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**Treating women with recurrent stress urinary incontinence; a hornet's nest
still needing proper clinical evidence**

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Main Editorial (max 1000 words)

Recurrent stress urinary incontinence (SUI) in women is a high-stakes setting. It appears to be common, though exact numbers are hard to ascertain. This is largely due to non-standardised definitions used by researchers, and potentially the reticence of women to engage with the medical profession following the failure of previous treatment to cure their SUI, or its recurrence of after a period of time. Naturally, those women who do return for further treatment expect an effective response. Modern society has high expectations of healthcare, and recurrence may be seen by some as a basic healthcare failure.

Sadly, an easy resolution is far from guaranteed. The evidence base for treatment of recurrent SUI is remarkably poor. No randomised controlled trials (RCTs) have addressed this uncertainty and the Cochrane analysis was inconclusive (1). An indirect systematic review of the sub-groups of women with recurrent SUI within a number of RCTs, did not detect a significant difference in efficacy or safety of various repeat surgical interventions (2). In 2017, the updated Canadian guideline recommendations for the evaluation and treatment of recurrent SUI was based upon level B or C evidence (3). Best practice for the management of SUI following a failed tension free vaginal tape operation was identified as a top ten issue by the James Lind Alliance (JLA) (4), an initiative which brings together patients, carers and clinicians in a Priority Setting Partnership (PSP). A decade later, the issue is still unanswered.

Doubt and anxiety are strongly evident. On the patients' side, there are concerns about the need for more diagnostic tests and interventions, which are balanced with potential

childcare, working or other responsibilities and awareness of the uncertainties regarding vaginal mesh complications (5). From the healthcare professionals' perspective, many surgeons deal only with a small number of affected women, the operative field is complex, and procedures presumed to be more effective may carry greater risk of unwanted side effects (such as intermittent self-catheterisation). Many surgeons choose to repeat the procedure which failed to resolve symptoms when first done – due to confidence in the outcomes of this procedure or sometimes lack of confidence in their ability to perform alternative surgical options. Patients' choices are usually based on an elimination of options, including that of a repeat failed procedure (6). Overall, the wide variation in preferences between patients and surgeons, and within healthcare professional groups, deepens uncertainty and affects trust.

Only a credible, robust and patient-advocated study can be expected to align the complex issues and influences. To address this, the UK National Institute of Health Research funded the “Proper Understanding of Recurrent Stress Urinary Incontinence Treatment in women” (PURSUIT) study (reference HTA 17/95/03). PURSUIT is a two-arm randomised controlled trial set in urology and urogynaecology units in 24 NHS hospitals across the UK. Women aged 18 years or over with bothersome recurrent or persistent SUI, following a primary SUI intervention, who are seeking further treatment are randomised to receive either endoscopic urethral bulking injection(s) or a surgical operation. Women randomised to the surgical arm decide which operation to have through a preference-based shared decision-making process with their surgeon. Surgical treatment options include all those available under usual NHS care (according to rules applicable at the time of treatment). Currently (in 2020) the use of midurethral

tape as a treatment for recurrent SUI is suspended so the surgical treatment options are colposuspension, autologous urethral sling and artificial urinary sphincter.

All women receive their allocated treatment and aftercare at hospital, as per routine NHS clinical care. 250 women will be recruited to the study over a 2-year period and followed up for 3-years, with equal numbers joining each arm (1:1). Within the recruitment period, a 6-month internal pilot phase, running at 5 hospitals, will ensure delivery of the study interventions is achievable. The pilot phase will also facilitate a QuinteT Recruitment Intervention (QRI) (7) designed to evaluate uptake and implement recruitment intervention strategies, if needed.

The study aim is to determine whether more invasive surgical treatment is superior to the minimally invasive endoscopic bulking injections in terms of improving symptoms and quality of life for women with recurrent SUI. The primary outcome is a patient-reported outcome measure (PROM) of continence at 1-year, using the International Consultation on Incontinence Questionnaire - Urinary Incontinence - Short Form (ICIQ-UI-SF). Secondary outcomes include assessment of longer-term clinical impact (2 and 3 years), improvement of symptoms, safety, cost effectiveness (from an NHS and societal perspective) and an evaluation of patient's and clinician's views and experiences of the interventions.

When PURSUIT reports in 2025, there will be high-quality, randomised, scientific evidence on endoscopic injections and definitive surgical treatments to aid the counselling of women presenting with recurrent SUI. In addition, the qualitative arm of the trial will provide evidence on therapeutic choices, patient and surgeon factors and

further insight into patient perception of the therapeutic pathway. The study will be greatly beneficial to patients, carer and health economies in providing a solid basis for guiding further treatment for women presenting with recurrent SUI.

Take Home Message (40 words): *Evidence is lacking on the best treatment for women presenting with recurrent stress urinary incontinence. PURSUIT is a randomised trial of urethral bulking agent injection versus surgical intervention. It will provide high-quality evidence to aid counselling and inform choice.*

Conflicts of Interest

Tamsin Greenwell is a personal consultant for Boston Scientific and Contura; is a speaker for Allergan, Boston Scientific, Contura, Ferring, Olympus, and Medtronic; is a GURS board member (AUA), ESGURS board member (EAU), and member of the EAU Urethral Stricture Guidelines Committee; has received institutional grants/sponsorship to run the annual Female Urology and Urogynaecology Masterclass at UCLH from Allergan, Astellas, Axonics, Boston Scientific, Contura, Ferring, June Medical, Laborie, Mediplus, Medtronic, Olympus, and Vesica Urology; has received sponsorship from Medtronic for a Neuromodulation Fellow at UCLH (now replaced by the Medipoints system); has received an education grant from Laborie for an ICS-approved UDS course at UCLH; and has received equipment and a staff loan from Olympus, Storz, Cook, and Mediplus. Wael Agur has received trainer and speaker fees from CR Bard, Contura, NHS Ayrshire and Arran, and the London Medical Education Academy; sponsorship from Boston Scientific and Neomedic; expert fees from NHS Scotland and various law firms in the UK, Ireland, the USA, and Australia in relation to mesh litigation; and institutional research support as principal

investigator for the SIMS Pilot, PROSPECT, and VUE studies, and as co-chief investigator for PURSUIT study. Wael Agur is also a member of an All Party Parliamentary Group on surgical mesh. The remaining authors have nothing to disclose.

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Department of Health Disclaimer: The views and opinions expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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