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Future developments and new technologies in the field of faecal incontinence: scanning the horizon using late-stage clinical trial registrations

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ABSTRACT

Aim The aim of this study was to examine how new technologies in late-stage clinical trials might address unmet patient, practitioner or caregiver need for faecal incontinence (FI) over the next 5 years.

Methods Horizon scanning techniques were used to provide insights into the current landscape of emerging health technologies. A search was performed across clinical trial registries using the National Institute for Health Research Innovation Observatory's ScanMedicine database (scanmedicine.com) to identify new, emerging interventions or health technologies (drugs, medical devices or diagnostics) that were addressing or investigating FI. Trials were then screened for relevance to FI in a non-blinded duplicate manner.

Results 1163 records were identified through searching ScanMedicine, and 136 trials were included in the final data extraction and mapping process. The most frequently investigated FI intervention topics were complementary therapies (n=17, 12.4%); electrical stimulation (n=13, 9.5%); pelvic floor muscle training/biofeedback/sphincter exercises (n=13, 9.5%) and implanted sacral nerve stimulation (n=12, 8.7%). There was little evidence of new pharmaceutical technologies in development. Existing drugs are, however, being repurposed and trialled for the treatment of FI (eg, linaclotide, colesevelam). Such repurposed drugs often have lower development costs, shorter timelines and report lower failure rates compared with new pharmaceutical products.

Conclusion Overall, the innovation space as indicated by late-stage clinical trials related to FI, is relatively stagnant. Patients, carers and healthcare professionals are demanding more effective treatment and containment options; however, these are unlikely to come to market in the immediate future.

Summary box

What are the new findings?

⇒ Horizon scanning techniques have been used to systematically identify health technologies related to faecal incontinence (FI) in active development.

⇒ Most late-stage trials focused on bowel management strategies, followed by strategies related to bladder and bowel dysfunction.

⇒ There was limited evidence found for new drugs in the development pipeline, however, some trials evaluated the effectiveness of existing repurposed drugs.

How might it impact on healthcare in the future?

⇒ Repurposed drugs are currently being tested, which might help treat FI over the next 5 years.

⇒ Other management strategies are being trialled to examine the treatment benefits to specific groups (ie, cancer patients).

⇒ More trials are needed to address the unmet need of those with FI, particularly identifying more effective containment options. An emphasis on education for self-management and the use of more effective existing treatment and management strategies would improve patient outcomes in the short term.

INTRODUCTION

Faecal incontinence (FI) is the involuntary passage of faecal material through the anal canal. The prevalence of FI is estimated to range from 2% to 17% among community-dwelling individuals and up to 40% among people aged over 65 years living in residential care settings.[1] Incontinence has a severe impact on quality of life and can profoundly affect an individual's health, family and sexual relationships, lifestyle choices, employment and finances.[2–4] Failure to seek appropriate treatment for FI can lead to recurrent visits to primary and secondary care placing an increased burden on the healthcare system.[5]

As the population continues to age and the prevalence of those living with complex multimorbidity rises, we will see further increases in FI prevalence. FI continues to be under-reported[6] even though improved identification and diagnosis have seen the prevalence among those living in community or supported living environments increase.[2] The causes of FI are multifactorial with occurrence via several mechanisms. Consequently, there is no single treatment approach suitable for all patients. Rather, the complex aetiologies, which result in symptoms of FI mean different treatments or combination of treatments may be best suited to different populations.[7] There has never been a greater need for research and innovations in FI therapies and medical technologies.

Few reports on the formal setting of research or innovation priorities to address FI have been undertaken. Two studies that do identify priorities highlight the need for new randomised controlled trials of effective treatments (particularly treatment combinations) and more generally the development of new drugs and surgical techniques.[8 9] A third study[10] focussing solely on research and funding priorities for incontinence nursing, found literacy and communication to be paramount, alongside dissemination of information on evidence-based interventions for incontinence management.

Here, we describe emerging health technologies (drugs, therapeutic and surgical procedures and medical devices) for the diagnosis and management of FI. This research formed part of a wider programme of work, funded by the National Institute for Health Research (NIHR), UK, through Cochrane Incontinence (CI) and the NIHR Innovation Observatory. This wider programme of work aimed to synthesise existing evidence and elicit stakeholder insights into the management and treatment of FI (eg, surgical and procedural approaches, drug treatments, mechanical devices) to ensure future research on FI is as relevant to patients and practitioners as possible. The methods and results of this are explored elsewhere.[11 12]

METHODS

Horizon scanning techniques provide insights into the current landscape of emerging health technologies. A search was performed across clinical trial registries using the NIHR Innovation Observatory's ScanMedicine database (scanmedicine.com) to identify new, emerging interventions and health technologies (drugs, medical devices or diagnostics) that were addressing or investigating FI. The topic terms used were initially taken from the MEDLINE search terms used by CI to identify FI-related studies for their Specialised Register and translated for use in ScanMedicine. For more details of the search methods used to build the Specialised Register, please see the Group's webpages, where details of the Register's development (from inception) and the most recent searches performed to populate the register can be found. ScanMedicine's built-in synonym search feature using the Unified Medical Language System identified clinical trials based on the FI topic terms. Details of the search terms are given in online supplemental appendix 1.

The initial search was performed on 11 August 2020. The results identified through 'ScanMedicine' were combined into a single collection of trials and then deduplicated using Microsoft Excel's built-in functions. The deduplicated and consolidated results were then filtered by their trial recruitment status and clinical trial registries. Trials with a date of first enrolment prior to 1 January 2015 were excluded to provide an insight into the most recent 5 years of active development. Trials were then screened for relevance to FI in a non-blinded duplicate manner. During the primary screening, the clinical trial title and primary indication(s) or health question(s) of interest in each clinical trial were evaluated by two independent reviewers. The primary end points, inclusion or exclusion criteria, and other features, were ascertained during the secondary screening and only trials specific to FI were carried forward (see online supplemental appendix 2 for inclusion/exclusion criteria). In case of disagreement between the two reviewers, a third reviewer was consulted. Existing and pipeline trials were categorised and mapped to the FI intervention topics identified by the Sixth International Consultation on Incontinence (online supplemental appendix 3).[13]

Patient and public involvement

Patients or the public were not involved in the study design or conduct of the horizon scanning. However, the horizon scanning was part of a larger programme of work, which included workshops incorporating patients, carers and healthcare professionals in an agenda setting process examining priority areas for FI research.[12] The results of the horizon scanning exercise were shared and discussed in this workshop, and the views of the patients captured are incorporated here, where appropriate, to illuminate patient perspectives on the future treatment landscape.

RESULTS

A total of 1163 records were identified through ScanMedicine searching. After duplicates were removed

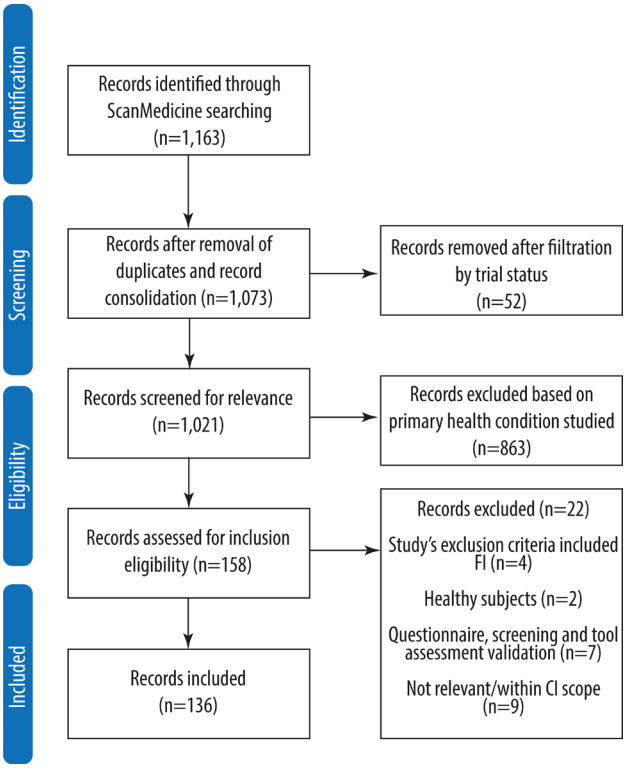

Figure 1 Horizon scanning of clinical trials and selection process flow diagram. CI, Cochrane Incontinence; FI, faecal incontinence.

and filtered by clinical trial status, trial registry and enrolment year, 1021 records were screened for relevancy and 863 studies were excluded based on the primary health condition studied. The remaining 158 records were investigated in detail by assessing the trials' primary end points and inclusion or exclusion criteria, and a further 22 studies were deemed irrelevant (see online supplemental appendix 4 for a full list of trial exclusions). In total, 136 trials were included in the final data extraction and mapping process (online supplemental appendix 5). Figure 1 shows the flow diagram of the horizon scanning and selection process.

The clinical trials were mapped to one or more FI domains (table 1). The most frequently investigated FI intervention topics (within the FI domains) were complementary therapies (n=17, 12.4%); electrical stimulation (n=13, 9.5%); pelvic floor muscle training/biofeedback/sphincter exercises (n=13, 9.5%) and implanted sacral nerve stimulation (n=12, 8.7%). Several trials also looked at the effect of laxatives on FI (n=8) and the impact of educational (n=6) and lifestyle interventions (n=9) on bowel management.

The impact of various interventions trialled for the treatment or management of FI in patients with cancer included pelvic floor rehabilitation, physical exercise and transanal irrigation (n=10). There was also evidence on tailored follow-up approaches offered to patients following rectal cancer surgery (eg, pelvic floor muscle training, dietary education). The most novel treatment option highlighted was the use of plasma-rich platelet injections to initiate and speed up reconstruction following low anterior resection of the bowel.[14] There were also clinical trials (n=15), both randomised and non-randomised, comparing the effectiveness of different therapeutic interventions and pharmacological treatments, including nerve stimulation, laxatives, supplements and cell transplantation. However, previous priority setting exercises highlighted the need for randomised trials assessing combined treatments,[8 9] and in our rapid horizon scanning, we found no evidence of this.

Table 1 Clinical trials mapped to one or more FI domains

Number of trials	FI domain
65	Bowel management
32	Bladder and bowel dysfunctions
24	Surgical techniques
23	Drug treatments
16	Bowel management for neurogenic conditions
12	Mechanical devices
11	FI interventions in particular populations
3	FI interventions in particular settings
1	Models of care
16	Trial records were termed 'other' and comprised a range of issues including incontinence associated dermatitis, financial support, psychological support and quality of life.

FI, faecal incontinence.

Emerging developments and novel health technologies

The horizon scan of the clinical trial landscape identified a range of emerging and novel therapeutic technologies. In total, 16 new and emerging technologies were identified: nine pharmacological therapies, two mechanical devices and five therapeutic technologies. Some of these trials focused on evaluating existing technologies that have been advanced, such as repurposed approved drugs for a new therapeutic use or within an alternate patient population and the evolution of neurostimulation devices (eg, improving control mechanisms).

Pharmacological therapies

There was limited emerging evidence of new drugs in the development pipeline (n=2) and there were no early-stage pharmacological trials of therapies specifically licensed for the treatment of FI. Most emerging evidence was on the effectiveness of repurposed drugs (n=11) in treating and managing FI. The evaluated repurposed drugs for the treatment or management of FI included linaclotide, colesevelam, imipramine and mosapride citrate, all of which were originally indicated for divergent conditions, only two of which were for gastrointestinal disorders (linaclotide and mosapride citrate). Some trials are also evaluating the effect

of laxatives in improving FI in the paediatric population, such as lubiprostone, lactitol, polyethylene glycol and lactulose.

ENT-01 (Kenterin) is a new investigational drug for the treatment of constipation, which may present a potential treatment option for some FI patients, depending on their cause or symptoms of FI. ENT-01 is a series of small compounds and aims to prevent the accumulation of alpha synuclein (a neuronal protein) in the nerves of the gastrointestinal tract to improve neural signalling and gut motility in patients with constipation related to Parkinson's disease (PD).[15] Results from the small, open label, phase II study (RASMET) with 34 participants reported that ENT-01 was thus far safe and 'improved bowel function' in over 80% of patients with PD. The reported systemic absorption was <0.3%, suggesting improvements resulted from local stimulation of the enteric nervous system.[16] A randomised phase II trial (KARMET) (152 participants) is currently in progress to evaluate the effect of orally administered ENT-01 compared with placebo on neurologic symptoms and constipation.[17] Results from larger, randomised trials will be needed to fully assess the efficacy and safety of ENT-01.

Mechanical devices

Fecobionics is a novel device that simulates faeces by integrating a balloon expulsion test (BET) and anorectal manometry to assess defecatory functions in patients with chronic constipation and FI.[18] The integration of several technologies and tests into one Fecobionics device aims to save time and reduce test variability. The innovations of this device compared with current anorectal functional assessment techniques include mechanical properties that mimic faeces, electronic (objective) measurement of the anorectal angle and pressure measurements in the orientation of the faeces trajectory. Early study results (randomised study, crossover design, 20 participants) suggest that Fecobionics may be an effective method for evaluating anorectal physiology and evacuatory efficacy.[19] Larger, randomised trials would be needed to fully assess the efficacy and safety of this device.

Current developments in neurostimulation devices for FI are focusing on increasing portability and patient use as well as ease of use. Geko is a self-adhesive, internally powered, disposable tibial nerve stimulator device. Intended for patient use, it is already marketed for the prevention and/or treatment of venous thrombosis and oedema. As a wound therapy device, it is also used to increase blood circulation and promote wound healing. Powered by OnPulse technology, the device provides 11 stimulation settings and 60 muscle contractions per 1 min at 1 Hz.[20] Geko was trialled in 13 patients for the treatment of FI in older people living at home or in residential care, potentially providing a feasible option for the elderly or their caregivers to manage FI in these settings.[21]

Therapeutic technologies and surgical or procedural treatment approaches

Clinical trials are currently investigating the role of regenerative medicine and cellular therapy for the treatment and management of FI in patients with neurological disorders. Novel developments in regenerative medicine may provide sustainable techniques that address the limitations of injectable bulking agents and their need for repeat treatment. The investigational surgical techniques in early phase I/II developments include scaffold-based treatment (NeuroRegen scaffold) and both autologous (fat grafting, stem cell transplantation and platelet rich plasma injection) and heterologous (faecal transplantation) therapies.

NeuroRegen scaffold is prepared from bovine aponeurosis by removing residual muscle, connective tissue and fat. NeuroRegen scaffold is then implanted into the resection sites and aims to promote axonal growth along collagen fibres and inhibit glial scar formation after spinal cord injury (SCI). Findings reported from a previous non-randomised study in eight patients with SCI suggest that NeuroRegen scaffold with human umbilical cord mesenchymal stem cells are safe and feasible for the repair of chronic SCI.[22] The efficacy and safety of NeuroRegen in scaffold transplantation is currently being assessed in a phase 1/2 trial in combination with various types of cell transplantations (bone marrow mononuclear cells, mesenchymal stem cells or neural stem cells) for SCI repair and neurological recovery.[23 24] Four clinical trials are currently investigating the role of regenerative medicine and cellular therapy for the treatment and management of FI in patients with neurological disorders. Novel developments in regenerative medicine may provide sustainable surgical techniques that address the limitations of injectable bulking agents and their need for repeat treatment.

Fat grafting technique using Lipogems is a reconstructive lipoplasty with microfragmented autologous adipose tissue. It is believed to increase circulation, nerve regeneration, muscle growth and tone in the anal sphincter muscles, leading to a decrease in FI with a long-lasting impact.[25] Transplantation of autologous, purified haematopoietic stem cells (HSC) positive for CD34 and CD133 (HSC markers) into the spinal cord, using bone marrow or leukapheresis as sources is currently being trialled. A randomised controlled trial (50 participants) aimed at assessing this approach as a potential treatment option for SCI, is underway. The effect on improving sensory and motor functions as well as urinary and stool incontinence is being evaluated.[26]

Another therapeutic intervention under evaluation, in a single-armed study with 20 participants, is platelet-rich plasma injection, a thrombocyte-enriched liquid portion of whole blood that increases cell proliferation and the formation of collagen, for treating incontinent patients after low anterior resection for rectal cancer.[14]

Finally, heterologous faecal microbial transplantation, which uses infusion of intestinal microbiota from healthy donors, is also in phase 1/2 development (single-armed study, 15 participants). This aims to increase microbial diversity, reduce symptom severity and improve quality of life.[27]

DISCUSSION

Our review of the emerging active trial evidence details what treatment and management options for FI may become available over the next 5 years. Treatments and approaches suitable for this population are only included and discussed if there is recent, active clinical trial evidence (within the remit of Cochrane Incontinence meaning constipation during pregnancy, cancer surgery and Hirschsprung's disease, for example, were excluded). Existing (licensed) or early-stage trial evidence for technologies to treat FI would not be considered here. Furthermore, the efficacy of the pharmaceutical or management options is not considered, as such it is likely that some treatment options will not go through regulatory approval.

Our results showed little evidence of new pharmaceutical technologies in development. Existing drugs were, however, being repurposed and trialled for the treatment of FI (eg, linaclotide, colesevelam). This is perhaps not surprising considering the vast costs of developing new technologies. After accounting for the costs of failed trials, the median capitalised research and development investment to bring a new drug to market was estimated in 2018 at US$985.3 million.[28] Given the vast costs associated with research and development, pharmaceutical companies are perhaps unwilling to invest in FI innovations. Repurposing previously licensed drugs for new indications outside of their original scope may be a more attractive proposition to companies as compounds are partially derisked, have potentially lower overall development costs, shorter development timelines and lower chances of failure as the safety profile of the compound is already partially established.[29] In the stakeholder workshops which were part of the wider priority setting exercise, participants identified that research topics are often dictated by research sponsors and that product development is heavily influenced by the potential for investment gains.[11] As such, they considered that there is limited interest in developing new, more innovative products, which may improve the management of FI in the medium and long term. Limited improvements in containment technologies were also found in the trial records, which again was a disappointment to stakeholders attending our workshop who felt such innovations would improve their everyday lives and were being sidelined compared with pharmacological innovations.[11]

This research highlighted the repurposing of drugs to treat FI. Currently, there are few drugs used for FI, and it is appropriate to examine whether an existing antidiarrhoeal drug, for example, can reduce FI (with few side effects). The results of a discrete-choice experiment by Nafess *et al*[30] showed that patients who had a diagnosis of SCI favoured treatments that offered any improvement compared with those currently available. So, even if the marginal gain by offering a repurposed antidiarrhoeal drug is low, the patient benefit in terms of improving health-related quality of life makes the treatment worthwhile. Other drugs, not originally indicated for FI, have also been studied. Darifenacin has, for example, been tested as an early invention for FI in women with double incontinence (32 participants, no control group) and may merit further exploration in the context of a randomised controlled trial.[31]

FI is often a symptom of other health problems and, therefore, as the disorder has a multitude of causes, treatment approaches need to be tailored to the individual patient. There are a variety of existing pharmaceutical and management approaches, and their administration by a greater number of skilled and knowledgeable practitioners could increase the number of patients who have improved FI symptoms. More emphasis on healthcare provider education and the dissemination of best practice approaches to treat FI symptoms would facilitate this.

The horizon scanning search undertaken here was comprehensive, covering 11 registries across the globe. However, other relevant clinical trials may not have been identified in this process if their registration records were not available through ScanMedicine. Some of the identified trial records were not recently updated, making it difficult to assess their current state of development, or whether they had been prematurely discontinued. The process we used to horizon scan for this project focuses on products that have gone through clinical trials and may have missed relevant products that do not require a review of efficacy and safety as part of the regulatory processes (eg, medical devices).

CONCLUSIONS

Horizon scanning has shown some emerging evidence for pipeline drugs currently in development, the use of repurposed drugs, new devices, surgical techniques and procedures to treat FI. Although incremental innovations in drug repurposing strategies offer hope to patients, major paradigm shifts in treatment will likely come instead from traditional drug discovery.[32] Raising the profile of FI and proactive screening will most likely lead to more people identified with the condition, which may, in turn, drive innovation. Given the stigma of FI, it was reassuring that there was some evidence looking specifically at quality of life. However, future trials must go further and assess the importance of psychological support concomitantly with conservative and pharmaceuticals for treating FI. As identified within our stakeholder workshop,[11] psychological support remains an important and

unresolved issue, despite previous research highlighting its importance.[10] This is especially important in the short-term to medium-term, as patients must be given the support and tools to live with FI and cope with a chronic condition for which there is no cure. At the same time, however, innovative technologies to better manage the condition, or reduce its severity, must also be prioritised to meet the needs of existing and future patients. Only with technological innovations and improved patient, carer and healthcare provider education and support will benefit to patients living with FI be realised.

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REFERENCES

1 Brown SR, Wadhawan H, Nelson RL. Surgery for faecal incontinence in adults. *Cochrane Database Syst Rev* 2013:CD001757.
2 Perry S, Shaw C, McGrother C, *et al*. Prevalence of faecal incontinence in adults aged 40 years or more living in the community. *Gut* 2002;50:480–4.
3 Rockwood TH, Church JM, Fleshman JW, *et al*. Fecal incontinence quality of life scale. *Diseases of the Colon Rectum* 2000;43:9–16.
4 Wilson M. The impact of faecal incontinence on the quality of life. *Br J Nurs* 2007;16:204–7.
5 Finne-Soveri H, Sørbye LW, Jonsson PV, *et al*. Increased work-load associated with faecal incontinence among home care patients in 11 European countries. *Eur J Public Health* 2008;18:323–8.
6 O'Keefe EA, Talley NJ, Zinsmeister AR, *et al*. Bowel disorders impair functional status and quality of life in the elderly: a population-based study. *J Gerontol A Biol Sci Med Sci* 1995;50:M184–9.
7 National Institute for Health and Care Excellence. *Faecal incontinence in adults: management. clinical guideline CG49*. London: National Institute for Health and Care Excellence, 2007. https://www.nice.org.uk/guidance/cg49
8 Whitehead WE, Wald A, Norton NJ. Priorities for treatment research from different professional perspectives. *Gastroenterology* 2004;126:S180–5 http://doi.org.uk/
9 Whitehead WE, Bharucha AE, Rao SS, *et al*. Mo2003 researchers identify priorities for fecal incontinence: survey of scientists. *Gastroenterology* 2014;146:S714.
10 Bliss DZ, Norton CA, Miller J, *et al*. Directions for future nursing research on fecal incontinence. *Nurs Res* 2004;53:S15–21.
11 Thomson KH, O'Connor N, Bliss DZ, *et al*. Rapid priority setting exercise on faecal incontinence for Cochrane incontinence. *BMJ Open Gastro* 2022.
12 O'Connor N, Thomson K, Dangova K, *et al*. The methods used to identify key priorities for faecal incontinence: a multi-step, multi-stakeholder priority setting exercise by Cochrane incontinence.
13 Abrams P, Cardozo L, Wagg A. *Incontinence: 6th International consultation on incontinence*. Bristol, UK: ICI-ICS. International Continence Society, 2017.
14 NCT04063293. PrP injection into anal sphincters for fecal incontinence, 2019. Available: https://clinicaltrials.gov/ct2/show/NCT04063293 [Accessed 11 Aug 2020].
15 Enterin Inc. *Kenterin (ENT-01)*. Philadelphia, PA: Enterin Inc, 2021. https://enterininc.com/enterin/
16 Hauser RA, Sutherland D, Madrid JA, *et al*. Targeting neurons in the gastrointestinal tract to treat Parkinson's disease. *Clin Park Relat Disord* 2019;1:2–7.
17 NCT03781791. Orally administered ENT-01 for Parkinson's disease-related constipation (KARMET), 2018. Available: https://clinicaltrials.gov/ct2/show/NCT03781791 [Accessed 11 Aug 2020].

18 NCT03317938. Studies in patients with defecatory disorders, 2017. Available: https://clinicaltrials.gov/ct2/show/NCT03317938 [Accessed 11 Aug 2020].
19 Gregersen H, Chen S-C, Leung WW, *et al*. Novel Fecobionics Defecatory function testing. *Clin Transl Gastroenterol* 2019;10:e00108.
20 Firstkind Limited. *geko™ devices high*. Wycombe, UK: Firstkind Limited, 2021. https://www.gekodevices.com/
21 NCT02875665. feasibility study of the use of the gekoTM device for faecal incontinence in older people living at home or in care homes, 2016. Available: https://clinicaltrials.gov/ct2/show/NCT02875665 [Accessed 26 May 2021].
22 Zhao Y, Tang F, Xiao Z, *et al*. Clinical study of NeuroRegen scaffold combined with human mesenchymal stem cells for the repair of chronic complete spinal cord injury. *Cell Transplant* 2017;26:891–900.
23 NCT02688062. NeuroRegen scaffold with bone marrow mononuclear cells transplantation vs. intradural decompression and adhesiolysis in SCI, 2016. Available: https://clinicaltrials.gov/ct2/show/NCT02688062 [Accessed 11 Aug 2020].
24 NCT02688049. NeuroRegen scaffold combined with stem cells for chronic spinal cord injury repair, 2016. Available: https://clinicaltrials.gov/ct2/show/NCT02688049 [Accessed 11 Aug 2020].
25 NCT03882632. fat grafting technique for fecal incontinence, 2019. Available: https://clinicaltrials.gov/ct2/show/NCT03882632 [Accessed 11 Aug 2020].
26 NCT02687672. transplantation of autologous bone marrow or leukapheresis-derived stem cells for treatment of spinal cord injury, 2016. Available: https://clinicaltrials.gov/ct2/show/NCT02687672 [Accessed 11 Aug 2020].
27 NCT04201821. fecal microbial transplantation for the treatment of fecal incontinence in women (FMT for FI), 2020. Available: https://clinicaltrials.gov/ct2/show/NCT04201821 [Accessed 11 Aug 2020].
28 Wouters OJ, McKee M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. *JAMA* 2020;323:844–53.
29 Pushpakom S, Iorio F, Eyers PA, *et al*. Drug repurposing: progress, challenges and recommendations. *Nat Rev Drug Discov* 2019;18:41–58.
30 Nafees B, Lloyd AJ, Ballinger RS, *et al*. Managing neurogenic bowel dysfunction: what do patients prefer? a discrete choice experiment of patient preferences for transanal irrigation and standard bowel management. *Patient Prefer Adherence* 2016;10:195–204.
31 Kissane LM, Martin KD, Meyer I, *et al*. Effect of darifenacin on fecal incontinence in women with double incontinence. *Int Urogynecol J* 2021;32:2357–63.
32 Gil C, Martinez A. Is drug repurposing really the future of drug discovery or is new innovation truly the way forward? *Expert Opin Drug Discov* 2021;16:829–31.