variants for the International Gastric Cancer Linkage Consortium), the majority being classified as deleterious and thus possibly pathogenic (R Seruca, personal communication, 2014).

Panel sequencing

Penetrance estimates for *CDH1* mutation carriers have been derived from the study of highly ascertained HDGC families and it is likely that the penetrance for mutations detected in non-HDGC families will be lower. With the introduction of next-generation sequencing-based gene panels, both in research and diagnostic settings, *CDH1* alterations may be found in patients without a personal or family history of GC.[49 50] In our opinion, one should be very cautious in the interpretation of coding variants identified in non-HDGC families, especially if the alterations do not lead to a premature stop codon.

CDH1 mutation database

Currently, there is no international database containing all germline *CDH1* mutations and variants identified to date. A database has been designed and is currently under construction with the collaboration of the LOVD team. The variant database is available at http://www.LOVD.nl/CDH1. This database can be consulted to assess whether a given *CDH1* mutation has been found by others and whether it has been considered deleterious and likely disease-causative or not based on population data, segregation analysis, *in silico* analysis and *in vitro* functional analysis, and/or recurrence in several individuals/families. We advise researchers and clinicians to submit unpublished mutations and variants to the database (contact C Oliveira, carlaol@ipatimup.pt), together with the requested information on families/patients and mutations. The publication/submitter of every mutation will always be referred to in the database.

Psychosocial effects of counselling

Even though it is well recognised that many individuals will benefit from genetic counselling and testing for hereditary cancer in general, there have also been reports that it may induce a number of psychosocial problems. In a review on individuals requesting genetic counselling and testing for hereditary cancer syndromes, six dominant problem areas were identified: (1) coping with cancer risk; (2) practical problems (such as obtaining life insurance/loans and employment when found to be a mutation carrier); (3) family-related problems (eg, communication problems with family members, feeling responsible for family members); (4) children-related problems (eg, concerns for children having increased risk, fear of leaving young children); (5) living with cancer (eg, fear of developing cancer, pain about the loss of family members) and (6) emotions (eg, anxiety, anger, feelings of loss, but also relief and reassurance).[51] These topics, when applicable, should be addressed during the counselling sessions.

Pregnancy and assisted reproduction

Although scientific data are lacking concerning timing of prophylactic gastrectomy and family planning, it is entirely possible for women to give birth to a healthy child after gastrectomy.[52] Nutritional advice and follow-up with a dietician within this context is essential.

Individuals from hereditary cancer families are frequently concerned about the transmission of their predisposition of cancer to their children.[53 54] Healthcare professionals, including geneticists and psychosocial workers, will be increasingly involved in discussions and decisional counselling regarding reproductive options in families with a known cancer predisposing mutation such as *CDH1*. In the past decades, genetic testing for hereditary cancers before birth has become available through prenatal diagnosis (PND) and preimplantation genetic diagnosis (PGD).[55] We recommend that carriers of a *CDH1* mutation with a desire to have children should be informed about all reproductive options, including PND and PGD.

Future research: other genes involved in HDGC predisposition

Currently, three families that meet the new criteria have been described to carry germline *CTNNA1* mutations.[23 24] Even though these families show a clinical picture similar to that of *CDH1* mutation-positive families,[23] insufficient data are available to make a statement on disease penetrance. Given the functional connection between the two genes, they may represent a genocopy. Mutation carriers could be given the option of prophylactic total gastrectomy (PTG) and other cancer prevention measures recommended for HDGC families, but with the precaution that such advice is being given based on very limited data.

Other families have recently been described with *BRCA2* and *PALB2* mutations;[24] however, we recommend that these families are managed no differently than other families with such mutations according to national guidelines. It is likely that other HDGC-associated genes will be discovered through whole exome, genome or other unbiased next-generation-sequencing empowered methodologies. Indeed, using a combination of this approach and linkage analysis, mutations in *MAP3K6* have recently been described.[56] More needs to be understood about families with *MAP3K6* mutations before they could be used to stratify risk in families. Until such data are available, a cautious approach in which all first-degree relatives of mutation carriers are followed is recommended. Without multiple mutation-positive families for newly identified genes, it will be extremely difficult to ascribe pathogenicity to such mutations and to develop management guidelines.

SCREENING AND SURVEILLANCE

Gastric endoscopic screening and surveillance

To clarify the terminology, we consider that individuals having endoscopy who do not know their mutation status or those who do not have a proven pathogenic *CDH1* mutation undergo screening whereas mutation-positive individuals undergo surveillance. The consensus reached at the workshop was that individuals who tested positive for a pathogenic germline *CDH1* mutation should be advised to consider prophylactic gastrectomy, regardless of endoscopic findings. However, the timing of surgery may vary according to the preferences and age, as well as the physical and psychological fitness of the individual. In patients proceeding for gastrectomy, a baseline endoscopy should be performed prior to surgery to look for macroscopic tumour as this may alter the treatment plan. This endoscopy is also performed to ensure that there is no other coincidental pathology, such as Barrett's oesophagus, which may alter the extent of the resection. When the stomach is macroscopically normal, the information on microscopic disease *foci* is useful to compare with findings in the surgical resection specimen and hence to increase knowledge on the likelihood of endoscopic detection of microscopic lesions.

For individuals with a *CDH1* mutation in whom gastrectomy is not currently being pursued (eg, through patient choice or existence of physical or psychological comorbidity), regular endoscopy should be offered. In patients declining surgery, surveillance can have the advantage of helping individuals to come