

Tackling burden in ART: an integrated approach for medical staff

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ABSTRACT: Discontinuation is a problem in fertility clinics. Many couples discontinue assisted reproductive technologies (ART) without achieving a live birth for reasons other than poor prognosis or the cost of treatment. Discontinuation has been attributed to the burden of treatment. The causes of burden can be broadly classified according to whether they originate in the patient, clinic or treatment. Interventions to alleviate these burdens include provision of comprehensive educational material, screening to identify highly distressed patients, provision of tailored coping tools and improvements in the clinic environment and medical interventions. Practical interventions to reduce the different causes of burden in ART exist, but further development and evaluation of the efficacy of these interventions requires more precise definition of terms and theory. In this paper, we propose a general integrated approach to cover different perspectives in dealing with burden in ART clinics. We firstly describe the integrated approach and present common sources of burden. We then describe interventions that could help reduce the burden in ART. Our paper is aimed at fertility clinic staff because of their day-to-day involvement with patients. However, this discussion should also be relevant to companies that develop treatments and to psychosocial experts. Reducing the burden of treatment should lead to improved outcomes, namely better quality of life during treatment and lower discontinuation rates.

Key words: assisted reproductive technology / *in vitro* fertilization / psychological / discontinuation / psychosocial interventions

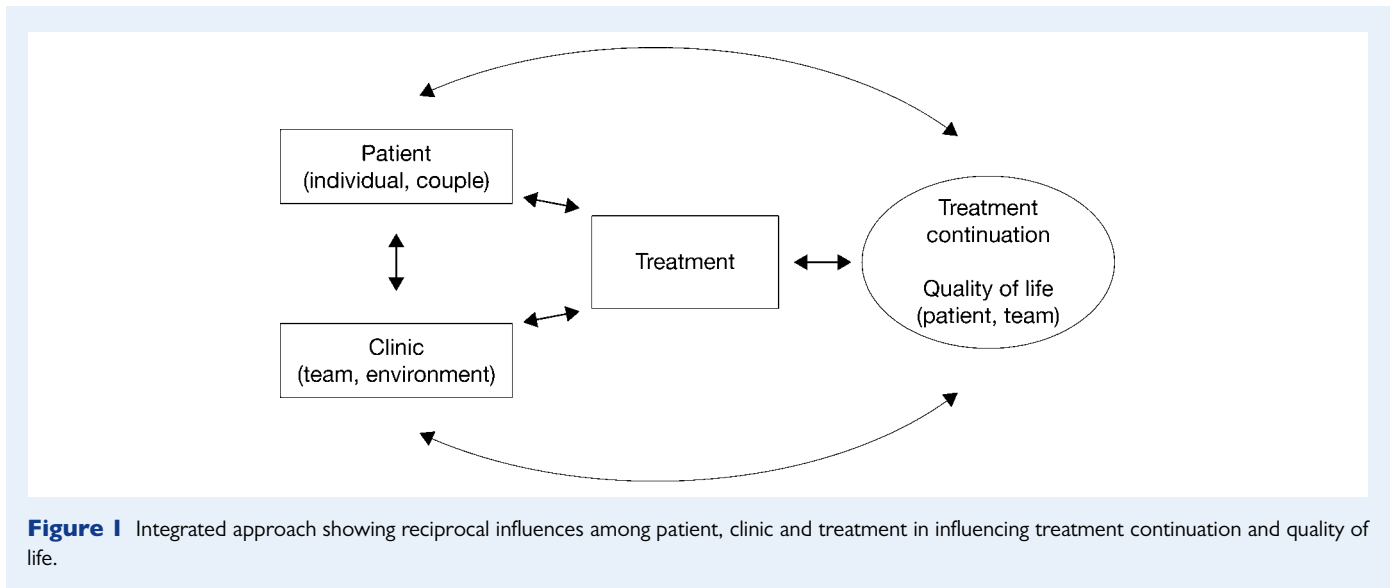
Introduction

Assisted reproductive technologies (ART) such as IVF provide an opportunity for patients to realize their goal of parenthood with cumulative pregnancy rates nearing 70% (Pinborg *et al.*, 2009). However, many couples discontinue ART without achieving a live birth for reasons other than poor prognosis or cost of treatment. In some cases this decision is satisfactorily achieved after deliberation about beliefs, values and perceived opportunities and costs of treatment (Elwyn *et al.*, 2000). In other cases the decision to discontinue is reluctantly made as a direct consequence of the burden of treatment. Whilst discontinuation in such cases may reflect patients' incapacity to deal with the demands of treatment, recent research also points to non-patient factors (e.g. clinic factors, nature of treatments) that add to the burden of treatment and that make treatment more onerous than necessary. Such findings bring into focus the need for medical teams and pharmaceutical companies to consider their role in the treatment experience. In this opinion paper, we propose a general integrated approach to cover different perspectives in dealing with burden in ART clinics. We firstly describe the integrated

approach and present common sources of burden. We then describe interventions that could help reduce the burden in ART. Our paper is aimed at fertility clinic staff (e.g. nurses, doctors, embryologists, administrators) because of their day-to-day involvement with patients. However, this discussion should also be relevant to companies that develop treatments and to psychosocial experts. Reducing the burden of treatment should lead to improved outcomes, namely better quality of life during treatment and lower discontinuation rates.

Patients, clinics and treatments: reciprocal influences

Discontinuation (dropout) in fertility treatment refers to patients with a failed cycle who opt not to proceed with further treatment despite a favourable prognosis and ability to pay or cover the costs of treatment. Discontinuation is most often discussed in the context of ART and has been identified as an issue in ART as early as 1988 (Callan *et al.*, 1988). (Discontinuation can also refer to people who opt not to start treatment, but in the literature reviewed it mainly refers to patients having



undergone at least one treatment cycle.) Discontinuation rates vary significantly among studies from as low as 7.7% (Verberg et al., 2008) to as high as 89% (Sharma et al., 2002), and even among the better-controlled studies the rates are in the range of 24–35% (e.g. Land et al., 1997; Olivius et al., 2004; Smeenk et al., 2004; Brandes et al., 2009). Heterogeneity is due to factors beyond the scope of this paper (e.g. heterogeneous definitions of discontinuation, methodological approaches, patient groups and/or treatment types). Despite this heterogeneity, the discontinuation literature does make clear that the patient (individual, couple), the clinic (team, environment) and the treatment (type, effect) all have reciprocal influences on each other in determining willingness to continue with treatment. This state of affairs suggested to us that in order to fully address discontinuation and other important outcomes in fertility treatment (e.g. quality of life for patients and staff), one would need an integrated approach that takes into account these reciprocal influences (i.e. patients, clinics, treatments). Figure 1 illustrates this integrated conceptualization. Reciprocal influences might be, for example, that pre-existing emotional problems originating in the patient (e.g. depression) add to the burden of providing treatment to these patients (Verhaak et al., 2010) but (conversely) that depression can also be a consequence of the many demands treatment makes on people (Boivin and Takefman, 1996). Staff can cause emotional distress in patients because of the bad news they must deliver (e.g. failed stimulation, Boivin, 2000) but patient reactions to this bad news can cause problems for staff (e.g. distress, time demand, Simpson and Bor, 2001).

The [causal] pathways depicted in Fig. 1 (i.e. double-headed arrows) have not received equal research or clinical attention. In the psychosocial literature much more is known about treatment impacts on patient well-being (Verhaak et al., 2007) and stress effects on the treatment outcome (Boivin et al., 2011a) than about the impact of treatment delivery on clinic staff (e.g. morale when treatment is not successful, Harris and Bond, 1987). In the medical literature more attention has been spent on improving pregnancy rates (Leushuis et al., 2009) than on reducing secondary effects of medication on patient well-being (Verberg et al., 2009). To optimize the treatment experience for patients and medical teams, we need to

examine the patient and the clinic and the treatment to identify from within these domains what could be the causes of burden. We use the discontinuation literature to achieve this goal insofar as we infer that the factors that lead to discontinuation are likely to also shed light onto the burdensome aspects of treatment that can eventually be minimized or even eliminated. Minimizing burden should ultimately lead to improved outcomes, for example reduced discontinuation or improved quality of life during treatment to name but a few. However, future research will be required to test this hypothesis.

What are main causes of discontinuation in ART?

Patient (individual, couple) factors

Table 1 lists three patient factors commonly linked to discontinuation in the literature: (i) fear and negative treatment attitudes; (ii) psychological and emotional factors; and (iii) relational strain. In 1391 couples with suspected fertility problems, about 25% discontinued due to negative attitudes to treatment, with 70% of these patients dropping out before undergoing first-line treatments (ovulation induction, insemination) and 30% before starting ART (Brandes et al., 2009). In studies that describe these attitudes, 26% of patients ended treatment due to a fear of complication or 'possible danger' of treatment (Moini et al., 2009). Fear and negative treatment attitudes have been shown to be particularly important considerations when initiating treatment and/or moving on to new types of treatment (White et al., 2006; Bunting and Boivin, 2007). This early influence of attitude is potentially because it is at such points that people consider the match between personal beliefs and values before opting in or out of proposed treatment options.

Psychological factors have been cited as a main cause of discontinuation, with a considerable range in frequency between studies (e.g. 7.4%, Verhagen et al., 2008 to 52% Van den Broeck et al., 2009) due to imprecise definitions and study methods (Osmanagaoglu et al., 1999; Hammarberg et al., 2001; Olivius et al., 2004; Domar et al., 2010). Intense negative emotions are difficult to tolerate for extended periods of time and ending treatment may be a way of

Table 1 Factors cited by patients as contributing to their decision to end treatment

Patient (individual, couple)	Clinic (team, environment)	Treatment
Fear and negative treatment attitudes <ul style="list-style-type: none"> • Unfavourable attitudes to treatment (e.g. fear about health of baby, perceiving treatment to be unnatural, perceived costs) • Values (ethical, moral) and preferences incompatible with treatment • Idiosyncratic barriers Psychological and emotional factors <ul style="list-style-type: none"> • Pre-ART psychological profile • Difficulty in tolerating negative emotions for extended time periods • Uncertainty • Strain of repeated ART cycles Relational strain <ul style="list-style-type: none"> • Fear that ART will negatively impact relationship • Perceived and actual asymmetry in treatment focus between partners (particularly prevalent in early phases of medical involvement) 	Sub-optimal organizational care <ul style="list-style-type: none"> • Stressful care (disorganized, assembly-line treatment, different staff on clinic visits) • Insufficient information on alternatives, inadequate co-ordination • Depersonalization (poor coordinated follow-up, results at work and without partner present) • Lack of continuity of care and negative doctor attitudes • Overly bureaucratic procedures Negative staff-patient interactions <ul style="list-style-type: none"> • Lack of empathy, poor listening skills, insufficient care of the man, insufficient time for questions 	Physical burden <ul style="list-style-type: none"> • Worry about physical burden, physical symptoms and discomfort • Injection protocols and adherence to treatment • Cycle monitoring • Disruption of work and daily activities • Worry about cost Handling of poor prognosis <ul style="list-style-type: none"> • Loss of hope for success (cycle number dependent)

copied with these emotions (Lazarus and Folkman, 1984). Studies mainly lack specificity about the psychological cause of discontinuation, for example: 'psychologically too stressful' (Osmanagaoglu *et al.*, 1999), 'psychological burden' (Olivius *et al.*, 2004; Domar *et al.*, 2010), 'psychological reasons' (Smeenk *et al.*, 2004), 'emotional costs' (Hammarberg *et al.*, 2001) and 'emotional exhaustion' (Daniluk, 2001). Where specificity exists, the potential for treatment failure and the strain of the 2-week waiting period are consistently reported as foremost compared with other aspects of treatment consistent with other research on treatment reactions (Boivin and Takefman, 1995). For example, 40% of patients rate the waiting period as the most stressful aspect of treatment compared with 13 and 15% stating pain/physical discomfort or disruption to daily routine, respectively (Benyamini *et al.*, 2005). Ending treatment because of distress may be especially likely for those who start treatment at a psychological disadvantage. Smeenk *et al.* (2004) reported that elevated pretreatment depression was the strongest predictor of patient-driven discontinuation in the first three ART cycles, and this link has been reported elsewhere (Strauss *et al.*, 1998).

Relational strain is also a frequently reported reason for discontinuing treatment (Strauss *et al.*, 1998; Daniluk, 2001; Verhagen *et al.*, 2008; Brandes *et al.*, 2009; Van den Broeck *et al.*, 2009). Withdrawal from treatment due to relational problems often occurs in the early phases of medical involvement, for example, before or after diagnosis (Brandes *et al.*, 2009) and while on the waiting list for treatment (van Dongen *et al.*, 2010). Anecdotally this has been reported to mean that only the stronger marriages survive the demands of treatment. Strauss *et al.* (1998) found in a prospective study that couples discontinuing treatment within 6 months of a failed cycle reported more relational strain (e.g. more concern about the impact of treatment failure on marriage, more unresolved couple conflicts) than those continuing, and similar findings were reported for donor insemination (Schover *et al.*, 1992). In contrast, Smeenk *et al.* (2004) found no relationship

between marital satisfaction and discontinuation (12-month follow-up), suggesting that it is strain rather than appraisal of the relationship that is critical. Others have reported that asymmetry in decision-making between spouses (e.g. worry and preoccupation with treatment or planning (Merari *et al.*, 2002) is related to strain and discontinuation (Daniluk, 2001).

Clinic (team, environment) factors

Numerous aspects of quality of care have been reported in connection with discontinuation (see Table 1). Stressful organizational care (e.g. clinic disorganized, assembly-line treatment, never the same staff; Olivius *et al.*, 2004), inadequate provision of information and inadequate coordination of care (Haagen *et al.*, 2008) have been cited as reasons for ending treatment. Follow-up studies on the well-being of patients show that these organizational problems make patients feel depersonalized (Daniluk, 1997). For example, in a study on communicating ART results, about half of the patients received pregnancy test results when at work and two-thirds when their partner was not present, which was perceived to be stressful (Groh and Wagner, 2005). Fertility staff can suffer from poor organizational care themselves, with time pressure (Simpson and Bor, 2001) and work overload as the main problems (Harris and Bond, 1987). In 112 ART centres in the USA, 49% of physicians, 74% of administrators and 64% of staff agreed that the clinic environment was stressful (Gerson *et al.*, 2004). Such pressures can mean that medical teams feel they cannot deliver the standard of care they would want and this probably affects patient perceptions of the treatment team. Indeed variations on 'assembly-line treatment' or 'too long waiting periods' are a common cause of patient dissatisfaction (Dancet *et al.*, 2010). Discontinuation due to moving to another clinic has been reported in several studies (Osmanagaoglu *et al.*, 1999; Verhagen *et al.*, 2008; Akyuz *et al.*, 2010; Domar *et al.*, 2010) and could also reflect dissatisfaction with the quality of care.

Problematic interactions, mainly communication, with fertility staff have also been cited in discontinuation studies. In a recent systematic review, there were variable findings about the quality of interactions between patients and fertility staff (Dancet et al., 2010). Patients in discontinuation studies have cited, for example, 'lack of empathy' (Olivius et al., 2004); negative interactions with staff (Rajkhowa et al., 2006); and poorly formulated explanations of healthcare plans (Meynol et al., 1997). In a Swedish study, a third of patients cited staff inability to deal with patient distress and need (e.g. lack of empathy, poor listening skills, insufficient care of the man, unkind treatment) as causal factors in their decision to end treatment (Olivius et al., 2004). The lack of specificity of most terms makes it difficult to ascertain causes but evidence suggests that it is mainly related to organization of care and communication (Souter et al., 1998; Malin et al., 2001; Schmidt et al., 2005).

Doctors, nurses and patients do not perceive the physical and psychological demands of treatment in the same way. When compared with patients, doctors tend to underestimate the strain of procedures/events (e.g. diagnostic tests, oocyte pick-up, cancelled cycles), whereas nurses tend to overestimate (Kopitzke et al., 1991). Discontinuation is another problem context where perspectives differ. One study observed that 30% of patients who cited poor prognosis as a reason for discontinuation actually had a favourable prognosis according to their doctors, suggesting that patients may lose hope for success before the medical staff do (Malcolm and Cumming, 2004) and/or that they define a 'poor prognosis' differently. Willingness-to-pay studies show that patients derive benefit from undergoing ART even if they do not achieve success because having tried reduces feelings of regret from not trying options that could have helped them become parents (Ryan, 1996). An early ART study reported that staff found the impossibility of getting all patients pregnant a primary source of difficulty in their job (Harris and Bond, 1987). The wish to do all for the patient may sometimes get in the way of seeing that the patient just wants to end treatment. Alternatively, discrepancy in perceptions of prognosis may represent genuine communication errors that need to be addressed.

Treatment factors

Treatment is physically demanding and patients have been known to end treatment for this reason (see Table I). What is understood by 'physical' varies between studies. The 'physical burden' of treatment (e.g. breast tenderness, pain at oocyte pick-up) can be significant, and a cause of worry, and be more pronounced than emotional distress (Boivin and Takefman, 1996; Franco et al., 2002; Klonoff-Cohen and Natarajan, 2004). Treatment procedures are worrying for many patients. For example, 20% of women were worried about injections (Franco et al., 2002) and 28% ranked giving injections as one of the most difficult topics for them to discuss with their partner (Cousineau et al., 2006). A qualitative study showed that fertility care providers were also concerned about adherence to stimulation protocols (Huisman et al., 2009), cycle monitoring and feedback (Boivin, 2000). It is noteworthy that despite the physical burden of stimulation and oocyte pick-up, patients report feeling overwhelmingly optimistic (Boivin and Takefman, 1996) and much less distressed than in the 2-week waiting period (Boivin and Lancaster, 2010). Attending the clinic and integrating treatment schedules (e.g. scans, blood tests) with work, family and social activities can disrupt daily activities

(Klonoff-Cohen and Natarajan, 2004; Benyamini et al., 2005; Brod et al., 2007, 2009) and can add to emotional distress (Benyamini et al., 2005). The most comprehensive prospective study to date indicated that 62% of patients reported IVF-related absence from work resulting in productivity loss of about €845 (greater for women with emotional problems) (Bouwman et al., 2008). Finally, the cost of treatment is a well-documented cause of stress and worry (Domar, 2004; Rajkhowa et al., 2006; Van den Broeck et al., 2009; Eisenberg et al., 2010).

Although these causes of burden represent important intervention targets willingness-to-pay studies show that patients are willing to trade off costs (e.g. administration ease, minor physical side effects, disruption to daily life) against gains in effectiveness, even marginal gains of 1–2% in the pregnancy rate (Palumbo et al., 2011). Further, this study found that patients would be willing to trade off these costs for a more reassuring communication experience with their treating physician, in particular shared decision-making about treatment options. The use of willingness-to-pay methods shows that patients are willing to put up with discomforts of treatment for the chance of parenthood but also could help identify which aspects of treatment are potential priority areas for improvement.

In this section, we have highlighted patient, clinic and treatment factors linked to discontinuation that shed light on what seems to make fertility treatment burdensome for patients. It is clear that much more work needs to be done to fully specify causes of burden linked to model domains presented in Fig. 1, particularly clinic and treatment domains. However, in the following section we use these findings to describe how interventions could be selected and implemented at different time points to minimize burden to ultimately lead to better outcomes (e.g. reduced discontinuation, improved quality of life).

What techniques could lessen the burden of treatment (and thereby reduce discontinuation and improve quality of life)?

Identifying the specific challenges in each domain (patient, clinic, treatment) will allow us to develop tailored interventions that have high 'goodness-of-fit' and more potential to optimize the treatment experience. Tailored interventions in other health areas have been found to be more effective than general interventions (Noar et al., 2007). Figure 2 shows specific problems during treatment according to the treatment stage and the domain (e.g. patient, clinic, treatment) matched with potential interventions, which shows how there could be better compatibility between the problems identified in the previous section and the types of interventions implemented in clinics. Figure 2 presents as a series of discrete interventions, but we recognize that greater synergy or benefit would probably be derived if these were integrated into a complex intervention. By a complex intervention we mean one that includes a number of the aforementioned components (e.g. coping, communication), and/or requires complex action from the person receiving or delivering the intervention (e.g. skill acquisition) and/or targets multiple outcomes (e.g. discontinuation, quality of life, ease of treatment administration) and/or requires effort at multiple organizational levels (e.g. clinic, industry) (Craig et al., 2008). Further, whether simple or complex the feasibility, acceptability and efficacy of the intervention would need to be evaluated. Figure 2 is

	Pretreatment	During treatment	Waiting for results	Post results	Interventions to address burden
Patient factors	Fear and negative attitudes to treatment				Develop tailored patient information and education materials using guidelines Use checklists and treatment questionnaires to ensure all treatment worries addressed
	Psychological vulnerability	Psychological burden			Identify patients at high risk using SCREENIVF, FertiQoL Implement general and/or tailored coping interventions for all patients Refer high-risk patients to appropriate mental health professionals for additional support
	Relational strain				Ensure partner fully involved in treatment
Clinic factors	Sub-optimal organizational care				Improve performance in areas known to be associated with discontinuation Monitor performance using FertiQoL-TM Involve patients in service evaluation and development
	Negative staff-patient interactions				Use communication strategies designed for brief patient-staff interactions Address workload issues and teach staff stress-management skills
Treatment factors		Physical burden			Simplify treatment protocols
		Poor prognosis			Incorporate persuasive communication in referrals for lifestyle change Accept that patients may want to end treatment

TM, Treatment Module

Figure 2 Cause of burden and associated interventions by stage of treatment.

therefore a starting point of what could be implemented but we recognize that the key stakeholders (e.g. patients, clinicians, researchers and pharmaceutical industry) will have to work together to develop, implement and evaluate intervention packages in fertility health care.

Targeting patient factors

There seems to be a clear need for educational interventions to address erroneous patient fears (e.g. worry about health of baby) and misconceptions (e.g. dangers about specific ART procedures) and to better prepare patients for the demands and potential success of treatment (e.g. realistic expectations). Improving the quality of information is one of the easiest ways to improve patient experiences (Dancet *et al.*, 2010), but this simple strategy has not consistently been adopted. In a survey of 2698 couples attending 16 clinics in the Netherlands only 57% received the detailed information recommended by national guidelines (Mourad *et al.*, 2009). In the USA, 50.8% of fertility clinic websites fail to meet any of the minimal quality standards for printed medical information (Okamura *et al.*,

2002). Therefore one way to optimize the treatment experience at relatively low cost is to ensure that clinic education material is developed according to quality criteria (Bunge *et al.*, 2010) which could include, for example, using structured checklists or treatment surveys (e.g. Treatment Module FertiQoL, Klonoff-Cohen and Natarajan, 2004; Mourad *et al.*, 2009; Boivin *et al.*, 2011b) to ensure that common misconceptions and worries about treatment are addressed; incorporating knowledge about the impact of cultural/religious perspectives in treatment discussions (Schenker, 2005; Adamson, 2009); and developing educational material in collaboration with patients for maximum fit (Pook and Krause, 2005). One caveat is that the quantity of information should be in line with what is needed at a particular stage of treatment because too much information has been shown to attenuate the benefits of an educational intervention in the diagnostic phase of infertility treatment (Takefman *et al.*, 1990). It should be noted that staff can benefit from educational interventions too, for example learning more about the impact of providing feedback about treatment progress on patient reactions (Boivin, 2000)

or about emotional reactions during treatment that may make treatment delivery more difficult for them (Verhaak et al., 2007; Boivin and Lancaster, 2010).

Psychological burden is a cause of discontinuation that is partly caused by patient history (for example, psychological vulnerability) and partly by demands of treatment. Clinics need to address both aspects to optimize treatment. The team can best help the highly distressed patient entering treatment by identifying them and then referring them to a mental health professional who, together with the patient, will formulate adjunct support plans during treatment (Ningel and Strauss, 2002; Hammer Burns and Covington, 2006; Wischmann et al., 2009). Two short tools to detect at-risk fertility patients already exist, SCREENIVF and FertiQoL. SCREENIVF is a 34-item questionnaire covering five risk indicators for high distress in ART (pretreatment depression and anxiety, negative infertility illness cognitions, low acceptance of infertility and poor social support) (Verhaak et al., 2005). A positive screen prospectively showed a minimum 3-fold increase in the risk of poor adjustment at the end of treatment (Verhaak et al., 2010). FertiQoL consists of 26 items about the impact of infertility in four core domains (emotional, mind/body, relational, social) and has been translated into 22 languages [www.fertiqol.org, (Boivin et al., 2011b)]. FertiQoL is reliable, significantly correlates to patient-centred care (Aarts et al., 2011a) and significantly discriminates between depressed and non-depressed patients on the Hospital Anxiety and Depression Scales (Aarts et al., 2010). Screening may also detect couples experiencing high relational strain (Pasch, 2001). However, more research on screening for marital strain needs to be carried out.

The procedural strain of treatment (e.g. uncertainty, tension, worry) also needs to be addressed. Recent reviews on psychosocial interventions delivered by mental health professionals have demonstrated that interventions reduce anxiety (Boivin, 2003) and depression (de Liz and Strauss, 2005) and can have a small but reliable effect on pregnancy rates, which may be due to behavioural change (e.g. lifestyle, treatment continuation) rather than a change in emotions (Hämmerli et al., 2009), but there is some inconsistency between reviews. Psychological interventions designed to improve stress management skills showed in a prospective, controlled, single-blind, randomized study that mind/body techniques were associated with decreased anxiety and depression, fewer physical symptoms and increased pregnancy rates in infertile women compared with a control group, but this effect depended on the number of sessions attended (Domar et al., 2011). Self-administered coping interventions for the waiting period have also been developed. The Positive Reappraisal Coping Intervention (PRCI) comprises 10 positive reappraisal statements designed to promote active attempts to reappraise the waiting period before the pregnancy test in a more positive light (Lancaster and Boivin, 2008). It consists of a small card with 10 statements on it that patients are instructed to read once in the morning, once in the evening and at any other time they need it. Compared with an attention and mood control group, PRCI patients reported feeling significantly more positive, felt that PRCI helped them carry on during the waiting period, and were more able to make plans for the future (Lancaster and Boivin, 2008). Ensuring that clinic staff involve the partner more in treatment plans could also help ease relational strain (Pasch, 2001) because lack of partner involvement is a major source of dissatisfaction with service delivery in clinics. Interventions

for the semen analysis (Pook and Krause, 2005) and even interventions to assist in more global lifestyle change have been developed (Moran et al., 2006). Many more interventions exist (e.g. online interventions, Aarts et al., 2011b) and clinics should familiarize themselves with the interventions that can practically be implemented in their setting. However, it should be reiterated that many of these interventions still require more evaluation to fully ascertain their value, as has been noted previously (Wischmann, 2008).

Targeting clinic factors

We are not the first to advocate a change in the clinic environment as an essential way to promote better quality of care (Alper et al., 2002; Gerson et al., 2004; Dancet et al., 2010). Change may be slow in coming because it is difficult to translate results of patient satisfaction surveys into improved quality of care without greater specificity of the cause of dissatisfaction (Riiskjaer et al., 2010). Further, less research has been devoted to reducing the burden of treatment by effecting change in clinic procedures and/or treatment protocols than change in the patient. Therefore the clinic and treatment factor sections are still at an embryonic stage. Nevertheless, we use what can be gleaned from the discontinuation and patient satisfaction literature to suggest possible targets for improvement. Dancet et al. (2010) performed a systematic review of 51 fertility patient satisfaction studies. From these they identified domains where there was consensus across the 51 studies that patients felt the domain was important to fertility care and problematic (i.e. level of satisfaction low). These findings could be used to identify problem areas that cause treatment to be more onerous and where clinics could target efforts to improve the patient experience. The domains were: (i) access to care (e.g. time for referral and treatment, frequency of appointments); (ii) staff technical skills (e.g. ability of staff to provide comprehensive treatment/testing in one clinic, quality of service provision); (iii) coordination, integration and continuity of care (e.g. staff turnover); (iv) information, communication and education (e.g. about alternatives to treatment, how to help oneself, making plans for the future); (v) emotional support and alleviation of fear and anxiety; and (vi) physical comfort (separate clinics from pregnant women) (Dancet et al., 2010). Clinics can also evaluate their own service using existing tools for example, using FertiQoL-Treatment Module www.fertiqol.org (10 items) (Boivin et al., 2011b) or the Patient-Centred Care Questionnaire, van Empel et al., 2010 (41 items) developed for infertility care. These assessments could be carried out regularly with patients to monitor service delivery but also evaluate impact of the interventions implemented to reduce burden of treatment.

Even simple interventions like making time for more personalized care (e.g. introducing yourself, establishing the main reason for the visit, providing information about treatment procedures), and asking whether the patient had other issues or concerns, have been shown to differentiate satisfied from dissatisfied infertility patients (Daniluk, 2001; Leite et al., 2005). Interventions designed to address medical staff uncertainty about the right words to use in various contexts have been designed and can easily be adapted to the context of fertility (Platt et al., 2001). A study with ART personnel revealed that about 20% of staff felt inadequately trained to deal with patient complaints at the same time as revealing that an enhanced focus on patients was associated with higher pregnancy success rates (Gerson et al., 2004). A closer collaboration with patients could help identify specific

problems and best solutions to problems in each clinic (Stewart *et al.*, 2001). For example, a significant proportion of patients want their pregnancy test results by telephone rather than at the clinic, a practice which could also result in significant time savings for staff (Stewart *et al.*, 2001). Fertility patients prefer shared decision-making with their health-care team (Peddie *et al.*, 2004) and interventions developed with patients tend to be more likely to motivate organizational change (Bunge *et al.*, 2010). Clinics therefore need to effect change with their patients. As noted previously, this is especially important in accepting that patients and medical staff may not define the optimal treatment trajectory in the same way (Daniluk, 2001; Boivin *et al.*, 2005).

Targeting treatment factors

Finally, some research suggests that simplifying treatment protocols would help reduce physical demands and minimize disruptions. The pharmacological options and regimens all have strengths and weaknesses. Mild ovarian stimulation protocols aiming to retrieve fewer oocytes reduce physical and emotional stress reactions (Hojgaard *et al.*, 2001; Verberg *et al.*, 2009) and have been shown to significantly reduce the chance of discontinuing from treatment (Verberg *et al.*, 2008). Ovarian stimulation using less complex treatment regimens and fewer injections may also result in a significant reduction in distress (3 versus 23%; Hojgaard *et al.*, 2001). However, the success of milder stimulation regimens may be dependent on the patient's willingness to undergo multiple cycles, as the live birth rate per cycle is lower than for conventional ART (Heijnen *et al.*, 2007). It may be useful to compare outcomes of various interventions (i.e. success rates, burden of treatment and cost) over a given period of time (which may involve multiple cycles) rather than per IVF cycle only (Vail and Gardener, 2003). Pen injection devices may offer significant benefits over syringe delivery in terms of patient convenience, acceptability and tolerance (Craenmehr *et al.*, 2001; Platteau *et al.*, 2003; Sedbon *et al.*, 2006; Christianson *et al.*, 2007; Abbotts *et al.*, 2011), just as the recently introduced sustained follicle stimulant preparations allow for a reduction in the total number of injections (Devroey *et al.*, 2009). Low cost ART is in its infancy and its cost-effectiveness needs to be fully evaluated but presumably it will eventually reduce the financial burden associated with treatment (Fauser *et al.*, 2010). Doctors will mainly guide the choice of regimens. However, shared decision-making would also involve taking into account which regimen would reduce the burden of treatment for a particular patient (Palumbo *et al.*, 2011). Importantly, it is noteworthy that willingness-to-pay studies suggest that people prefer to pay more to improve chances of success (Palumbo *et al.*, 2011). Therefore reduced costs, if they incur reduced chances of success, may not be in line with patient preferences.

Future directions and Conclusion

To make treatment less onerous for patients and medical teams, we propose an integrated approach that takes into account the patient, the clinic and the treatment and their reciprocal influences on each other (Fig. 1). This integrated approach focuses attention more broadly and allows for better matching of interventions to specific problems (Fig. 2). However, much more needs to be done to identify the challenges that patients and medical teams face. In this opinion article

we used the discontinuation literature to infer what were the causes of burden. However, to support/refute the hypothesis that burden is a cause of discontinuation and a lower quality of life (and potentially other outcomes), we need to identify independent markers of burden (e.g. ratings from FertiQoL optional treatment module, observer ratings of patient–staff communication, number of injections) and investigate whether these predict discontinuation from treatment and quality of life. Alternatively, one could also reduce the source of burden (e.g. using a named nurse programme, improved leaflets) and see whether these are associated with concomitant improvements in discontinuation and quality of life in randomized controlled trials. To date discontinuation studies have relied on survey techniques to question people about discontinuation and its causes. However, other techniques, for example willingness-to-pay methods, could potentially help to investigate these issues in greater depth, establish patient preferences and determine how people view the costs/benefits of treatment. The development and evaluation of interventions, especially complex interventions that involve many components, should follow theory-based intervention guidelines (Campbell *et al.*, 2000; Craig *et al.*, 2008) because such interventions are more likely to reach their therapeutic goals (Boivin, 2003; Michie, 2008). In this article we address burden-related causes of discontinuation. However, we recognize that, for many patients, ending treatment will be a satisfactory choice achieved after consideration of beliefs, values and preferences.

In conclusion, compelling longitudinal research demonstrates that patients are better off and more able to reconstruct their lives if they have had a positive treatment experience (Daniluk, 2001). Fertility clinics can do more in this regard. Clinics have made important strides in improving the efficacy and safety of fertility treatments, and now more attention needs to be given to making treatment less onerous. Altogether, tackling burden in ART will be a considerable endeavour but this needs to be a priority for fertility clinics and industry.

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Authors' roles

J.B. drafted the manuscript with input from all authors and all authors participated in the revisions.

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