

# Stem Cell Clinics Online: The Direct-to-Consumer Portrayal of Stem Cell Medicine

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Despite the immature state of stem cell medicine, patients are seeking and accessing putative stem cell therapies in an “early market” in which direct-to-consumer advertising via the internet likely plays an important role. We analyzed stem cell clinic websites and appraised the relevant published clinical evidence of stem cell therapies to address three questions about the direct-to-consumer portrayal of stem cell medicine in this early market: What sorts of therapies are being offered? How are they portrayed? Is there clinical evidence to support the use of these therapies? We found that the portrayal of stem cell medicine on provider websites is optimistic and unsubstantiated by peer-reviewed literature.

Few areas of science have generated as much public interest as stem cell research. Advances in stem cell medicine promise novel, cell-based therapies for many diseases in which conventional medicine is ineffective (Bongso and Richards, 2004; Mimeault et al., 2007). But numerous scientific questions remain unanswered, and scientists generally do not recommend these therapies for general access (Braude et al., 2005; Coutts and Keirstead, 2008; Daley et al., 2003; Lassmann, 2005). Nonetheless, patients are accessing putative therapies from privately operated clinics across the world (Lang, 2007; Bodeen, 2008; Baker, 2005; Enserink, 2006). Beike Biotech, a Chinese clinic specializing in neurologic disorders, claims to have treated over 3000 patients at its 24 hospital clinics in China (McCullough, 2008). ACT, from Turks and Caicos, and Emcell, from Ukraine, claim to have treated over 700 and over 2000 patients, respectively (see Table S1 available online). Many of these clinics advertise directly to patients via the internet. This mode of communication is an important means of reaching patients, with 8 million Americans searching for health informa-

tion on the internet on any given day (Fox, 2006). Indeed, given the uncertain regulatory status of stem cell therapies, the internet may be the *only* means by which these clinics are able to reach patients in North America.

To characterize the direct-to-consumer portrayal of stem cell medicine, we performed a content analysis of websites obtained by a Google ([www.google.com](http://www.google.com)) search for “stem cell therapy” or “treatment” in August, 2007 (Weare and Lin, 2000; Zhang, 2005). This “snapshot” of online stem cell clinics returned 19 websites claiming the use of stem cells for the treatment of disease (detailed search and analysis procedures are provided in the Supplemental Data; included websites are listed in Table S1). In addition to treating disease, eight (42%) of these sites treated otherwise healthy patients for cosmesis (three sites, 16%) or health enhancement (eight sites, 42%). Importantly, these clinics self-reported the administration of stem cells. Clinics’ uses of the “stem cell” label were taken at face value. Despite adopting this label in the following analysis, we have no knowledge of the true “stemness” of clinics’ interventions. Indeed, given the heterogeneity of cell populations and scientists’ limited abilities to sort them, it is likely that “stem cell therapies” contain numerous other cells in addition to stem cells, to the extent that they contain stem cells at all. This caveat applies equally to therapies promoted to consumers by stem cell clinics, and to therapies now under investigation in clinical trials.

What therapies are being offered? Adult autologous stem cells were most commonly provided (9 sites, 47%), followed by fetal stem cells, cord blood stem cells, and embryonic stem cells (see Table 1). Stem cells were most often obtained from the patient’s bone marrow (7 sites, 37%) and/or peripheral blood (5 sites,

26%), although some sites obtained stem cells from patient fat, blood or marrow donors, aborted fetuses, patient’s skin, animal tissues, and human placental tissue. Treatments were most commonly administered by infusion into cerebrospinal fluid (6 sites, 32%). Peripheral intravenous administration was common as well (6 sites, 32%). Four sites (21%) obtained access to deep body cavities. For example, [www.nrrfr.com](http://www.nrrfr.com) and [www.puhuachina.com](http://www.puhuachina.com) both advertised stem cells transplanted by injection deep into the brain via craniotomy or by injection into the spinal cord parenchyma via laminectomy. Although a wide range of treatments are represented, the most frequently provided treatment was autologous stem cells obtained from bone marrow or peripheral blood reintroduced into the body by lumbar puncture or IV infusion.

Numerous indications for treatment were observed, representing diverse categories ranging from neurologic disease to allergies (indications are listed in Table S2). The most commonly mentioned categories were neurologic and cardiovascular disease, mentioned by 16 (84%), and 12 (63%) sites, respectively. Among the neurologic diseases, multiple sclerosis (MS), stroke, Parkinson’s disease, spinal cord injury (SCI), and Alzheimer’s disease were most common. Cardiovascular indications were typically ischemic heart disease related. Seven sites (37%) treated congenital diseases, mainly cerebral palsy, autism, and Duchenne muscular dystrophy. Regarding risks and benefits, all websites (19, 100%) advertised improvement in disease state as a benefit of therapy. In contrast, most (14, 74%) sites did not mention particular risks. A few sites mentioned procedural risks or other risks, such as nonspecific fever or tingling.

How are stem cell therapies portrayed? This question called for the

**Table 1. Nature of Therapies Offered across Surveyed Websites**

Stem Cell Type	Frequency	%
Adult, autologous	9	47
Fetal	6	32
Cord blood	4	21
Embryonic	2	11
Adult, allogeneic	2	11
Adjuncts	0	0
Unspecified	0	0
Stem Cell Source	Frequency	%
Bone marrow	7	37
Blood or marrow donors	5	26
Peripheral blood	5	26
Fetuses	4	21
Fat	2	11
Unspecified	2	11
Other	3	16
Transplantation Procedure	Frequency	%
Intrathecal, into the CSF	6	32
Intravenous	6	32
Subcutaneous or intramuscular	4	21
Surgical transplantation	4	21
Catheterization of deep body vessels	3	16
By mouth	1	5
Topical	1	5

We extracted information from each clinic's website on the stem cell types provided, the source of these stem cells, and on each clinic's transplantation procedure. Frequencies do not sum to n = 19 or 100% because several sites fitted into more than one category per concept. Stem cell source is patient's own unless otherwise noted. The stem cell type denoted "fetal" was composed of neural cells, hematopoietic cells, olfactory ensheathing cells, placental cells, and amniotic cells harvested from aborted fetuses. "Other" stem cell sources include animal sources (shark and sheep) and skin stem cells.

measurement of holistic impressions about each site's portrayal of the indications, risks, benefits, and readiness of the therapy offered (See [Supplemental Results](#) for examples illustrating each impression). Indications for treatment were scored for determinacy, i.e., the extent to which indications were well bounded and specific, as opposed to open ended or vague. Indications scored *very* or *somewhat unclear or indeterminate* in 68% of sites (see [Figure 1A](#)). The impression of indeterminacy was typically generated by the presence of catch-all categories like aging, "increased feelings of energy," and by long lists of diseases spanning numerous clinical categories. Indeed, indications on 12 of 19 sites (63%) spanned 4 or more broad disease categories.

Portrayals of risks and benefits were scored for relevance, defined as the

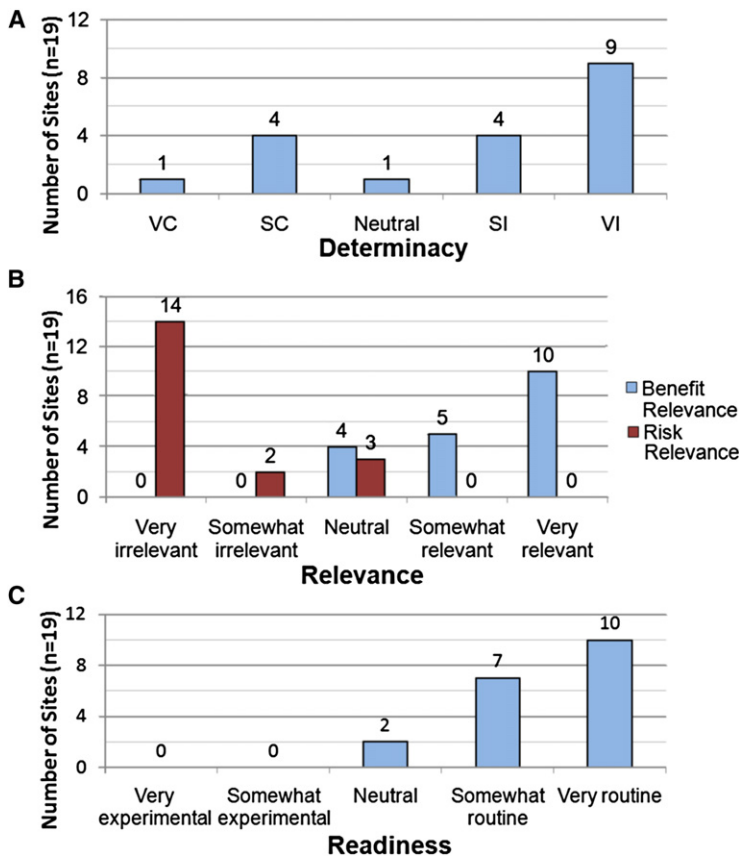
extent to which the risk or benefit is likely in frequency or dramatic in magnitude (see [Figure 1B](#)). Seventy-nine percent of websites portrayed benefits as *somewhat* or *very relevant*. In contrast, websites' risk portrayals scored as *very irrelevant* in the majority (14, 74%) of sites. This asymmetric portrayal of relevance of risks and benefits contributed to an overall impression that therapies were safe and effective. Finally, websites were scored for the readiness of their therapies for public access. Ten (53%) sites scored at the "very" positive end of the five point scale for readiness (see [Figure 1C](#)). This impression was encountered when websites appeared to have accumulated copious experience with the therapy, signifying a degree of expertise and optimization. Sites also established credibility by advertising the "latest medical equipment and technology" and by

featuring publications, news articles, patents, and numerous patient endorsements, giving rise to impressions of readiness.

These results demonstrate a general portrayal of therapy as safe and effective for a broad range of diseases in the context of routine clinical use. However, a few websites resisted the general trend. For example, indications for treatment with autologous bone-marrow-derived cells were clear and well bounded in [www.vescell.com](http://www.vescell.com). This site only treated ischemic heart disease refractory to conventional therapy. As another example, the portrayal of benefits in [www.nrrfr.com](http://www.nrrfr.com) was unique. This clinic was guarded in describing the benefits patients would obtain. Indeed, reports of unsuccessful treatment could be found on its site.

We next asked whether there was peer-reviewed clinical evidence to support the use of these therapies in a routine clinical setting. We performed a PubMed (<http://www.ncbi.nlm.nih.gov>) search in July 2008 for primary human studies reporting the clinical effects of *any* stem cell therapies for indications mentioned ten or more times in our top two disease categories, i.e., neurologic and cardiovascular diseases. Targeted indications were as follows: MS, Parkinson's disease, stroke, Alzheimer's disease, and SCI. Heart disease also appeared frequently among provider websites. However, our search for evidence related to heart disease was limited to systematic reviews of RCTs evaluating autologous hematopoietic stem cell transplantation (AHSCT) for acute myocardial infarction (AMI). Forty-one studies and four systematic reviews were appraised using evidence-based medicine (EBM) principles (Sackett et al., 1996; Guyatt et al., 2008) (see [Supplemental Procedures](#); [Table S3](#) summarizes the number of records screened, included, and excluded; and [Tables S4](#) and [S5](#) contain data extracted from each included study). In describing the current state of stem cell medicine, we caution against drawing conclusions about the potential of stem cell medicine from our analysis. Our purpose is to evaluate the direct-to-consumer portrayal of stem cell medicine.

Studies reporting a range of non-AHSCT stem cell therapies for spinal cord injury and stroke were included. For example, two studies treated stroke with



**Figure 1. Impressions Conveyed by Websites' Portrayals of Stem Cell Therapies**

(A–C) The following holistic impressions about each site's portrayal of the indications, risks, benefits, and readiness of the therapy offered were measured: determinacy of indications (i.e., the extent to which indications were well bounded and specific, as opposed to open-ended or vague), relevance (i.e., the extent to which the risk or benefit is likely in frequency or dramatic in magnitude), and readiness (i.e., the extent to which the therapy is ready for general clinical access, as opposed to restricted access in the context of a trial protocol only). VC, very clear, bounded; SC, somewhat clear, bounded; SI, somewhat unclear, indeterminate; VI, very unclear, indeterminate.

NT2/D1 teratocarcinoma-derived neurons, and five studies treated SCI with olfactory ensheathing cells. These studies were generally of small size, low methodological quality (e.g., no control group), and uncertain, negative, or contradictory findings. AHSCT was employed by several studies treating SCI and stroke. Only one case report reported positive outcomes from the use of AHSCT for stroke. Regarding AHSCT for SCI, we found two unblinded, nonrandomized controlled trials with 36 and 48 patients. While the former found higher improvements in American Spinal Injury Association (ASIA) scores among treated patients versus controls, significance was tested within groups only. The latter did not report control outcomes. The evidence for stem cell therapies for SCI and stroke is generally underdeveloped.

We were unable to find any studies of stem cell therapy for Parkinson's disease. Notably, transplantation with fetal mesencephalon grafts containing dopamine neurons has been employed experimentally to treat Parkinson's disease since the late 1980s (Freed et al., 1990). These transplants may contain stem cells, and further trials are now underway (e.g., [ClinicalTrials.gov](http://ClinicalTrials.gov), 2008). However, the safety of the therapy is not certain (e.g., Olanow et al., 2003), and recent opinions suggest that much optimization work remains before the treatment can be recommended for clinical use (McKay and Kittappa, 2008; Suchowersky, 2008; Braak and Del Tredici, 2008; Snyder and Olanow, 2005). Similarly, we were unable to find a study of stem cell therapy for Alzheimer's disease.

Stem cell therapies have had a slightly longer history with MS. AHSCT for MS

has been employed in trials as early as 1997 (McAllister et al., 1997). Findings from one large case series suggest that AHSCT may have a role to play in slowing the progression of disease (Saccardi et al., 2006). However, clinical outcomes are variable and "not obviously better than the natural history of patients with multiple sclerosis" (Burt et al., 2007). This conclusion reflects a preponderance of noncomparative studies and substantial uncertainty in patient selection and conditioning techniques. Additionally, the MS trials included in our review employed myeloablative conditioning regimens, commonly the chemotherapy combination BEAM or total body irradiation, followed by cyclophosphamide. In contrast, immunoablation played no role in any therapy mentioned by our websites.

Finally, we considered four systematic reviews with meta-analyses for AHSCT to treat AMI (see [Supplemental Data and Table S5](#)). Reviewed studies were mostly RCTs of varying quality. Heterogeneity notwithstanding, all six reviews reported a small but statistically significant advantage in change in left ventricular ejection fraction (LVEF) among treated patients versus controls, with pooled point estimates among these reviews ranging from 2.88% to 3.46%. All four reviews also reported no increase in adverse events related to treatment. Thus, there is evidence that AHSCT for AMI is safe and, to a limited extent, efficacious. However, LVEF is a surrogate outcome, and whether the observed 2.88% to 3.46% higher improvement in LVEF leads to meaningful clinical/functional improvements, like decreased mortality, is uncertain.

For stem cell therapies for MS, Parkinson's disease, stroke, Alzheimer's disease, and SCI, we consider any treatment recommendation made on the basis of the reviewed evidence to be low grade (see Phillips et al., 2001). For AMI, evidence of physiologic improvements exists, but any treatment recommendation must be tempered by the limitations of small treatment effects and the use of physiologic outcomes. In any event, only [www.vescell.com](http://www.vescell.com) offered AHSCT exclusively for cardiologic indications. Eighty-four percent of websites advertised therapy for neurologic indications. We therefore find that the treatments offered on stem cell websites are generally unsupported by the clinical evidence.

In this study, we outlined the range of treatments being offered directly to consumers via the internet. Websites generally portrayed therapies as safe, effective, and ready for routine use in a wide variety of conditions. In contrast, the published clinical evidence is unable to support the use of these therapies for the routine treatment of disease. The direct-to-consumer portrayal of stem cell medicine is optimistic and unsupported by published evidence.

This finding might suggest that providers are making inaccurate claims in their direct-to-consumer promotional materials. Patients may not be receiving sufficient and appropriate information and may be shouldering inordinate risks. Clinics may also be contributing to public expectations that exceed what the field can reasonably achieve. However, this interpretation is subject to the following limitations: information available from websites may not be indicative of the information actually shared with patients during their clinical encounters; the aggregate data, collected from a heterogeneous group of clinics, cannot be used to evaluate the claims of any particular clinic; and finally, we do not test the accuracy of websites' claims directly by analyzing actual outcome data. We show, instead, that there is a lack of *high quality* evidence supporting stem cell clinics' claims. Even supposing that clinics have indeed observed successful recovery from chronic disease posttreatment, a lack of good evidence precludes a valid or precise inference that the observed improvement is attributable to the interventions. If, in fact, the interventions were not effective, then patients would have been subjected to inappropriate risk and financial burden. The average cost of a course of therapy among the four websites that mentioned costs was \$21,500, excluding travel and accommodation for patients and care givers. And examples of serious treatment side effects can be found (Dobkin et al., 2006). In conclusion, patients should be wary of claims made by stem cell clinics on the internet. The direct-to-consumer portrayal of stem cell medicine is overoptimistic given the

peer-review literature. More research is needed either to substantiate these clinics' claims or to develop stem cell therapies that actually work.

#### SUPPLEMENTAL DATA

The Supplemental Data include Supplemental Procedures, four boxes, five tables, Supplemental Results, and Supplemental References and can be found with this article online at [http://www.cellstemcell.com/supplemental/S1934-5909\(08\)00573-0](http://www.cellstemcell.com/supplemental/S1934-5909(08)00573-0).

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