Stem cell clinics in the UK: a web-based study

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STEM CELL CLINICS IN THE UK: A WEB-BASED STUDY

Keywords: Ethics, marketing, direct to consumer, stem cell clinics, unproven treatments, online clinics, vulnerable patients, stem cell therapy.

ABSTRACT

Aim: Explore the nature and extent of web-based promotion of stem cell treatments marketed by clinics in the UK. **Materials & Methods**: Web-based analysis of clinics in the UK using pre-defined variables, with analysis of eligible clinics according to pre-set criteria of ethical relevance. **Results:** A majority (79%) of UK clinics were judged to be problematic. Information was found to be lacking, misleading, or otherwise problematic in several respects, including a lack of information on risks of adverse effects, unjustifiably optimistic depictions of therapeutic effectiveness, and questionable presentational approaches such as the use of celebrity patient testimonials. **Conclusions:** In a majority of cases, commercial clinics in the UK portray stem cell therapies on their websites in ethically questionable ways.

INTRODUCTION

The allure of stem cells to patients and consumers has been growing, boosted by substantial marketing and positive media portrayals of stem cell therapies [1-6]. An increasing number of stem cell clinics have emerged across the world, with a range of treatments are on offer to purportedly treat a plethora of conditions, particularly neurological disorders (including multiple sclerosis (MS), Parkinson's disease, stroke, and spinal cord injury), together with various anti-ageing therapies (including dermatological, muscular, and connective tissue regeneration) [7-10]. While stem cells promise much in terms of therapeutic and aesthetic cellular repair and rejuvenation, the literature is replete with case reports of serious adverse effects, including permanent debility and death, that have resulted from unproven stem cell treatments [11-14].

At present, stem cell treatments are only approved for a limited range of disorders, including leukaemia, certain haematological disorders, and specific disorders of the immune system (e.g. Pearson's syndrome), and multiple sclerosis. However, it is clear that, across the world, some clinics offer to treat a wide range of other conditions, for which cell-based therapies are unproven and unapproved (including dermatological, musculoskeletal neurological, and orthopaedic conditions) [15-19]. Moreover, while some conditions are treatable using approved (but not widely available) stem cell therapies, some clinics offer to treat these conditions using unproven methods. MS is a paradigm example: while specific autologous haematopoietic stem cell transplantation (AHSCT) protocols have been approved in a number of countries (including the UK) [20,21], some commercial clinics target MS patients with their own unproven and unapproved mesenchymal or neural stem cell therapies [22,23]. In all cases, it is clear that serious ethical issues exist where unproven, ineffective, or unapproved stem cell therapies are promoted and provided by rogue clinics.

In the regulated medical markets of rich nations, the scope for such malpractice is lower than in middle-income countries with lenient medical regulatory systems, such as China and India. Nevertheless, novel and experimental stem cell therapies have increasingly become commercially available in high-income countries, including the USA and UK [24-26]. The clinics concerned frequently exploit regulatory loopholes which allow for the use of stem cells isolated from the patient's own body (autologous stem cells) [27], for example the 'same surgical procedure exemption' in the USA, which avoids FDA oversight of cell-based products that are collected and reimplanted in a single procedure

[28]. By contrast, stem cell therapies using non-autologous cells are subject to rigorous assessment and regulation [27,29].

How serious a problem this may be in the UK has not been fully answered to date. In a 2019 study, Erikainen *et al.* conducted a valuable review of UK stem cell clinics, focusing on their marketing approaches [25]. However, the extent to which unproven stem cell therapies may be offered and promoted by commercial clinics in the UK has not been explored in terms of the issues that might influence patient choice. To address this important question, we conducted a systematic Web-based study of stem cell-based treatment providers in the UK in 2020, in order to comprehensively categorise UK stem cell clinics and evaluate the scope for potential patients being misled by the information provided by the clinics.

METHODS

Design

A web-based content analysis was conducted for this study [30]. The approach used by a prior study was adapted for this purpose [7]. Google was used as a search engine and keywords were followed by the adjunct 'UK' to limit search results to pages from the United Kingdom. The following keywords were utilised: 'stem cell treatment', 'stem cell therapy' and 'stem cell clinic', employed as 'stem cell treatment OR stem cell therapy OR stem cell clinic'. The first 30 pages of search results were screened to find websites that are most likely to be identified by potential patients. The data were collected in March 2020, thus giving a snapshot of online marketed unproven stem cell-based interventions at that time. The eligibility and website selection criteria are detailed below.

Eligibility

Websites were included if they met the following conditions: 1) the website is owned by a stem cell treatment provider, 2) unproven stem cell treatments were advertised or described to potential patients and 3) the clinics were located in the United Kingdom.

Website selection

Website titles and their description were initially screened, and it was determined whether the results were relevant, i.e. clinics are offering stem cell treatments. Then, for final inclusion, the entire website was screened, and it was determined whether the eligibility criteria were met. Websites that represented the same clinic but appeared multiple times were only analysed once.

RESULTS

Out of 529 web search results, 24 stem cell clinics were identified after screening the title and description. Out of these, 19 were clinics offering unproven stem cell treatments which were considered for the analysis. All the identified clinics in the UK were located in the major cities of England, with approximately three-quarters located in the capital, London.

Analysis

21 pre-defined variables were used to characterise the clinics. The variables sought to define the services they provide in a standardised way so clinics can be easily compared. The main data collected characterised the services provided, and the claims made to evaluate their legitimacy. Data were collected for the categories shown in Table 1.

Table 1 Variables used in the analysis of UK-based unproven stem cell treatment provider websites.

General Qualitative Data	Transparency Data	Safety Data	Other Direct-to-Consumer Portrayal	Location Data
Conditions for which treatment options were offered	Outcome data	Risks, including claim that procedure has no risk	Treatment effectiveness claimed	Location(s)
Stem cell sources	Number of patients treated	Side effects	Other marketing, including exaggerated language used and claims not covered by other variables	Number of clinic(s)
Stem cell types	Clinical trials linked	Contraindications		
Number and duration of treatments required specified	Curative potential	Eligibility requirements		
Costs		Recommendation to discuss treatment with GP		
		Referral required		
		Access to patients record requested		

Scoring and Rating Scale

All identified clinics offering unproven stem cell treatments were assigned a score to determine whether there is likely potential for prospective patients without medical or scientific knowledge to receive misleading information. The following criteria were applied:

(1) Risks and/or side effects of the procedure not made public or trivialised (e.g. usage of the word 'theoretical risk')
(2) Treatment effectiveness claimed incorrectly or without evidence (peer-reviewed clinical trials)
(3) Curative potential claimed incorrectly
(4) Usage of exaggerated language (e.g. usage of the phrase 'expect results' without context).

If any of the above criteria were positive for a clinic a 'fail' was assigned, otherwise, a 'pass' was assigned. This scoring system is not designed as an objective quantification, rather it is intended to provide a broad indication of which clinics engaged in at least one unethical practice (criteria 1-4). The reasoning behind this approach is that the medical profession enjoys a high level of trust in the public and that any breach of this trust that impacts a patient's choice in any way is ethically unacceptable. This corresponds with generally established practice in medical ethics in the UK. For example, Paragraph 71 of the GMC Good Medical Practice guidelines [31] states:

> *You must be honest and trustworthy when writing reports, and when completing or signing forms, reports and other documents. You must make sure that any documents you write or sign are not false or misleading.*
> *a. You must take reasonable steps to check the information is correct.*
> *b. You must not deliberately leave out relevant information.*

We consider this guidance to be equally apposite in the context of stem cell clinics' website material. The potential for clinics' direct-to-patient portrayal to be misleading was then determined by examining the scoring criteria. Where none of the criteria were deemed positive, a 'low' was assigned,

where one of the criteria were deemed positive a 'moderate' was assigned, and where more than one of the criteria were deemed positive a 'high' was assigned. As with the above 'pass/fail' scoring, these scores are subjective, but we believe justified by accepted ethical standards.

Conditions treated

The single most-treated condition type was orthopaedic/musculoskeletal conditions, offered by 60% of clinics. The other indications, which 40% of the clinics offered to treat, were alopecia, dermatological (cosmetic) conditions, erectile dysfunction, and multiple sclerosis. (See Supplemental file 1.)

Stem cell source

Most clinics indicated that they derived their stem cells from either or both adipose or bone marrow (84%), with a small minority (8%) of clinics using blood as a source. All cells were autologous. (See Supplemental file 2.)

Pricing

Only 3 clinics gave information about pricing on their websites. The prices that were provided ranged from £995 to £7000+ for mesenchymal stem cell injections for cosmetical use, alopecia, and joint issues. (See Supplemental file 3.)

Provision of information on effectiveness

While no clinic guaranteed results, some websites used positive phrases such as 'expect improvement' and 'patients usually demonstrate a rapid and progressive improvement' (see Supplemental file 4). One clinic claimed a curative potential of their hair restoration procedure. Only three clinics made it clear that results cannot be assured, with only one clinic mentioning that stem cell therapy for the offered indications is still experimental. One clinic described a stem cell-based treatment from adipose tissue as FDA approved. No clinic linked a finished clinical trial that demonstrates the effectiveness of the offered treatments; however, two clinics offered links to studies that were not clinical trials. One clinic stated that the confidence in regenerative orthopaedics is 'based on sound knowledge, research, training, and experience' (see Supplemental file 5).

Provision of information on safety

67% of clinics did not make any statements with regard to the risk and side effect profile of their therapies. One clinic claimed that *"no serious side effects"* were reported and three mentioned a risk of infection out of which one stated it is 'theoretical'. Two clinics compared the risks to conventional operations. One clinic explicitly described their procedure as safe and claimed that there was neither a risk of rejection nor of communicable disease transmission. Only two clinics mentioned contraindications or eligibility requirements on their websites. One clinic explicitly required a referral, and one did not, the rest did not, nor did they recommend a consultation with a GP prior to an appointment. No clinic mentioned access to patient records as a requirement, however one asked for an MRI scan prior to the appointment. (See Supplemental file 6).

Direct-to-patient promotional claims

Clinics advertised their procedures on their websites and made claims such as *"This is a brand-new procedure that delivers clinically proven results, time after time"* (Belvedere Clinic), that they offer alternative *treatments "without the need for invasive or major surgery"* (Pall Mall Medical) and *"Our private hospital is one of few places in the UK offering regenerative therapy with stem cells - a new and rapidly expanding branch of medicine made famous by celebrity users such as actors John Cleese, Charlie Sheen and sports stars including Cristiano Ronaldo, Luis Suarez, Rafael Nadal and martial arts commentator Joe Rogan"* (Pall Mall Medical). On the website of one clinic, it was explained that the "*current problem with regenerative orthopaedic studies is that the power of evidence is mostly not the strongest"* and recommended discussion with a doctor whenever a treatment is offered (Algocells). (See Supplemental file 4.)

DISCUSSION

This study characterises the direct-to-patient portrayal of stem cell therapies by UK stem cell clinics, and evaluates its potential effect on prospective patients. 19 clinics were identified, of which 15 were judged to potentially violate patient autonomy and risk causing them harm, through the provision of misleading medical information. Of the 15 problematic clinics, 9 were judged to carry a moderate risk, and 6 a high risk, of misleading patients. These are notable findings, with strong implications for regulatory authorities.

UK stem cell clinics have been surveyed in recent years by other researchers. An international study published in 2016 reported the existence of 12 such clinics [1], and a 2019 report referred to 71 UK clinics [25]. However, the latter survey included platelet rich plasma (PRP) therapies, a medical treatment that seeks to use blood factors to promote tissue repair. PRP therapy is not a true stem cell therapy, and therefore clinics offering only this type of treatment were excluded from the present study. Thus, in terms of the number of clinics in the UK offering stem cell therapies, it is apparent that this has increased by 58% since 2016. This is a substantial level of growth which is of itself of ethical relevance, since the greater the quantity of provision of (often questionable) stem cell therapies, the higher will be the numbers of patients at risk from the sort of misinformation that our study indicates is commonplace in this commercial domain.

Of the 15 ethically problematic clinics, the most common issue identified was a trivialisation of the risks associated with the therapies on offer, or a failure to refer to any risks at all. Other key issues we discovered included inaccurate or non-evidenced claims of treatment effectiveness, unwarranted claims of a curative outcome, and the use of exaggerated language to promote therapies. In addition to these positively misleading forms of direct-to-patient portrayal, many clinics failed to provide key information that would be important for informed consent. For example, only 2 (11%) of the 19 clinics surveyed provided any of their clinical outcomes data, and where such information was presented on the websites it generally lacked rigour or clarity, and it was not possible to independently verify their data.

Across the clinics surveyed in this study, it was noticeable that stem cell therapies were offered for a remarkably (indeed implausibly) wide range of disorders. The treated conditions ranged from the most serious to the relatively trivial, including orthopaedic and musculoskeletal disorders, multiple sclerosis, erectile dysfunction, alopecia, and various dermatological conditions (including simply the effects of ageing). To date, there are 8,427 ongoing clinical trials investigating stem cell-based treatments worldwide [32], but for the vast majority of the conditions treated by the UK clinics, there presently exists insufficient evidence to support the effectiveness of stem cell therapies [28,33,34]. Compared to the situation that prevails in several other nations [7,14], UK-based clinics appear to be more careful in how they present themselves, with none making outright promises with regards to health outcomes. However, the fact that UK clinics are offering treatments lacking proven efficacy (or safety) is inherently troubling.

By informally surveying the literature, it can be readily observed that most of the evidence supporting the efficacy of stem cell therapies comes from underpowered small-scale studies, most of which are not double-blind placebo-controlled trials. While being careful not to guarantee clinical success, several UK clinics present such published work on their websites as evidence of effectiveness, a practice that this study discovered to be commonplace. It cannot be expected that laypeople will be able to properly evaluate such claims and recognise the weak and putative nature of most of these studies. Thus, we consider that the presentation of such published work from respectable academic journals on clinics' websites is highly likely to mislead potential patients.

In terms of risk, the websites of 12 (63%) of the surveyed clinics did not include any indication that their procedures may carry a risk of adverse effects. Of the clinics whose websites did allude to the

possibility of side-effects, none made any mention of the more severe adverse reactions to stem cell injections that have been documented in the medical literature, including life-threatening and long-term effects (for example, autoimmune reactions, loss of vision, pulmonary embolism, tumour formation) [14]. Mention of dangers was largely limited to the risks associated with the basic clinical procedures employed as part of the overall therapy, such as general anaesthesia and methods for administering therapies. For example, one clinic offering stem cell therapy for knee damage stated that the risk of adverse effects is *"the same as those for routine hip or knee arthroscopy operations"* and that there is only a *"theoretical risk for infection".* In addition to failing to convey the more serious risks associated with stem cells per se, such descriptions are ethically problematic in that they were rarely accompanied on any clinic's website by clear information on the effectiveness (or otherwise) of the promoted therapy. Thus, the potential patient is not able to make a risk vs benefit judgement. The risk of infection after arthroscopy is low but non-trivial, ranging up to 0.4%. If a stem cell therapy for knee damage has a very low proven effectiveness, then even a low level of risk may be unacceptable. A related concern is that none of the clinics present alternatives to the proposed stem cell therapy. If a conventional procedure is available with better effectiveness than has been demonstrated for the stem cell approach and carries the same (or lower) level of risk, then this may well be a better option. In all cases, the potential patient ought to be furnished with full information on risk, effectiveness, and alternative treatments, in order to attain their informed consent. The fact that this is not happening in most clinics' websites, as revealed by the present study, is ethically unacceptable.

Another issue with the clinics' websites was one of general presentational approach. The study discovered that most clinics employed exaggerated language, and selected examples of success that were more suited to consumer marketing than to the serious matter of conveying clinical information to potential patients. Examples of exaggerated language include the use of the term *"evidence-based"* and claims such as (a stem cell therapy can) *"potentially treat your condition and avoid major surgery",* when in fact the actual supporting evidence is weak and contentious. Examples of what we consider to be an inappropriate 'marketing' based approach include the use of anecdotal accounts of 'success stories', sometimes featuring celebrities. It seems likely that this kind of approach to 'informing' potential patients is liable to mislead, and thus risks violating patient autonomy.

To have given their informed consent, it is essential that patients have been presented with sufficient and appropriate information to understand the likely benefits and risks associated with the proposed treatment, and from the above discussion it should be clear that many of the clinics fail in this regard. However, informed consent requires more than an understanding of benefits and risks; it also requires that patients are provided with an understandable account of the causal mechanisms underlying the therapy, insofar as these have been elucidated by medical science [35]. This study discovered that most clinics failed to explain, apart from a general or theoretical description of how stem cells work, the mechanism of their therapies. This failure to convey information on physiological mechanism further compounds the violation of patient autonomy arising from the misleading and partial information that is provided by many of the clinics' websites.

This study has some limitations, including the fact that it was limited to the information provided by clinics on their websites. Clinics do of course have further opportunities to provide patients with information, in particular during in-person consultations. This may include important effectiveness and safety data of the sort that the present study found to be lacking in many clinics' websites. Nevertheless, the potential impact of clinics' flawed website information is of substantial importance, since this will be the initial source of information that the potential patient is exposed to. Even where misleading information is subsequently corrected via a medical consultation, there still remains a number of significant ethical concerns. To get to the consultation stage only to then realise that the website information was unreliable is likely to entail a waste of the patient's time. Worse, if the patient had high hopes from the website's information and these hopes are

subsequently dashed, it may inflict psychological harm on the patient. It may also be more likely for patients who are desperately seeking treatment to be misled, especially when treatment options are approached as a 'last hope' or with a 'nothing to lose' attitude [36]. The likelihood for patients to be misled by direct-to-patient website information may therefore be higher for these subgroups. Further, it is possible that some patients may become convinced from a clinic's website that a stem cell therapy is what they need, such that subsequent (more realistic) information may fail to change their minds.

Another limitation of the study is that it is a snapshot of the period in which the data were collected. As time moves on, new regulations may emerge, some existing clinics may cease operations, and new ones may open; thus the landscape may change significantly over time. This is an unavoidable limitation of such survey-based research.

The scope of this study has been limited to the UK. A more geographically extensive study would be ideal, as it would permit detailed comparisons between the situation in the UK and elsewhere in the World. However, the exclusive focus on the UK has been necessary in order both to maintain focus and to constrain the work within a manageable scale. While several studies (some of which are referred to within this paper) have been published considering the situation beyond the UK, it would be beyond the scope of the present paper to analyse and synthesise these findings in detail.

The foregoing discussion is premised on the view that failing to provide full and accurate information and evidence on clinic websites is prima facie unethical. This premise may appear self-evidently correct to many (including the present authors), however it not entirely uncontentious. In opposition to this perspective, it can be argued that a clinic's website is not really the place for full and complete information on the nature and frequency of side effects potentially associated with a treatment. This contrasting position does not hold that such information is unnecessary per se; rather, it presumes that the necessary information will be provided outside the website, when the potential client engages further with the clinic. In counterpoint, it can be argued that the modern website is the ideal place to reposit all relevant information and links – the process of doing so is not unduly onerous, and in general provision of full information to customers is now commonplace on the Internet. On this view it would be unethical to omit such material, as it would at a minimum be tantamount to negligence, and at worst it could be designed to mislead.

Future research could clarify the degree to which patients are actually misled by the sort of problematic websites discovered in this study. Such research could also explore the events that happen beyond the websites, when potential patients actively engage with clinics. Ideally, the medical consultation process would be investigated. A better understanding of the *modi operandi* of the UK's private stem cell clinics would provide valuable guidance for legislators to regulate appropriately, such that patients are no longer at risk of having their autonomy undermined by the sort of misleading information that, as this study demonstrates, presently dominates the websites of UK stem cell clinics.

CONCLUSIONS

This study describes how commercial clinics in the UK portray stem cell therapies on their websites, and identifies a number of serious issues with the information provided to potential patients by a majority of clinics. This raises important ethical concerns around patient autonomy and informed consent. While it is possible that full information will duly be provided to patients, i.e. during in-person consultations, the initial provision of misleading information via websites retains the potential to impinge upon patient autonomy and cause harm. These are important findings, with strong implications in terms of regulatory action in the UK.

Summary Points

- Unproven stem cell treatments are available in the UK for a wide range of indications.
- The online direct-to-consumer portrayal of stem cell clinics was misleading in a majority of cases.
- A number of clinics portrayed their treatments as innovative and safe alternatives to proven, conventional treatments.
- Underpowered studies were used as "evidence" for unproven procedures; this may be highly difficult for laypeople to evaluate.
- Clinics depicted their treatments as generally safe, yet permanent disabilities and fatalities have occurred, and the safety of more invasive procedures was downplayed.
- Questionable marketing tactics were used, including the inclusion of celebrity patient testimonials.
- The cost of such treatments is significant.
- Significant ethical issues are raised when conventional treatments are delayed for unproven alternatives, especially if in the meantime disease progression occurs.
- Informed consent may be affected if they are misled through clinics' online portrayal and thus patient autonomy may be impaired.
- Regulatory action is needed to ensure patient safety.

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SUPPLEMENTAL FILES

Supplemental file 1

Conditions treated	
Indication	**Number (and percentage) of clinics**
Orthopaedic/ musculoskeletal	15 (60%)
Alopecia	5 (20%)
Dermatological (cosmetic)	3 (12%)
Erectile dysfunction	1 (4%)
Multiple sclerosis	1 (4%)
TOTAL (note that some clinics offered treatments for multiple conditions)	25

Supplemental file 2

Source of stem cells	
Tissue type	**Number (and percentage)**
Adipose	11 (44%)
Bone marrow	10 (40%)
Blood	2 (8%)
Not specified	2 (8%)
TOTAL (note that some clinics used more than one source)	25

Supplemental file 3 - Stem cell clinics – general qualitative data.

Clinic (& website)	Conditions	Type and source of stem cells	Administration technique	Cell number	Costs
Algocells **https://www.algocells.com/**	Rotator cuff tears, arthritis of the shoulder joint, thoracic outlet syndrome, labral tears or degeneration, rotator cuff tendonitis and tendinosis, AC joint separation, recurrent shoulder dislocations, and other orthopaedic conditions of hand, wrist, hip, knee, foot, ankle and spine	Mesenchymal stem cells (from bone marrow)	Injection into affected site, not further specified	No info	£7,000 +
Belvedere Clinic **https://belvedereclinic.co.uk/stem-cell-hair-restoration/**	"Early" hair loss, not further specified	Mesenchymal stem cells (adipose-derived)	Injection, not further specified	No info	No info
HCA Healthcare at London Bridge Hospital **https://www.hcahealthcare.co.uk/our-services/treatments/stem-cell-treatment-for-ms**	Multiple sclerosis	Haematopoietic stem cells (from bone marrow)	Transplantation into bone marrow	No info	No info
HR Orthopaedics **https://www.hrorthopaedics.co.uk/hips/stem-cell-therapy/**	For hip & knee problems, not further specified	Mesenchymal stem cells (from bone marrow)	Injection with arthroscopy	No info	No info
International Andrology **https://london-andrology.co.uk/news/stem-cell-treatment-for-erectile-dysfunction/**	Erectile dysfunction	Mesenchymal stem cells (from blood, bone marrow and adipose-derived)	Not specified	No info	No info
London Bridge Plastic Surgery & Aesthetic Clinic **https://www.lbps.co.uk/stem-cell-therapy/**	Anti-ageing skin care, wrinkle reducing filler, body shaping, alopecia areata, joint osteoarthritis	Mesenchymal stem cells (adipose-derived)	Injection subcutaneous or into affected site	No info	No info
London Spine Unit **https://www.londonspine.com/treatments/spinal-stem-cell-therapy/**	Variety of orthopaedic/musculoskeletal conditions	Not specified	Not specified	No info	No info
London Stem Cell Centre **https://londonstemcellcentre.com/**	Hip and knee conditions, not further specified	Mesenchymal stem cells (from blood/bone marrow)	Injection with arthroscopy	No info	No info
Manchester Hip Clinic, Spire Hospital **http://manchesterhipclinic.com/stem-cell-therapy/**	Variety of orthopaedic/musculoskeletal conditions	Mesenchymal stem cells (from bone marrow)	Injection with arthroscopy	No info	No info
Manchester Hip Surgeons (Manchester Knee Surgeons) **https://www.manchesterhipsurgeons.co.uk/stem-cell-like-therapy-hip-surgery-manchester-cheshire.html** **https://www.manchesterkneesurgeons.co.uk/stem-cell-like-therapy-knee-surgery-manchester-cheshire.html**	Hip and knee conditions (incl. arthritis), not further specified	Adipose derived mesenchymal stem cells, mesenchymal stem cells	Injection, not further specified	No info	No info
Medica Stem Cells Pain Management Clinic **https://medicastemcells.com/**	Joint injuries, sports injury, managing symptoms of arthritis, osteoarthritis or any other degenerative condition of the joints, cosmetic applications	Mesenchymal stem cells (from bone marrow and adipose-derived)	Injection into affected site, not further specified	3500	No info
Olivier Amar (plastic surgeon) **https://olivieramar.co.uk/news/stem-cell-treatment-for-hair-loss-discover-the-revolutionary-one-off-treatment-for- thinning-hair-and-alopecia/**	Hair loss, not further specified	Mesenchymal stem cells (adipose-derived)	Not specified	No info	No info
Pall Mall Medical **https://www.pallmallmedical.co.uk/consultants-and-specialists/our-consultants-and-specialists/regenerative-medicine**	Variety of orthopaedic/musculoskeletal conditions	Mesenchymal stem cells (from bone marrow)	Injection with or without arthroscopy	No info	£6195-7795
Rejuvence Clinic **https://www.rejuvenceclinic.co.uk/**	Wrinkles, scars, joint issues (not further specified), hair loss (not further specified)	Mesenchymal stem cells (adipose derived)	Injection, not further specified	No info	£995-1250

Spire Cambridge Lea Hospital **https://www.spirehealthcare.com/spire-cambridge-lea-hospital/treatments/a- z/stem-cell-therapy/**	Damaged joint tissues and structures, possibly arthritis and cartilage regeneration in the knees and hip	Mesenchymal stem cells (source not specified)	Injection into affected site with arthroscopy	No info	No info
The Harley Street Hospital **https://theharleystreethospital.co.uk/regenerative-and-stem-cell-service/**	Osteoarthritis, joint and spine pain from worn discs and ligaments	Mesenchymal stem cells (adipose-derived)	Injection, not further specified	No info	No info
The Manchester Stem Cell Centre **https://www.manchesterstemcellcentre.co.uk /regenerate/stem-cell-therapy/**	Arthritis (not further specified)	Mesenchymal stem cells (from blood, bone marrow and adipose-derived)	Injection with arthroscopy	No info	No info
The Regenerative Clinic **https://www.theregenerativeclinic.co.uk/**	Osteoarthritis of the joints, rotator cuff tears, cartilage tears in the knee, lower back pain, tennis elbow, plantar fasciitis, tendon tears	Mesenchymal stem cells (adipose-derived): "Lipogems"	Injection into affected site, not further specified	5000	No info
Westminster Clinic **https://www.westminsterclinic.co.uk/hair-transplant-studies/stemvita/**	Hair loss (alopecia areata, frontal fibrosing alopecia), Lyme disease, joint arthritis	Mesenchymal stem cells (adipose-derived)	Not specified	No info	No info

Supplemental file 4 - Other direct-to-consumer portrayal

Name of clinic	Was treatment effectiveness claimed?	Other marketing, including exaggerated language used and claims not covered by other variables	Links to where data was gathered from, if not from website in table 1 (applies to table 1-4)
Algocells	No	Patients "(..) prefer our stem cell treatments and platelet-rich plasma therapy over a risky operation", testimonials advertised, video linked claiming "Ferrari team driver Martin Fuentes chooses Regenexx over meniscus surgery", "Key benefit: Avoiding surgery", “current problem with regenerative orthopaedic studies is that the power of evidence is mostly not the strongest"	
Belvedere Clinic	No	"This is a brand new procedure that delivers clinically proven results, time after time." "This is the latest and most advanced hair restoration treatment in the world today for early stage hair loss."	n/a
HCA Healthcare at London Bridge Hospital	No	Clinic has "accumulated enough convincing clinical data to suggest that HSCT may have a sustained benefit in halting the progression of MS and in some cases reversing disability."	n/a
HR Orthopaedics	No, but "early results of this procedure are very encouraging in this group of patients with early degenerative change"	"Unfortunately, biological therapies are not an established treatment when advanced arthritis is present. Once there is full thickness loss of cartilage in the joint, the results of biological therapies are not predictable and it may be better to consider more established treatments such as hip or knee joint replacement surgery."	n/a
International Andrology	No, "stem cell therapy is still experimental"	n/a	n/a
London Bridge Plastic Surgery & Aesthetic Clinic	Expect "improvement of skin texture" and "thickness of	Testimonials and Trustpilot score shown on website	n/a

	subcutaneous collagen improves"		
London Spine Unit	No	n/a	n/a
London Stem Cell Centre	No, "relatively new procedure"	n/a	n/a
Manchester Hip Clinic, Spire Hospital	No	"Stem Cell therapy is a relatively new procedure, however, extensive work has been carried out in both animal and human clinical studies"	n/a
Manchester Hip Surgeons (Manchester Knee Surgeons)	No	Patient testimonials and links to doctor rating websites offered under "clinical outcomes" tab	n/a
Medica Stem Cells Pain Management Clinic	No	Testimonials advertised	https://medicastemcells.com/blog/ https://medicastemcells.com/testimonials/
Olivier Amar (plastic surgeon)	Claimed that "All patients saw an average of 23 per cent additional hair growth with up to 53 per cent increase in the number of hairs within six months." in clinical trial, could not be verified	"Kerastem has successfully completed the STYLE Trial, a randomized double blind, placebo-controlled Phase 2 clinical trial for the US FDA and the Phase 3 trial is in design. The Kerastem treatment is also CE approved in Europe and is approved by the Korean and Chinese regulators.", "Reverse hair loss"	n/a
Pall Mall Medical	"Patients usually demonstrate a rapid and progressive improvement in pain and function by 3- 6 months"	"Don't wait to feel great!" "Our private hospital is one of few places in the UK offering regenerative therapy with stem cells - a new and rapidly expanding branch of medicine made famous by celebrity users such as actors John Cleese, Charlie Sheen and sports stars including Cristiano Ronaldo, Luis Suarez, Rafael Nadal and martial arts commentator Joe Rogan."	n/a
Rejuvence Clinic	No	n/a	n/a
Spire Cambridge Lea Hospital	No	n/a	n/a
The Harley Street Hospital	No	n/a	n/a
The Manchester Stem Cell Centre	No	"Our evidence based biological treatments will help potentially treat your condition and avoid major surgery" "We successfully manage and treat (…)" Patient testimonials offered on website.	n/a
The Regenerative Clinic	Effectiveness not guaranteed	Lipogems are FDA approved	https://www.theregenerativeclinic.co.uk/evidence/one-year-knee-outcome-vas-and-oks-results-of-patients-treated-with-lipogem-treatment-at-the-regenerative-clinic-uk/ https://www.theregenerativeclinic.co.uk/frequently-asked-questions/ https://www.theregenerativeclinic.co.uk/clinical-evidence/
Westminster Clinic	No	"StemVita is a professional, reputable stem cell treatment protocol, backed by science, dedicated to pursuing the highest standards of stem cell research" "Where StemVita is different, is that their protocols ensure a documented quantity of living stem cells. Other clinics who are claiming to offer stem cell treatments, use what is known as a "blind protocol.""	n/a

Supplemental file 5 - Transparency data

Name of clinic	Was outcome data provided?	Number of patients treated	Were clinical trials linked?	Was curative potential of the procedure claimed?
Algocells	Yes, based on self-reported data	Not provided	No, but claim that confidence in regenerative orthopaedic is "based on sound knowledge, research, training and experience"	Not mentioned
Belvedere Clinic	No	Not provided	No	Not mentioned
HCA Healthcare at London Bridge Hospital	No	Not provided	No	Possibly: 70% chance of stability, if successful patients may become MS drug free after 3 months
HR Orthopaedics	No	Not provided	No	No, "to potentially delay the need for joint replacement surgery"
International Andrology	No	Not provided	No	If successful, "permanent symptomatic ED treatment"
London Bridge Plastic Surgery & Aesthetic Clinic	No	Not provided	No	Not mentioned, but possible results are presented under "What to expect?"
London Spine Unit	No	Not provided	No, clinical trials are mentioned but not named or linked	No, but described as regenerative medicine
London Stem Cell Centre	No	Not provided	No	Not mentioned
Manchester Hip Clinic, Spire Hospital	No	Not provided	No	Not mentioned
Manchester Hip Surgeons (Manchester Knee Surgeons)	No	Not provided	No, "There is a general lack of data about the long-term effects of stem cell-like therapy as it is a newer procedure and represents a newer form of treatment."	Not mentioned
Medica Stem Cells Pain Management Clinic	No	3500	Yes, but not specific to the conditions procedures are offered for	Not guaranteed, multiple treatments may be needed
Olivier Amar (plastic surgeon)	No	Not provided	Yes, but only a phase II clinical trial was finished	In patients without other medical conditions results "expected" to be permanent
Pall Mall Medical	No	Not provided	No	Not mentioned
Rejuvence Clinic	No	Not provided	No	Not mentioned
Spire Cambridge Lea Hospital	No	Not provided	No	Not mentioned
The Harley Street Hospital	No	Not provided	No	Not mentioned
The Manchester Stem Cell Centre	No	Not provided	No, results of some clinical studies mentioned but not named or linked	Not mentioned
The Regenerative Clinic	Success rate >80%, based on self reported data	5000	Yes, but insufficient to support their treatments	Pain reduction 3- and 6-months post-injection but not maintained at 12-month mark. No claim it cures from pain
Westminster Clinic	No	Not provided	No, but claim that "It is an evidence-based treatment that are proven to benefit patients, using both peer reviewed studies and in house protocols to ensure a consistent quality product."	Not mentioned

Supplemental file 6 - Safety data

Name of Clinic(s) and Location(s)	Risks, including claim that procedure has no risk and side effects	Were contraindications or eligibility requirements mentioned?	Was it recommended that the treatment is discussed with a GP or was a referral required?	Was access to patient records required?
Algocells	Not mentioned	No	Not mentioned	Yes, MRI required
Belvedere Clinic	Not mentioned	No	Not mentioned	Not mentioned
HCA Healthcare at London Bridge Hospital	Not mentioned	Yes, patients must be aged 18-65 and disease modifying drugs must have not worked after 6 months	Not mentioned, but referral by consultant neurologist or GP required	Not mentioned
HR Orthopaedics	Not mentioned	No	Not mentioned	Not mentioned
International Andrology	Not mentioned	No	Not mentioned	Not mentioned
London Bridge Plastic Surgery & Aesthetic Clinic	Not mentioned	No	Not mentioned	Not mentioned
London Spine Unit	Not mentioned	No	Not mentioned	Not mentioned
London Stem Cell Centre	Risks "same as those for routine hip or knee arthroscopy operations" and risk of infection	No	Referral from GP or practitioner required	Not mentioned
Manchester Hip Clinic, Spire Hospital	Not mentioned	No	Not mentioned	Not mentioned
Manchester Hip Surgeons (Manchester Knee Surgeons)	"Generally safe procedure with minimal complications", risk of infection, immune reaction and general anaesthesia	No	Not mentioned	Not mentioned
Medica Stem Cells Pain Management Clinic	Risk of infection and mild pain but also claim that "Safe procedures with No risk of rejection and No communicable disease transmission"	No	Not mentioned	Not mentioned
Olivier Amar (plastic surgeon)	Not mentioned	No	Not mentioned	Not mentioned
Pall Mall Medical	Risk of infection and risk same for routine hip or knee arthroscopy	No	Not mentioned	Not mentioned
Rejuvence Clinic	Not mentioned	No	Not mentioned	Not mentioned
Spire Cambridge Lea Hospital	Risks are "same as those for routine hip or knee arthroscopy operations", "theoretical risk for infection"	No	Not mentioned	Not mentioned
The Harley Street Hospital	Not mentioned	No	Not mentioned	Not mentioned
The Manchester Stem Cell Centre	Risks "same as those for routine hip or knee arthroscopy operations" and risk of infection. No risk of rejection due to use of own cells	No	Not mentioned	Not mentioned
The Regenerative Clinic	No serious side effects reported	Steroid injections in last 3 months	Not mentioned, no referral required	Not mentioned
Westminster Clinic	Not mentioned	No	Not mentioned	Not mentioned