 90%.

Professor Bazzoli: There is no evidence to show that this is achieved however.

Question: **Should we draw conclusions from a post hoc analysis of dyspepsia subgroups, as was done in the ORCHID and OCAY studies? If the analysis was not included when patients were entered into the study, then is there any validity in this kind of "data dredging"?**

Dr Veldhuyzen van Zanten: We need to be very cautious, and it would have been better if the analysis had been done a priori. However, there is still room for this type of analysis as it may be that ulcer-like and reflux-like dyspepsia patients do better.

Question: **Peptic ulcers are transient, recurrent, and can be healed. A 20% rate of improvement is often quoted for patients with dyspepsia, no matter what is used to treat them. This percentage is close to the expected rate of recurrence of peptic ulcer disease. Is it possible that improvement in dyspepsia is related to cure of undiagnosed peptic ulcer disease?**

Professor Bazzoli: There is probably a common mechanism for dyspepsia and peptic ulcer disease that we cannot identify. However, I cannot believe that there is a 20% rate of misdiagnosis and that 20% of peptic ulcers are undiagnosed.

Dr Veldhuyzen van Zanten: I think that the background prevalence of peptic ulcer disease in the population is important. All studies have well defined inclusion criteria. For example, patients must have been off acid suppressive therapy for four weeks and, if you look at the relapse data for duodenal ulcer, many ulcers recur after four weeks. So, theoretically, some patients with peptic ulcer disease may be included. One study in Scotland has found a prevalence of peptic ulcer disease of 40% in dyspeptic patients.[3] I believe therefore that if you have a high background prevalence of peptic ulcer disease you are more likely to include patients who eventually will develop an ulcer, and you are more likely to find a beneficial effect of the "test and treat" strategy in such populations.

Professor Tytgat: If you look at the data there is no doubt that *H pylori* eradication has little to offer the patient with dysmotility-like symptomatology. However, *H pylori* eradication might have something to offer the patient with ulcer-like symptoms. In this subgroup, there is definitely a percentage of ulcers that do not have an active crater at the time of endoscopy but they might have one some time later. As far as we know, the development of an ulcer is a very sudden event. The ulcer then starts to heal, and then it recurs. Thus a snapshot in time will not pick up all those who truly have the ulcer diathesis.

Professor Axon: Is it helpful to select patients in whom you intend to eradicate *H pylori* using these data? Does it matter whether *H pylori* eradication gets rid of functional dyspepsia? Are these data going to affect the way we behave? Are those of us who believe that we should eradicate *H pylori* going to change what we do? It is unlikely that those who do not eradicate the bacterium will change their management.

Professor Bazzoli: We are speaking of functional dyspepsia, in which, by definition, at least one endoscopy has been performed; it is also likely that a biopsy has been taken and *H pylori* status defined. The patient will have chronic upper gastrointestinal pain and will have been seen by the doctor at least two or three times. What do you say to this patient? Do you say that we will not treat you because we do not have enough data on the effectiveness of *H pylori* eradication in functional dyspepsia? Or do you say that *H pylori* may actually have a potential dangerous effect and that it should be eradicated?

Dr Veldhuyzen van Zanten: Personally, I would eradicate the bacterium not because it will definitely improve symptoms but because it is a true pathogen.

Question: **Dr Veldhuyzen van Zanten, in your talk you made a plea for results to be given as proportions of patients who achieve the desired outcome. In the "old days" we used patient and doctor satisfaction. Why is the former a better outcome?**

Dr Veldhuyzen van Zanten: The unit of measurement should be the patient—the proportion of patients who achieve an outcome that you state you want to achieve. If you state that on a seven point Likert scale you are aiming for a three point improvement, then you can interpret the results. However, there are a lot of dyspepsia trials, particularly with H_2 receptor antagonists and prokinetics, that simply report an average improvement. With these, you do not know whether, say, 10% of patients had a large improvement while the rest of the patients showed no improvement at all. I think that it is very important that the Rome group, when looking at the design of clinical trials, has made a plea that the proportion of patients who achieve the outcome is reported.[4]

Professor Tytgat: Do you feel that the time is right to translate some of the more objective gradings into routine clinical practice?

Dr Veldhuyzen van Zanten: At the end of the day, whether you are treating patients with irritable bowel syndrome, inflammatory bowel disease, or dyspepsia, one of the questions we ask patients when we have given them a trial of therapy is whether or not they feel better. We then like to quantify this.

Professor Axon: We are talking about two things, one is looking at symptoms in a clinical trial, the other is the way that we manage patients in reality. When you have a patient in front of you, you can ask them a variety of questions and form a better assessment of their improvement than by administering a questionnaire. The reason for a questionnaire is to apply statistics and make the findings consistent in a large number of people. Therefore, I do not think that giving every patient a quality of life questionnaire will help in the management of individual patients.

Dr Veldhuyzen van Zanten: I think that a global question—"Overall how are you, or overall what is the severity of your dyspepsia symptoms or heartburn?"—is very valid. I think that it is very useful in clinical practice.

***Question:* Does *H pylori* eradication induce or unmask reflux symptoms? Is there such a phenomenon and why doesn't everybody find the same thing?**

Dr Veldhuyzen van Zanten: My understanding from the better designed trials with large sample sizes is that there is no increase in reflux symptoms following *H pylori* treatment. The data from the ORCHID and OCAY studies were based on the gastrointestinal symptom rating scale and this is not the ideal way to assess the effect.[1 2] I think that an important aspect is the severity of gastritis in the body and cardia. There are very few good, prospective, randomised trials that have looked at this as a predictor of what happens with reflux symptoms, and I think that needs to be done.
Professor Bazzoli: I fully agree with Dr Veldhuyzen van Zanten. I think that a further explanation, given by McColl and colleagues,[8] is the possibility that these patients have a change of lifestyle; they eat more and they smoke more when they feel better, and this could be a good reason for developing GORD after eradication of *H pylori*.

***Question:* Is it clinically meaningful or even ethical to eradicate *H pylori* in patients with functional dyspepsia when 70–80% of them will have no symptomatic improvement after treatment?**

Professor Axon: Certainly, there is every reason to eradicate *H pylori* in these patients. Eradication treatment is relatively free from side effects. If 20% of patients improve it is worthwhile. In addition, you get rid of a pathogen that may cause problems in the future.

***Question: H pylori* infection starts in childhood. We know that adults who have childhood onset diseases under report their symptoms because they have had them all their life. These patients are therefore less likely to report a change in their symptoms. In the studies to date, how many *H pylori* positive patients had symptoms that began in childhood or adolescence? This may be contributing to the lack of a clear answer because such patients with chronic disease may be under reporting their symptoms.**

Dr Veldhuyzen van Zanten: Chronic abdominal pain is common in children. There is very little evidence that *H pylori* is associated with that common childhood syndrome, and I think that it would go against *H pylori* playing a major role. I agree that it may be interesting to look at the question of whether onset of dyspepsia at a young age influences treatment response. Such trials will however be difficult to perform.
Questioner: There are a lot of causes of abdominal pain in children and so trying to tease out what is relevant to *H pylori* may not be effective.
Professor Tytgat: I think that paediatricians have a tremendous role to play, to sort out what the long term outcome is and when symptoms arise. I am convinced that irritable bowel syndrome, for example, takes a long time before it becomes clinically overt.
Questioner: We have looked at 1000 children from 12 centres in the USA, and the results in children who had *H pylori* infection were significantly different in symptomatology compared with children who were *H pylori* negative. I think therefore that you need to wait until the data are confirmed.

References

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2 **Blum AL**, Talley NJ, O'Morain C, *et al*. Lack of effect of treating *Helicobacter pylori* infection in patients with non-ulcer dyspepsia. *N Engl J Med* 1998;**339**:1875–81.

3 **McColl KEL**, El-Nujumi A, Murray L, *et al*. The *H. pylori* breath test: a surrogate marker for peptic ulcer disease in dyspeptic patients. *Gut* 1997;**40**:302–6.

4 **Veldhuyzen van Zanten SJO**, Talley NJ, Bytzer P, *et al*. Design of treatment trials for functional gastrointestinal disorders. *Gut* 1999;45(suppl II):II69–77.