

# Congress Review

## Review of the 26<sup>th</sup> United European Gastroenterology (UEG) Week

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“UEG Week provides a fantastic opportunity for clinicians and researchers to come together from all corners of the world to discuss advances in digestive health,” Prof Herbert Tilg, Chair of the UEG Scientific Committee, declared proudly, speaking at UEG Week 2018. He went on to extoll the virtues of the event and explained that “the high volume of submissions, coupled with the first-class standard of abstracts, confirms that UEG Week is the most important forum to present gastrointestinal research.”

A select team from EMJ were privileged to travel from the UK to Vienna for this occasion. Rather than to marvel at the splendour of Vienna’s imperial palaces or delight in the skill of the riders at the Spanish Riding School, we arrived in Austria’s capital to immerse ourselves in Europe’s gastroenterological capital: UEG Week. We are now delighted to be able to present to you all of the headline news disseminated at the event within the pages of this Congress Review. Some of this news included results from the UNIFI Phase III trial into ustekinumab as an induction therapy for moderate-to-severely active ulcerative colitis, a comparison between laparoscopic ileocaecal resection and infliximab for the treatment of immunomodulator-refractory Crohn’s disease, and research from the USA into the risk factors for colorectal cancer in those aged 20–49 years.

A snapshot of the event by the numbers gives some indication of its magnitude:

- › Attendees came from around the globe, with 114 nations represented.
- › Previous attendance records were surpassed, with 12,600 travelling to Vienna.
- › 3,705 abstracts were submitted, with 2,214 of them accepted.
- › 62 abstract presentation prizes were awarded.
- › There were 194 scientific sessions.
- › The number of lectures delivered totalled 1,129.

- The exhibition space spanned a vast 5,084 m<sup>2</sup>, which was larger than the 4,957 m<sup>2</sup> at UEG Week 2017.
- There were 148 exhibitors and sponsors at the event. You can find further details of those present in our Buyer's Guide.

However, numbers alone are insufficient to demonstrate the full scale of this scientific gathering. For one thing, it was not only those physically present in Vienna who were able to share in this year's UEG Week. The congress organisers had worked hard behind the scenes to ensure a significant online presence, further extending the event's global following. This endeavour to make UEG Week even more widely accessible saw 113 sessions being streamed live over the internet. To complement this, viewers were able to use the mobile app to ask questions of the presenters in real time. The EMJ team saw this facility in full effect at a session that took place as part of the Young GI Network; the details of this highly topical discussion on balancing work with your personal life, and whether it is necessary to make sacrifices, are explored in our Congress Review. With >3,000 viewers tuning into the streamed sessions, the efforts of the organisers certainly paid off. Furthermore, the UEG Week social media accounts saw 1,481 posts over the course of the meeting, highlighting the increasing relevance of interacting across multiple channels. UEG Week's virtual presence was not only in real time; of the 1,129 lectures given, an impressive 571 were recorded for the benefit of those unable to attend the event.

Prof Tilig extended his gratitude to all those who played a part in UEG Week: "Finally, I would like to pass on a huge thank you to everyone that attended the congress, including the passionate speakers, the engaged delegates, and the enthusiastic young gastroenterologists." We here at EMJ would also like to extend our thanks to every attendee: all of you combined to make UEG 2018 a thoroughly enjoyable and memorable event. Next year will see UEG Week return to Barcelona, Spain and we hope to have the pleasure of seeing you there as well.

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## More Screening Required for Young-Onset Colorectal Cancer

COLORECTAL cancer cases in young European adults are becoming more common, according to an analysis of incidence rates across the continent, presented for the first time at UEG Week 2018. Reported in a UEG Week press release dated 23<sup>rd</sup> October 2018, this upward trend in the number of colorectal cancer cases suggests that more widely available screening programmes are necessary across Europe for young people.

The investigation involved analysis of data on the incidence of colorectal cancer in adults aged 20–39 years from 20 European national cancer registries, including those of Belgium, Germany, Italy, France, and the UK. While investigations of this type have been performed in North American populations, the researchers noted that, until now, the information on colorectal cancer incidence in young people in Europe has been limited.

*“Increased awareness and further research to elucidate causes for this trend are needed and may help to set up screening strategies to prevent and detect these cancers at an early and curable stage.”*

After analysing the trends in incidence rates, the number of cases of colon cancer was shown to

increase by 2.2% (95% confidence interval [CI]: 1.4–3.0) per year from 1990–2010 and by 7.3% (95% CI: 2.3–12.5) per year from 2010–2016 in men aged 20–39 years, whereas in women in the same age range, the incidence rate increased by 1.5% (95% CI: 0.4–2.7) per year from 1990–2008 and by 8.9% (95% CI: 4.8–13.2) per year from 2008–2016. A similar increased incidence rate was observed for rectal cancer: in men, rates decreased by 3.9% (95% CI: -7.1– -0.7) from 1990–1997, and increased 1.6% (95% CI: 0.8–2.3) per year from 1997–2016; in women the increase per year in 1990–1996 was 8.3% (95% CI: 4.7–12.0), but this stabilised in the years 1996–2016.). Since the malignancy is traditionally considered to affect people aged >50 years, with incidence rates higher in men than women, the research team noted that the finding that colorectal cancer is increasing in the young is worrying, particularly because young-onset cases are often more aggressive and advanced.

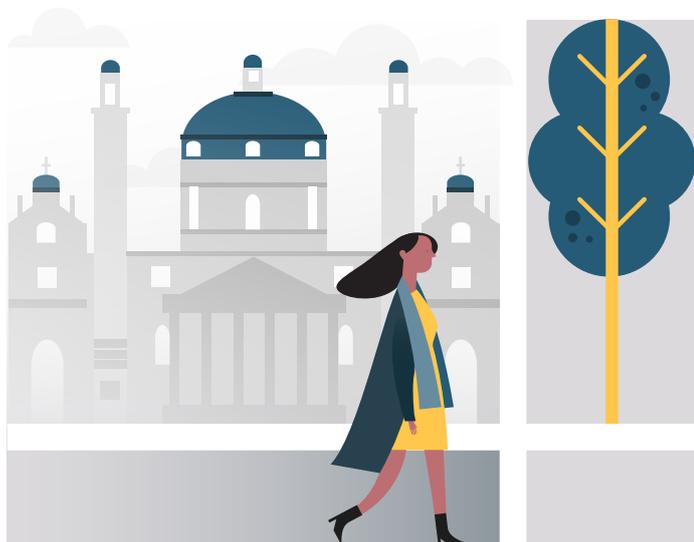
Hypothesising that the observed upward trend may be related to risk factors such as obesity, poor diet, and increasingly sedentary lifestyles, study presenter Dr Fanny Vuik, Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, Netherlands, commented: “Increased awareness and further research to elucidate causes for this trend are needed and may help to set up screening strategies to prevent and detect these cancers at an early and curable stage.” Reductions in the incidence and mortality rates of colorectal cancer have been shown to result from effective screening strategies; however,

many European screening programmes are only available for people aged >50 years. Therefore, with colorectal cancer being the second most common cancer in Europe, screening adults at a younger age who may be at a high risk is essential to optimise patient outcomes and ensure an early diagnosis.

## Oesophageal Cancer Risk Linked to Oesophageal Microbiota

UNIQUE microbe signatures have been found to be linked to oesophageal cancer, according to results presented in a UEG Week press release dated 23<sup>rd</sup> October 2018. It is hoped that the identification of these oesophagus microbe signatures will aid in both the diagnosis and management of oesophageal cancer.

To assess whether there is a relationship between the microbiota of the oesophagus and oesophageal cancer, researchers obtained biopsy samples from 6 newly diagnosed oesophageal cancer patients, 10 patients with Barrett's oesophagus, and 10 controls that were analysed for microbiota comparison. When the biopsies were analysed, higher levels of bacterial diversity were reported in those taken from patients with cancer compared with controls. It was identified that there was an abundance of Bacteroidetes and lower levels of Firmicutes in oesophageal cancer patients compared with controls. Comparing oesophageal cancer patient results with Barrett's oesophagus patients and controls, there were lower levels of *Streptococcus* and higher levels of *Veillonella*, *Porphyromonas*, and *Prevotella*.



Oesophageal cancer is the eighth most common cancer worldwide and, coupled with the fact that most people only present with established disease and mortality rates are high, there is a profound need to identify a way of screening for those most likely to develop the disease and to develop alternative treatments to best tackle the disease. Well-known risk factors associated with oesophageal cancer include obesity, smoking, low fruit and vegetable intake, and alcohol consumption; now, this researcher suggests that microbiota can also be added to this list.

*"If these findings are confirmed in our further analyses, it may be possible to imagine innovative diagnostic and therapeutic tools to help us manage this condition more successfully."*

Dr Loris Riccardo Lopetuso, lead researcher, Catholic University of Rome, Rome, Italy, commented on the importance of these findings: "These results indicate that there is a unique microbial signature for oesophageal cancer that might represent a risk factor for this condition." Dr Lopetuso also spoke of the future applications for this research: "If these findings are confirmed in our further analyses, it may be possible to imagine innovative diagnostic and therapeutic tools to help us manage this condition more successfully."

## Cannabis Oil and Crohn's Disease

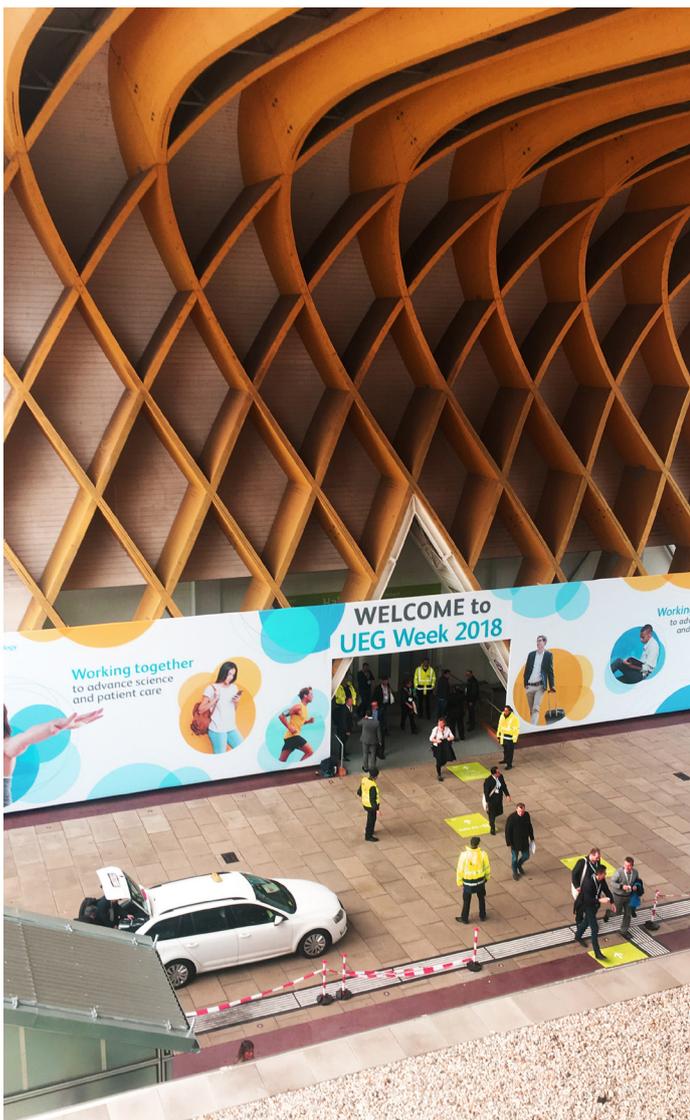
CANNABIS OIL has been demonstrated to result in the improvement of symptoms in patients with Crohn's disease and additionally lead to an improvement in the quality of life of these patients. The results of this study were discussed in a UEG Week press release dated 22<sup>nd</sup> October 2018.

Cannabis has been used in the treatment of a number of medical conditions for centuries. It is also utilised for symptomatic relief by many patients with Crohn's disease. The researchers conducting this study set out to examine whether the improvement in symptom relief was as a result of cannabis alleviating gut inflammation.



The researchers enrolled 46 patients with moderately severe Crohn's disease. These patients were randomised to one of two treatment arms: one arm received placebo and the other arm received cannabis oil that contained 15% cannabidiol and 4% tetrahydrocannabinol. The treatment period was 8 weeks. Prior to treatment beginning, the symptom severity and quality of life of the participants were measured, as well as gut inflammation. These measurements were also taken after the treatment course.

*"...to our surprise, we saw no statistically significant improvements in endoscopic scores or in the inflammatory markers we measured in the cannabis oil group compared with the placebo group."*



After the 8-week treatment course, 35% of the patients in the placebo arm met the criteria for clinical remission compared with 65% of patients in the cannabis oil arm. Furthermore, those in the cannabis oil group demonstrated a significant improvement in quality of life in comparison to those in the placebo group. However, the authors were surprised by one of their findings. "We have previously demonstrated that cannabis can produce measurable improvements in Crohn's disease symptoms, but, to our surprise, we saw no statistically significant improvements in endoscopic scores or in the inflammatory markers we measured in the cannabis oil group compared with the placebo group," explained the study's lead researcher, Dr Timna Naftali, Tel Aviv University, Tel Aviv, Israel.

Bearing this finding in mind, the researchers' next steps are to study in more detail whether the endocannabinoid system is a potential treatment target for Crohn's disease and other gastrointestinal diseases. However, Dr Naftali explained that: "For now [...] we can only consider medicinal cannabis as an alternative or additional intervention that provides temporary symptom relief for some people with Crohn's disease."



## Link Between Black Death and Crohn's Disease Revealed

CROHN'S disease occurrence across Europe has been linked to overcoming devastating plague outbreaks during the middle ages by new research into the genetic origins of the inflammatory disease revealed at UEG Week 2018 and reported in a UEG Week press release dated 22<sup>nd</sup> October 2018.

Inflammatory bowel disease, comprising ulcerative colitis and Crohn's disease, affects roughly 3 million individuals in Europe and costs healthcare systems across the continent >€5 billion annually. Although not fully understood, there is strong evidence to suggest that genetic factors play a role in the pathogenesis of inflammatory bowel disease, and, therefore, the researchers focussed their attention on *NOD2*, a gene known to play an important role in the immune system and mutations of which are associated with Crohn's disease.

*"This research goes some way to explaining the genetic origins of Crohn's and we hope it will enable us to better understand the disease, and how to treat it, in the future."*

Previous investigations have shown that genetic variation of *NOD2* was also involved in the mechanism of resistance against the causal organism responsible for millions of European deaths due to the Black Death during the 14<sup>th</sup> century. Therefore, by studying historical data, the researchers concluded that the prevalence Crohn's disease-associated *NOD2* mutations correlates with intensity of plague outbreaks, which may help to explain the modern-day incidence rates of Crohn's disease in Europe.

"Considering the potential severity of Crohn's disease when untreated, it is unlikely that it was a frequent disease before the 20<sup>th</sup> century. As healthcare systems have developed and care for Crohn's disease patients has improved, more and more people are living with the disease," elucidated researcher Prof Jean-Pierre Hugot, Paediatric Digestive and Respiratory Diseases Department, Robert Debré Hospital, Paris, France. "This research goes some way to explaining the genetic origins of Crohn's and we hope it will enable us to better understand the disease, and how to treat it, in the future," he added.

## Monitoring Microplastics: The Story Continues

PLASTICS are ubiquitous with modern society, polluting the world's oceans, seas, and rivers to

an extent that, even now, is only just becoming fully understood. The effect this pollution may be having on the human gastrointestinal tract has been of growing concern for some time in the gastroenterological community and the results of a first of its kind study, reported in a UEG Week press release dated 23<sup>rd</sup> October 2018, have identified the presence of microplastics in human stool samples. The results are set to add further fuel to the fire demanding a change to the current use, manufacture, and disposal of plastics.

Eight individuals were included in the study, recruited from Finland, Austria, Poland, Italy, Japan, the Netherlands, Russia, and the UK. Participants were asked to keep a food diary for the week prior to stool sampling, and review of the food diary and the stool sample highlighted that all the participants were exposed to plastics through the consumption of plastic wrapped food and the use of plastic drinks bottles.

*"Now that we have the first evidence for the microplastics inside humans, we need further research to understand what this means for human health."*

Analysis of the stool samples, conducted at the Environment Agency Austria (UBA), showed that per 10 g of stool sample 20 microplastic particles

were identified on average. Up to nine different microplastics, sized between 50 and 500  $\mu\text{m}$ , were identified in the samples; polypropylene and polyethylene terephthalate were the most common microplastics.

The study is relatively small, encompassing only eight individuals, yet it raises an important point about the pervasiveness of microplastics. Study lead Dr Philipp Schwabl, Medical University of Vienna, Vienna, Austria, concluded: "While the highest concentrations in animal studies have been found in the gut, the smallest microplastics particles are capable of entering the blood stream, lymphatic system, and may even reach the liver. Now that we have the first evidence for the microplastics inside humans, we need further research to understand what this means for human health."

## The Best of the Best: Top 5 Abstracts from UEG Week 2018

As ever, the annual UEG Week provided a platform for the most pivotal trials, studies, and investigations conducted over the last year to be presented to the members of the gastroenterological community. With >2,000 abstracts presented, UEG Week 2018 proved to be a record-breaking year. Among the thousands of research teams presenting their results across the 5-day event, five were singled out and presented with awards for their work.







**Austria Center Vienna**  
Home of UEG Week 2018

This year, the awards were split between researchers from the Netherlands, France, Germany, Switzerland, and the USA.

### The Use of Early Surgery for Obstructive Chronic Pancreatitis Management

In the first of three award-winning studies investigating the pancreas, Dr Marinus Kempeneers and the research team behind the ESCAPE trial were awarded for their work. The team compared the effect of early surgery on the pain chronic pancreatitis patients experienced in comparison with the current standard optimised medical therapy. Overall, 88 chronic pancreatitis patients, with a  $\geq 5$  mm dilated pancreatic duct, continuous or intermittent severe pain, and previous use of strong opioids for  $< 2$  months or weak opioids for  $< 6$  months, were randomised in a 1:1 ratio to receive either early surgery or medical therapy. During the 18-month follow-up, the research identified that early surgery gave rise to a significantly lower Izbicki pain score than their optimised medical therapy counterparts ( $36 \pm 24$  compared to  $47 \pm 24$ ;  $p < 0.001$ ).

The improved patient pain experience in combination with a reduced overall cost associated with early surgery (€17,522 compared with €22,366) makes early surgery a very attractive option for the management of obstructive chronic pancreatitis.



### Open versus laparoscopic surgery

Continuing the theme of pancreatic surgery, the research team from the Dutch Pancreatic Cancer Group, Amsterdam, the Netherlands, investigated whether open or laparoscopic surgery gave rise to a faster time to functional recovery.

*"We think that further research should focus on safety outcomes and volume thresholds for laparoscopic pancreatoduodenectomy."*

Patients were randomised in a 1:1 ratio to receive laparoscopic or open surgery and were blinded to the procedure used via large dressings visually obscuring the surgical site. Laparoscopic surgery was shown to improve time to functional recovery (10 days versus 8 days for open versus laparoscopic surgery, respectively;  $p = 0.80$ ). However, the study was stopped early after only 99 patients had undergone the surgery, as 10% of the laparoscopic surgery cohort died due to complications (two from intraoperative damage; two from postoperative haemorrhage; and 1 from postoperative fistula) compared to only one patient in the open surgery group, as a result of haemorrhage.

Discussing the results, Dr Jony von Hilst highlighted the concerning safety aspects of the procedure: "We think that further research should focus on safety outcomes and volume thresholds for laparoscopic pancreatoduodenectomy."



## Gene Expression Analysis in Inflammatory Bowel Disease

Investigators from France, Spain, Germany, and the USA collaborated to further explore the genes involved in two major inflammatory bowel diseases. They performed the first integrated gene expression analysis of >1,500 samples obtained through intestinal biopsy of patients with Crohn's diseases, ulcerative colitis, and controls.

Combining the data from six major heterogeneous studies, obtained through microarray and RNA sequencing techniques, analysis of gene expression identified a number of disease and region-specific gene clusters, including the REG genes that had a prominent effect in colonic diseases. Comparison of ulcerative colitis with ileal and colonic Crohn's diseases samples highlighted cluster of shared inflammatory genes, including *DUOX2*, *MMP1*, and *MMP3*, present in all three disease subtypes.

Dr Kevin Perez, who presented the study acknowledged the variation in sample composition was a limitation of the study, but future single cell studies will soon provide better data.

## Promoting the Survival of T Helper Cells: NLRP6

"We propose that naïve T cells start to express NLRP6 upon differentiation of Th1 cells and this prevents apoptosis. We therefore suggest that NLRP6 promotes the survival of CD4 T cells," explained Dr Jan Hendrik Niess, University of Basel, Basel, Switzerland after the completion of multiple *in vitro* studies examining the effect of NLRP6 on the differentiation of T cell.

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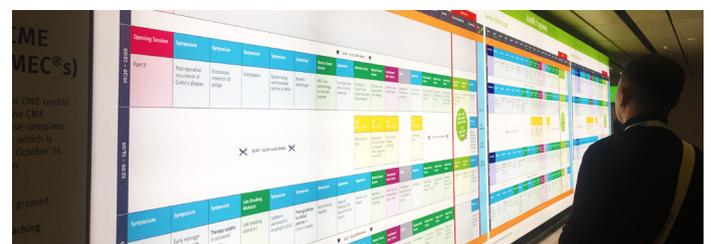
Using differentiated T cells and T cells after the co-transfer of wild-type and NLRP6-deficient cells on RAG hosts, the researchers discovered that NLRP6 deficiency did not impact upon T cell proliferation or development in mice. Additionally, the protein is not expressed by naïve CD4 and CD8 positive cells, B cells and bone marrow-derived macrophages, but is expressed by Th1 cells.

However, analysis of apoptosis markers, including TNF- $\alpha$  levels and IFN $\gamma$  signalling, indicated that cell death is accelerated in NLRP6-deficient cells; this hypothesis was confirmed through Annexin V+ staining, highlighting the importance of the protein to the innate immune response.

## Early Biliary Decompression Versus Conservative Treatment

In the last of three award-winning studies investigating pancreatic surgeries, the Dutch Pancreatic Study Group presented data that analysed the effect of early biliary decompression in comparison with conservative treatment in 232 patients with severe acute biliary pancreatitis.

The composite primary endpoint of death or major complications during the 6-month study period was observed in 45 of the 117 patients in the early biliary decompression compared with 50 of the 133 conservatively treated patients ( $p=0.37$ ). The study showed that there was no statistically significant difference between the two study arms.

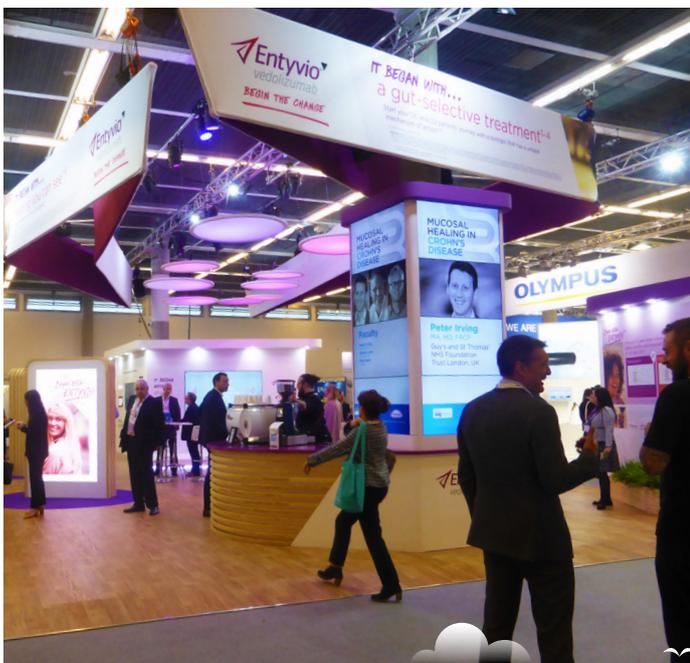




Dr Nicolien Schepers, who presented the award-winning data on behalf of the Dutch Pancreatic Study Group concluded: "In patients with predicted severe acute biliary pancreatitis without cholangitis, the APEC trial did not show the superiority of early ERC (endoscopic retrograde cholangiography) with sphincterotomy as compared with conservative treatment."

## Conclusion

This year proved to be a landmark year for gastroenterological research, with the Dutch investigative teams leading the way for pancreatic research. An additional selection of some of the other top studies presented at UEG Week 2018 can be found within the Abstract Reviews section of the eJournal.



## Worthy Winners at UEG Week 2018

EXCELLENCE across the field of gastroenterology was recognised at this year's UEG Week via presentation of three prestigious, individual awards. Best Research, Best Paper, and Overall Lifetime Achievement awards were the prizes on offer to many deserving nominees, leaving the deciding bodies spoilt for choice this year.

*"I hope that this work can contribute to the pioneering research on building personalised models of coeliac disease, which can be utilised in many different ways."*



Firstly, the 2018 UEG Research Prize was awarded to Prof Cisca Wijmenga, Lodewijk Sandkuijl Endowed Chair and Professor of Human Genetics, University Medical Centre Groningen, Groningen, Netherlands. As recognition for excellence in her outstanding work investigating a coeliac mucosal barrier-on-chip model in coeliac disease initiation, Prof Wijmenga was presented with €100,000. "I hope that this work can contribute to the pioneering research on building personalised models of coeliac disease, which can be utilised

in many different ways,” she commented. Devoting much of her career to identifying novel genetic factors that underlie coeliac disease to better the lives of coeliac patients, as well as being the first to understand the power of genome-wide association studies using cases versus controls, Prof Wijmenga’s interdisciplinary work makes her a worthy winner of the UEG Research Prize. Also appointed Knight in the Order of the Dutch Lion this year for exceptional service to the Dutch community, Prof Wijmenga is at the height of her career and her work will have a crucial impact on digestive health for years to come.

*“I am honoured and humbled to receive such a prestigious award and extremely grateful to the Council for bestowing on me this unique Lifetime Achievement Award.”*

Recognising high-quality, significant research published in the UEG Journal during the past year, this year’s UEG Journal Best Paper Award was presented to the first named author of the article entitled ‘Correlation between adenoma detection rate in colonoscopy and faecal immunochemical testing-based colorectal cancer screening programs’. Lead author Joaquín Cubiella, Complejo Hospitalario Universitario de Ourense, Ourense, Spain proudly received the award for his team’s post-hoc analysis of the COLONPEV trial, involving 5,722 patients to investigate adenoma detection rate in primary and work-up colonoscopy. Known for being one of the most significant colorectal cancer screening projects, Dr Cubiella commented on the importance of the COLONPREV trial: “This study will complete the follow-up in the coming years and will provide relevant information on the effect of the two most accepted screening strategies: colonoscopy and faecal immunochemical test.”

The third and most prestigious standalone award presented at the annual UEG Week event is the UEG Lifetime Achievement Award, which acknowledges remarkable individuals who have contributed greatly to the UEG community, as well as to the entire field of gastroenterology and hepatology.





The first question the experts were asked was whether a choice had to be made and whether something had to be sacrificed. Prof Hegyi explained that this was a matter of prioritisation and focussing on the task at hand, which was a theme returned to often throughout the course of the discussion. He elaborated that when you were at work, you should be focussed on work, when you were at home with your family, you should be focussed on being a parent, and when you were on the sports field, you should be focussed on that. Prof Ciacci largely concurred with this statement, explaining that multitasking was a confusing message as “you cannot be at home and at work at the same time.” She did however acknowledge that forgetting about work was the part she found the hardest.

Ways to ensure your time was as productive as possible were also suggested by the experts. Both extolled the virtues of outsourcing or delegating work that you did not necessarily need to do yourself. Prof Hegyi described saying ‘no’ to such tasks as being the biggest challenge of the twenty-first century. When combined with prioritising, delegating represents a powerful tool.

It may, however, be difficult for younger gastroenterologists to delegate as effectively if they have fewer people they are able to delegate to or perhaps lack the financial resources to

outsource household tasks. Therefore, having a clear plan, as proposed by Prof Hegyi, is potentially a more useful tip. He declared that it was vital to have specific aims over a period of time, because otherwise you can be very busy but achieve nothing of value. Prof Hegyi also suggested that as part of this plan it was important to allot yourself some time in the day for other activities and that you should be strict with yourself about sticking to this. He mused on the importance of undertaking extracurricular activities, pointing out that, in his experience, most successful people took part in something else other than work. The need for a measure of flexibility in even the strictest of plans was highlighted by Prof Ciacci, who noted that if, for instance, your child has a problem at school and they call you, then all your plans must change immediately.

With many of the tips put forward by the experts somewhat dependent on personal circumstances, perhaps the most universally applicable suggestion was to ensure you are fully focussed on the situation in which you are currently in. This should ensure you are making the most of the time available to you. After all, as Prof Hegyi explained, sometimes you might technically be spending hours with your family, but if you are not focussed on them, you are not really present with them. If your priorities mean you must spend less time in a place, then having a 100% focus will maximise that time.

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