

## CASE STUDY

# Successful In Vitro Fertilization in a Poor Responder While Under Network Spinal Analysis Care: A Case Report

Simon A. Senzon, MA, DC

### ABSTRACT

**Objective:** This case report describes the successful in vitro fertilization (IVF) of a 34 year old female who had one previous aborted IVF attempt prior to Network Spinal Analysis (NSA) care. This case report is being presented to add to other case reports that show positive physiological changes in patients receiving NSA care.

**Clinical Features:** The IVF was attempted due to her partner's azoospermia. The first IVF attempt was on 3/26/02. The patient had a poor follicular growth after the standard hyper-stimulation process of the ovaries, including pre-treatment with Mircette (birth control pills) and 1mg/0.2ml of Lupron (a gonadotropin releasing hormone agonist), and 3-6 amps of Gonal-F (a recombinant fsh) starting on cycle day 3. Her baseline day 3 estradiol and LH levels were only 21.2pg/me and 5.0 I.U./L respectively. On cycle day 8, estradiol was only 56% and LH was 6.6 I.U./L. The Gonal-F was increased to 6amps. This first attempt was canceled due to the poor follicle growth. Only 3-4 follicles of insufficient size between 10-14mm each were found.

**Chiropractic Care and Outcomes:** On 4/11/02, the patient commenced regular NSA care. The second IVF attempt began

on 6/6/02. The change in IVF protocol was the addition of Repronex (also a gonadotropin a combination of LH and fsh). The total increased dose of Gonal-F and Repronex was 6amps, compared to the first attempt of only 3amps which was then increased to 6amps of Gonal-F only.

**Conclusion:** On the second IVF attempt, estradiol was 1001pg/ml on day 8, and 2019pg/ml on day 11, with LH at 9.3. The Oocyte retrieval after the second attempt was 10 eggs, each approximately 18mm. A successful aspiration of eggs was completed on 6/17/02, and a successful pregnancy followed. The patient is still under NSA care, and is now in her second trimester with normal fetal heart sounds. The possible role of NSA care in the vigorous follicular growth and other health benefits is discussed.

**Key words:** *Network Spinal Analysis, NSA, In Vitro Fertilization, IVF, poor responder, hypothalamic-pituitary-ovarian axis, GnRH pulse generator, vertebral subluxation, chiropractic, infertility*

### Introduction

This case is reported as a contribution among other reports of physiological changes occurring in patients while under NSA care.<sup>5-7</sup> The present report describes a 34-year-old female Caucasian undergoing in-vitro fertilization (IVF). Prior to Network Spinal Analysis care (NSA), the patient underwent an aborted attempt at ovarian hyperstimulation at a private fertility clinic. Her follicle growth was only 4 four small follicles, which classified her as a poor responder. After commencing NSA care, which is a non-allopathic, non-therapeutic, form of health care,<sup>1</sup> the patient underwent a second successful attempt at IVF. Her follicle growth increased to 10 preovulatory sized follicles. This success was more than expected. The only change in the IVF protocol was a standard increase in gonadotropins, which is

not a predictor of increased oocyte growth,<sup>2</sup> and may not improve the chances of a successful pregnancy in poor responders.<sup>3</sup> In one study, poor responders to 3amps of gonadotropin per day have a low pregnancy and birth rate even if the hMG is increased to 6amps and a high number of follicles and oocytes grow (as in this case). This may be due to poor quality of follicles and oocytes.<sup>4</sup>

Poor responders have a low chance of success. In fact, poor responders show characteristics of ovarian aging<sup>8</sup> and ovarian failure.<sup>9</sup> Protocol seems to make no difference in improving the chances of poor responders,<sup>10</sup> including an increase in gonadotropin. Although a minidose of GnRH is the first line of therapy,<sup>11</sup> one study showed 39.6% of poor responders out of 111 subjects did not respond at all to increased GnRH protocol.<sup>12</sup> The use of birth control pills as a preliminary approach to the GnRH flare-up protocol (as in this case), does not always

Simon A. Senzon, MA, DC, Private Practice  
188 Charlotte Street, Charlotte, NC 22801, sasenzon@aol.com

make a difference with poor responders.<sup>13</sup> One study showed that lower doses of gonadotropins may be more predictive of a successful pregnancy than higher doses, and that higher doses may affect oocyte quality or endometrial receptivity.<sup>14</sup> In light of these facts, this patient had a successful ovarian stimulation which led to pregnancy. The possible correlation of NSA to the success of her pregnancy is explored.

**Case Report**

**Patient Presentation and Relevant History**

The patient presented for NSA care on 4/11/02. She complained of a “sore throat,” and a “stiff and painful neck”, she stated a desire to gain “overall balance and a release of neck pain” as an outcome of her care. She also stated that, “We’ll be doing in vitro fertilization in the near future and I want to be receptive, balanced, and prepared.” Thus one of her reasons for seeking NSA care was help with the IVF process. She stated a hope that NSA care would help her to be relaxed through the stressful IVF protocol, enhancing her ability to conceive.

The patient initially sought help for fertilization in June of 2001. Her laboratory findings from 6/19/01 showed a normal progesterone count of 14.50ng/mL. Her laboratory report from 7/23/01 showed a normal Prolactin count of 10.6ng/mL as well as normal FSH at 5.0mIU/L and TSH at 1.87mIU/mL. She started regular visits at the reproduction clinic on 10/5/2001 with her partner. Her partner was diagnosed with azoospermia with a lack of vas deferens bilaterally. On 1/21/02 they were referred for genetic counseling due to their history of infertility. Viable sperm were available, due to percutaneous sperm aspiration, and so they were good candidates for IVF.

On 3/26/02, the patient underwent an IVF cycle, which began with 1mg/0.2ml of Lupron (a gonadotropin releasing hormone agonist), combined with Mircette (birth control pills). Her baseline estradiol was 21.1pg/ml and LH 5.0 IU/L. She was then given 3 ampules of Gonal-F (a gonadotropin) for five days, and on the eighth day of her contraceptive cycle, she had a low development of follicles: only 2 or 3 exceeded 10mm. Her estradiol was 56pg/ml, and LH 6.6 IU/L. Gonal-F was increased to 6amps for two more days. On the tenth day, there were only three follicles on the left ovary between 10- 12mm, and one on the right measuring 14mm. Due to the possible difficulty of conception with the azoospermia which otherwise relies on epididymal or testicular sperm for insemination, and such a low follicle count, the procedure was canceled. She was instructed to discontinue the medications and await a normal menstrual cycle before the procedure was attempted again. Her doctor explained to her the “poor prognosis” that is normal for “poor responders” and hence the decision to cancel the IVF attempt.

On 5/10/02, the patient presented on day three of her cycle with a 24mm cystic structure on the right ovary. This was diagnosed as a possible functional cyst from the previous cycle. Another scan was scheduled for the next menses.

**Clinical Findings and Impression**

Evaluation of the patient on 4/11/02, following presentation for NSA care, reflected a standing postural evaluation of a left head tilt, an elevated right shoulder, and an elevated left hip. There was some cervical pain with flexion and extension, a restriction to left and right lateral bending, with pain and re-

striction on both left and right rotation. Anterior head carriage was approximately one inch. Prone spinal analysis revealed bilateral heel tension, bilateral inversion stress, bilateral leg adduction resistance, as well as bilateral leg abduction resistance.<sup>1</sup> On a scale of 1-5, 5 being the highest level of tension, all of the prone analyses were between 3-5. Seated muscle palpation<sup>15</sup> revealed moderate active muscle tension over the entire cervical spine, with mild muscle tension in the upper thoracic region. Mid and lower thoracic active muscle tension was moderate, while the lumbar spine held a high level of muscle tension. Passive vertebral (bony) palpation revealed mild tension in the upper cervical region, high tension in the mid-cervical region, and moderate tension in the lower cervical region. A high level of passive subsystem tension was found in the thoracic and lumbar spine. Sacral passive tension was moderate.

Paraspinal surface electromyography (semg) using the Insight Millenium Second Generation Subluxation Station, showed readings of normal muscle activity at T2(L), T8(L), T12(R), L1(L), L3(R), L5(L), and S1(L). Readings indicating mild elevation of muscle activity were recorded at T4(R), T6(L),

**Table 1a**  
**April**

%DF	NSD	Norm	UV	Site	UV	Norm	NSD	%DF
>>>	1.6	3.8	21.4	C1	24.4	3.9	1.8	14
17	1.8	4.4	33.3	C3	28.5	4.3	1.7	<<<
30	1.8	4.2	12.5	C5	9.6	4.1	1.8	<<<
140	1.9	4.8	52.0	C7	21.6	4.6	2.0	<<<
>>>	2.7	4.9	14.2	T1	50.9	4.9	2.6	257
>>>	2.8	5.0	6.3	T2	34.6	5.0	2.9	451
118	3.0	6.5	24.8	T4	11.4	6.4	3.2	<<<
>>>	3.5	8.4	13.4	T6	22.8	8.2	3.5	71
>>>	4.1	9.6	9.9	T8	22.6	9.5	4.5	129
39	4.2	10.0	26.0	T10	18.7	10.0	4.3	<<<
>>>	4.5	9.8	7.4	T12	12.6	9.8	4.4	72
>>>	4.1	8.7	8.5	L1	16.5	8.7	4.0	94
>>>	3.1	6.1	5.5	L3	6.7	6.2	3.4	22
>>>	3.2	5.2	7.4	L5	9.6	5.3	3.5	31
>>>	2.7	4.4	4.6	S1	7.4	4.4	2.8	62

**Table 1b**  
**August**

%DF	NSD	Norm	UV	Site	UV	Norm	NSD	%DF
>>>	1.6	3.8	2.6	C1	5.4	3.9	1.8	110
>>>	1.8	4.4	4.1	C3	4.6	4.3	1.7	13
>>>	1.8	4.2	4.6	C5	5.4	4.1	1.8	16
>>>	1.9	4.8	5.3	C7	7.3	4.6	2.0	38
>>>	2.7	4.9	5.2	T1	7.5	4.9	2.6	45
>>>	2.8	5.0	4.8	T2	7.3	5.0	2.9	53
>>>	3.0	6.5	7.7	T4	10.7	6.4	3.2	39
1	3.5	8.4	12.1	T6	12.0	8.2	3.5	<<<
>>>	4.1	9.6	12.3	T8	12.9	9.5	4.5	5
>>>	4.2	10.0	9.2	T10	11.3	10.0	4.3	22
>>>	4.5	9.8	7.3	T12	10.2	9.8	4.4	40
>>>	4.1	8.7	4.6	L1	6.9	8.7	4.0	52
>>>	3.1	6.1	2.7	L3	3.6	6.2	3.4	31
32	3.2	5.2	2.5	L5	1.9	5.3	3.5	<<<
>>>	2.7	4.4	1.8	S1	2.0	4.4	2.8	9

<b>Postural Analysis</b>	<b>April</b>	<b>August</b>
Anterior Head Carriage	2 inches	1 inch
Head Tilt	Right	None
Right Shoulder-Elevated	Yes	Yes
Left Pelvis-Elevated	Yes	Yes
Cervical Rotation (R)	Restricted	None
Cervical Rotation (L)	Restricted	None
Cervical Flexion	Pain	None
Cervical Extension	Pain	None
Lateral Bending (R)	Pain and Restriction	None
Lateral Bending (L)	Pain and Restriction	None

L1(R), L5(R), and S1(R). Indications of moderate elevation of muscle activity were found at T8(R) and T10(R). High levels of muscle activity were noted by three standard deviations above normal means found at C1(L), C1(R), C3(L), C3(R), C5(R), C5(L), C7(L), C7(R), T1(L), T1(R), T2(R), T4(L), T6(R) and T10(L). Areas of significant asymmetry between the left and right side were noted at C7(L), T1(R), T2(R), T4(L), T6(R), T8(R), T10(L), T12(R), L1(R), and S1(R). The clinical impression for this patient was multiple facilitated subluxations at C5, C2, C1, as well as the sacrum. Light contacts were made at C5/6 on the right, C1/2 on the left as well as C2/3 on the right, and at S2 on the left to correct for an anterior and inferior sacrum on the left.<sup>16</sup> The initial plan of care involved 3 visits per week for 12 weeks, followed by 2 visits per week for the next 4 weeks. Thus, the patient was seen 2 or 3 times per week for 16 weeks, at which time a re-evaluation was conducted. At each visit, she was administered the appropriate NSA care based on clinical findings revealed through the analyses described above.<sup>1</sup>

### Results

On 6/6/02 the second IVF procedure was initiated on the second day of her menstrual cycle. The patient was placed on 1mg/0.2ml Lupron on cycle day 21, in a pretreatment cycle. On day 3 of the next cycle, she was reduced to 0.05ml. On the third day of her menstrual cycle, she was placed on 3 amps of Gonal-F (which is recombinant fsh) and 3 amps of Repronex (which is human menopausal gonadotropin). On day eight of her menstrual cycle, her estradiol was 1001pg/ml, and five follicles were developing on each ovary. The patient's medical report stated a surprise on the part of the attending physician that such a vigorous response was observed in consideration of the previous poor response. On day ten of her menstrual cycle, the Gonal-F and Repronex were decreased to 2amps twice daily. At this time, the estradiol was 1617 pg/ml, and LH was 93%. On day 11 of her menstrual cycle, the estradiol was 2019pg/ml, with nine follicles approximately 18mm each (with two that

<b>Exam Findings</b>	<b>April</b>	<b>August</b>
Abduction Restriction (L)	4	3
Abduction Restriction (R)	4	3
Adduction Restriction (L)	5	2
Adduction Restriction (R)	5	2
Heel Tension (R)	5	2
Heel Tension (L)	4	2
Inversion Stress (R)	3	1
Inversion Stress (L)	4	2

were greater than 18mm). A human chorionic gonadotropin (HCG) injection was given, and the aspiration was completed 36 hours later. On day 13, nine eggs were found. Pregnancy was successfully established. From 4/11/02 through 6/13/02, the patient completed 21 NSA visits. A re-examination was completed on 8/1/02 after a total of 34 visits. Improvement was noted in all elements of the spinal evaluation including range of motion, prone spinal examination, seated palpation, and semg (tables 1a & b). There was no pain or restriction in any range of motion (table 2). Posture remained with a slight elevation of the right shoulder and left hip. Prone indicators of heel tension, inversion stress, abduction stress, and adduction stress were all below 3 on a scale of 1-5, 5 being the greatest tension<sup>1</sup> (table 3). Seated muscle and segmental palpation rated all areas from moderate to mild (table 4 & 5).

Paraspinal surface electromyography (semg) found decreased muscle activity at L1(L), and L3(L). Normal muscle activity was found at C1(L,R), C3(L,R), C5 (L,R), C7(L), T1(L),

<b>Muscle Palpation</b>	<b>April</b>	<b>August</b>
Upper Cervical	2	1
Middle Cervical	2	1
Lower Cervical	2	2
Upper Thoracic	1	1
Middle Thoracic	2	1
Lower Thoracic	2	1
Lumbar	3	2
Upper Sacrum	1	1

<b>Bony Palpation</b>	<b>April</b>	<b>August</b>
Upper Cervical	1	1
Middle Cervical	3	2
Lower Cervical	2	1
Upper Thoracic	3	2
Middle Thoracic	3	2
Lower Thoracic	3	2
Lumbar	3	1
Upper Sacrum	2	2

T2(L,R), T4(R), T8(L,R), T10(L,R), T12(L,R), L1(R), L3(R), L5(L,R), and S1(L,R). Indications of mild elevation of muscle activity were found at C7(R), T1(R), T4(R) and T6(L,R). There were no areas of high muscle activity. Areas of significant right versus left muscle activity asymmetry were noted at, C1(R), C7(R), T1(R), T2(R), T4(R) and L1(R). It should be noted that asymmetry from the first scan showed 9 areas that were greater than 60%, while asymmetry from the re-scan showed only one area greater than 60% (Table 1a & 1b).

An NSA intermediate care self-reported assessment was administered on 8/12/02. Instructions were, "Please answer the following questions with regard to the time since beginning care in this office." The patient's self-reported assessments are presented in table 6.

### Discussion

The IVF process is based on the neuroendocrine regulation of the female reproductive system.<sup>17</sup> Normal follicle stimulation is dependent on a number of factors such as the release of

**Table 6**

Self Reported Assessment	Rating
Musclar Comfort	3
Ease of mm Recovery from injury	3
Feelings of ease, peace	3
Ease of Breathing	2
Areas where I experience Breath	2
Experience of gratitude/joy	2
Ease of mm Movement	1
Depth/Vol of respiration	1
Ease of breath during exercise	1
Experience of release of spinal tension	1
Experience of body's rhythms	1
Muscular Strength	0
Nervousness	-1
Depression or lack of interest	-1
Difficulty concentrating	-1
Difficulty falling asleep	-2
Moodiness or temper	-2
Fidgety or restlessness	-2
Over reach to life stresses	-2

GnRH (gonadotropin releasing hormone) from the pulse generator in the hypothalamus, the response to this from the pituitary gland, and its release of gonadotropins (lutienizing hormone (LH) and follicle stimulating hormone (fsh)).<sup>18</sup> If GnRH is released at a frequency of 1 pulse per hour, then normal follicular growth ensues.<sup>19</sup> The first 14 days of the 28 day menstrual cycle is associated with an increase of frequency and amplitude of the GnRH pulse as well as folliculogenesis. The second fourteen days is associated with a decrease of amplitude and frequency of the pulse.<sup>20</sup> The frequency change and amplitude are related to plasma levels of estradiol and progesterone. Progesterone is thought to be a regulator of the pulse generator.<sup>21,22</sup> In order for IVF to occur, the ovaries are stimulated by exogenously increasing the FSH and LH. One study found normal follicle growth for Caucasian women between the ages of 28-37 undergoing standard IVF protocol and ovarian stimulation to be 8.7 +/- 4.4 oocytes, while appropriate estradiol levels were approximately 1006pg/ml.<sup>23</sup> In another study, women between 30-34 years of age, also undergoing ovarian stimulation, had an average oocyte retrieval of 10.2 +/- 7.1, with estradiol levels at 871pg/ml.<sup>24</sup> Another investigation has shown that poor responders had 4.5 follicles, versus 7.5 in successful responders, with peak estradiol at 752pg/ml versus 1346pg/ml.<sup>25</sup> Based on these findings, the NSA patient discussed in this report was justifiably classed medically as a poor responder.

Due to the low success rate of overall pregnancy in poor responders, the positive response of this patient is significant. Especially since the known methods of follicle stimulation in poor responders does not show a significant increase in successful pregnancy. Poor responders may even represent early ovarian aging or failure.<sup>8,9</sup> Many factors can contribute to poor follicular growth and the disruption of the hypothalamic pulse generator, including stress, environment, exercise, sleep, and drugs.<sup>20,26</sup> The most primary disruption of the cycle is to the frequency and amplitude release of GnRH from the hypothala-

mus.<sup>20</sup> The pulse generator in the medial basal hypothalamus is due to oscillations of electrical activity. Any deviation of normal pulse frequency will disrupt the menstrual cycle.<sup>19</sup> Other factors that could disrupt this cycle are a breakdown in the hormonal feedback mechanisms. Both progesterone and estradiol are crucial to the success of the cycle. A decrease in estradiol will diminish progesterone production, and progesterone is essential to signal the amplitude and frequency of the pulse generator.<sup>17,27,28</sup> This may not directly affect the pulse generator in this patient's case, since progesterone is not released until after ovulation in a normal cycle. It may be possible that the normalization of stress levels prior to this cycle had an effect. There is no way of definitively knowing this in this case. IVF procedure does not rely on the pulse generator to boost gonadotropin, since Lupron effectively shuts down the pulse generator. So, while a normalization of the pulse generator in normal cycles would have a great effect on the follicular cycle, it may not be effected during an IVF cycle.

It is not possible in this case report to distinguish the possible effects of NSA and the increase in Repronex, both of which occurred prior to the successful IVF. That is, the increased vigorous response of the patient's oocyte growth could be related to the addition of Repronex, which was consistently at 3amps for the entire six days on the successful IVF (in addition to the 3amps of Gonal-F), as opposed to 3amps of only Gonal-F, which was then increased to 6amps on the first attempt. However, the possible role of NSA care is also of interest as reports suggest that such care may influence physiological processes.

There is some evidence that NSA care may elicit a neurological response that has been referred to as a "sympathetic quieting affect,"<sup>26</sup> the possible restoration of normal immune function,<sup>5</sup> and other neurophysiological changes over time.<sup>7</sup> As well, other factors relating to an increased state of wellness have been self-reported.<sup>29</sup> The positive outcomes associated with NSA care<sup>5-7,29</sup> may be mediated through the spinal stabilizing subsystems which have been termed: active subsystem (muscles and tendons of the spinal column), passive subsystem (vertebra, discs, articulations, ligaments of the spine, as well as joint capsules and passive mechanical aspects of muscles), neural control subsystem (force and motion transducers of the ligaments, tendons and muscles, as well as the neural control centers),<sup>15</sup> and emotional subsystem ("informational substances" such as neuropeptides, which occupy the same anatomical and physiological locations as the other subsystems)<sup>16</sup> or emotional motor system (proposed to dissipate tension from the limbic system through large muscle movements).<sup>30</sup> The dissipation of spinal tension, as observed with this patient, may be mediated through the subsystems described above, most notably through the active muscle system, and the emotional motor system which has branches from the limbic system through every segmental level.<sup>30</sup>

The effect of stress on the menstrual cycle is well documented. In one study, endotoxin was injected into ovary-intact ewes to simulate the stress inflammatory response.<sup>31</sup> The endotoxin disrupted the frequency pulses of LH (which is a good indicator of the pulse generator frequency).<sup>27</sup> Follow-up studies on ovariectomized ewes demonstrated that endotoxin inhibited pulsatile LH secretion at both hypothalamic and pitu-

itary levels.<sup>31</sup> Many factors can affect the activity of the pulse generator, including stress, drug intake, exercise, and sleep.<sup>26</sup> The release of corticotropin releasing hormone and vasopressin during the stress response mediated two actions on the menstrual cycle, the first is the inhibition of the gonadotropin-releasing hormone pulse generator, and the other stimulates gonadotropin secretion.<sup>32</sup> Impaired follicular development may be the most common reproductive dysfunction attributable to stress.<sup>33</sup>

NSA care may influence the neurophysiology of the stress response. The patient showed indications of this effect, including: a decrease of neurological findings in the spinal analysis at reassessment periods, a decrease of muscle activity as indicated by the semg readings, and post self-reported questionnaire responses. This suggests an improvement in health and quality of life while under NSA care. Since a qualitative change in the frequency or amplitude of the pulsatile gonadotropin signal is known to disrupt follicular development,<sup>19,20</sup> the proposed “sympathetic quieting effect”<sup>6</sup> associated with NSA care may have allowed for a normalization of frequency from the pulse generator in this patient. Data derived from unpublished semg studies have provided preliminary evidence that the somatopsychic wave<sup>16</sup> has dynamical properties, which become more predictable as the level of NSA care increases.<sup>16,7</sup> It is possible that the dynamics of such care are linked to the menstrual cycle as it is also proposed to be a dynamic and robust system.<sup>34</sup> Examining the evidence from Knobil,<sup>19</sup> and Filicori,<sup>20</sup> among others, while examining what they call, “physiology on the edge of chaos,” Solé and Goodwin write, “The follicle, tuned to a narrow frequency range of pulsatile gonadotropin signal, fails to grow and mature if this range is violated.”<sup>31</sup> Frequency control is one way for the dynamic regulation of the cycle. Solé and Goodwin continue, “A great many different processes, operating on different time scales, are all interacting. An extraordinary range of frequencies are integrated into a single coherent cycle: hypothalamic firing patterns of 3,000 cycles per minute (50Hz) alternating with 17 Hz firing frequency of 1 cycle per 28 days (4.14 x 10<sup>-7</sup> Hz). This is eight orders of magnitude in the frequency range!” Other influences they note are signals associated with emotional and nutritional states that can disrupt the menstrual cycle.<sup>34</sup> With so many interacting variables, the disruption of one aspect of the system can have many health consequences.

## Conclusion

In conclusion this report contributes to the literature supporting the positive physiological changes associated with NSA care. A postulated “sympathetic quieting affect” may have been a contributing factor in this patient’s successful IVF and pregnancy. Further research is necessary to examine the role of NSA care in relation to sympathetic tone, the menstrual cycle, and the hypothalamus. It may be of interest to investigate the influence of NSA care in normally menstruating women who have had plasma levels of Lutenizing Hormone (LH) assessed regularly. Frequency pulsation of LH is a good indicator of the pulse generator’s frequency and amplitude.<sup>27</sup> Optimally, this testing would be done every ten minutes for thirty days. Such findings could be compared to other such studies.<sup>15</sup> Or, the LH plasma

could be monitored at less frequent intervals, this would give a useful though incomplete picture of LH frequency.<sup>17,31</sup> As well, a more general study would be useful to compare the success rates of a group of poor responders who are receiving NSA care, to a similar control group not receiving NSA care.

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