HEART RATE VARIABILITY
All patients were asked to avoid caffeine for 6 hours prior to the visit. Autonomic nervous system function was evaluated using heart rate variability (HRV) analysis of a 24-hour epoch of electrocardiographic recordings using a Holter monitor (LifeCard CF; Del Mar Reynolds, Spacelabs Healthcare Inc., Snoqualmie, WA, USA). The initial period of recording was commenced with the patients undertaking 10 minutes of controlled breathing (15 breath minute$^{-1}$) in the supine position and standing positions. HRV was assessed throughout the 24-hour recording period (Pathfinder Software, Version 9.019, Spacelabs Healthcare Inc.) with waveforms manually reviewed for any evidence of artefact. The 24-hour value of R-R intervals, standard deviation of normal to normal intervals, HRV within 5-min cycles (SDANN), and the root mean square of the difference of successive normal R-R intervals (RMSSD) were recorded, see Table 1 in the main manuscript. All parameters were recorded and interpreted according to internationally agreed guidelines (1).

QUESTIONNAIRES
**Michigan Neuropathy Screening Instrument (MNSI):** The Michigan Neuropathy Screening Instrument (MNSI) is designed for use in the outpatient setting, and is structured to screen for the presence of diabetic neuropathy. The first part of the screening instrument consists of 15 self-administered "yes or no" questions on foot sensation including pain, numbness and temperature sensitivity. A higher score (out of a maximum of 13 points) indicates more neuropathic symptoms (2). A score of > 7 is considered abnormal. During the MNSI examination, a health professional inspects each foot for deformities, dry skin, calluses, infections and fissures. Each foot with any abnormality receives a score of 1. The maximum score is 8 points and a score > 2.5 is considered abnormal. **PAGI-SYM questionnaire:** GI symptoms in the preceding 2 weeks were assessed by using
the Patient Assessment of Upper Gastrointestinal Symptoms (PAGI-SYM). The Gastroparesis Cardinal Symptom Index (GCSI), which is based on the three subscales of the longer PAGI-SYM, and has proved to be a reliable tool for measuring symptom severity in patients with gastroparesis and GI dysmotility (3). The GCSI score is composed of three subscales (postprandial fullness, nausea and bloating) and ranges from 0 (no symptoms) to 5 (very severe symptoms), see supplementary table 1.

**WIRELESS MOTILITY CAPSULE**
The capsule measures 26 mm x 11 mm, and contains sensors that measure temperature (25-49°C), pH (0.05-9.0) and pressure (0-350 mmHg). The WMC has a battery life of a minimum of 5 days operational use. The WMC continuously measures intra-luminal pressure, pH, and temperature as it traverses the GI tract. Data is wirelessly transmitted from the WMC and stored in an external receiver worn by the participant. Following ingestion of the WMC, participants consumed a meal of known nutritional composition (SmartBar, Medtronic, Minneapolis, Minnesota, USA) with a glass of water in order to standardize the initiation of postprandial motility patterns (4). Successful ingestion of the WMC was confirmed by observation of an acidic pH on the display of the external receiver, thereby demonstrating that the WMC had entered the stomach. Participants were then released from the clinical settings and could resume normal diet and daily living activities, although they were asked to avoid eating for another 6 hours following WMC ingestion, in order to re-establish a fasting motility pattern and achieve an accurate measurement of gastric emptying time (GET) (5). In addition, the participants were asked to complete a diary recording bowel movements, food intake, sleep, and GI symptoms such as abdominal pain/discomfort and bloating. Four days after the WMC ingestion (or earlier if the person observed the capsule in the toilet), participants returned to the study centre with the diary and the receiver. Individual WMC
traces were analyzed by a single investigator (AGP) manually and using standardized software
(MotiliGI, Medtronic, Minneapolis, USA). Traces were then manually reread independently by a
further two experienced investigators (CB and ADF). Disagreement was resolved by consensus.
TABLE 1

<table>
<thead>
<tr>
<th>Gastroparesis Cardinal Symptom Index component scores</th>
<th>Patients (Mean ± SD/Median &amp; IRQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting</td>
<td>0.2 ± 0.5</td>
</tr>
<tr>
<td>Fullness</td>
<td>0.6 ± 0.73</td>
</tr>
<tr>
<td>Bloating</td>
<td>0.7 ± 1</td>
</tr>
<tr>
<td>Total Score</td>
<td>0.51 ± 0.64</td>
</tr>
</tbody>
</table>

Table 1 - Gastroparesis Cardinal Symptom Index (GCSI) is based on three subscales, comprising of nausea/vomiting, fullness and bloating, of the longer PAGI-SYM. Fullness is based on 4 items, nausea/vomiting on 3 items and bloating on 2 items. Responses are recorded on a 6-point scale ranging from 0, representing no symptoms to 5 representing very severe symptoms. From these subscales a composite GCSI can be derived.
Table 2 - Differences in segmental and whole gut transit times and change in pH across the ICJ in patients in comparison to controls. GET- gastric emptying time, SBTT – small bowel transit time, CTT – colonic transit time, WGTT – whole gut transit time, ICJ – ileocaecal junction.
REFERENCES


