



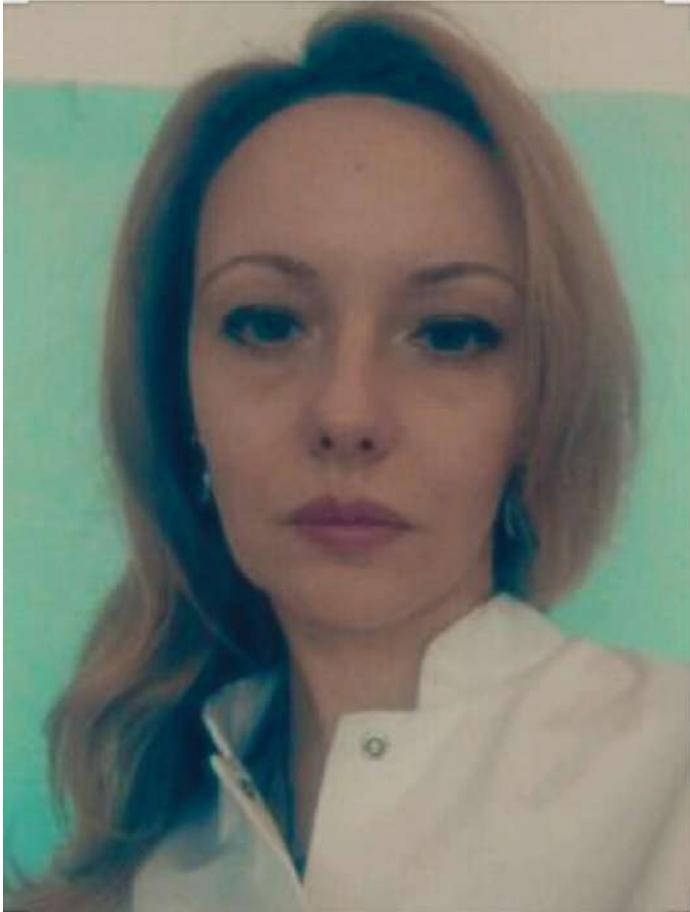
***Restorative reproductive
medicine approach for
infertility and recurrent
miscarriage in the outpatient
ob/gyn practice in Ukraine***

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Objectives

- To assess the outcomes of treatment the couples with infertility or miscarriage with NaProTechnology (NPT) and to identify predictors of success
- The protocol of the study was approved by the Bioethic committee of the Vinnitsa National Medical University, protocol number 7 of 24.04.2014, in Vinnista, Ukraine.

Methods

- retrospective study of 282 couples, who were included in program in 2 outpatient ob/gyn centers in May 2010 - December 2014.
- outpatient gynecological practice, 3 physicians gynecologists with specialization in NPT
- The couples were observed to the end of pregnancy (or pregnancies) or withdrawal from the program (June 2017)

Inclusion criteria

- inability to conceive for at least 1 year with random intercourse, or for at least 6 months with fertility focused intercourse using the CrMS or other fertility awareness based system
- 2 or more visits and at least agreed to begin observations of the cycle

Excluded

- pregnant at the moment of the 1st visit
- evident anatomic disorders which couldn't be surgically corrected (severe tubal factor, Asherman's syndrome)
- menopause
- couples with azoospermia
- patients who failed to complete the initial investigations or return to discuss the results

- **Primary outcome**
 - cumulative proportion of conceptions or conceptions leading to live birth
 - Crude proportions
 - Adjusted proportion (life-table analysis)
- **Secondary outcomes**
 - multiple births
 - birth weight
 - prematurity
 - unsuccessful pregnancies

Characteristics of Couples Beginning Treatment by Subsequent Conception Status (n=282)

Woman's age, <i>median (min-max)</i>	29 (21-46) [26-34]
N years trying for baby <i>median (min-max)</i>	3 (0.5-20) [2-5]
Previous live births, n (%)	38 (13.4%)
Previous unsuccessful pregnancy (miscarriage, ectopic) n (%)	81 (28.5%)
Previous unsuccessful IVF	11 (3.9%)

Diagnoses of couples before and after evaluation: N=282, couples could have multiple diagnoses

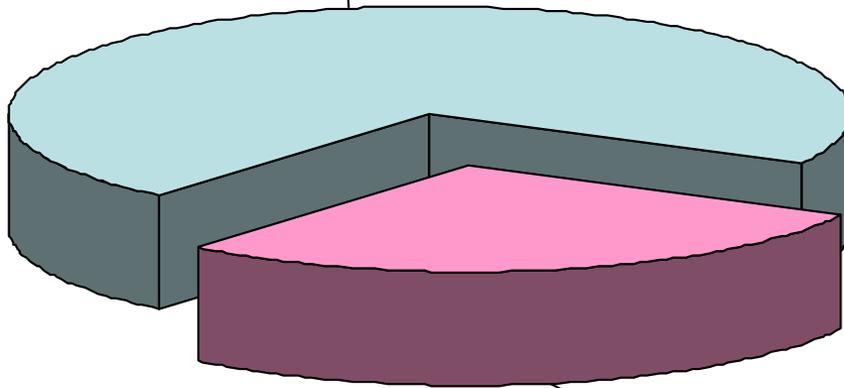
Diagnostic category	Before evaluation, N (%)	After evaluation N (%)
Unexplained infertility	125 (44,3%)	0 (0)
Unexplained recurrent miscarriage	15 (5,3%)	0 (0)
Hyperprolactinemia*	22 (7.8%)	203 (72.0%)
PCOS	38 (13.5%)	104 (38.9%)
Thyroid autoimmunity	4 (1.4%)	29 (10.3%)
Endometriosis	20 (7.1%)	21 (7.4%)
Uterine fibroids	9 (3.2%)	11 (3.9%)
Low ovarian reserve	2 (0.7%)	9 (3.2%)
Male factor	51 (18.1%)	31 (11.1%)
Hypothalamic amenorrhea	1 (0.36%)	2 (0.7%)
Disorders of ovulation	21 (7.4%)	265 (94%)
Inflammatory diseases**	28 (9.9%)	17 (6%)
Tubal factor	15 (5.3%)	25 (8.9%)
Hypothyrosis	0 (0)	30 (10.6%)
Limited cervical mucus	0 (0)	252 (83%)

* Included patients with prolactin levels within normal limits but symptoms of hyperprolactinemia

** Included sexually transmitted diseases, salpingitis, endometritis

System of observation used

**CrMS; 202;
71,6%**



**Sympto-
thermal ;
80; 28,4%**

Medical treatment used among women, N=282

Treatment	Couples n (%)
Folic acid, vitamins and minerals	189 (67%)
Luteal progesterone	237 (84%)
Prolactin lowering drugs	179 (63.5%)
Letrozol	114 (40.4%)
Medications to enhance cervical mucus production	84 (29.7%)
Metformin	83 (29.4%)
Human chorioic gonadotropin	40 (14.2%)
L-thyroxin	24 (8.5%)
Corticosteroids	21 (7.4%)
Clomiphene	20 (7.1%)
Antibiotics	17 (6%)

Results: Cumulative Outcomes: conceptions & live births

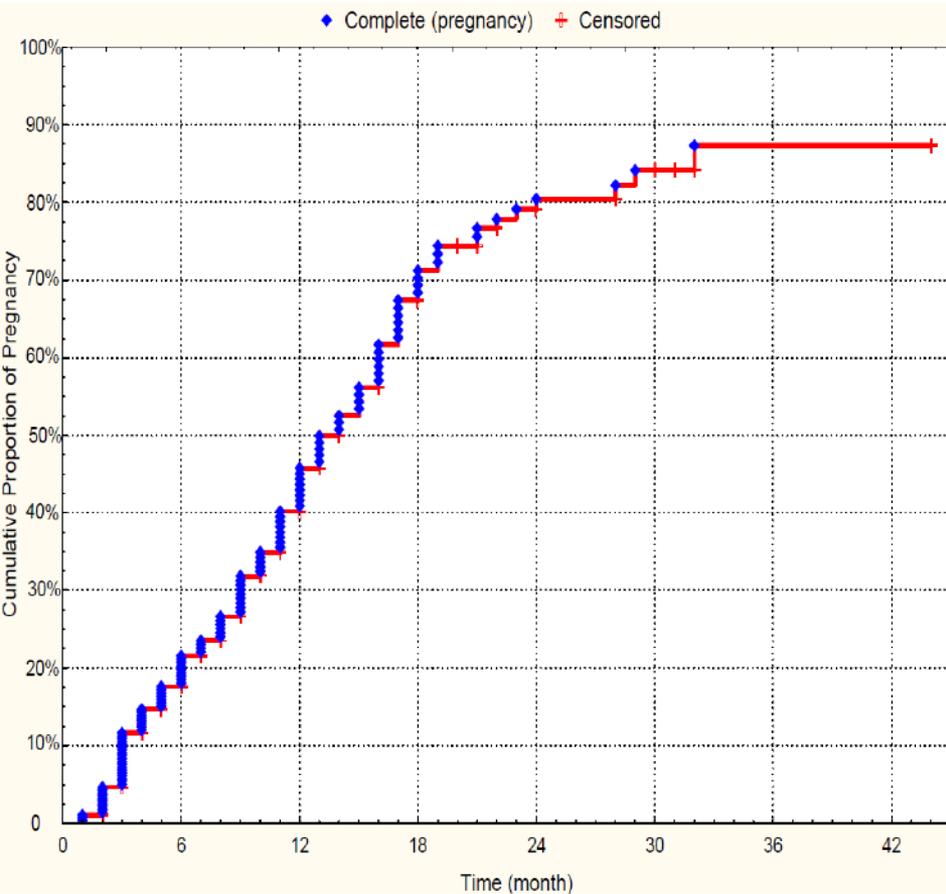
Time interval (months)	Cumulative withdrawals* * from NPT (n)	Conceptions				Live births*			
		Starting at time interval (n)	Cumulative conceptions (n)	Crude proportion	Adjusted proportion†	Starting at time interval (n)	Cumulative live births (n)	Crude proportion	Adjusted proportion†
0-3	10	282	13	4.6%	4.7%	282	9	3.2%	3.3%
4-6	39	259	47	16.7%	18.3%	259	41	14.5%	16.3%
7-12	59	186	88	31.2%	39.7%	186	75	26.6%	34.6%
13-18	20	86	120	42.6%	65.1%	86	102	36.2%	58.7%
19-24	7	34	131	46.5%	77.7%	34	113	40.1%	73.6%
24-30	5	16	134	47.5%	82.6%	16	116	41.1%	79.5%
30-36	6	1	135	47.9%	86.1%	8	117	41.5%	83.6%

* Live births are assigned the time interval when the conception occurred rather than when the birth occurred.

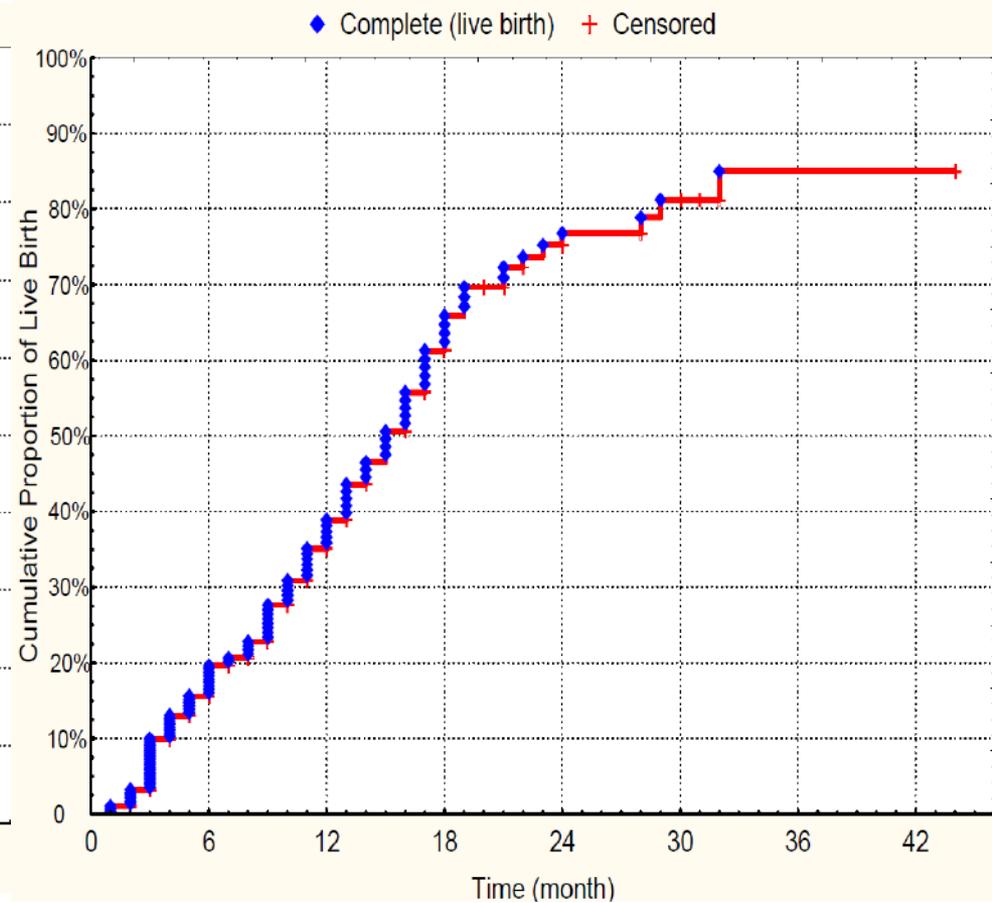
** Included continuing treatment at the end of study follow-up.

† Adjusted by life-table analysis, where withdrawal or continuing treatment at the end of study follow-up are censoring events.

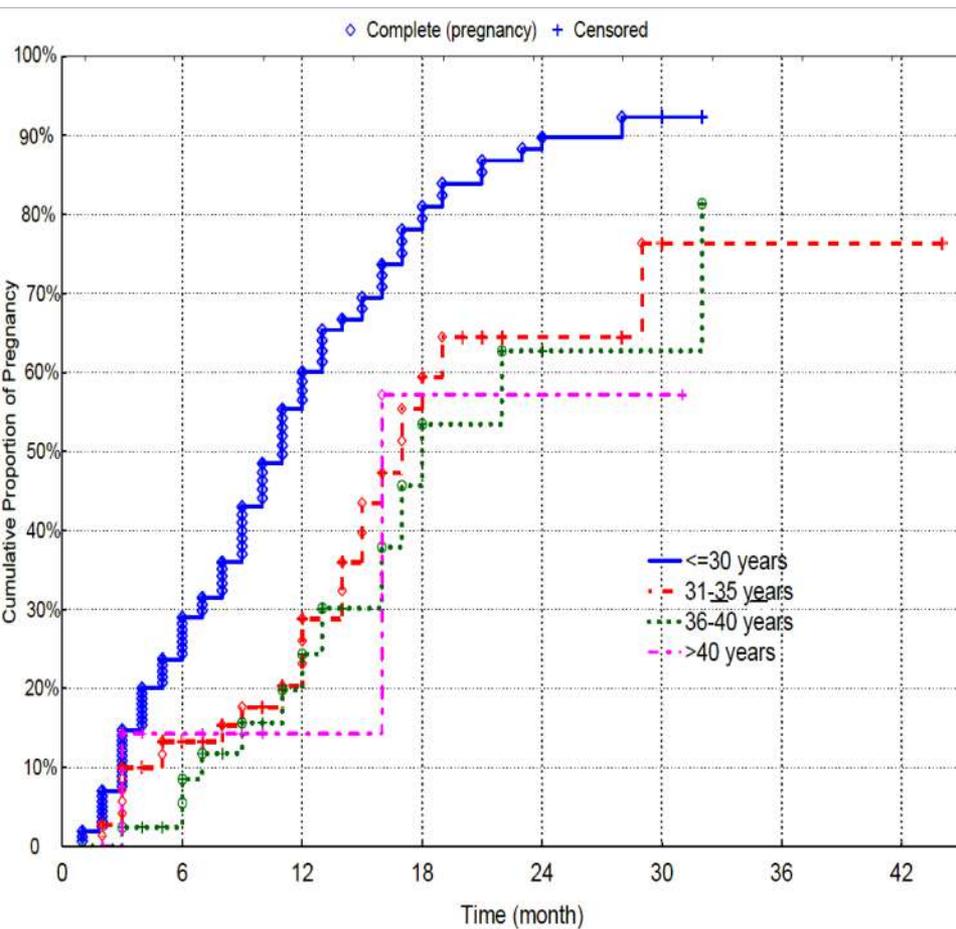
Results: Cumulative Outcomes: conceptions



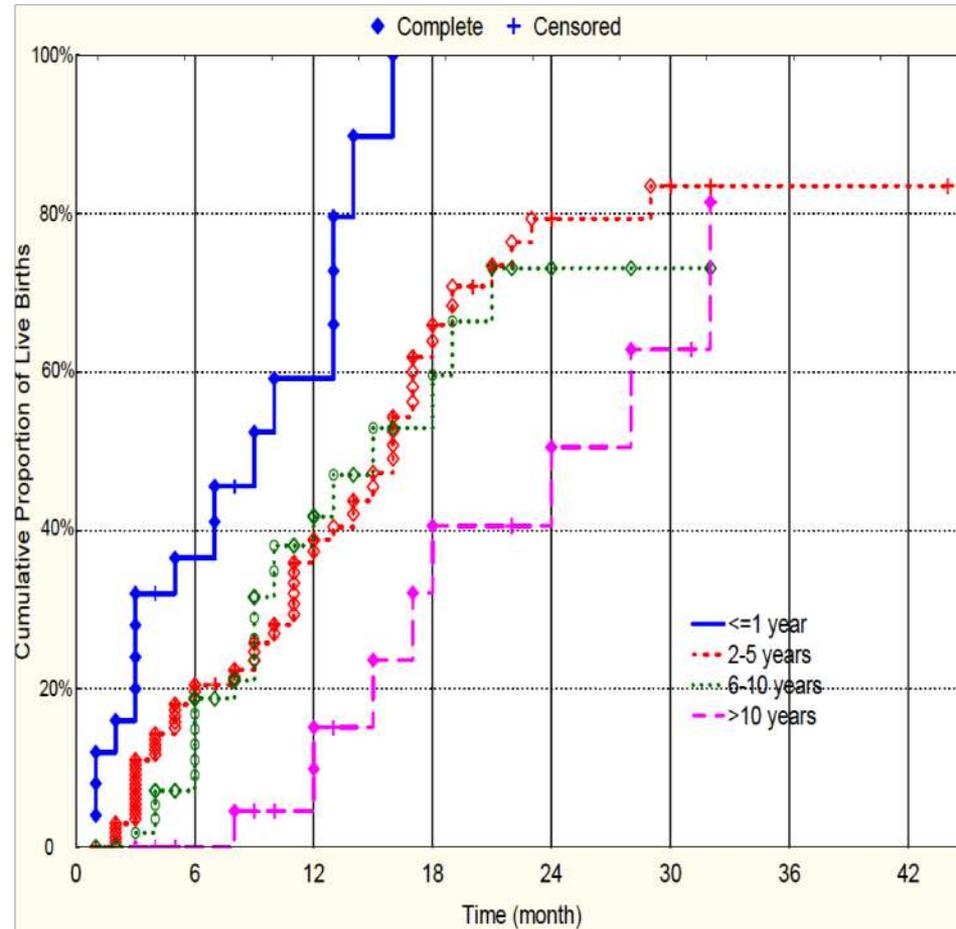
Results: Cumulative Outcomes: live births



Predictors of conception: woman's age



Predictors of conception: N of years trying for baby



Results:

predictors of conception/live birth

- favorable:

- pregnancy in history (even unsuccessful),
- birth in history,
- recurrent miscarriage,
- age of the women less than 30 years,
- compliance with treatment

- unfavorable

- increasing age of woman
- increasing previous years to conceive ($p < 0.0001$)
- hyperprolactinemia,
- uterine fibroids,
- endometriosis,
- male factor (significant difference, $p < 0.05$; Cox's F-test).
- hypothyroidism,
- thyroid autoimmunity,
- surgery after initiation of treatment (marginally significant difference, $p < 0.1$; Cox's F-test).

Outcomes for the first live births, n=117

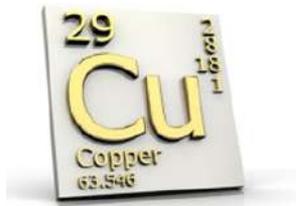
Outcome	n (%)
Gestation age (weeks)	114 (97.4%)
≥37	
<37	3 (2.6%)
Birth weight	114 (97.4%)
≥ 2500	
1500-2500	2 (1.7%)
<1500	1 (0.8%)

Of all first unsuccessful pregnancies:

- 5 ectopic (4,2% of all pregnancies)
- 15 miscarriages (12,8% of all pregnancies)
- 7 delivered healthy babies later

Conclusions

- The current study showed that NPR in outpatient gynaecological setting resulted in cumulative proportions of live births that were comparable with NPT general practice in Ireland and Canada.
- The perinatal outcomes (prematurity, low birth weight) were also similar.
- This approach is positively accepted by patients because the treatment program is minimally invasive and much cheaper than IVF, and that's why it can significantly improve timely access to couples looking for infertility treatment.



- Mother 37, father 38
- Trying for baby for 7 years
- 3 miscarriages
- **Wilson's disease in mother**
- Pregnancy in the 5th perfect cycle
- **Delivery per vias naturalis on December 29, 2015**
- **Boy 3530 g , 50 cm**

- **Now mom pregnant again 25 weeks...**



Thank you!

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