**Supplementary Table 5. Some UK CIGH-Related Deaths 1992–2017 Not Reported to the MHRA Yellow Card System**

| **Patient sex, age (yr)** | **Clozapine dose (mg/d)** | **Clozapine duration** | **Clinical features** | **Investigations** | **Treatment** | **Outcome** |
| --- | --- | --- | --- | --- | --- | --- |
| M, 40-50 | 750 | 4 y | Day before death reported feeling ‘bunged up’. Neutrophilia, monocytosis, acidosis | Autopsy: small bowel dilated, with blood-stained mucus, particularly in jejunum. Large bowel dilated with foul-smelling, blood-stained fluid and small amount of stool | 4 x Movicol; failed to defecate. Next morning vomited copious quantities of tea-coloured fluid. Given 2 x Movicol. Severe, uncontrollable diarrhoea | Found collapsed and not breathing. Resuscitation attempt failed (Flanagan and Ball, 2011) |
| M, 40-50 | 200 + quetiapine 500 mg/d | 4 y | Emergency admission with discomfort, abdominal swelling, and vomiting that had been present and increasing for some 2 weeks | Autopsy: dilatation of the small and large bowel with no obvious obstruction. Dilated, flabby heart (720 g) with left ventricular hypertrophy. Liver extensive centrilobular hepatic necrosis; 5.2 L of straw-coloured ascitic fluid in abdomen |  | Died after 2 d |
| M, 40-50 | 625 |  | 12 d history of constipation. Found collapsed; could not be resuscitated. 1 h before speech slurred | Autopsy: massive gaseous distension of large bowel, faecal loading of the distal sigmoid and rectum. No stercoral ulceration, perforation, or toxic bowel changes. |  | Died |
| M, 40-50 | 500 |  | Breathlessness, distended abdomen. Recently stopped smoking. Clozapine dose at that time 550 mg/d and plasma clozapine/ norclozapine 1.15/0.88 mg/L. Constipation, vomiting. Hypertensive, ascites, mild hepatomegaly | Autopsy: large bowel caecum to splenic flexure distended at maximum point. Hard faeces throughout large bowel; no other cause for obstruction | Prescribed laxatives, clozapine stopped on admission. Plasma clozapine/norclozapine 2.84/1.60 mg/L 4 days post-admission | Died 5 d. post-admission |
| M, 40-50 | 450  + chlor-promazine | 10 y | Hyperventilating, agitated and anxious. Repeated episodes of hypotension. | Severe liver damage (INR 2.5); renal function deteriorating. Autopsy: faecal loading in left colon |  | Collapsed and could not be resuscitated. |
| M, 40-50 | 600 | >10 yr | Found lying on floor. Nausea, but not constipation. Examination: soft abdomen, possibly slightly distended | Autopsy: large intestines and sigmoid colon markedly dilated with firm faeces. No other cause for obstruction |  | Found unconscious; could not be resuscitated |
| M, 40-50 | 900 | 15 yr | History of constipation. Drowsy and agitated. Suddenly labored breathing, restless and unwell. BP 55/36 mm Hg | Autopsy: marked faecal overloading of the colon with proximal bowel distension. No other cause for obstruction |  | Appeared to fit, then vomited blood, became unresponsive; could not be resuscitated |
| M, 60-70 | - | - | Suffered cardiorespiratory arrest at mental health unit. Revived by first responders. Presented in spontaneous circulation, intubated, unconscious. | Autopsy: Bowels markedly distended, appeared sluggish and showed a heavy retained amount of liquid and solid faeces, strongly suggest­ing paralytic ileus possibly within a setting of sepsis from the chest. No evidence of perforation. Small bowel full of liquid residue; rectum normal | Admitted to ITU. Ventilated. CT head scan 4 d post-admission: hypoxic brain injury. | Died 4 days post-admission. Post-mortem blood clozapine and norclozapine concentrations 1.75  and 0.74 mg/L, respectively |
| M, 40-50 | 300 (also amisulpride 400 mg/d) | - | Constipated, although ‘soiling’ of sheets noted. Faecal vomiting. Had felt ‘bunged’ and 4 hours later had a large bowel movement. Collapsed in A&E. Low blood pressure and raised pulse rate. Abdomen distended and tender | Abdominal X-ray: dilated large bowel without free gas under his diaphragm. CT scan: mildly dilated loops of intestine (jejunum) and possible small bowel adhesions. Faecal loading and moderate dilation of the large bowel | Intubated and sedated. Pro­gress­ive abdominal distention. Required i.v. noradrenaline, adrenaline and vasopressin | Developed significant metabolic acidosis. Continued to deter­iorate died < 24 h post-admission. Post-mortem blood concentrations (mg/L): clozapine and norclozapine 1.0 and 0.7, respectively; amisulpride 10 |

Abbreviations: BP, blood pressure; CT, computerized tomography; d, day(s); F, female; GI, gastrointestinal; h, hour(s); INR, international normalized ratio; IV, intravenous; m, month(s); M, male; PEG, polyethyleneglycol; w, week(s); yr, year(s).