

# From Victim to Survivor to Thriver: Helping Women with Primary Ovarian Insufficiency Integrate Recovery, Self-Management, and Wellness

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## ABSTRACT

Most women discover that they are infertile in a gradual manner after many failed attempts at conception. By contrast, most women with primary ovarian insufficiency (POI) uncover their infertility as part of an evaluation of other presenting complaints, frequently before attempts at conception have even been contemplated. The most common words women use to describe how they feel in the hours after getting the diagnosis of POI are “devastated,” “shocked,” and “confused.” Clearly, the news propels some patients onto a difficult journey. POI is a serious and incurable chronic disease. The diagnosis is more than infertility and affects a woman’s physical and emotional well-being. Management of the condition must address both. Patients face the acute shock of the diagnosis, associated stigma of infertility, grief from the death of dreams, anxiety from the disruption of life plans, confusion around the cause, symptoms of estrogen deficiency, worry over the associated potential medical sequelae such as reduced bone density and cardiovascular risk, and the uncertain future that all of these factors create. There is a need for an evidenced-based integrated program to assist women with POI in navigating the transition to acceptance of the diagnosis, ongoing management of the condition, and ongoing maintenance of wellness in the presence of the disorder. A health-centered approach can gradually replace the disease-centered approach and put patients in partnerships with professional health-care providers. Ideally, the journey transitions each patient from seeing herself as a victim, to a survivor, to a woman who is thriving.

**KEYWORDS:** Primary ovarian insufficiency (POI), premature ovarian failure (POF), integrative care, recovery, self-management

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"To survive or to thrive: that is the question."  
Yongey Mingyur Rinpoche<sup>1</sup>

"And whatever else history may say about me when I'm gone, I hope it will record that I appealed to your best hopes, not your worst fears, to your confidence rather than your doubts." Ronald Reagan<sup>2</sup>

Primary ovarian insufficiency (POI), also known as premature menopause or premature ovarian failure, involves the cessation of normal ovarian function before the age of 40. It affects 1 in 10,000 by age 20, 1 in 1000 by age 30, and 1 in 100 women by age 40.<sup>3</sup> The condition is considered to be present when a woman <40 years old has had oligo-amenorrhea for  $\geq 4$  months and two serum follicle-stimulating hormone (FSH) levels in the menopausal range (obtained at least 1 month apart) (Nelson 606–14).<sup>4</sup> POI is a long-term incurable condition that causes infertility, menopausal symptoms, estrogen deficiency, and other general health concerns. As such, POI is a life-altering diagnosis that affects all aspects of a woman's life: physical, emotional, and spiritual.

Living with a chronic condition is complicated and involves multiple challenges, such as coping with medical crises, managing treatment regimens, controlling symptoms, organizing one's time efficiently, preventing social isolation, adjusting to changes in the condition, and normalizing interaction and life despite the disease.<sup>5</sup> As compared with control women, women with POI have increased shyness and social anxiety, impaired self-esteem, a perceived lower level of social support, and increased symptoms of anxiety and depression.<sup>6–8</sup> Many women with POI report experiencing severe emotional distress at the time of diagnosis and indicate wanting more guidance on how to cope with their disorder.<sup>9</sup>

The World Health Organization defines health as a "state of physical, mental, and social well-being and not merely the absence of disease or infirmity."<sup>10</sup> In addressing this broader goal for health, three distinct, yet related, concepts—*recovery*, *self-management*, and *wellness*—have gained widespread usage (Table 1). These

**Table 1 Characteristics of an Approach to Primary Ovarian Insufficiency through Recovery, Self-Management, and Wellness**

**Recovery:** Living a life that is satisfying, hopeful, meaningful, purposeful, and productive despite limitations caused by illness.

**Self-Management:** The patient is an active participant in treatment.

**Wellness:** Constant and deliberate effort to stay healthy and achieve the highest potential in living, even in the presence of disease.

terms have different lineages: the term *recovery* derives from the mental health consumer movements, the term *self-management* derives from the chronic illness and rehabilitation literature, and the term *wellness* has its origin in the complementary and alternative medicine field. Despite their varied origins, each term shares a common perspective that centers on health rather than disease. Wellness and disease are not mutually exclusive from the perspective of recovery, self-management, and wellness. One can continue to maintain wellness in the midst of disease. The three approaches emphasize the central role of patients in managing their own health and health care in partnership with clinicians. Still, each term is complex, multifaceted, and often defined differently by various constituencies and stakeholder groups.

In this article, we focus on how recovery, self-management, and wellness apply to women with POI. By integrating key concepts that promote recovery, self-management, and wellness, women with POI can learn to manage their condition effectively instead of letting it rule them (Table 2).

## RECOVERY

Starting in the mid-1930s, the recovery approach removed the blame for the disease or condition from the individual and empowered people to take control over their own lives and health. Eventually, recovery became a much broader movement seeking to shift the focus from symptom suppression to overall health and well-being. In the 1980s, patients began to challenge the notion that for those with chronic conditions without cures, the best one can hope for is stability. Instead, recovery is a way of living a satisfying, hopeful, and contributing life even with limitations caused by the illness. Recovery involves the development of new meaning and purpose in one's life as one grows beyond the catastrophic effects of their illness.<sup>11</sup> Still, the concept of recovery is not without its critics. Some practitioners and researchers have raised concerns that the case for

**Table 2 Major Issues to Address in Partnership with the Patient Given the Diagnosis of Primary Ovarian Insufficiency**

### Recovery

The shock of the diagnosis

Stigma

### Self-Management

Grief

Disruption of life plans

Associated medical conditions

### Wellness

Estrogen deficiency

Bone loss

Uncertain future

recovery is overstated. Also, there is concern that the approach may contribute to patients setting unrealistic expectations as well as experiencing additional stigma if these expectations are not met.<sup>12</sup>

### The Shock of the Diagnosis

Clinicians can begin playing a major role in helping patients recover from POI by communicating the news of the diagnosis properly. How bad news is communicated can have a profound effect on patient satisfaction,<sup>13,14</sup> treatment compliance,<sup>13</sup> quality of life,<sup>15</sup> and other health outcomes.<sup>16,17</sup> POI confronts the clinician with communicating difficult information. This is a sudden, unexpected diagnosis that is life altering but not life threatening. Research has demonstrated that the manner in which patients are informed of this diagnosis can significantly impact their level of distress.<sup>9</sup> Patients with POI perceive a need for clinicians to spend more time with them and provide more information.<sup>9</sup> Indeed, illness uncertainty in this population is associated with higher levels of anxiety.<sup>8</sup> Lack of understanding and uncertainty about their disorder have been associated with greater depression and anxiety and less effective coping in patients with diverse chronic health problems.<sup>18,19</sup> Developing a cadre of nurse educators to assist women with POI may be indicated, and this could follow a model that has been applied to the management of diabetes.<sup>20,21</sup>

Evidence suggests that many clinicians underestimate the potential emotional significance of this diagnosis. Nearly half of women reported having been informed of the diagnosis by telephone, for many while at work.<sup>9</sup> Buckman<sup>22</sup> outlines a help approach to giving bad news. Such an approach will likely set a tone for patients with POI that will help them along the road to recovery. His first point is to get the physical context right. Have the patient come to the office for an unhurried appointment. The patient will appreciate getting the news in person and also benefit from the tangible emotional support that a caring clinician can provide. Start the discussion by asking the patient to summarize her understanding of what laboratory tests have been done and why. Then, Buckman recommends a "warning shot" such as "I have some bad news for you that is difficult for me to tell you about. The problem has to do with your fertility and the functioning of your ovaries."<sup>9</sup> Then pause, and wait for the patient's response and invitation to proceed. An iterative process such as this provides the patient information at the rate she is ready to receive it. When emotions are expressed, it is important for the clinician to validate the patient's feelings with a statement such as "I understand your sadness. Most women find this diagnosis difficult to accept emotionally."<sup>9</sup> Emotions may progress such that additional information is not being processed and a follow up

appointment is indicated. At this point inquire about what sources of emotional support the patient has available and suggest additional sources of support if appropriate.<sup>9</sup>

### Stigma

Infertility is stigmatized in most cultures.<sup>23,24</sup> Stigma has been shown to be significantly positively correlated not only with infertility-related distress but also with symptoms of anxiety and depression.<sup>8,25</sup> Also, social alienation with a sense of isolation and withdrawal from social relationships is an important component of stigma. Women with POI score significantly lower than controls on perceived social support and self-esteem, suggesting that strategies to improve these factors might reduce the emotional suffering that accompanies this life-altering diagnosis.<sup>7</sup> Educational intervention can be used to reduce stigma.<sup>26-28</sup>

### SELF-MANAGEMENT

One of the first uses of the term *self-management* appeared in 1976 in a book written by Creer and Christian on the rehabilitation of chronically ill children.<sup>29</sup> The thesis is that the term *self-management* encourages patients to become active participants in their treatment. Self-management programs are based on developing "self-efficacy" or one's confidence in his or her ability to deal with health problems.<sup>30,31</sup> Instead of viewing the chronically ill as having a disease that waxes and wanes simply due to physiological changes within their bodies, self-management emphasizes the natural shifting of perspectives that patients have about their illnesses regardless of their physical health. This broader perspective permits patients to adapt as their specific needs and situations change over time. The critical component of any self-management program is to increase the participant's confidence level so the person can more effectively cope with their disorder and adapt to change. By integrating self-management concepts into existing health-care delivery systems, patients are able to collect information, communicate, analyze options, and make decisions more effectively. Self-management programs can also provide new skills, allowing patients to manage negative emotions such as fear and depression that often accompany any chronic disease.<sup>31</sup>

### Grief

One study found that by patient report, only 2% of clinicians provided a plan for managing the emotional and mental health aspects of POI as part of informing them about the diagnosis.<sup>9</sup> Women who receive a diagnosis of POI embark on a "psychosocial transition" that requires adaptation;<sup>32-35</sup> skilled clinicians can guide

them along the way and help them to self-manage the process. Learning of the diagnosis of POI and the associated sudden unexpected loss of the ability to conceive can induce an emotional response that in some ways parallels the grief response to the death of a loved one.<sup>36</sup> The loss creates a discrepancy between the world that is and the world that "should be." This induces grief, the emotion that draws us toward something or someone that is missing.<sup>32</sup> In fact, in this situation patients may experience "disenfranchised grief," meaning others in their social network or culture do not adequately validate and recognize the legitimacy and impact of the loss.<sup>37</sup>

Events in life that represent significant loss are associated with major depressive disorder and other psychopathology.<sup>38-44</sup> This is especially true when (1) the loss is unanticipated, (2) it requires major revisions with regard to the person's assumptions about the world, and (3) it has lasting implications.<sup>32</sup> All three of these factors are at play when women receive the diagnosis of POI. This makes it all the more important that clinicians take a proactive role in helping patients self-manage this major psychosocial transition. They can direct these patients to available support, opportunities, and resources with which to address the loss.<sup>32</sup> Support and resources are the factors that relate to successful adaptation to loss.

### Disruption of Life Plans

Women with POI face a disruption in their pursuit of childbearing, a life goal that is central for many people.<sup>45</sup> Clinicians can help patients deal with this disruption by helping them build on the inherent positive psychological resources they possess, such as their flexibility in setting goals and their desire to define purpose in their life.<sup>8</sup> In general, evidence supports finding new opportunities in life as a way to navigate psychosocial transitions successfully.<sup>46-49</sup> Women with POI who have evidence of greater goal flexibility on a validated instrument have been shown to experience greater positive affect.<sup>8</sup> The same is true for women with POI who demonstrate a stronger sense of purpose in life.<sup>8</sup>

Positive affect is a potent resource available to help individuals recover from difficult experiences.<sup>50</sup> Approaches that help women find new goals and purpose in life may be one way to increase positive affect. Also, many women report that their spirituality or faith is a resource that can assist them in the psychosocial transition induced by the diagnosis of POI. Evidence has shown that women with POI who score higher on a validated measure of spiritual well-being also score higher on a validated measure of functional well-being.<sup>51</sup> Interestingly, evidence supports the view that there is little need for women with POI to relinquish the goal of

getting pregnant as part of the psychosocial transition. The ability to disengage from this goal is not strongly associated with measures of distress or well-being.<sup>8</sup> The findings suggest that patients need not detach from this loss to free up energy to move forward in other ways. It is important for clinicians to recognize these factors when counseling women with POI. However, there is clearly a need to develop and test interventions that can be proven safe and effective in helping women with this challenging life transition.

### Associated Medical Conditions

Those women who develop primary ovarian insufficiency due to Turner syndrome related to a missing or structurally abnormal X chromosome have associated medical conditions that have been reviewed elsewhere.<sup>52</sup> Other medical disorders may be associated with spontaneous 46,XX POI that need to be identified and managed appropriately. Women who have POI related to steroidogenic cell autoimmunity are at increased risk of developing adrenal insufficiency, a potentially fatal condition. Steroidogenic cell autoimmunity represents only ~4% of women with 46,XX spontaneous POI. This subset of patients is identified by testing for the presence of adrenal autoimmunity as measured by indirect immunofluorescence and 21-hydroxylase immunoprecipitation.<sup>53</sup> Those who test positive should have an annual corticotrophin stimulation test to assess adrenal function. It is important to educate all women with 46,XX spontaneous POI regarding the symptoms of adrenal insufficiency, which include loss of appetite, weight loss, fatigue, weakness, salt craving, and darkening of the skin.

Autoimmune thyroid disease is also more common in women with POI, so it is reasonable to test serum thyroid-stimulating hormone and for serum thyroid peroxidase autoantibodies.<sup>54,55</sup> In addition, although the mechanism is not clear, ~20% of women with POI meet diagnostic criteria for dry eye syndrome and ocular-surface disease and will benefit by referral to an ophthalmologist.<sup>56</sup> Although many other autoimmune disorders have been reported in association with POI, testing for these should not be routine but rather based on symptoms and signs that suggest the presence of the condition.

Women with 46,XX spontaneous POI are at increased risk of carrying a premutation in the *FMR1* gene, which conveys a risk of having a child with mental retardation due to fragile X syndrome. In familial cases of POI the premutation is found in ~14% of women, whereas in isolated cases it is present in ~2% of women.<sup>57</sup> Women with POI should be tested for a premutation in the *FMR1* gene.<sup>58-60</sup> In most cases of POI the cause of the disorder remains a mystery even after a thorough evaluation. In a few cases the disorder

presents as part of one of a host of rare syndromes outlined in a recent review.<sup>4</sup>

## WELLNESS

Traditionally, illness, whether mental or physical, has been the primary focus of the medical community.<sup>61</sup> A wellness approach is far more than just encouraging certain lifestyle changes.<sup>62</sup> Instead, a wellness approach emphasizes the constant and deliberate effort to stay healthy and achieve the highest potential for total well-being, even in the presence of disease.<sup>63</sup> In the United States, this approach originated as a reaction to discontent with mainstream medicine. A wellness approach can be applied not only to specific diseases but also as a way to approach everyday problems, including stress, frustration, and fatigue.<sup>64</sup> Wellness, not simply the absence of disease, is a phenomenon to itself, one toward which we all should strive. The wellness approach includes a strong sense of personal responsibility, commitment to physical fitness, good nutrition, positive social interactions, a positive outlook, a strong interest in critical thinking, spiritual health, and openness to new discoveries and perspectives.<sup>65,66</sup>

## Estrogen Deficiency

POI is a pathological condition that causes abnormally low serum estradiol levels in women who have the disorder as compared with other women their age. As such, hormone replacement therapy is a critical component of maintaining wellness in girls and young women who have POI. Accumulating evidence has associated an early age of menopause with an increased incidence of fractures,<sup>67</sup> increased total mortality, and mortality due to ischemic heart disease.<sup>68-70</sup> Furthermore, evidence from the Framingham study has demonstrated an increased risk of ischemic stroke for women who experience an early natural menopause.<sup>71</sup> The Women's Health Initiative study demonstrated increased cardiovascular risk with continuous oral equine estrogen and progestin treatment of menopausal women, who were on average 63 years of age.<sup>72</sup> These results from menopausal women are not applicable to young women with POI. Most experts agree that estrogen and progestin replacement is indicated for young women with POI and should be continued until they reach an age when menopause would normally occur.<sup>4,73-76</sup>

No studies have prospectively compared the many possible approaches to hormonal replacement therapy for young women with POI. Estradiol is the major natural estrogen produced by the human ovary in terms of effect on the estrogen receptor. In the absence of comparative studies, one practical approach is to attempt to mimic normal physiology as closely as possible using transdermal administration of estradiol. Oral contra-

ceptives provide more steroid hormone than is needed for physiological replacement and are therefore not recommended as first-line management. Providing estradiol delivered by a transdermal system in a dose of 100  $\mu\text{g}$  per day effectively relieves symptoms and achieves mean serum estradiol levels of  $\sim 100$  pg/mL, which mimics the average level in women of similar age who have normal regular ovulatory menstrual cycles.<sup>77</sup> As compared with oral estrogen, transdermal estradiol delivery has the advantage of having little effect on clotting factors and in case-control studies has been associated with a lower risk of venous thromboembolism.<sup>78-80</sup> Because 100  $\mu\text{g}$  per day of estradiol is a full replacement dose of estrogen, it is important to also administer a full replacement dose of a progestin in a cyclic manner to protect against endometrial cancer. Evidence best supports the use of medroxyprogesterone acetate at a dose of 10 mg per day for 12 days each month because this regimen fully induces secretory endometrium and provides protection against endometrial cancer at an equivalent dose of estrogen as recommended here.<sup>81,82</sup> Patients should keep a menstrual calendar, obtain a pregnancy test if an expected menses is late, and stop the hormonal replacement if the test is positive. Oral micronized progesterone lacks supporting endometrial efficacy data when given in conjunction with a full replacement dose of estrogen and is thus not recommended as first-line therapy in this population.<sup>4,83</sup>

## Bone Loss

Many women with POI experience a delay in diagnosis of their estrogen-deficient state, which evidence has demonstrated clearly causes them to pay a price in terms of reduced bone mineral density. In 25% of women the delay in diagnosis from onset of menstrual irregularity is  $>5$  years.<sup>84</sup> Women with POI have reduced bone mineral density compared with control women, and the reduction in bone mineral density is significantly correlated with the delay in diagnosis.<sup>85</sup> Thus, to maintain wellness, a baseline bone mineral density should be measured at the time of diagnosis, and women should be educated regarding strategies to maintain bone health. Although specific data for this population are not available in this regard, it seems reasonable to follow the guidelines developed for perimenopausal women by the North American Menopause Society.<sup>86</sup> These include maintenance of adequate vitamin D status, defined as a serum 25-hydroxyvitamin D level of  $\geq 30$  ng/mL (74 nmol/L). Adults with inadequate exposure to the sun should take at least 800 to 1000 units of vitamin D<sub>3</sub> per day.<sup>87</sup> It is also important to maintain adequate calcium intake of 1200 mg of elemental calcium per day.<sup>86</sup> Adequate weightbearing exercise is also important in maintaining bone health.<sup>85</sup> A case can be made for a program that involves mixed loading exercise, such as a

combination of jogging and other low-impact loading activity such as walking and stair climbing, along with high-magnitude resistance training.<sup>88</sup> Bisphosphonates have long skeletal half-lives, and the effects of these agents on a developing fetus are unknown. Therefore, these agents are not advised in women with spontaneous 46,XX POI because pregnancy can occur unexpectedly in some of them.

### Uncertain Future

After recovering from the shock of the diagnosis that has disrupted long incubating life plans, and after the options for managing the disorder have been presented to the patient and discussed, the next item on the agenda for most women who get a diagnosis of POI will be to determine what the future holds in terms of family planning. As articulated by one patient advocate,<sup>89</sup> patients with POI have "what if" questions, as outlined in Table 3. It is important to inform patients that spontaneous remission with return of ovarian function can occur and ~5 to 10% of women with this condition will conceive subsequent to diagnosis without medical intervention.<sup>90</sup> A barrier contraceptive method or intra-uterine device is indicated in those who wish to avoid pregnancy. The effectiveness of the oral contraceptive has not been proven in this population, and there are concerns they may not effectively suppress ovulation due

**Table 3 "What If" Questions Articulated by a Patient Advocate for Primary Ovarian Insufficiency<sup>87</sup>**

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What if my pregnancy test never turns positive?
What if I never fill my baby scrapbook page?
What if my infertility robs me of my sexiness and I'm never "in the mood" again?
What if we finally save up enough money for our one egg donation cycle and it fails?
What if we can't afford to adopt?
What if I can't counter the thought that I had to "buy" a baby?
What if I have to read another pregnancy announcement in an online social media today?
What if we have to learn to live child free . . . with a smile?
What if he leaves me for a fertile woman?
What if I never let go of the resentment and jealousy of the woman who got to do this naturally?
What if I lose myself along the way?
What if I stop defining myself by my infertility?
What if I stop hiding behind my fears?
What if I stop hiding behind my grief?
What if I redefine what it means to be woman?
What if I redefine what it means to be mother?
What if I redefine what it means to be family?
What if I let go of the doubt, the fear, the worry, and the self-judgment for one day?
What if I lived in the moment rather than in an uncertain future?

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to the high serum FSH levels characteristically seen in this disorder.<sup>4,91</sup>

Family planning decisions are highly personal and individual, and it is important to recognize that not all women aspire to society norms with regard to desire for marriage and parenthood. Some couples electively decide not to become parents. Some couples are uncomfortable with the prospect of adoption or reproductive technologies and are content not to become parents by these methods. There is no urgency to make these decisions. In fact, for many couples, a proactive decision to delay decision making and give natural conception a chance to take place may be in order. For example, a 3-year delay can provide couples with the time to process the grief related to the diagnosis and to investigate other options for parenthood if no conception occurs in the interval.

When the time is right, those couples who decide to pursue parenthood actively may choose adoption, foster parenthood, egg donation, or embryo donation. The rates of pregnancy with egg donation are similar among older and younger women.<sup>92</sup> Some but not all evidence suggests that women who become pregnant by oocyte donation may be at increased risk for pregnancy-induced hypertension, small for gestational age infants, and postpartum hemorrhage.<sup>93-96</sup> In the rare situation where there is an identical twin discordant for the POI, an ovarian transplant is an option.<sup>97</sup>

For women who get a diagnosis of POI, the journey from recovery, to self-management, to wellness presents a series of challenges, hurdles, and frustrations. Wellness can be found by moving from a place of fear and doubt to a place of hope and confidence. For many women the ultimate challenge is finding a place of self-acceptance with regard to their family plans.

### CONCLUSION

POI is a serious and incurable chronic disease. The diagnosis is more than infertility and affects a woman's physical and emotional well-being. Management of the condition must address both. There is a need to develop an evidence-based integrated program to assist women with POI in navigating the transition to acceptance of the diagnosis, ongoing management of the condition, and ongoing maintenance of wellness in the presence of the disorder. A health-centered approach gradually replaces the disease-centered approach and puts patients in partnerships with professional health-care providers. Ideally, the journey transitions each patient from seeing herself as a victim, to a survivor, to a woman who is thriving.

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