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EFFECTS OF PRE-TREATMENT HABITUAL PHYSICAL ACTIVITY ON COURSE AND OUTCOME MEASURES OF ASSISTED REPRODUCTIVE THERAPY

Ph.D. Thesis

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Dedication

To my daughters

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Abbreviations

ACOG: American Congress of Obstetricians and Gynaecologists
ACSM: American College of Sports Medicine
AH: Assisted Hatching
ART: Assisted Reproductive Therapy
BDI: Beck Depression Inventory
BMI: Body Mass Index
CES-D: Epidemiologic Studies Depression Scale
COH: Controlled Ovarian Hyperstimulation
EIM Consortium: European In-Vitro Fertilization Monitoring Consortium
ET: Embryo Transfer
ESHRE: European Society of Human Reproduction and Embryology
FER: Frozen Embryo Replacement
FertiQol: Fertility Quality of Life Tool
FF: Follicular Fluid
FPI: Fertility Problem Inventory
FYSS: Physical Activity in the Prevention and Treatment of Disease | Fysisk aktivitet i Sjukdomsprevention och Sjukdomsbehandling
GHQ: General Health Questionnaire
GLTEQ: Godin Leisure-Time Exercise Questionnaire
GPAQ: Global Physical Activity Questionnaire
HADS: Hospital Anxiety and Depression
HCSO: Hungarian Central Statistical Office | KSH: Központi Statisztikai Hivatal
HSG: Hysterosalpingogram
HY: Hatha Yoga
ICD-11: International Classification of Diseases 11th Revision
ICHI: International Classification of Health Interventions (WHO)
ICMART: International Committee for Monitoring Assisted Reproductive Technology
ICPM: International Classification of Procedures in Medicine
ICSI: Intracytoplasmic Sperm Injection
IPAQ-SF: International Physical Activity Questionnaire - Short Form
IQR: Interquartile Range
IUI: Intrauterine Insemination
IVF: In-Vitro Fertilization
KMO: Kaiser-Meyer-Olkin (KMO) Test
KPAS: Kaiser Physical Activity Survey
MDD: Major Depressive Disorder
MVPA: Moderate to Vigorous Physical Activity
MeSH: Medical Subject Headings in MEDLINE®/PubMed®
MET: Metabolic Equivalent of Task
NHCSC: National Health Care Service Centre | ÁEEK Állami Egészségügyi Ellátó Központ
NHIF: National Health Insurance Fund | NEAK Nemzeti Egészségbiztosítási Alapkezelő
NIQODHC: National Institute for Quality- and Organizational Development in Health Care | GYEMSZI: Gyógyszerészeti és Egészségügyi Minőség- és Szervezetfejlesztési Intézet
NUTS: Nomenclature of Territorial Units for Statistics
OHSS: Ovarian Hyperstimulation Syndrome
OI: Ovulation Induction
PAQs: Physical Activity Questionnaires
PAGA: Physical Activity Guidelines for Americans

PAGAC: Physical Activity Guidelines Advisory Committee
PICS: Psychological Immune Competence System
PR: pregnancy rate
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyzes
QoL: Quality of Life
RCT: Randomized Controlled Trial
SIRT: Sirtuin
SrH: Self-rated Health
STAI: State-Trait Anxiety Inventory
TESA: Testicular Sperm Aspiration
TFR: Total Fertility Rate
TAC: total antioxidant capacity
USG: Ultrasound-guided
WHOQOL-BREF: World Health Organization Quality of Life-Bref Questionnaire
8-OHdG: 8-hydroxy-2'-deoxyguanosine

Definitions

The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary on ART Terminology 2009 was used in general by defining infertility related nomenclature [1].

The Global Recommendations on Physical Activity for Health, the Physical Activity Strategy for the WHO European Region [2-4], and The Physical Activity Guidelines for Americans [5, 6] were used to define terms in relation to physical activity.

Introduction

Reproductive epidemiology

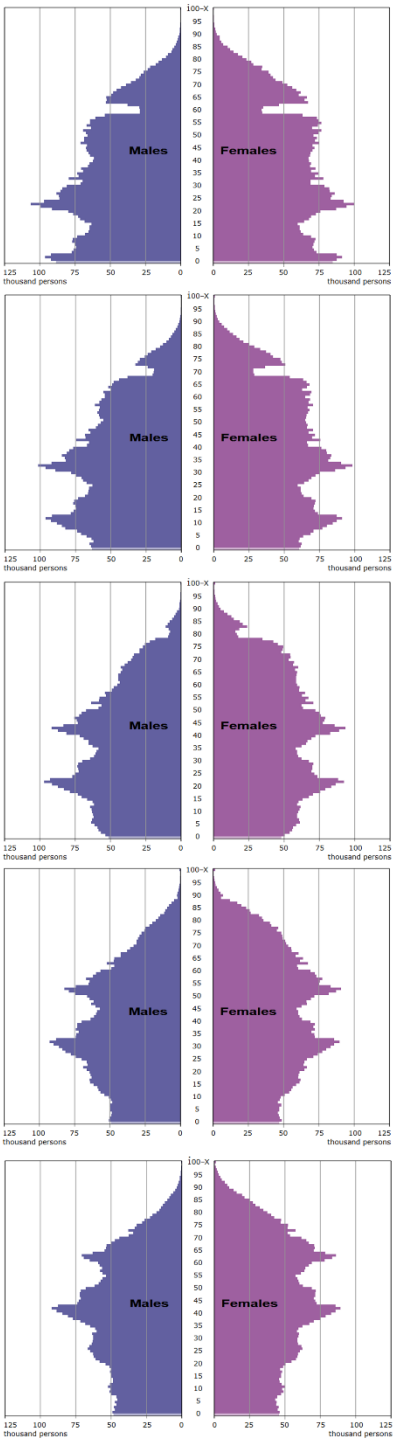
In June 2019 the Population Division of the United Nations Department of Economic and Social Affairs published a warning overview of global demographic patterns and prospects on size, composition, and distribution of the population: the World's population expected to reach 9.7 billion by 2050 and 11 billion by the end of the 21st century. The number of countries experiencing a reduction in population size is growing, but growth rates vary greatly across regions: several countries look toward aging population due to increasing life expectancy, postponement of childbearing and falling fertility levels [7-9].

Similarly to other developed countries, the decline in the birth rate, the decrease in total population, and the increase in the average age of the population in Hungary pose a serious demographic challenge. The phenomenon in the 1980's was mainly due to the high mortality rate relative to other European countries, but since the 1990's it is due to low fertility rate. As a third factor, the balance of international migration influences the population, the positive balance of which could only moderate the natural decline of the population in Hungary in the 21st century [10]. Although this factor is not the main subject of the dissertation and has not been discussed in detail.

Since 1981, the population of Hungary has been steadily declining with varying intensity. Figure 1. illustrates this decline in the number of the population in ten-year terms, which was 9 778 000 on 1 January 2019, 892 000 fewer than 40 years ago. (Figure 1.) The changes over 10 years of the population structure are well illustrated by the 120-year Interactive Population Pyramid of the Hungarian Central Statistical Office (HCSO) [Központi Statisztikai Hivatal (KSH)]. This application presents the changes in the number and age structure of the Hungarian population by gender from 1870 to 2060. The source of retrospective data is based on censuses from 1870-1949 and statistical yearbooks of 1950-2019. For the period of 2020-2060, the Population Research Institute provided estimates based on its 2015 population forecast [11].

According to the HCSO's Demographic Snapshot, after the absolute low point in 2011 (88 049), despite a slight increase, the number of live births still does not reach the level before the 2008 economic crisis (96 000) [10]. Figure 1. shows that the total number of live births in 2018 was still very low, only 94 000, which is 46% decrease from 1978.

Figure 1.



1978 **10 670 802 pers.**

Data — Clear selection

0 years old (born: 1977)

Males:	88 634
	51.1%
	48.9%
Females:	84 670
Combined:	173 304
% of Total:	1.62%

1988 **10 604 360 pers.**

Data — Clear selection

0 years old (born: 1987)

Males:	63 430
	51.2%
	48.8%
Females:	60 456
Combined:	123 886
% of Total:	1.17%

1998 **10 135 358 pers.**

Data — Clear selection

0 years old (born: 1997)

Males:	51 403
	51.7%
	48.3%
Females:	48 061
Combined:	99 464
% of Total:	0.98%

2008 **10 045 401 pers.**

Data — Clear selection

0 years old (born: 2007)

Males:	49 333
	51.2%
	48.8%
Females:	46 934
Combined:	96 267
% of Total:	0.96%

2018 **9 778 371 pers.**

Data — Clear selection

0 years old (born: 2017)

Males:	48 272
	51.3%
	48.7%
Females:	45 814
Combined:	94 086
% of Total:	0.96%

KSH HUNGARIAN CENTRAL STATISTICAL OFFICE

Population number of Hungary by age and number of livebirths rate by gender as of 1. January, between 1998-2018 in Hungary

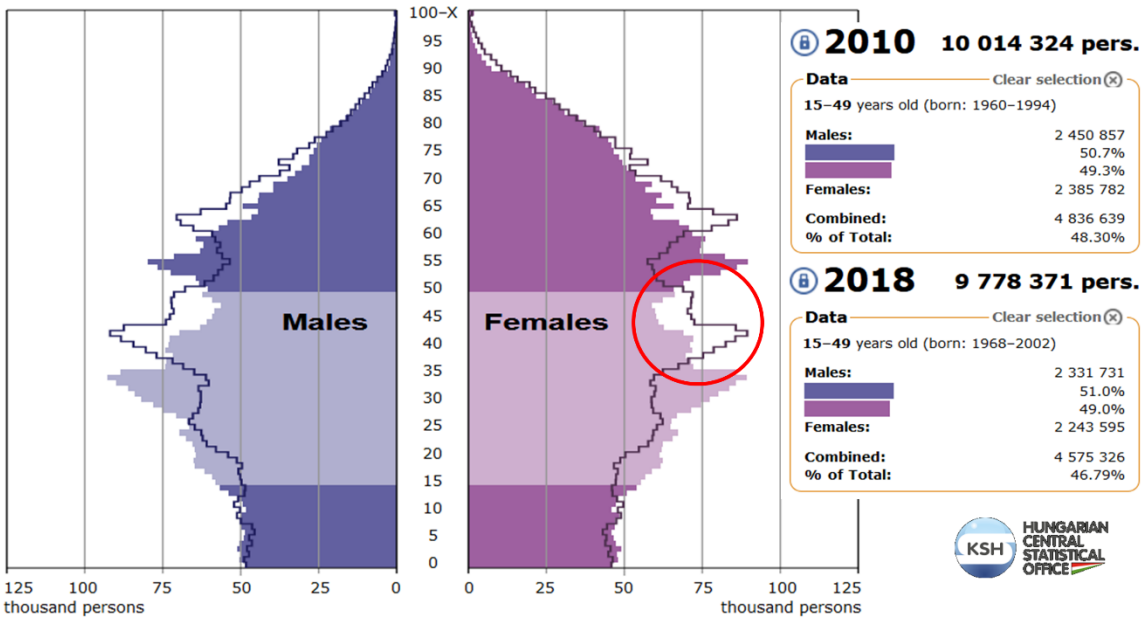
(Source: https://www.ksh.hu/interaktiv_korfa, Downloaded 26/07/2019)

If we analyse the number of livebirths per thousand inhabitants (9.2 per thousand inhabitants nationwide in 2018), we find regional differences. While in some counties the number of livebirths per thousand inhabitants can be considered extremely low (Zala County 7.6, Békés County 8.1, Baranya County – where the main studies of this dissertation were carried out –, Csongrád, Vas, and Veszprém County 8.2), while in other counties this ratio is relatively higher (Hajdú-Bihar County 10.1, Szabolcs-Szatmár-Bereg County 10.2, Borsod-Abaúj-Zemplén County 11.2) [12]

By using current age-specific fertility rates as an indicator, the Total Fertility Rate (TFR) could be calculated, which shows the average number of children that would be born to a woman over her lifetime. If TFR is higher than two, it ensures the replacement of the population. The United Nations reported in World Population Prospects 2019 that the global TFR, which decreased from 3.2 births per woman in 1990 to 2.5 in 2019 on average over a lifetime, fertility still remains above 2.1 births per woman, [7]. On average, 1.59 live births per woman was characteristic in the EU-28 in 2017, ranging from 1.26 in Malta to 1.90 in France [13]. TFR positively changed in Hungary: compared to 1.24 in 2011, it was around 1.54 in 2017. While the relative position of Hungary has improved in TFR ranking and the overall fertility rate has increased, there has been no significant increase in birth rate. After 2010 the number of births and the total fertility rates did not move together anymore, which, according to Kapitány and Spéder, is justified by the special age structure of the Hungarian population. Although the WHO describes reproductive age of women between 15 to 49 years [14], child-wish by the age of 20-40 years is more pronounced in our culture, and after 2012 the number of women in this particular age-cohort quickly dropped. While fertility per woman increased, the total number of live births did not change [15, 16].

Figure 2. indicates two alarming trends. On the one hand, the size of female population in the age group of 15-49 (considered as reproductive age according to the WHO's definition) decreased in Hungary between 2010 and 2018. On the other hand, the age structure within this age group also changed, with a strong increase in the proportion of women over 30 years. The outbreak of childbearing age has started to slow down in recent years. In 2017 mean age of women at birth of first child was 28.0 years in Hungary compared to the EU28 mean 29.1 years and the mean age of women at all childbirth was 29.8 compared to the EU28's 30.7 [10, 17]. Past experience has shown that postponed childbirth is not always realized and raises health consequences. The Committee Opinion (No. 589.) of the ACOG warns of the female age-related fertility decline, notably that the fecundity of women decreases gradually but significantly beginning approximately at age 32 years and decreases more rapidly after age 37 years [18].

Figure 2.



Change in the number of the population in reproductive age (15-49 years) in Hungary at 1. January, between 2010-2018 in Hungary. Lines indicate data from 2018, filled colours indicate data from 2010. (Source: https://www.ksh.hu/interaktiv_korfa, Download 26/07/2019)

Decreasing number of the female population in reproductive age and postponed childbearing raises the issue of increased incidence of disorders that impair fertility, and the higher risk of pregnancy loss [18].

Fertility impairments and their treatment

Infertility is clinically defined as "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" in the International Classification of Diseases (ICD-11) [19].

Multiple definitions of infertility are used in parallel. The demographic definition used for describing global and regional fertility trends interprets infertility in a larger time interval as "an inability of those of reproductive age (15-49 years) to become or remain pregnant within five years of exposure to pregnancy" [20] based upon "a consistent union status, lack of contraceptive use, non-lactating and maintaining a desire for a child" [21]. Epidemiological studies for monitoring and surveillance of infertility prevalence typically apply the definition as "women of reproductive

age (15–49 years) at risk of becoming pregnant (not pregnant, sexually active, not using contraception and not lactating) who report trying unsuccessfully for a pregnancy for two years or more" [14]. Infertility could be also considered as a disability, and among women under the age of 60 was ranked the 5th highest serious global disability [22].

A global prevalence of 12% to 15% of 1-year infertility was described by McLaren in 2012 [23]. Although infertility rates remain unchanged over two decades, an increasing trend in fertility therapy was reported. Even 20 years ago at least 1 500 cycles per million population per year was the estimated need for ART globally [24].

From 1978 to 2012 a calculated total of 5 million, to 2018 approximately 8 million babies, between 1% and 4% of all infants worldwide, have been born through ART [25]. However, it is challenging to find a reliable and up-to date report on current global trend. The latest world report was published in 2018 with the reference year of 2011 by the International Committee for Monitoring Assisted Reproductive Technology (ICMART) covering the data from 65 countries and 2,560 clinics, which means 72.7% of the total number [26].

Fertility treatments are available in 45 countries covering 78% of the world's population and approximately 50% of all reported treatment cycles are initiated in Europe. (ESHRE Capri Group, 2001). The monitoring report of the European Society of Human Reproduction and Embryology (ESHRE) presents a growing number of assisted reproductive therapy (ART). 776,556 cycles were initiated in 2014, which means an almost fourfold increase (3.82) in the number of cycles compared to 1997 (since ART data generated by national registries have been collected, and analysed by the European IVF-monitoring (EIM) Consortium and double (2.11) increase compared to ten years ago. The most frequent treatment modalities were intra-cytoplasmic sperm injection (ICSI, 362,285 cycles, 46.6%), frozen embryo replacement (FER, 192,017, 24.7%), and in vitro fertilisation (IVF, 146,148, 18.8%) [27].

The number of treatments continues to expand and the contribution to the birth rates is still rising in Europe. 849,811 treatment cycles were reported in the reference year of 2015 and 918,159 in 2016 from 40 European countries, where the Nordic countries and Belgium have traditionally high ART availability in terms of cycles per million population, while large increase in treatment numbers was reported by Russia and Spain. In the ESHRE Annual Report 2017 Spain has been mentioned as "the most active country in ART" with 110,000 reported cycles in the reference year. The proportion of infants conceived by ART varies between 6.6% and 2.3% in Europe (Denmark and Italy, respectively), except Malta with 0.6%. By contrast, the proportion in the USA was estimated to be approximately 1.0% of total births [24, 28-30].

Although the number of treatments is growing dynamically, for IVF cycles the clinical pregnancy rates (PR) per aspiration and per transfer were stable with 29.4% and 33.8% respectively, reported for 2012. Rates are similar for ICSI with 27.8% and 32.3 %, respectively [31]. PR were marginally higher for IVF in 2014 than in 2013, at 29.9% and 35.8% versus 29.6% and 34.5%, and with ICSI 28.4 and 35.0% versus 27.8 and 32.9%, per aspiration and per transfer, respectively. PR for FER with own embryos continued to rise also, from 27.0% in 2013 to 27.6% in 2014 [27].

Quite similar situation was reported by Bernard and Krizsa in the early 2000s regarding the Hungarian fertile age population, as 10 to 15% of couples of fertile age struggled with fertility problems [32]. Similarly, 12% to 15% of fertility impairment was described in 2012 [23] and age-standardized prevalence of secondary infertility (as the percent of women who seek a child aged 20–44 years) was reported in a World Health Organization (WHO) study as one of the highest with 18.0% (13.8%-24.1%) in Central-Eastern Europe in 2010 [21].

The results of ART in Hungary in 2012 were the following: 920 IVF and 3502 ICSI were conducted with 31.7% and 34.5 % of pregnancies per aspiration [31]. Although the frequency of treatments increased from 2012 to 2014 (3857 ICSI and 1179 IVF were conducted in that year), ESHRE reported 28.8% and 25.0% of pregnancies per aspiration by ICSI and IVF, respectively. Deliveries per aspiration are published with 0.0% values and any data on FER or IUI and on the percent of ART infants per national births are available in the report.

As published by the EIM Consortium, 170 163 ART infants were born in 2014 which means that on average one in 50 children born in Europe were the result of ART treatments [27]. Due to the abovementioned discrepancies and deficiencies it cannot be compared with the Hungarian data.

In Hungary the National Health Care Service Center (NHCSC) [Állami Egészségügyi Ellátó Központ (AEEK)] – and before 2015, its legal predecessor the National Institute for Quality- and Organizational Development in Health Care (NIQODHC) [Gyógyszerészeti és Egészségügyi Minőség- és Szervezetfejlesztési Intézet (GYEMSZI)] – are responsible for data reporting on frequency, indication, type of procedure, and success rates of ART procedures. Comparison of data from the reference years 2010-2014 are expressed in Table 1. During this five-year period, the number of reported cases increased by 20.16%, from 5854 to 7034. Due to missing data the number of valid cases was lower, yet it also increased by 28.25%. It should be noted that there was on average 21% difference between the number of cases reported by the institutions and the number of procedures which were reported to the National Health Insurance Fund (NHIF) [Nemzeti Egészségbiztosítási Alapkezelő (NEAK)] for the purpose of financing. Most of the patients belonged to 30-34 years (34.89%) and 35-39 years (38.26%) age cohort and typically the first

(48.95%) or second (27.25%) cycles were initiated at the institutions. 34.40% of the patients were diagnosed with female indications. Regarding the type of treatment, only IVF and ICSI data were consequently reported during the years; the number of cases increased by 28.71% and 31.72%, respectively, and the ratio of ICSI was approximately three-fold compared to IVF. Number of metaphase II oocytes varies around 8 and number of transferred embryos around 2 on average.

Number of cases increased by oocyte retrievals from 4859 to 6084 by 25.21%, by embryo transfers from 4987 to 6277 by 25.87%, and by clinical pregnancies from 1649 to 1803 by 9.34% also. PR varies between 25.67%-32.36% per aspiration and between 28.72%- 35.14% per transfer, but an increasing tendency cannot be described. PR should be interpreted with caution, because NHIF statistics do not establish with certainty whether a birth registered following an IVF procedure has occurred as a result of this procedure or independently. Obstetric events were calculated when they occurred within 290 days after ART. Additionally, the database contains only the funded service procedures.

Table 1.

Comparison of Annual Statistical Reports on Human Reproductive Procedures' Performance in Hungary, from the reference years of 2010-2014

Reference years	2010[1]	2011[2]	2012[3]	2013[4]	2014[5]
Reported cases	5854	4912	5056	6306	7034
Valid cases	5476	4550	4830	5562	7023
Difference with NHIF financed cases*	11%	27%	25%	46.7%	**
Investigations by age					
-30 years	711	563	577	539	549
30-34 years	2177	1748	1729	1952	1974
35-39 years	1855	1524	1782	2598	2747
40-44 years	691	661	678	1070	1544
44 - years	42	54	64	132	209
Number of cycles at the institution					
1	2616	2249	2395	2570	
2	1502	1245	1304	1420	
3	769	595	653	709	
4	366	271	273	311	
5	168	143	137	148	
≥5	55	47	68	66	
Diagnosis					
Tubal factor	710	535	661	817	924
Other female factor	1063	910	1094	1473	1623
Male factor	1882	1621	1585	1477	1607
Combined	1129	905	819	1468	1742
Unexplained	679	575	659	1052	1125

Type of treatment					
IVF	1146	923	878	1267	1475
ICS	3585	2977	3351	4233	4722
TESA	85	60	44		
FER	419	427	379		
IVF/ICSI + ET with donor oocytes	41	35	49		
ET with donor embryos	3	4	6		
No intervention	197	124	123		
Outcomes					
Oocyte retrieval	4859	3999	4333	5434	6084
Nr of oocytes in average	8.4	8.3	7.9	8.1	7.6
ET	4987	4161	4453	5699	6277
Nr of transferred embryos average	2.2	2.1	2.1	1.8	2
Nr of clinical pregnancies	1649	1462	1563	1721	1803

Legend to Table1.
*Difference between the number of cases reported by the institutes and the number of procedures reported to the National Health Insurance Fund (NHIF) for the purpose of financing.
** 30/2015. (II. 25.) Government Decree 37. § a) modified collecting and reporting methods of ART treatments. As the data collection in the reference year 2014 was not carried out in accordance with the new requirements, warns against drawing meaningful conclusions or comparisons.
(Sources:

[1] https://www.aeek.hu/documents/20182/607007/IVF_adatszolgaltatas_2010eves.pdf/079480aa-ff3b-51da-d8a7-595d174b9205

[2] https://www.aeek.hu/documents/20182/607007/IVF+adatszolgaltatas_weboldal_2011+eves.pdf/6a964b28-a26-51aa-dfda-0231f955a0bb

[3] https://www.aeek.hu/documents/20182/607007/IVF+adatszolgaltatas_weboldal_2012+eves_ki_v%C3%A9gleges_mod.pdf/54ad2bfc-b197-dca0-b8d9-7ab63e70f192

[4] https://www.aeek.hu/documents/20182/607007/IVF+adatszolgaltatas_weboldal_2013+eves_ki.pdf/a8f06b5e-e7b0-c014-b7c4-ab889e71f465

[5] http://www.ijsz.hu/UserFiles/ivf_jelentes_2014.pdf)

The order of reporting data on the Human Reproductive Procedures' Performance in Hungary was modified by the 30/2015. (II. 25.) Government Decree 37. § a), because it was impracticable to produce data on live births and the number of live births associated with a given birth (i. a. number of twins).

Utilization of assisted reproductive treatments (ART) in Hungary

The significance of a certain health impairment is well illustrated by the utilization of data on the intervention to treat it. In case of assisted reproduction, we can compare social needs of fertility treatments with respect to the growth in number of annual cases.

The structure, operation, and resource management of the Hungarian health care system are discussed in detail [33-39] and the application of one-day procedures in general and in the field of gynaecology and obstetrics from the purchaser's point of view is also analysed in Hungarian context [40, 41].

The Nr. 339/2008. (XII. 30.) Government Decree regulates the scope, method, place of publication, and control of the required statistical data on human reproductive procedures' performance in Hungary [42]. According to the Decree, since 2009 health care providers performing ART procedures shall report information electronically to the Health Minister on publicly financed and non-funded cases. The Minister shall maintain the Database of Reproductive Procedures, compile an Annual Statistical Report based on the Database following international reporting principles, and publish it in the second year following the year under review.

Our aim was to assess the case numbers of assisted reproductive interventions in Hungary between 2010 and 2018 with regards to the type of intervention, patients, regional distributions, and form of financing. Cases were classified in fashion of the International Classification of Health Interventions (ICHI, earlier the International Classification of Procedures in Medicine ICPM), which is a code system containing a list of examinations and interventions eligible for outpatient care, used primarily for financial accounting, and also for patient documentation and professional data collection [19]. Regarding ART investigations, follicle puncture, embryo transfer, intracytoplasmic sperm injection, controlled ovarian hyperstimulation, and assisted hatching are listed in Table 2.

Table 2.

Description of assisted reproductive treatments based on International Classification of Health Interventions (WHO) codes in Hungary

ICHI	ABRV	Procedure	Description
14703	FP	Follicle puncture	Ultrasound-guided follicular fluid extraction from spontaneously or medically stimulated ovaries for the purpose of obtaining oocytes (Aspiratio ovarii p. fertilisationem artef. USG dir.)
92722	ET	Embryo transfer	Injection of fertilized oocytes into uterus
97722	ICSI	Intracytoplasmic sperm injection	Fertilization of an oocyte by injection of sperm into the oocyte (ICSI)
97723	COH	Controlled ovarian hyperstimulation	Controlled ovarian stimulation involving the use of fertility medications to induce ovulation by multiple ovarian follicles (Stimulatio ovarii medicamentosa p. fertilisationem)
97724	AH	Assisted hatching	Artificially disrupting (mechanical, chemical, or laser treatment) of the zona pellucida surrounding the embryo to facilitate implantation.

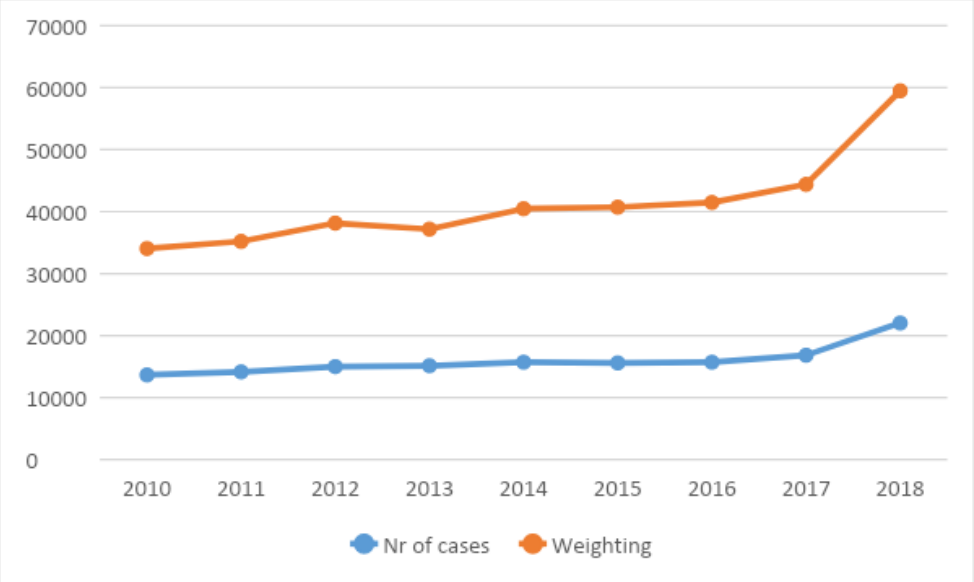
Source: WHO: International Classification of Health Interventions (ICHI)

https://www.who.int/classifications/ichi/en/,

Our database was derived from the funding records of the National Health Insurance Fund (NHIF) [Nemzeti Egészségbiztosítási Alapkezelő (NEAK)]. In the period under review, until 1 January 2017, the health insurance organization and thereby the data provider was the legal predecessor of the National Health Insurance Fund (NHIF) [Országos Egészségbiztosítási Pénztár (OEP)]. The database covers the number of cases of infertility treatments between 2010-2018, accounted in the publicly funded and also in billable/chargeable form following Annex 9 of the 9/1993. (IV.2.) Decree of the Ministry of National Economy [43].

Cumulative number of cases increased by 61.39%, from 13 643 to 22 019 during the reference years as shown on Figure 5. Follicle Puncture (FP) (4 790 – 6 249) followed by Controlled Ovarian Hyperstimulation (COH) (3 351 – 6 419) were carried out in the largest number and the most dynamic rise was shown by Assisted Hatching (AH), with 126% increase.

Figure 3.



Year over year growth of the utilization of assisted reproductive treatments based on International Classification of Health Interventions (WHO) codes in Hungary between 2010-2018

Table 3.

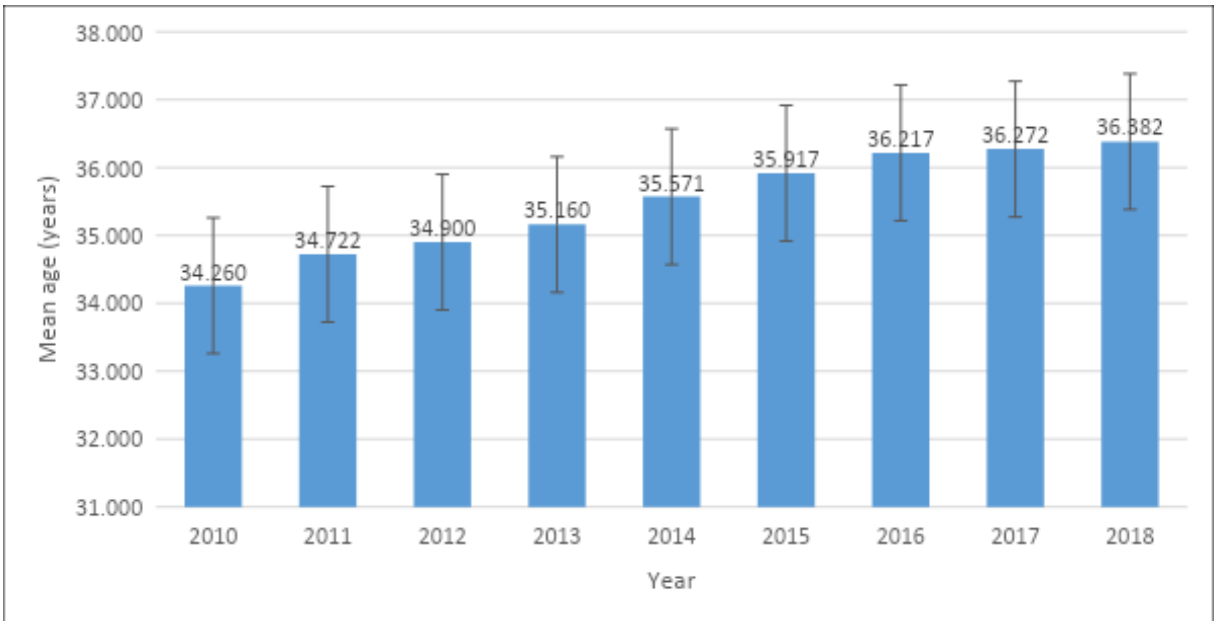
The utilization of assisted reproductive treatments based on International Classification of Health Interventions (WHO) codes in Hungary by type of interventions between 2010-2018

*number of treatments

ICHI	**ABRV**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**Total***
14703	FP	4 790	4 929	5 174	5 178	5 333	5 413	5 213	5 525	6 249	47 804
92722	ET	2 448	2 445	2 587	2 738	2 847	2 842	2 890	3 030	3 658	25 485
97722	ICSI	1 834	1 898	2 119	1 879	1 918	1 649	1 639	1 719	2 938	17 593
97723	COH	3 351	3 466	3 618	3 990	4 226	4 290	4 528	4 999	6 419	38 887
97724	AH	1 220	1 403	1 493	1 350	1 372	1 391	1 423	1 550	2 755	13 957
Total		**13 643**	**14 141**	**14 991**	**15 135**	**15 696**	**15 585**	**15 693**	**16 823**	**22 019**	**143 726**

To demonstrate changes in the patient population receiving care, the growth of utilization, and share of care providers, the database included gender (in this case patients were only females), age, patients domicile per counties, name of care establishment, type of care provider, names of care providers, and number of cases treated and accounted for by NHIF during the study period. The trend of postponed childbearing could be observed on the growing age of women receiving the treatments. Mean age of patients was 35.564 years during this nine-year period, but it increased with 2.122 years from 2010 to 2018. (Figure 4.)

Figure 4.



The utilization of assisted reproductive treatments based on International Classification of Health Interventions (WHO) codes in Hungary by mean age of patients between 2010-2018

As it was assumed, 97.25% of the cases were financed by the standard medical care under Hungarian health insurance, although the number of self-financed cases expanded. Despite a hundredfold increase, it remained modest, barely exceeding 2% of the total number of treated cases. (Table 4.)

Table 4.

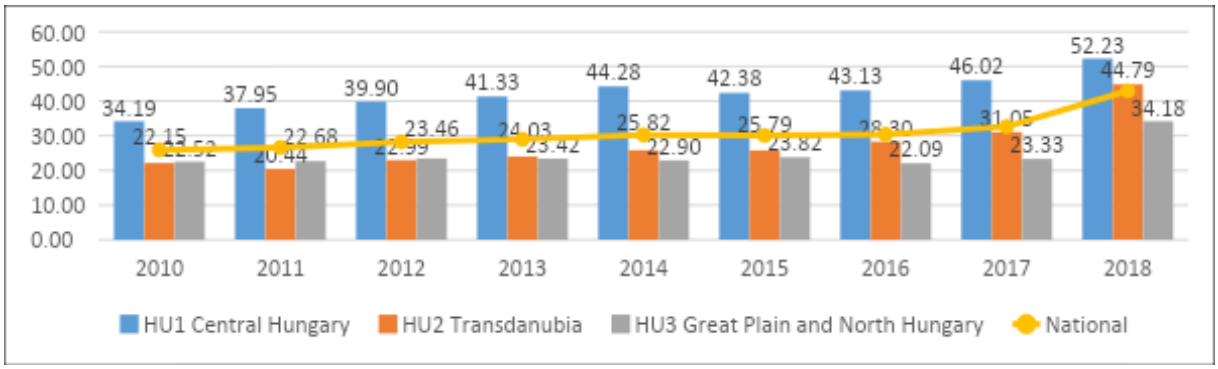
The utilization of assisted reproductive treatments based on International Classification of Health Interventions (WHO) codes in Hungary by financial categories between 2010-2018

*number of treatments

Financial categories	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**Total***
Medical care covered by Hungarian health insurance	13 629	14 126	14 952	14 940	15 356	15 220	15 179	15 634	20 883	139 919
Other, self-financed medical care for persons without Hungarian health insurance	10	15	34	195	340	365	375	895	1 136	3 365
Provision of services on the basis of international contracts	0	0	5	0	0	0	0	0	0	5
Medical care of Hungarian insured patients, including intervention with medical research purposes	4	0	0	0	0	0	139	294	0	437
Total	**13 643**	**14 141**	**14 991**	**15 135**	**15 696**	**15 585**	**15 693**	**16 823**	**22 019**	**143 726**

Regional and territorial distribution of the utilization of the treatments as described by the patient's residence shows a robust variance. During the studied timeframe most patients who received the interventions lived in Central Hungary NUTS 1 region. If we analyse the number of cases per 10 000 inhabitants by counties, utilization values of Baranya County (79.569) were significantly higher in 2018 compared to the national mean value (43.117). (Figure 5.) The amount of increase is worrisome in Baranya, where cases doubled compared to 2010. In addition to Baranya, Hajdú-Bihar, Tolna, and Somogy counties had outstanding utilization values as well. (Figure 6.)

Figure 5.



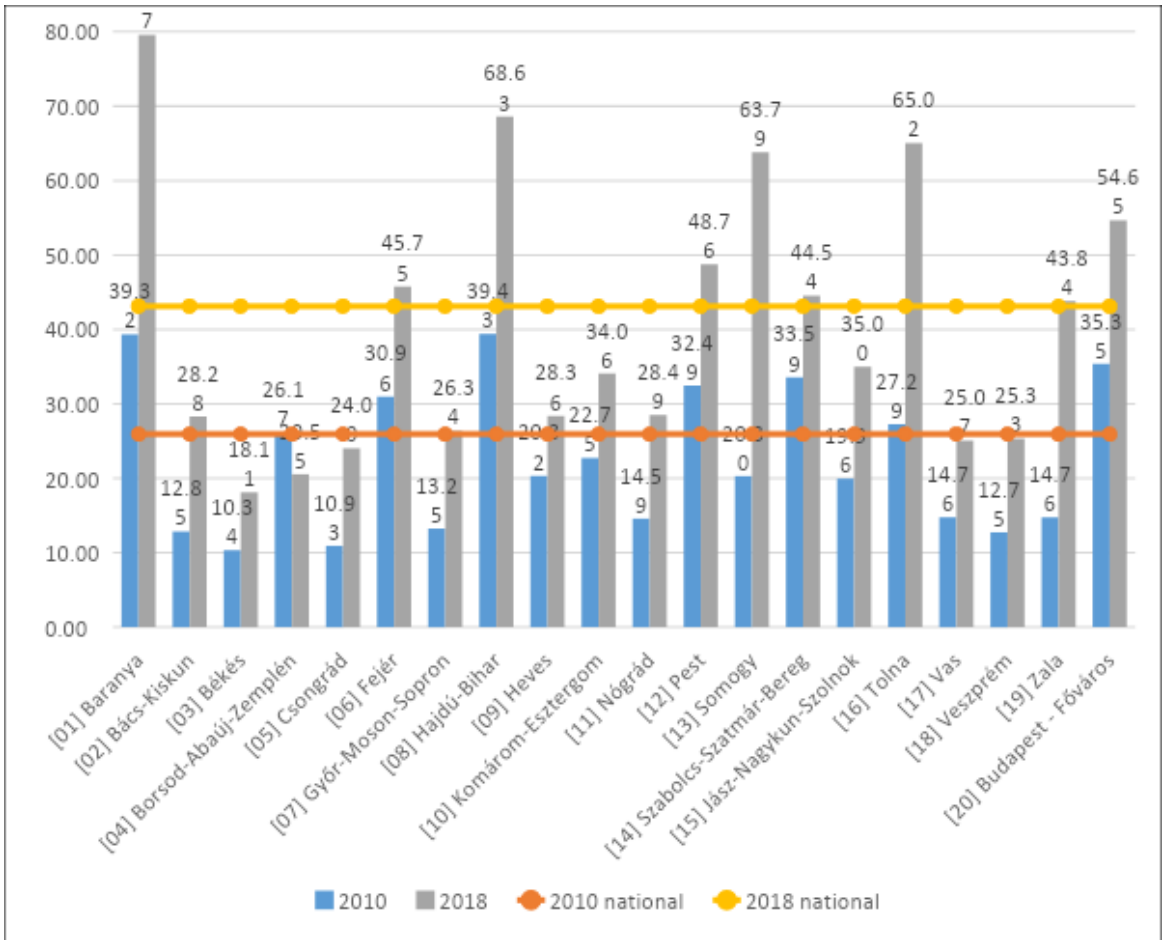
Regional distribution* of the utilization of assisted reproductive treatments** based on International Classification of Health Interventions (WHO) codes in Hungary

by NUTS 1 statistical regions between 2010-2018

*As described by the patient's residence

**Number of cases per 10 000 inhabitants

Figure 6.



Territorial distribution of the utilization of assisted reproductive treatments* based on International Classification of Health Interventions (WHO) codes in Hungary by counties between 2010-2018

*Number of cases per 10 000 inhabitants

Unfortunately, NHIF does not record whether a given livebirth was the result of ART and it is not possible to establish the exact relationship for twins born. However, the utilization data of fertility interventions demonstrate the changing patterns and the importance of this issue well.

Legislative changes in the field of ART

Recognizing the above trends, to halt population decline and make infertility treatments widely available, the government has decided on a series of measures to address infertility. Legislative changes came into force on 1th of February 2020 with the No. 2/2020. (I. 30.) Regulation of the Minister of Human Resources amending certain ministerial decrees on health insurance and the No. 4/2020. (I. 31.) Government Decree on certain financing issues related to the management of infertility [44, 45]. According to the published government decrees, the investigations were classified as of national strategic importance in the public interest. Medicines and interventions used in infertility treatment will become free, and infertility testing will be free from July 2020, the performance-volume limit will be abolished, there will be no waiting lists, and six private infertility centres will be under the control of the state.

Efforts to improve success rates

Despite all micromanipulation, microsurgery, and embryo transfer techniques, pregnancy and birth rates are far behind expectations. Efforts were also made by the Human Reproduction Scientific Research Group of the Hungarian Academy of Sciences – University of Pécs to improve success rates of ART. The main task of the research group since 1 May 2012 has been to detect and investigate potential biomarkers for ART from both the follicular fluid surrounding the oocyte and the culture medium of the human embryo. The research is focused on the identification of biomarkers that may indicate embryo viability, implantation ability, and genetic intactness [46]. As a junior research fellow, I assisted studies on follicular fluid examination. In observational clinical studies the research group examined, inter alia, the role of levels of total antioxidant capacity (TAC) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) [47] and also the levels of sirtuin 1, sirtuin 6 and resveratrol [48] of serum and follicular fluid (FF) in women undergoing in vitro fertilization.

The impact of these biomarkers on IVF outcome was analysed. It was demonstrated that TAC and 8-OHdG responded to controlled ovarian hyperstimulation (COH) differently. No relationship could be detected in their FF levels, although their cumulative serum levels were inversely related. Both FF TAC and FF 8-OHdG had a negative impact on the number of good

quality embryos, while such influence on their maternal serum levels could not be observed. When patients with and without endometriosis were evaluated separately, inconsistent results were obtained. However, patients without endometriosis had higher levels of serum and FF TAC when they progressed to clinical pregnancy. These findings support the notion that oxidative stress (OS) had an important contribution to the reproductive potential in IVF patients [47].

COH resulted significantly higher levels of serum Sirtuin1 (SIRT1) in pregnant (8 patients) compared to non-pregnant (22 patients) group (p=0.039); SIRT6 remained unchanged and it was markedly reduced in the pregnant group (before and after hyperstimulation p=0.002 and p=0.049). Both SIRTs could be detected in FF but they appeared to be independent of their serum levels. After correction for confounders, FF SIRT6 was positively related to matured oocytes (F=6.609, p=0.016), whereas serum SIRT1 and SIRT6 to clinical pregnancies (F=10.008, p=0.005; F=5.268, p=0.031). It was demonstrated that SIRT1 and SIRT6 but not resveratrol is involved in human reproduction and they may have a role in oocyte maturation and clinical pregnancy in IVF [48].

After learning about the above biomedical aspects on to improvement of success rates, with respect to former research experience on the importance of PA on female health [49-52] we decided to shift the focus of the current study from the main field of the research group, under the guidance of Dr Ákos Várnagy and Dr Kinga Lampek. Our research interest turned to psychosocial and lifestyle factors, with the aim to extend investigation methods with a multicausal approach. (Figure 7.)

Figure 7.

Biomedical	**Multicausal approach**
• Examination of biomarkers (metabolites) in follicular fluid and culture medium • Morphology and morphokinetics • Endometrial receptivity	+ PSYCHOSOCIAL FACTORS + LIFESTYLE

Change in research interest

Physical activity (PA) and health status

During our analysis, we considered physical activity (PA) as an emphasized lifestyle aspect. PA is an important factor among the determinants of health due to its protective factor and preventive role [6]. More than half of the Hungarian population is overweight and two thirds do not do sports regularly [53, 54]. Such behaviours have been associated with chronic metabolic and

musculoskeletal disorders such as type two diabetes, hypertension, obesity, and coronary heart disease, as well as psychological impairments and imbalanced mental health status [55-59].

PA Recommendations

Physical Inactivity is considered by the WHO as a Global Public Health Problem. Global age-standardised prevalence of insufficient PA was 27.5% in 2016, with more than 8% of gender difference [23.4% (21.1–30.7) in men vs 31.7% (28.6–39.0) in women]. Between 2001-2016 the levels of inactivity were stable as reported by Guthold et al. based on pooled analysis of 358 population-based surveys with 1.9 million participants [60, 61]. To counteract these worldwide trends, WHO Member States have agreed to aim to reduce physical inactivity by 10% by 2025 and by 15% by 2030 [4, 62].

The PA strategy for the WHO European Region 2016–2025 focuses on physical activity as a leading factor in health and well-being in the Europe, with particular attention to the burden of non-communicable diseases associated with insufficient activity levels and sedentary behaviour. Regarding females, the strategy only highlights that member states should provide information about the importance of PA during pregnancy about the benefits of being physically active and of maintaining a healthy body weight prior to and during pregnancy, including during antenatal classes. It suggests risk assessment and screening approaches to identify pregnant women requiring more support for behavioural change [3].

The World Health Organization (WHO) guidelines and recommendations state that to maintain health, adults younger than 65 years old should perform at least 150 minutes of moderate intensity PA or at least 75 minutes of vigorous intensity PA throughout the week. For additional health benefits, adults should increase moderate-intensity PA to 300 minutes per week, or equivalent. In this case PA has been defined as “any bodily movement produced by skeletal muscles that results in energy expenditure” [3, 4, 63].

In the United States (US) all adults (approximately 117 million people) suffer from at least one preventable chronic disease. In the meantime, seven of the ten most common chronic diseases could be prevented, or their risk may be reduced by regular PA. To counteract this warning situation, the Physical Activity Guidelines for Americans (PAGA) has been published by the Physical Activity Guidelines Advisory Committee (PAGAC) of the US Department of Health and Human Services in 2008.

Regarding the second edition of the guidelines published in 2018, still nearly 80% of adults were yet to meet the key guidelines for both aerobic and muscle-strengthening activity, while only about half met the key guidelines for aerobic PA, which is linked to approximately 117 billion USD

annually in health care costs and about 10% of premature mortality in the US [5, 6, 64]. The PAGAC guideline recommends 150 to 300 minutes of moderate-intensity PA per week for adults to be considered as active. This target is recommended to be met either by 60 to 75 minutes of moderate-intensity activities per day, or by 30 to 40 minutes vigorous-intensity activities per day. A new aspect of the guideline is sedentary behaviour due to its high prevalence; it is noted that at the greatest volume of moderate to vigorous physical activity (MVPA), the risk of all-cause mortality is low even for those who sit the most [64].

Similarly to the FYSS (Physical Activity in the Prevention and Treatment of Disease*)* in Sweden or PAGA in the US, specific guidelines for Hungarians is not yet available [55, 64]. Nevertheless, there is a growing emphasis on the topic, i.e. in the frame of the Exercise is Medicine Programme adapted by the Hungarian Society of Sport Sciences or by the National Sport Strategy [65, 66]

Significance of PA in women's reproductive health

In the case of female reproduction, the American Obstetrics and Gynecology Association's (ACOG) recommendation of PA for 150 minutes per week is noteworthy, suggesting moderate PA of 20-30 minutes almost every day of the week [67] that can help prevent pregnancy diabetes mellitus, preeclampsia, and chronic musculoskeletal disorders; maintain a healthy weight; and improve mental health [68-72]. In contrast, the recommendations of the American Sports Physicians Association (ACSM) and the World Health Organization (WHO) not only count exercise for the recommended 150 minutes per week, but also consider all physical activity that involves energy [73, 74]. PA should therefore also include activity in leisure or recreation, or in other areas of life such as transport (active transport) or work (as a professional). Particular emphasis should be placed on PA during housekeeping, domestic work, child-rearing, caring for the elderly or sick when examining pregnancy [56, 75]. In our cross-sectional preliminary survey, we conducted a pilot evaluation of socio-demographic, anthropometric, gestational, health, and quality of life (WHOQOL BREF) and physical activity (GPAQ) data in uncomplicated pregnancies. The purpose of our study was to describe the type, frequency, duration and intensity of physical activity in pregnant women, to determine whether these women achieve the activity determined in the recommendations, and whether activity patterns correlate with their self-rated health and quality of life.

Respondents spent an average of two hours per week (133.93 ± 137.06 min/week; 535.73 ± 548.26 MET) with active traffic, one hour per week (62.80 ± 98.17 min/week, 251.19 ± 392.66 MET) with moderate recreation, and an average of six hours a day (357.46 ± 178.38 minutes) with

sitting. Their moderate to vigorous physical activity (MVPA) reached 1457.97 ± 1970.90 MET, with 47.46% achieving at least 150 min/week MVPA. There was a significant negative correlation (R=-0.318, p=0.014) between physical health and work-related moderate movement and significant negative correlation (R=-0.318, p=0.019) regarding active transport. Negative correlation existed between psychological subject matter and moderate work (R=-0.291, p=0.027) and there was a significant positive correlation regarding moderate recreational activity (R=0.258, p=0.048). Our results confirm that moderate intensity recreational and transport-related physical activity has a positive effect on quality of life during pregnancy [76].

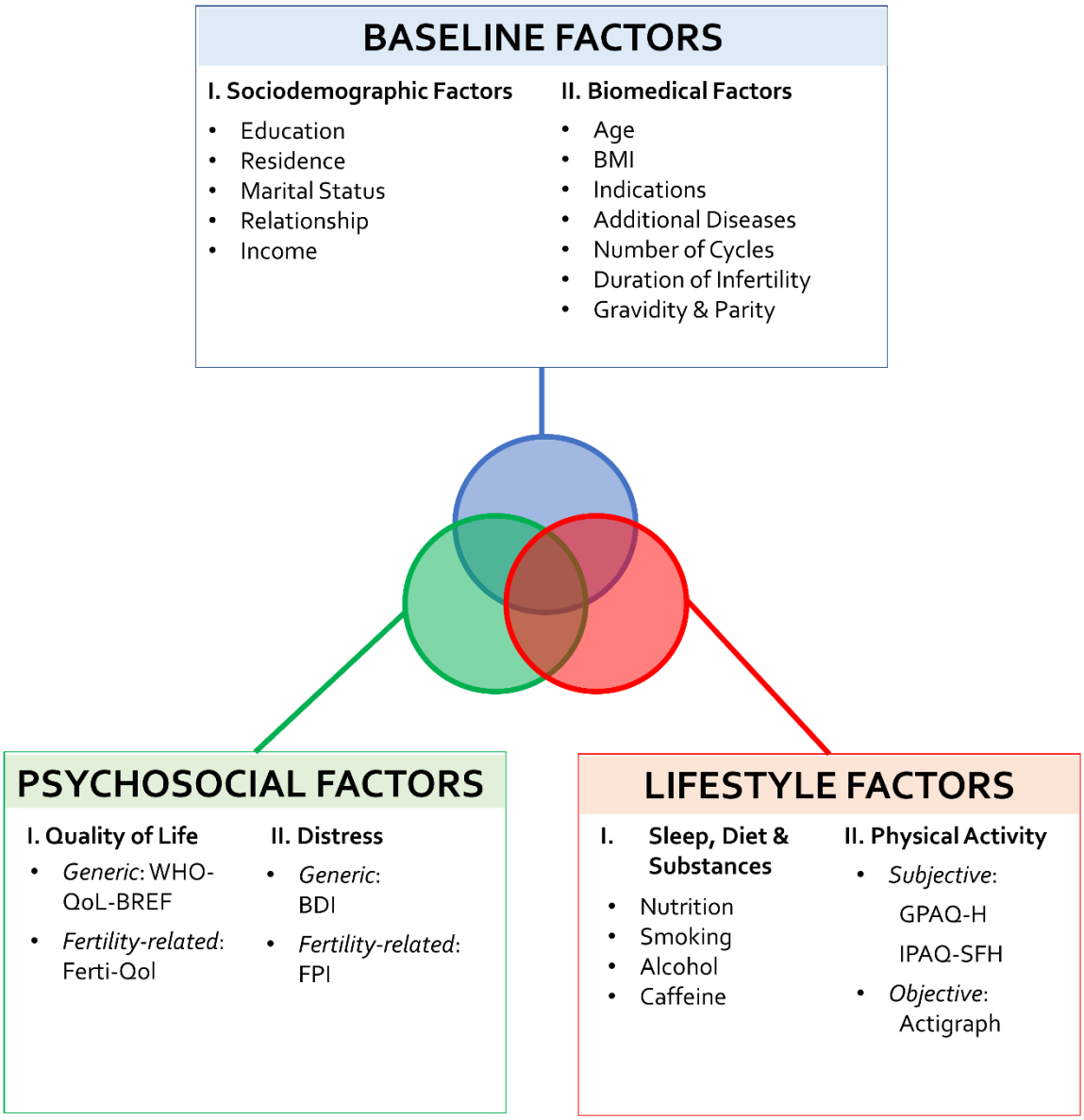
Theoretical framework of the dissertation

Researchers can rely on a wide-ranging theory related to infertility, while the scientific paradigm in the conceptualization of infertility varies considerably. The study of Lakatos et al extensively presented these linear vs complex theoretical models on individual and community level and described the biomedical, sociodemographic, evolutionist and psychological paradigms. While Lakatos considers the biomedical aspect to be reductive as it interprets infertility as a personal reproductive dysfunction, she nevertheless admits that the results of biomedical researches helped a large number of couples to become parents, parallel to the decrease of several undefined indications. Contrary to linear paradigms, evolutionist and circular models have a holistic approach. The circular model is also a psychological model, which analyses the somatic symptoms of psychiatric distress, while also responds to the diagnosis of infertility, medical interventions, and the psychic consequences of childlessness from a biopsychosocial perspective.

Following the authors' opinion, couples with infertility problems should become familiar with the adverse effects and should take steps to manage and change them. Therefore, in addition to the medical diagnosis, non-biological aspects of the reproductive dysfunction may be just as important as environmental factors, psychosocial distress, negative judgement, impact of diagnosis, negative consequences of interventions or non-adaptive coping. To ensure successful reproduction, monitoring of and disarming the negative psychological factors are necessary [77].

Using the abovementioned theoretical framework, the following multi-causal model was developed, which does not only consider the biomedical and psychosocial factors, but also focuses on the importance of lifestyle and, in particular, PA.

Figure 8.



Multicausal model to examine the factors influencing outcome measures of ART

Aims

The overall aim was to investigate the effects of pre-treatment habitual physical activity on course and outcome measures of assisted reproductive therapy.

Specific aims

•To analyse the utilization of assisted reproductive treatments in Hungary.

•To investigate the relationship between self-reported frequency of exercise and success of assisted reproduction in a pilot study.

•To explore in a qualitative synthesis of a systematic literature review on appropriate measurement methods of physical activity in association with ART.

•To assess the effects of psychosocial and lifestyle factors with special regard to physical activity on course and outcome of ART.

Pilot study - Relationship between self-reported frequency of exercise and success of assisted reproduction

Background

The increasing incidence of infertility, the stagnation of success rates of the treatments, and the reasons for success vs. failure are current research topics both from psychosocial and lifestyle points of view. It could be hypothesized that by decreasing the level of infertility related distress, abundance of pre-treatment moderate intensity physical activity will increase the success rate of ART. Therefore, the purpose of the present study was to examine the effect of physical activity (PA) and distress on success of ART.

Materials and methods

A cross-sectional, observational cohort study was conducted with consecutive sampling using a self-administrated questionnaire in paper-pencil form. Data collection was carried out at the Assisted Reproduction Unit, Department of Obstetrics and Gynaecology, University of Pécs, Baranya County, Hungary. Patient enrolment into ART procedure was approved by two independent physicians. Participants were recruited into this study according to the date of the consultation. The routine examination on the 3rd day of the unstimulated cycles presented a good possibility to get in contact with the patients and invite them to participate. The test battery was given to 100 female patients and 45 has returned until July 2017. The follow-up of outcome measures was conducted in May 2018.

All female patients with both female and male factors of infertility who were indicated for fertility treatment (IVF/ICSI) were consecutively invited to participate in the study according to the following inclusion criteria. Participants had a BMI $\geq$ 18 kg/m^2 and $\leq$ 38 kg/m^2 and had any significant abnormality relevant to the ART procedure and outcome (metabolic and vascular diseases including diabetes mellitus, metabolic syndrome, fatty liver diseases and atherosclerosis, severe endometriosis (stage III or IV) and/or adenomyosis. Participants were not at significant risk of severe ovarian hyperstimulation syndrome (OHSS), were not diagnosed with major depressive disorder (MDD) or any other mental disorders and had no significant physical or mobility impairments.

Assessment scales

The variables of the conceptual framework were measured by a survey: self-reporting questionnaires were filled out at home in a conventional paper-pencil form. Questionnaires were returned at the 21st day of the unstimulated cycles.

Socio-demographic characteristics were obtained by using questions regarding age, educational level, income, marital status, duration of partnership, duration of infertility, BMI, and lifestyle habits. Psychosocial characteristics were assessed by measuring the domains of depression/subjective well-being, anxiety, perceived stress, and infertility-related stress. To identify PA and exercise habits in general, participants reported on the frequency of exercise.

A total score was computed from the General Health Questionnaire (GHQ-12) as a screening tool of mental health. It is used as the outcome index of psychological distress experienced within the past few weeks. This scale focuses on breaks in normal functioning rather than on life-long traits. The questionnaire is scored on a 4-point Likert-type scale, and the cut-off point was 5 to determine the respondents' level of psychological well-being [78].

Beck Depression Inventory (BDI-13) was applied for reporting respondents' mental health status. BDI is widely used to measure the intensity of depression in general population [79-82], and in infertile patients as well [83, 84]. The questionnaire represents how the subject has been feeling in the last week. Each question has a set of at least four possible responses, ranging in intensity. A total score is computed and reflects the outcome index of depression. The validated Hungarian version of the short-form of the inventory with 13 items was completed by the respondents [85, 86].

To examine infertility-related stress with a specific scale, the Fertility Problem Inventory (FPI) was queried. FPI is a 46-item questionnaire developed to measure the level of infertility-related stress [87]. Patterns of infertility-related stress differed depending on gender, fertility history, and infertility diagnosis. The scale consists of five subscales identifying the following domains: social concerns (FPI1), sexual concerns (FPI2), relationship concerns (FPI3), rejection of childfree lifestyle (FPI4) and need for parenthood (FPI5). Permission for using the validated Hungarian version of FPI was sent to the authors [88].

In line with positive psychology, Psychological Immune Competence System (PICS) was applied. The questionnaire consists of 80 items and includes sixteen factors, which are divided into three subsystems: Approach Belief System, Monitoring-Creating Executing System and Self-

Regulating System. The subsystems are based on key psychological functions and refer to the mental resistance and adaptive coping capacity of the subjects [89, 90].

Ethical approval

The study was reviewed and approved by the University of Pécs, Clinical Center, Regional and Local Research Ethics Committee (Nr. 6955). Participants provided written informed consent prior to initiation of any study-related procedures, as shown by a signature on the Informed Consent Form. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Data analysis

Statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). Normality of data distribution was tested by Kolmogorov-Smirnov test. Depending on distribution, Student t-test or Mann-Whitney U-test were used to compare continuous variables. The association between two continuous variables was tested by Spearman's or Pearson's correlation coefficients and between two categorical variables was tested by Chi-square Test. Data was expressed as mean ± SD and the significance level of $p<0.05$ was considered in each case.

Results

General characteristics

The major socio-demographic characteristics of the study population are presented in Table 5. 45 female patients in reproductive age (33.2±5.4 years), with mostly normal weight (64,1%, BMI 18.5–24.9 kg/m2) participated in the study. They were sampled from a larger proportion with higher educational degree (46.7%) and with satisfactory economic status (87.5%). Each participant was either married or lived with a partner, and the duration of the partnership was 7.7±4.3 years on average with 3.1±2.0 years long child-wish.

Participants rated their health particularly good or very good, only 3 women reported 'fair general health' and another 3 women reported 'worse health during the treatment than before'. Participants experienced in average 5.0±2.9 psychosomatic symptoms during ART. In general, they self-reported a healthy lifestyle regarding diet, tobacco use and PA. Around 60% of them claimed to be physically active. We found various cases of infertility, duration and type of treatments. However, participants typically received IVF/ICSI (51.1%) with one year long (11.9±13.3 months) treatment because of female indication (33.3%).

Table 5.

Socio-demographic characteristics of the pilot study population

Socio-demographic Data N=45	
Age (years)	
Mean (SD)	33.2 (±5.4)
Education	
Low	6 (13.3%)
Intermediate	18 (40.0%)
High	21 (46.7%)
Marital status (N=44)	
Married	24 (53.3%)
Partner	20 (46.7%)
Place of residence	
County seat	16 (35.6%)
City	15 (33.3%)
Village	14 (31.1%)
Income	
Completely satisfied	4 (8.9%)
Rather satisfied	31 (68.9%)
Rather dissatisfied	10 (22.2%)
Health Status and Lifestyle	
BMI (kg/m^2, N=39)	
Mean (SD)	24.2 (±5.3) 5.32)
Underweight (<18.5)	2 (5.1%)
Normal weight (18.5–24.9)	25 (64.1%)
Overweight (25–29.9)	3 (7.7%)
Obesity (>30)	9 (23.1%)
Self-Rated Health - Before ART	
Excellent	3 (6.7%)
Very good	16 (35.6.0%)
Good	23 (51.1%)
Fair	3 (6.7%)
Self-Rated Health - Undergoing ART	
Much better	3 (6.7%)
Something better	7 (15.6.0%)
Same kind	32 (71.1%)
Somewhat worse	3 (6.7%)
Psychosomatic Symptoms	
Mean (SD)	5.0 (±2.9)
Healthy Diet	
Pay particular attention	6 (13.3%)
Pay some attention	31 (68.9%)
Not really	8 (17.8%)
Tobacco Use (N=44)	
Heavy	0 (0.0%)
Light	10 (22.7%)
Non-Smoker	34 (77.3%)
Exercise (N=44)	
Often	13 (29.5%)
Sometimes	14 (31.1%)
Not	17 (37.8%)
Infertility	
Case of infertility	
Female	15 (33.3%)
Male	4 (8.9%)
Dual	2 (4.4%)
Undefined (by med. professionals)	8 (17.8%)
Unknown (to the respondents)	16 (35.6%)
Type of ART Treatment – at baseline (N=31)	
IVF/ICSI	23 (51.1%)
IUI	3 (6.7%)
OI	5 (11.1%)
Examination in progress	14 (31.1%)
Duration of the Treatment (months)	
Mean (SD) months	11.9 (±13.3)
Min - Max	0 - 48.0
Child-wish	
Mean (SD) years	3.1 (2.0)
Relationship (years)	
Mean (SD)	7.7 (4.3)

Psychosocial characteristics

GHQ-12 resulted in average 2.3±2.1 points. Only four patients exceeded cut-off point 5, indicating the presence of mental health disorder.

At BDI-13, 73.3% of patients self-reported normal mood state. However, the study revealed various levels of depression within the cohort: results revealed that eight women were living with mild-, three women were living with moderate-, and one woman was living with severe depression. By invitation to the study, psychological support was offered for every patient who deemed it necessary. In comparison with previous reports on community samples, we can claim that the mean 5.0±4.1 depression level of this ART population lies within the normal range [84, 91-93]. (Table 6.)

Table 6.

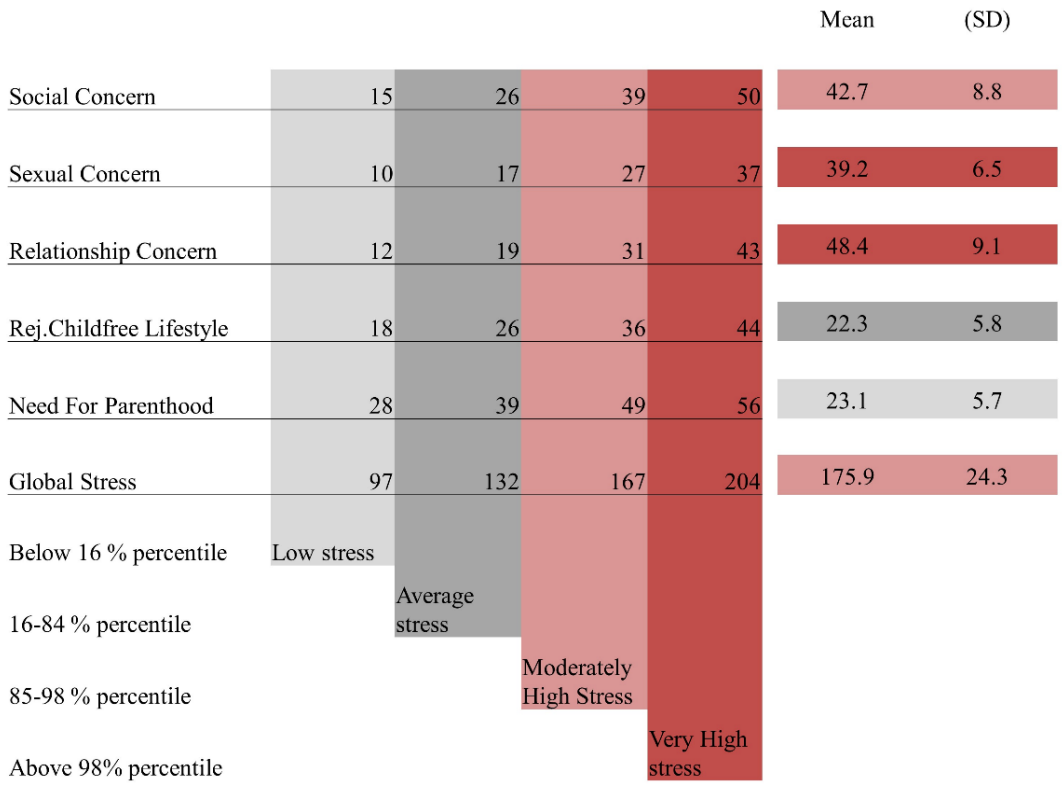
Pre-treatment psychosocial characteristics of women undergoing ART in the pilot study

Measure	Mean	SD	Median	Range	IQR lower	IQR upper
Child-wish (years)	3.2	2.0	3.0	8.5	2.0	3.9
Duration of treatment (months)	11.9	13.3	6.5	48.0	.3	20.3
GHQ-12 Score	2.3	2.1	2	10	1	3
BDI Score	5.0	4.1	5	18	2	7.5
Σ FPI	175.9	24.3	179.5	89.0	161.3	193.0
FPI1 Social Concerns	42.7	8.8	43.5	36	35	49
FPI2 Sexual Concerns	39.2	6.5	41	26	35	44.5
FPI3 Relationship Concerns	48.4	9.1	49	35	42	58
FPI4 Rejection of Childfree Lifestyle	22.3	5.8	23	23	18	25
FPI5 Need for Parenthood	23.1	5.7	24	22	17	27
Σ PICS	38.9	3.9	38.5	18.5	36.4	41.1
PICS Approach Belief System	13.7	1.6	13.6	6.1	12.4	13.6
PICS Monitoring-Creating Executing System	13.0	1.8	12.8	9.3	12.2	12.8
PICS Self Regulating System	12.0	2.2	12.3	9.0	10.5	12.3

We examined the psychosocial variables (BDI-13, GHQ-12) according to the duration of treatment (less or more than 3 years), but we could not find any differences between the variables (BDI-13: p=0.536, GHQ-12: p=0.803).

For the purpose of measuring the level of infertility-related stress, a more specific tool, the FPI was applied and moderately high *Global stress* (175.9±24.3) was explored. In the five domains of the questionnaire we found low stress by *Need for parenthood* (23.1±5.7), average stress by *Rejection of childfree lifestyle* (22.3±5.8), moderately high stress by *Social concern* (42.7±8.8) and very high stress level by *Sexual-* (39.2±6.5) and by *Relationship concern* (48.4±9.1). (Figure 9.) shows these results.

Figure 9.



Infertility related stress measured by Fertility Problem Inventory (FPI) in women undergoing assisted reproductive therapy (ART) (N=45)

Relationship between psychosocial characteristics and physical activity

Based on PA patterns, women were divided into two groups and means of baseline measures (child-wish, duration of the treatment and psychosocial scores) were compared regarding PA as the grouping variable (active/inactive). Results showed statistically significant difference between the

groups only for PICS *Self Regulating System* (p=0.034). (See Table 7.) *Synchronicity, Impulse control, Emotion control and Irritability control* belong to this subsystem, which stabilizes the person's inner emotional life and thus ensures the functioning of the first two subsystems.

Table 7.

Exercise Induced Differences in Psychological Health Domains in ART

	Active		**Inactive**		
Measure	Mean	SD	Mean	SD	p
Child-wish (years)	3.4	2.3	2.9	1.5	0.980
Duration of treatment (months)	13.5	14.1	9.9	11.9	0.453
GHQ-12 Score	2.6	2.5	2.1	1.9	0.692
BDI Score	4.8	4.8	5.1	3.9	0.422
Σ FPI	178.8	22.9	175.1	25.4	0.660
FPI1 Social Concerns	45.1	7.2	41.3	9.6	0.227
FPI2 Sexual Concerns	39.7	6.0	39.3	6.8	0.894
FPI3 Relationship Concerns	47.6	10.7	49.3	8.0	0.875
FPI4 Rejection of Childfree Lifestyle	22.8	6.2	22.1	5.8	0.502
FPI5 Need for Parenthood	23.1	6.0	23.1	5.7	0.979
Σ PICS	38.9	3.6	39.1	4.6	.502
PICS Approach Belief System	13.2	2.1	12.9	1.8	.283
PICS Monitoring-Creating Executing System	12.0	2.5	12.0	2.1	0.772
PICS Self Regulating System	13.2	1.6	14.2	1.4	**0.034***

*p≤ 0.05

During the follow-up of outcome measures we received limited information for various reasons. Some patients continued the treatments elsewhere or interrupted the therapy. From the 38 known women six successfully conceived, all of whom belonged to the physically active group. Positive significant relationship between pre-treatment PA and successful pregnancy (p=0.036) was found.

In this sample neither univariate tests nor multivariate analysis showed any difference on pre-treatment psychological measures between the two outcome groups, which may possibly be due to the relatively small sample size.

Discussion

It was assumed that by decreasing the level of infertility related distress, abundance of pre-treatment physical activity may increase the success rate of ART. In our survey 60% of the women studied announced regular physical activity. Measured by general scales, 73.3% of the whole study population self-reported normal mood state (average 5.0±4.1) with BDI-13 and 91.1% normal level of distress (average 2.3±2,1) with GHQ-12. Regarding an infertility specific scale, moderately high stress by social concern (42.7±8.8) and very high stress level by sexual- (39.2±6.5) and by relationship concern (48.4±9.1) of FPI was found. Significant difference between active and inactive groups was described for PICS Self Regulating System ($p=0.034$). During the follow-up of outcome measures only six successful pregnancies were noted, all of which were carried out by women who belonged to the physically active group. Positive significant relationship between pre-treatment PA and successful pregnancy ($p=0.036$) was found.

Stress and female reproduction are extensively investigated topics [94-97]. Clinical and empirical research proved the notion that infertility is distressing and that emotional instability due to grief and depression, anger, guilt, shock or denial, anxiety or loss of control influence the outcome of fertility treatments [94, 98].

Smeenk et al demonstrated in a multicentre prospective study with survey methods that pre-treatment levels of perceived anxiety ($p=0.01$) and depression ($p=0.03$) are significantly positively related to treatment outcome in IVF/ICSI. Similarly to our results, they measured 5.6±5.1 BDI-13 scores in 291 women who reached embryo transfer [84]. Their findings on the level of depression belong to the normal range of community samples [84, 91-93]. Jacob et al. investigated this particular question by examining studies that use standardized (general) scales on distress. Most of them found that the infecund patients are not significantly more clinically depressed than fertile controls [99]. The only study with differing results was carried out by Domar et al., who reported the results of BDI-21 using cut-off score 9 (instead of the commonly recommended cut-off score of 21), and 13 when using for clinical diagnosis of depression. With the first scoring 36.7% of the participants were diagnosed with depression, and with the second scoring 8.4% of women studied were recognised as living with depression [100].

To investigate the negative effect of pre-treatment levels of anxiety and depression on the outcome of IVF/ICSI, Smeenk et al. also administrated a *mixed method* study with 168 female patients. They compared the role of self-reports and endocrine variables, measured by concentration of adrenaline and cortisol, applying two general scales, BDI and State-Trait Anxiety Inventory (STAI) scales in ART. Similarly to their previous study, BDI scores were 5.4±4.7 on average. Significantly positive correlation was found between urinary adrenaline concentrations at baseline, embryo transfer (ET), and the scores on depression at baseline. By successful treatment, lower concentrations of adrenaline at oocyte retrieval and lower concentrations of adrenaline and noradrenaline at ET were observed. We extended our research with endocrine aspects in line with the work of abovementioned authors.

Kee et al. in their study on psychological strain in IVF compares average stress levels of 138 women with BDI. Women with unsuccessful IVF history had significantly higher level of depression than women with successful IVF history [101]. We did not found differences in BDI scores in the two outcome groups ($p=0.747$). Regarding the duration of infertility, BDI was moderately elevated in the first stage (<3 years), and the authors described a decreasing trend in psychological stress with an advanced infertility duration. On depression scales, the intermediate and final duration of infertility patients showed less symptomatology than the first-stage patients. In our research we did not find differences in BDI scores between the two outcome groups or regarding the duration of infertility ($p=0.536$).

Cserepes and co-authors investigated the infertility-related stress in a Hungarian infecund population and examined the effects of gender roles, child wish motives, subjective well-being, and marital relationship on the experience of infertility according to the conceptual framework using a general (BDI) and a fertility specific (Fertility Problem Inventory (FPI)) scale as well. Depressive symptoms correlated with infertility-related distress and fertility specific quality of life. In case of female patients, the researchers highlighted the importance of social (24.96±7.86) and relationship concerns (18.70±6.59) or rather the domain of need for parenthood (44.07±7.61) [88]. In our study conflicting results were found, as social and relationship concerns triggered moderate and very high stress levels, whereas the need for parenthood remained on average level.

Another fertility specific instrument, the Fertility Quality of Life (FertiQoL) questionnaire was developed to reliably measure the impact of fertility problems and its treatment on quality of life (QoL) [102]. Cserepes et. al conducted research using FertiQoL on Hungarian sample and in cross-cultural comparison. Comparing fertility specific and general questionnaires can be found in the literature in relation to FertiQol-BDI [103], FertiQol - Hospital Anxiety and Depression (HADS) [104, 105], FertiQol - WHOQOL [102].

Impact of psychological interventions on pregnancy rates in infertile women is underlined by Domar et. al [106, 107]. Other studies shift focus to lifestyle behaviours of women undergoing IVF and efficacy of mind/body intervention [108, 109]. In general, systematic reviews describe non-pharmacological interventions, such as exercise improving not only physical performance but other domains of quality of life [110-114].

We found a study on the connection between PA and psychological factors in IVF by Valoriani et al. Authors studied Hatha Yoga (HY) not only as exercise, but also as a psychological adjuvant, and found that women who are more distressed are more likely to accept psychological support before starting an IVF cycle and that in these women HY practice was associated with distress reduction ($p<0.0001$ for GHQ-12) [115].

PA appears to be beneficial during pregnancy as well. PA seems to reduce risks of gestational chronic diseases without adverse effects on the neonates [5, 116, 117]. In the absence of any contraindications, following the American Congress of Obstetricians and Gynaecologists recommendations pregnant women should engage in moderate intensity exercise for at least 30 minutes on most, if not all, days of the week [67, 118]. However, there are no definitive physical activity guidelines for women attempting conception, particularly for the window of implantation and luteal phase. Most of the studies take attention to risk of frequent vigorous PA on fertility [119, 120] and on success of ART [108, 121]. To describe PA levels both instrumental and self-report studies were published.

In line with our findings on the benefits of pre-treatment activity, Moran et al. reported positive effect of lifestyle intervention including exercise and diet in conjunction with ART in overweight and obese women and described elevated successful pregnancy rate (12／18 vs 8／20) in the intervention group compered to controls [122].

Conclusions

Infertility-specific scales provide more appropriate description on mental status of ART patients than general scales. Pre-treatment PA could positively influence success of ART. However, for more impressive results, detailed assessment of physical activity, increased number of participants, and further examinations are needed.

Limitations

Results of this study are advised to be interpreted in light of the low number of research participants. Further research should explore the correlation between pre-treatment PA and

infertility rates with larger sample size, applying more accurate measurement of moderate-intensity PA.

Qualitative synthesis - a systematic literature review on measurement of physical activity in association with ART

Background

Apart from the general positive effects of regular physical activity on health [123] it is a well-accepted fact that adequate amount of regular exercise plays a vital role in maintaining health during pregnancy and not only in promoting pregnancy [124]. The guidelines of the American College of Obstetricians and Gynecologists (ACOG) recommend approximately 150 minutes per week (20-30 minutes almost every day) of moderate-intensity physical activity in case of physiological pregnancies, i.e. in lack of any contraindication [125]. The results of this cross-sectional survey based on questionnaire data collection reflect that low-intensity recreational and active transport-related physical activity has a positive impact on quality of life during pregnancy [76].

Prior to this systematic review, the focus of our research interest was not only on pregnancy, but also on the delayed onset and failure of pregnancy. On the one hand increasing rates of infertility and the halt in the rate of success (30%) of assisted reproductive techniques (ART) [126] or examining the psychosocial and lifestyle causes of success/failure are current research topics [127]. On the other hand, no recommendation has been made to provide guidance specifically for women with infertility or for physical activity before and during treatment for reproduction. Therefore, we investigated the relationship between the success rates of pre-treatment physical activity and distress caused by infertility in women undergoing assisted reproductive therapy. In the previous cohort study, standard psychological questionnaires and pre-treatment habituation physical activity questions were included. From that study we were able to draw the following conclusions: infertility specific questionnaires give a more accurate picture of the mental state of patients undergoing reproductive therapy than general scales. Moderate but regular physical activity prior to treatment may have a positive effect on the outcome of ART treatment. Further and more detailed examination is needed to determine the effect of physical activity on pre-treatment psychosocial status [128].

The aim of this sub-study is to select the most appropriate method of measuring physical activity in the context of assisted reproduction by qualitative synthesis of a systematic literature review.

Material and methods

The systematic review was based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) criteria [129] which provides a clear protocol over traditional literature reviews analysing as much of the literature as possible in a non-selective, bias-free, and reproducible way with respect to a given research topic. Although PRISMA is primarily used for the analysis of randomized controlled clinical trials, it can also be used as a basis for reporting other types of studies [130].

We continued our research in the Web of Science, Medline (PubMed), Cochrane Library, and Science Direct databases, as well as through additional search. During the search, we focused on the words physical activity, exercise, human, assisted reproduction and In Vitro Fertilization. See Table 8 for a detailed definition of MeSH terms. A selection of English-language studies published over the last 15 years was selected for the analysis, with the last search conducted in January 2019. (Table 8.)

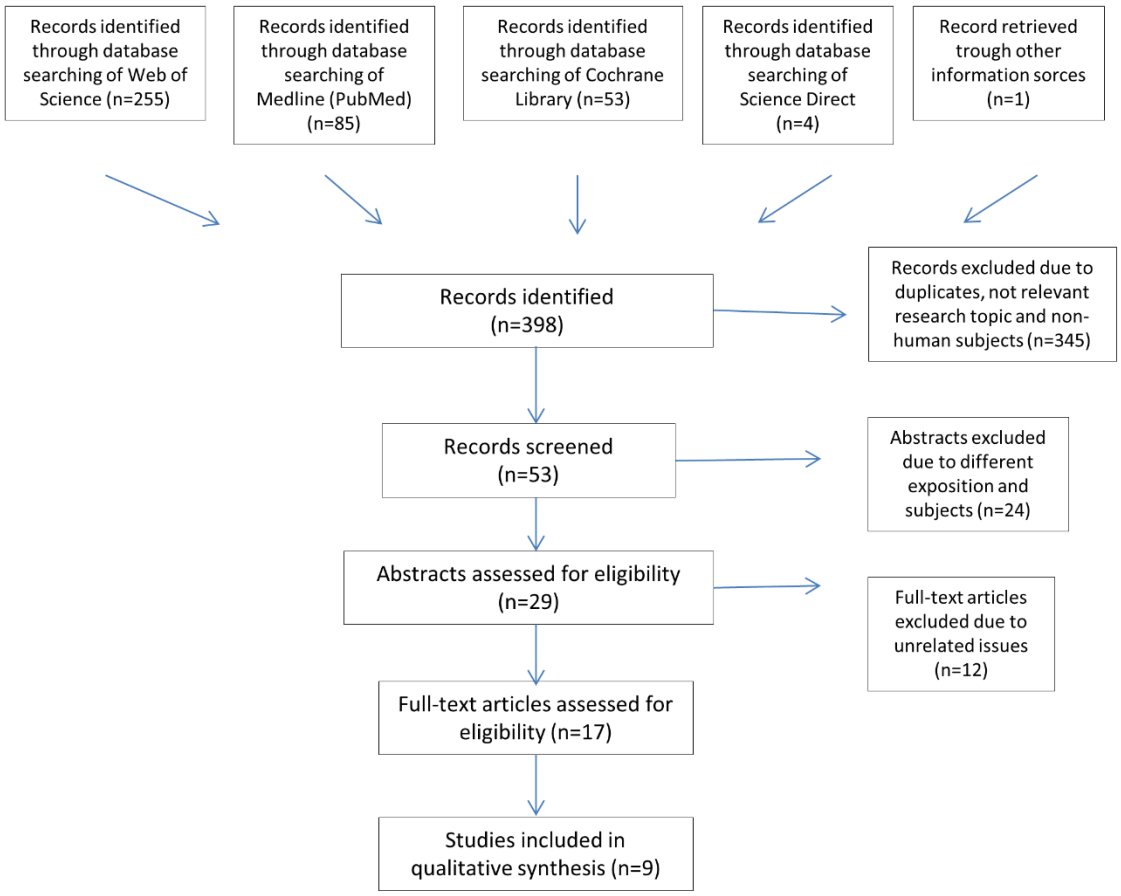
Table 8.

Literature Search Strategies for Measurement of Physical Activity in Association with Assisted Reproduction

Medline (PubMed)	(((((("Exercise"[MeSH Terms]) OR "Sport*"[MeSH Terms]) OR "Physical Activit*"[MeSH Terms]) AND "Female"[MeSH Terms]) AND "Humans"[MeSH Terms]) AND "Reproductive Techniques, Assisted"[MeSH Terms]) OR "In Vitro Fertilization*"[MeSH Terms]))
Web of Science	TS=((Exercise OR Sport* OR Physical Activit*) AND (Assisted Reprod* OR In Vitro Fertilization*))
Science Direct	title-abs-key((Exercise OR Sport* OR Physical Activit*) AND (Assisted Reprod* OR In Vitro Fertilization*))
Cochrane Library	#1 mh Exercise or mh Physical next Activity #2 mh assisted next reproduction* or mh In next Vitro next Fertilization

The 398 related studies found were reviewed by two independent researchers, with a third opinion involved in case of disagreement. After applying the exclusion criteria (non-relevant/different to the research topic and non-human subjects), 53 results were identified, of which further 24 were excluded after reading the abstracts with respect to parallelism, different exposure, and research subject. Finally, 17 in extenso publications were examined, 9 of them were relevant and included in the qualitative synthesis. (Figure 10.)

Figure 10.



Process of study selection on the measurement methods of physical activity in relation to assisted reproduction - PRISMA Chart

The studies included women with infertility diagnosis, with female ART indication alone, with prima- and multipara subjects of different ages, different body mass indexes, for whom exercise was not contraindicated. Studies on non-human subjects and cohorts with specific indications (eg. endometriosis, insulin resistance) were excluded. Our analysis focused on examining the relationship between pre-treatment habitual physical activity or exercise and any of the output indicators of ART treatment, with particular reference to the quantifiability and objectivity of the physical activity measurement methods used.

Results

The total number of patients studied in the 9 studies involved in the qualitative study was 3404 (Tables 9a and b). In most cases there was no intervention and control group, with the exception of one study in which Palomba and co-authors investigated the effectiveness of lifestyle change programs in patients with obesity prior to the ART cycle [131]. The studies were carried out with approximately 100-200 participants, with the exception of the study of Morris et al. in which 2232 women enrolled from Boston and its agglomeration, measuring lifetime activity patterns prior to IVF [121].

Authors predicted the extent of physical activity according to subjective surveys based on self-esteem, in some cases including questions of simple frequency, as in the study above. Morris and co-workers asked the following 5 questions about exercise: “Do you exercise regularly? If yes, as an adult, how many years did you exercise regularly? How many hours do you exercise per week? How many months a year? What is your most common training method?”.

Apart from the questions referring to smoking, alcohol, caffeine, vegetable/fruit consumption, use of herbs, acupuncture, and sleep during IVF cycle, Domar and co-authors used the following dichotomous question in a more fundamental form as part of the Lifestyle and Health Habits Questionnaire (LHHQ): “ Do you exercise regularly? Yes/No”, “If so, how many days a week?” [108]

We found a total of 5 specific questionnaires used in interview or self-report to measure physical activity in infertility treatment. The bottleneck can be found in the study of Kucuk et al on the extent of physical activity. The Godin Leisure-Time Exercise Questionnaire (GLTEQ) only asked about the frequency of leisure time activities (Godin and Shephard 1985), although supplemented by its intensity: "In a typical 7-day period, how often do you do strenuous/moderate/mild exercise?" To which patients can give categorical answers: often/sometimes/never or rarely [132].

Gaskins and his team, based on the Self-Administered Physical Activity Questionnaire (PAQ), have assessed weekly physical activity over the past year for specific recreational activities, such as walking, jogging, running, biking, swimming, tennis, squash, weight lifting, aerobics, and moderate to heavy outdoor work, based on which metabolic equivalent (MET: Metabolic Equivalent of Task) can be calculated [133, 134].

The next study by Kucuk and his research team has sought to measure physical activity in a more quantifiable way and by using the International Physical Activity Questionnaire - short form

(IPAQ-sf) [135] after measuring the duration of low, medium, and high intensity physical activity, inactive, minimally active, HEPA active (health-enhancing physical activity), and high activity categories they could develop combined total physical activity by calculating MET min/week as the sum of walking + moderate + intensive MET-min/week [136].

Applying the complete, 27-question version of the International Physical Activity Questionnaire (IPAQ-lf) [137] Ramezanzadeh and co-workers evaluated the total energy consumption (total MET) based on the Moderate to Vigorous Physical Activity (MVPA) in connection with work, recreation, and active transport and they also calculated MET values and MET-minute values [138].

Palomba et al. used the Global Physical Activity Questionnaire [139] to measure physical activity during ART process design and treatment. The multidomain questionnaire, which consists of 16 questions, covers many components of physical activity, such as intensity, duration, and frequency, and examines three areas in which physical activity is performed (work-related/occupational physical activity, transport-related physical activity, and recreational or leisure time physical activity). The fourth part relates to the sedentary inactive time. Based on the result, PA was categorized into 4 activity categories. Researchers aimed to examine in this study the efficiency of lifestyle change programs among obese women with fertility problems [131].

In the studies of Calhoun et al. and Evenson et al., we come across a multidomain questionnaire supplemented with an objective measurement method. Both studies used the Kaiser Physical Activity Survey (KPAS) and asked patients to wear an ActiGraph accelerometer from the day of embryo implantation to the βHCG test [140, 141]. KPAS is also a multidomain questionnaire specifically designed for women's physical activity, a summary index of 4 physical activities: based on housework/family care, active lifestyle, sports and work [142].

Table 9.a

Summary of Measurement Methods of Physical Activity in Association with Assisted Reproduction

Author - Title	Research tool - Efficiency	Findings
Calhoun, K. C., et al. (2012). "Association of short-term and long-term physical activity on implantation in in vitro fertilization (IVF) cycles."	**ActiGraph accelerometer** From day of embryo transfer until the day of βHCG testing **The Kaiser Physical Activity Survey (KPAS)** Designed specifically to assess activity in women 4 summary activity indexes: housework/caregiving, active living habits, sports, and occupation	• Women who conceived had higher median KPAS scores for active living (3.0, interquartile range (IQR): 2.3-3.3) and sports (3.8, IQR: 2.8-4.0) than women who did not conceive (2.5, IQR: 2.3-3.0 and 2.8, IQR: 1.8-4.0,) (P 0.04 and 0.05, respectively) • Time spent sedentary or in moderate/vigorous activity following embryo transfer did not differ by IVF outcome
Domar, A. D., et al. (2012). "Lifestyle behaviors in women undergoing in vitro fertilization: a prospective study."	**Lifestyle and Health Habits Questionnaire (LHHQ)** on exercise, smoking, alcohol, sleep, caffeine, herbs, acupuncture, and fruit/vegetable consumption. Have you exercised? Yes/No	• Lifestyle history and daily habit survey. Result(s): In the month before their IVF cycle • Patients continued to exercise regularly and drink caffeine daily, and almost half continued to drink alcohol • During their ART cycle, 100% exercised, 2% smoked, 49% drank alcohol, 77% drank caffeine, 12% took herbs, and 47% underwent acupuncture.
Evenson, K. R., et al. (2014). "Association of physical activity in the past year and immediately after in vitro fertilization on pregnancy."	**Accelerometer** From embryo transfer to serum pregnancy testing **Kaiser Physical Activity Survey (KPAS)** Evidence for both validity and reliability among pregnant women	• The adjusted odds of intrauterine gestation were higher among those that had higher continuous active living (odds ratio [OR] 1.96, 95% confidence interval [CI] 1.09-3.50), sports/exercise (OR 1.48, CI 1.02-2.15), and total activity (OR 1.52, 95% CI 1.15-2.01) indices related to past year • Accelerometer-measured physical activity and sedentary behaviour after embryo transfer were not associated with any IVF outcome
Gaskins, A. J., et al. (2016). "Maternal physical and sedentary activities in relation to reproductive outcomes following IVF."	**Self-Administered Physical Activity Questionnaire (PAQ)** Sensitivity at issue: Only specific physical activities was associated with higher probability of live birth in IVF	• Physical and sedentary activities in the year before IVF treatment • Time spent in moderate-to-vigorous physical activities and total metabolic equivalent task hours before IVF were not associated with outcome • Specific physical activities, only greater time spent in aerobics, rowing, and on the ski or stair machine was associated with higher probability of live birth

Table 9.b

Summary of Measurement Methods of Physical Activity in Association with Assisted Reproduction

Author - Title	Research tool - Efficiency	Findings
Kucuk, M., et al. (2010). "Assessment of the physical activity behavior and beliefs of infertile women during assisted reproductive technology treatment."	**Godin Leisure-Time Exercise Questionnaire (GLTEQ)** During a typical 7-Day period in your leisure time, how often do you engage in strenuous / moderate / mild exercise? often / sometimes - /never or rarely	• Women's physical activity may decline during ART treatment because of the misconception that pursuing their pre-treatment physical activity routine would decrease their chance of conceiving
Kucuk, M., et al. (2010). "Effect of energy expenditure and physical activity on the outcomes of assisted reproduction treatment."	**Physical Activity Questionnaire short form (IPAQ-sf)** Categories: low, moderate and high physical activity, inactive / minimally active / HEPA active (health enhancing physical activity; a high active) category A combined total physical activity MET-min/week can be computed as the sum of Walking + Moderate + Vigorous MET-min/week scores	• Women undergoing ART significantly decreased their activity level during the treatment period • However, women who were physically more active were more likely to have an increased implantation rate and live birth
Morris, S. N., et al. (2006). "Effects of lifetime exercise on the outcome of in vitro fertilization."	**5 questions about exercise** 1) Do you regularly exercise? 2) If so, as an adult, how many years have you engaged in regular exercise? 3) How many hours per week do you exercise? 4) How many months per year do you exercise? and 5) What is your most frequent type of exercise?	• Women who reported regular exercise were no more likely to have a live birth compared with those who did not report exercise • Women who reported exercising 4 hours or more per week for 1-9 years were 40% less likely to have a live birth (OR 0.6, CI 0.4-0.8) and were almost three times more likely to experience cycle cancellation (OR 2.8, CI 1.5-5.3) and twice as likely to have an implantation failure
Palomba S., et al. (2014). „Physical activity before IVF and ICSI cycles in infertile obese women: an observational cohort study."	**Global Physical Activity Questionnaire;** PA was administered during counselling and rechecked at the beginning of the treatment and graded a-d due subjective feelings and then categorized into two groups on the basis of regular physical activity (yes/no) it examine the role of lifestyle modification programmes in infertile obese women	• 216 obese infertile women at first ART with stable BMI • relative risks for a clinical pregnancy and livebirth were 3.22 (95% CI 1.53–6.78;P= 0.002) and 3.71 (95% CI 1.51–9.11;P= 0.004) in case of RPA before ART, irrespectively from losing weight
Ramezanzadeh, F., et al. (2012). "Impact of body mass index versus physical activity and calorie intake on assisted reproduction outcomes."	**International Physical Activity Questionnaires (IPAQ)** Assesses total energy expenditure by moderate- and vigorous-intensity exercise Metabolic equivalent of task (MET) values and formula for computation of MET-minutes were used.	• The number of oocytes retrieved was significantly higher in women of normal weight compared with overweight women, regardless of the level of PA. • Increased BMI, independent of calorie intake and PA, has an adverse effect on the number of oocytes retrieved in women aged 36 years, but does not affect the number of high-quality embryos or the success of the treatment cycle.

Discussion

Results of the examined researches showed that the activities of ART-treated women with regular, sufficient physical activity can contribute to the improvement of primary and secondary outcomes. By developing an appropriate PA monitoring methodology in conducting the research, we could further fine-tune the level and nature of pre-treatment physical activity to avoid potential risks.

Measuring the level of physical activity is not only a challenge for ART. While the positive effects of regular physical activity on health and well-being are evident (Lee, Shiroma et al., 2012, Husu, Suni et al., 2016, Ács, Prémusz et al., 2018) and there are many different methods available to determine its extent, it is challenging to include this aspect in real-life epidemiological studies [143, 144]. Physical activity volume measurement can either be objective (eg. accelerometers, heart rate monitors, exercise lab tests, etc.) or subjective (eg. questionnaire, diary, observations, etc.). Research with a large number of items generally uses questionnaires for cost-effectiveness and simpler data collection. However, they often greatly overestimate activity [145, 146].

Given the variety of the applied methodology, it is difficult to find analyses of physical activity based on representative statistical data that compare the same variables with the same methods. The following two questionnaires have been developed to eliminate the biased results of measurements and the lack of internationally comparable data: International Physical Activity Questionnaire (IPAQ) and WHO Global Physical Activity Questionnaire (GPAQ) [137, 139]. Both questionnaires have already been included in several Hungarian studies but their official translation, cultural adaptation and the Hungarian versions have not been validated so far. In the study carried out by our research group the translation process, the cultural adaptation and the validation in the general population were performed [147, 148].

Of the relevant studies found – perhaps in view of the less detailed questioning as only 5 questions were asked regarding the frequency, duration and type of exercise – the results of Morris et al. were different from the articles in the topic and our own results. According to their data, women who reported regular physical exercise were not more likely to have a live birth than those who did not train at all. These results on excessive physical activity are consistent with the literature. Women who reported more than 4 hours/week of exercise for 1 to 9 years (OR 0.6, CI 0.4-0.8) had a 40% lower chance of live birth, and were three times more likely to miss a cycle (OR 2.8, CI 1.5-5.3) and twice the chance of implant failure (OR 2.0, CI 1.4-3.1) or miscarriage. (OR 2.0, CI 1.2-3.4) [121]. Kucuk refuted the previous statement and concludes that women's

physical activity may decline during ART due to the misconception that continuing a pre-treatment physical activity routine would reduce the ability to conceive [132].

The following study draws attention to moderation. According to the PAQ questionnaire, in the study of Gaskins et al. women receiving IVF (N = 273) attended moderate to vigorous physical activity (MVPA) 2.8 (IQR 1.0, 6.0) hours/week and spent 49.0 (36.0, 62.5) hours per week sitting. MVPA levels were associated with a diagnosis of infertility (p = 0.04), particularly in women in the upper quartile who typically had ovulation disorders (13%) or decreased ovarian reserve (16.7%) compared with women in the lower quartile (3.7% és 11.1%) [149].

In determining the correct measure one may have the thought that in contrast to its ease of completion the disadvantage of IPAQ-sf is that respondents are unable to provide activities linked to different domains, i.e., work, recreation, and active traffic like in the complete version of the questionnaire [135]. Nevertheless, Kucuk et al., by measuring their energy use (MET min / week) based on IPAQ-sf, successfully demonstrated that women undergoing assisted reproductive therapy significantly reduced their activity during the treatment period ($p < 0.05$). They established a low (N=68) and a moderately active (N=63) group which showed that more physically active women had higher implant rates (31/160 (19.4%) vs 45/152 (29.6%), p=0.035), clinical pregnancy (23/68 (33.8%) 34/63 (54.0%) p=0.02) and live birth (15 (22.1%) vs 30 (47.6%), p= 0.002) [132]

Ramezanzadeh et al. also reported BMI as a prominent covariate in addition to PA. In their study of 240 women, the number of oocytes obtained was significantly higher in normal-weight than in overweight women (p=0.01), regardless of the degree of physical activity measured by IPAQ-lf. High BMI, irrespective of caloric intake and physical activity, had a negative effect on the number of oocytes removed at 36 years of age, but had no effect on the number of implantable embryos and the success of the treatment cycle [138].

Also dealing with obesity, Palomba et al. examined 216 obese women with stable BMI during fresh embryo implantation in IVF treatment in their study using GPAQ. Regarding change in lifestyle they found a three-fold odds of pregnancy and childbirth in regular physical activity prior to cycle, irrespective of weight loss: pregnancy (16/41, 39.0% active vs 28/175, 16.0%, inactive; p = 0.002), and live birth (10/41, 24.4% active vs 13/17 5, 7.4%, inactive; p = 0.004) [131].

Calhoun and his team have shown the most accurate results, along with a positive relationship with the Kaiser Physical Activity Survey in a 100-person study of women undergoing non-donor IVF embryo transfer. Higher median KPAS values have been documented for successful insemination due to active lifestyle (3.0, IQR: 2.3-3.3) and sport (3.8, IQR: 2.8-4.0) in all women who have not become pregnant (2.5, IQR: 2.3-3.0 and 2.8, IQR: 1.8-4.0,) (p= 0.04 and p=0.05).

Sedentary time and moderate / intense physical activity were not associated with IVF outcome [140].

Evenson and his research team surveyed 121 women undergoing a non-donor IVF embryo transfer under similar research circumstances, also using KPAS. The adjusted odds ratio for intrauterine pregnancy was higher for those with a higher index of active life expectancy (OR 1.96, 95% CI, 1.09-3.50), sports/exercise (OR 1.48, CI 1.02-2.15), and total activity (OR 1.52, 95% CI 1.15-2.01) over one year prior to treatment. Refuting the bed rest myth, physical activity and sedentary lifestyle measured by accelerometer after the embryo transfer showed no association with any IVF outcome [141]. Although impressive results were obtained, unfortunately the Hungarian version of the questionnaire is not available and to our knowledge, it has not been validated so far.

Conclusions

Based on our preliminary studies on the measurement of physical activity and its role in female reproduction, the use of questionnaires, the data based on international comparisons, the availability of questionnaires, and the availability of a validated Hungarian version, it can be concluded that the IPAQ-sf and GPAQ questionnaires combined with an accelerometer seem to be the most appropriate ones, which seems effectively contribute to the future development of a PA recommendations prior to ART treatment.

Effects of psychosocial and lifestyle factors with special regard to physical activity on course and outcome of ART

Introduction

The increasing incidence of assisted reproductive therapies (ART) and unchanged success rates highlight the need for inspection of social, psychological and lifestyle covariates. To examine the impact of interventions or health conditions in a broader context we applied the generic quality of life (QoL) concept of the WHO, defined as "people's perception of their position in life in the context of the culture and value systems in which they live in relation to their objectives, expectations, standards and concerns" [150]. This comprehensive framework involves physical and psychological health aspects as well as social relationships, environment and spiritual aspects and widely used on subjects with different conditions, inter alia in infertility [151]. The failure to become pregnant may specifically affect various life dimensions such as depression, anxiety, social isolation, sexual dysfunction, social and psychological distress, and poorer marital adjustment [152].

It has also been hypothesized that depression and anxiety may negatively affect female reproduction or ART due to hormonal, neuroendocrine, or immunologic functioning and lead to poor outcomes [94-97, 153]. The relationship between psychosocial stress in relation to the success of IVF/ICSI is still moderately discussed [154, 155]. On the other hand, Smeenk et al demonstrated with survey methods that pre-treatment levels of perceived anxiety and depression are significantly positive related to treatment outcome in IVF/ICSI [84, 156]. For this reason, it is necessary to explore the fertility related QoL and PSD as well.

Benefits of regular physical activity to maintain physical, mental and social health is not called into question [4]. Depending on intensity or duration, certain studies disagree on the health effects of exercise or even PA in relation to ART [121, 131, 157, 158]. These studies primarily focus on outcomes of ART and less on the QoL and PSD aspects on the course.

Therefore, the aim of the current research was to describe PA, QoL and PSD patterns and their relationships in ART patients on the course and outcomes of the treatment.

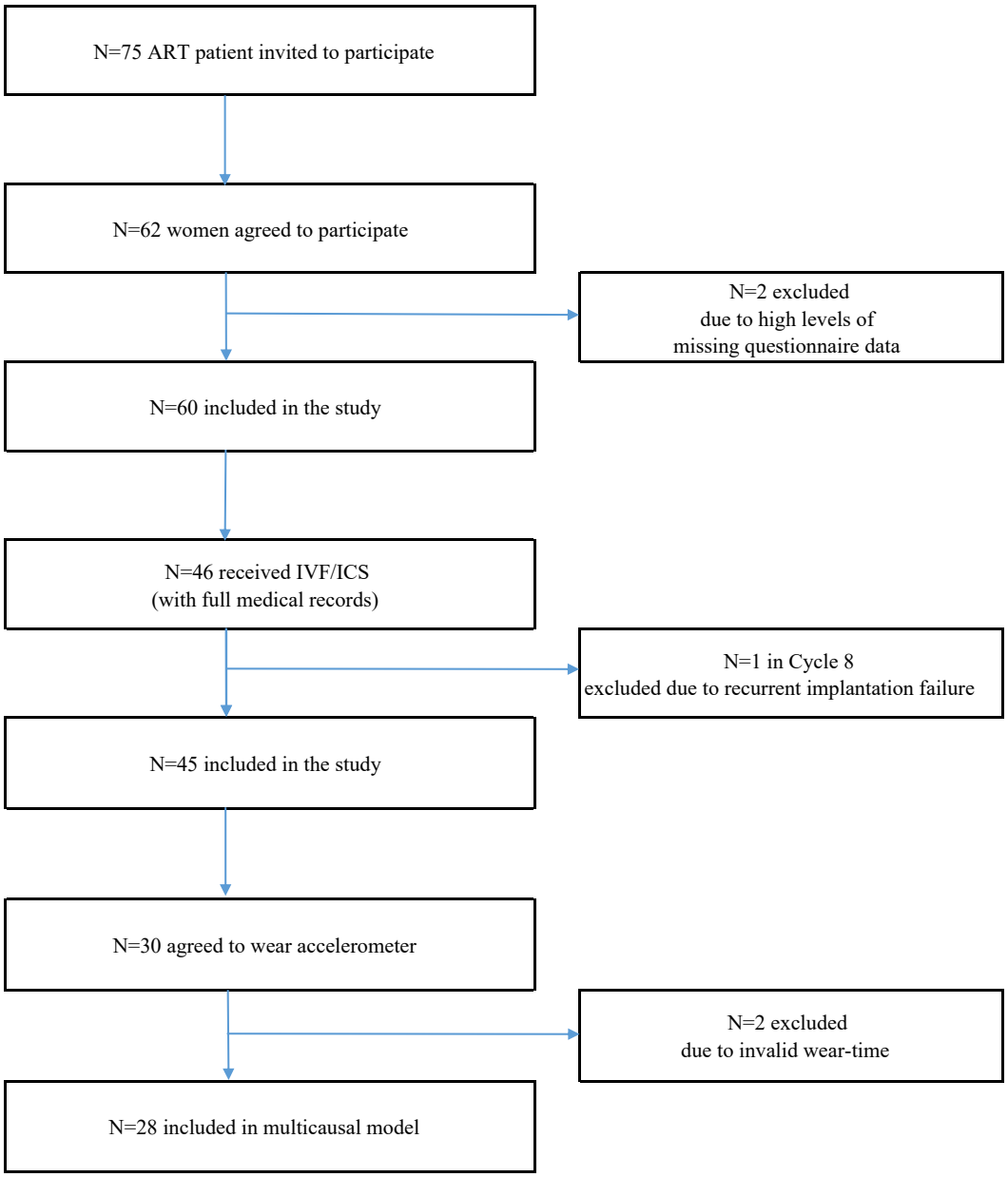
Methods

A cross-sectional, observational cohort study was conducted with consecutive sampling at the Assisted Reproduction Unit, Department of Obstetrics and Gynaecology, University of Pécs, Hungary. All female patients with both female and male factors of infertility who were indicated

for fertility treatment (IVF/ICSI) in the institute were consecutively invited to participate in the study. Participants were recruited according to the date of the fertility consultation. Inclusion criterions were BMI ≥ 18 kg/m^2 and ≤ 38 kg/m^2, 18 to 40 years of age, having undergone not more than three unsuccessful cycles and no significant health risk relevant to the ART procedure and outcome (metabolic and vascular diseases including diabetes mellitus, metabolic syndrome, fatty liver diseases and atherosclerosis, severe endometriosis (stage III or IV) and/or adenomyosis). Participants were not diagnosed with any mental disorders and had no significant physical or mobility impairments.

Data collection was carried out during the routine examination on the 3rd day of the unstimulated cycles. 62 women participated in the study between December 2018 and June 2019, which means 82.66% response rate. Self-administrated questionnaires were given to participants, who filled them at home in a conventional paper-pencil form. Questionnaires were returned on the 21st day of the unstimulated cycles. 2 participants were excluded due to high rate of missing questionnaire data. The selection of the study populatin including patient recruitment, exclusion criteria, and refusals are presented on the flow chart. (Figure 11.)

Figure 11.



Flow chart of the study population selection including patient recruitment, exclusion criteria, and refusals.

Assessment scales

Socio-demographic characteristics were obtained using questions regarding age, educational level, income, marital status, duration of partnership, duration of infertility, BMI and lifestyle habits.

Assessment of quality of life

Quality of life was measured in general and as infertility-related quality of life as well. The validated Hungarian version by Paulik et al. of World Health Organization Quality of Life-BREF (WHOQOL-BREF) generic questionnaire was used. The instrument comprised 26 items, which measured the following broad domains: physical health, psychological health, social relationships, and environment. Raw data was expressed 4-20 linearly or transformed for a 0-100 scale. We decided to express our data in the scale format where the value of 100 means the best QoL [159, 160]

Fertility-related QoL was measured with the Hungarian version of the Fertility Quality of Life Questionnaire (FertiQoL). FertiQoL is an internationally validated instrument to measure QoL in individuals experiencing fertility problems in diverse life areas. The Core module described general health, self-perceptions, emotions, partnership, family and social relationships, work life and future life plans (26 items). Additionally, the optional FertiQoL Treatment module assesses the environment and tolerability of fertility treatment for patients who have used fertility medical services regarding medical consultation or intervention. (10 items) [102]. One version of FertiQoL already existed in Hungarian [103]. However, we decided for a repeated review due to linguistic reasons. The publication of the results of the redefined Hungarian version is in progress.

Assessment of distress

As in the pilot study, Beck Depression Inventory (BDI-13) was applied again for reporting respondents' mental health status [79-84]. The questionnaire represents how the subject were feeling the week before. Each question has a set of at least four possible responses, ranging in intensity. A total score is computed reflecting the outcome index of depression. The validated Hungarian version of the short-form of the inventory with 13 items was completed by the respondents [85, 86].

To examine infertility-related distress with a specific scale, the Fertility Problem Inventory (FPI) was included. FPI is a 46-item questionnaire developed to measure the level of infertility-related stress [87]. The scale consists of five subscales identifying the following domains: social concerns, sexual concerns, relationship concerns, rejection of childfree lifestyle and need for

parenthood. Higher score indicates that the individual is experiencing more psychological stress than the average individual seen for infertility (85-98% reflects moderately high stress, and above 98% reflects very high level of stress). The former Hungarian version [88] was accurately redefined, results will be published separately.

Assessment of PA

To describe PA and exercise habits, participants self-reported on the type and frequency of exercise in a PA diary and reported all kinds of physical activity in two types of PAQ. These self-reports were compared with objective measures collected by the Triaxial ActiGraph GT3X+ accelerometers.

International Physical Activity Questionnaire (IPAQ-SFH)

The International Physical Activity Questionnaires – Short Form (IPAQ-SF) was used to obtain internationally comparable data on health–related physical activity that women do as part of their everyday lives. IPAQ-SF is a single domain questionnaire, 7 items surrounding last 7-day recall of PA and reports on types of intensity of PA and sitting time [137, 161-163]. The data were expressed in min/week and was summarised in moderate and vigorous activities min/week, MVPA min/week, and sitting time min/week also. The scoring protocol proposes to classify population in three levels of physical activity: low, moderate and high [135]. The Hungarian version of the questionnaire (IPAQ-SFH) is under validation by the EUPASMOS project on Hungarian general sample [164].

Global Physical Activity Questionnaire (GPAQ-H)

The GPAQ version 2 used in our research was developed by the WHO. This self-administered form comprises 16 items that measure the physical activity levels of a typical active week (7 days) of adults. The questionnaire contains three domains of PA: work, transportation, and recreational activities. The duration and frequency of physical activity (min/day) were recorded in case of all three abovementioned domains. The evaluation of the intensity of certain activities is well described for respondents in the introduction section of the questionnaires: “'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate”[165]. Results were expressed in time (minutes) or in energy expenditure (MET: Metabolic Equivalent of Task). According to intensity, moderate and vigorous activities can be classified and walking activities should be also distinguished.

Our study indicates data in min/week format for easier comparison with accelerometer data. Total MVPA min/week (all vigorous + all moderate activities' mins), moderate and vigorous activities in min/week, and weekly sitting time in min/week values were calculated [165, 166].

The cultural adaptation, efficient translation, and validation of the Hungarian version were composed by our scientific research group [139, 166, 167] . The aim of this former study was to adapt and validate the self-administered GPAQ - Hungarian version (GPAQ-H) against accelerometer data and IPAQ-Hungarian long version (IPAQ-HL) in Hungarian healthy young adults. In this cross-sectional comparative study, the last 7 days PA by GPAQ-H was compared with IPAQ-Hungarian Long version and Actigraph GT3X accelerometer data to measure concurrent validity and reliability. A convenient sample of 300 young adults was recruited in January – July 2018 at the University of Pécs and finally 120 participants (age 21.53±1.75 years, 46.66% male) were included in the validity and reliability study.

Significant differences between the three instruments were found ($p<0.001$) in all scores, except PAQs vigorous activities ($p=0.332$) and GPAQ-H and accelerometer MVPA score ($p=0.424$). A moderate KMO measure was found (0.538) with a significant Barlett's test of Sphericity (279.51; $p<0.001$). The total variance was explained as 81.10%. The reliability of the GPAQ-H instrument with all domain's scores was 0.521 (CI 0.371-0.644). We found in all intensity scores and sitting time good reliability scores ($R=0.899$-987, $p<0.001$) between the baseline and follow-up (N=33 random subsample). The Bland-Altman plots were showed that GPAQ-H overestimates vigorous activities by 212.75 min/week (331.82-757.42) and MVPA by 104.93 min/week (-1016.98-807.11). A high difference, 6336.79 min/week (CI 3638.18-9035.40) was revealed regarding sitting, as GPAQ-H largely underestimated the time spent sedentary.

However, the validity GPAQ-H was fair to moderate (MVPA $R=0.290$, $p=0.001$) but it was acceptable, as by similar European studies. Consequently, it could be claimed that the GPAQ-H measurement tool is a valid and reliable questionnaire to measure the healthy Hungarian general population's physical activity patterns [147].

For calculation of energy expenditure (METmin/week) of PA following the guidelines of both of the questionnaires MPA by 4 MET, VPA by 8 MET and walking by 3.3 MET should be multiplied [135, 165, 167, 168]. We decided to apply the values of the updated "Physical Activity Guidelines for Americans", calculates with 3, 6 and 2.5 METs respectively [64].

Accelerometry monitoring

Triaxial ActiGraph GT3X+ accelerometers (ActiGraph, Pensacola, FL) were used to collect data on PA with standard device initialization (sample rate of 30Hz, 60 second epochs and normal filter option).

Participants were instructed to wear the accelerometer on the right hip (near the iliac crest) for a week, from the time they woke up in the morning until they retreated at the end of the day, except for the duration of any water-based activities, such as swimming or bathing. The Actigraph GT3X + device measures the strength of the movement in three spatial directions, as well as their duration. The device converts acceleration into a quantifiable and measurable digital signal. It allows us to accurately assess daily activities and classifies it into categories.

60 or more motionless minutes was defined as "non-wear time". A minimum of 480 minutes of wear-time was required daily and a minimum of 5-7 days with valid wear time including at least one weekend day was required for inclusion in the analysis [169]. Finally, all valid days of recording were averaged and multiplied by seven to provide the comparability with the questionnaires.

ActiLife 6 software was used to initialize the accelerometer and to download results, and row data was converted with Freedson cut points [170]. The average of daily moderate to vigorous physical activity (MVPA) (min/day) and sedentary behaviour (SB) (min/day) was calculated with a sensitivity and specificity of more than 98% and 99%, respectively [171].

Based on the additional physical activity diaries any contact sports or water-based activities were performed, which may restrain the participants to wear the accelerometer. Although, four participants were excluded due to invalid wear-time. The average number of valid days was 6.32.

Physical Activity Categories by Guidelines

On the basis of the results, physical activity was categorized by meeting the key guidelines of PAGAC for adults as Inactive (any activity beyond basic movement from daily life activities), *insufficiently active (less than 150 minutes* of moderate-intensity physical activity (MPA) or 75 minutes of vigorous-intensity physical activity (VPA) or the equivalent combination of them per week), *active (equivalent of 150 minutes to 300 minutes* of MPA a week), or *highly active* (more than 300 minutes of MPA a week) [64].

Following the ACOGs recommendations, pregnant women should engage in *moderate intensity exercise for 150 minutes* per week [67, 118]. However, there are no definitive physical activity guidelines for women attempting conception, particularly for the window of implantation and luteal phase. We integrated this into our model, and application of this category was confirmed

with the similarity of PA patterns of ART patients to women during gestation (See the detailed categories below).

Most of the studies draw attention to risk of frequent or vigorous PA on fertility [119, 120, 172] and on success of ART [108, 121]. Therefore, *exercising 240 minutes* or more per week was considered an independent category.

Fertilization protocol

Publications of the Human Reproduction Scientific Research Group by Bódis and Várnagy described the detailed protocol of fertility treatments as follows [46, 47, 173]. Superovulation treatment was started after cervical smear, serum hormone measurements (follicular stimulating and luteinizing hormones /FSH, LH/, prolactin, estradiol, progesterone, testosterone, thyroid-stimulating hormone) on the 3rd and 21st days of the unstimulated cycles, human immune-deficiency virus and hepatitis-B surface antigen screening, hysteroscopy or HyCoSy and andrologic examination. Patient enrolment into IVF procedure was approved by two independent physicians.

The fertilization is performed with traditional IVF or intracytoplasmatic sperm injection (ICSI) depending on the andrological status (sperm count less than 15M/ml), the maternal age (> 35) and the number of the previous IVF cycles the patient had before (>2). The oocytes selected for ICSI were denuded with hyaluronidase and were assessed for maturity. Only metaphase II oocytes, identified by the presence of the first polar body, were chosen for fertilization. ICSI was performed 3-6 hours after oocyte recovery in the medium G-MOPS ™. The remained oocytes were fertilized with the conventional IVF method in a bicarbonate buffered medium (G-IVF ™, Vitrolife®, Göteborg, Sweden). Fertilization was assessed 24 hours later in the medium G-I™v5 (Vitrolife®, Göteborg, Sweden).

Embryo transfers were done 3-5 days after the oocyte retrieval. From day 3 to blastocyst stage we used the medium G-21Mv5 (Vitrolife®, Göteborg, Sweden). Only Grade 1 staged embryos were transferred (according to the Consensus embryo scoring system of ESHRE). According to the patient request we transferred one, two or three embryos. To evaluate the success of the treatment, transvaginal ultrasound examination was performed 21 days after the embryo transfer to detect gestational sac [47].

One patient was excluded due to high risk of implantation failure, in her 8th cycle. The remaining patients took part in cycles 1-4.

Ethical approval

This study was approved in advance by the University of Pécs, Clinical Centre, Regional and Local Research Ethics Committee (Nr. 6533). Each participant voluntarily provided written informed consent before participating. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Data analysis

Statistical analyses were performed using IBM SPSS Statistics 25.0 for Mac (SPSS Inc., Chicago, IL, USA). Normality of data distribution was tested by Kolmogorov-Smirnov test. Mann-Whitney U-test was used to compare continuous variables. The association between two continuous variables was tested by Spearman's rank correlation. To define predicting factors of primary and secondary outcomes of IVF from pre-treatment habitual PA, psycho-socio-demographic and baseline biomedical variables, we conducted a multivariate linear regression using the stepwise method. Logistic regression analysis was conducted to evaluate the effects of all the above parameters on livebirths. A post-hoc statistical power analysis was performed using G*Power software, version 3.1.9.6 for Mac (Franz Faul, Christian-Albrechts-Universität Kiel, Kiel, Germany) [174]. Data was expressed as mean ± SD as well as medians with 25th and 75th percentiles and the significance level of $p<0.05$ was considered in each case.

Results

General characteristics of the sample

The major socio-demographic and clinical characteristics of the study population are presented in Table 10. 60 female patients in reproductive age (34.6 ±5.2 years), with mostly normal weight (70.0%, BMI 18.5–24.9 kg/m^2) participated in the study. They were sampled from a larger proportion with higher educational degree (58.6%) and with satisfactory economic status (96.6%). 95.0% of them worked and 75.0% had urban residence. Each participant was either married or lived with a partner, and in average the duration of the partnership was 8 years (7.6±3.8) with an around 5-years-long (59.0±38.4 month) child-wish. We found various cases of infertility, duration and type of treatments. However, these primarily nulliparous women (84.4%) typically received IVF/ICSI (82.3%) with mostly non-male indication (75.6%). Complete clinical data was available regarding 45 IVF/ICSI patients.

76.7% of the participants rated their physical health particularly good or excellent. In general, they self-reported a health-conscious lifestyle regarding diet, tobacco use and PA, and quality of sleep was satisfactory (86.2%) as well. Lifestyle change was also examined, but we cannot report relevant changes back to 5 years ago, from the beginning of ART, or in the current month. 50.0% of the participants claimed to be physically active, one tenth of them exercised 4-7 times per week.

Table 10. General characteristics of women undergoing ART ***(N=60)***

Socio-demographic Data (N=60)		**Health Status and Lifestyle (N=60)**		**Reproduction (N=60)**		**Medical records by IVF/ICSI (N=45)**	
Age (years)		BMI (kg/m^2)		***Indication (Self-report)***	N (%)	***Indication***	
Mean (SD)	34.6 (±5.2)	Mean (SD)	24.2 (±4.9)	Female	26 (43.3)	Poor semen quality	11 (24.4%)
Education		Underweight (<18.5)	5 (8.3%)	Male	4 (6.7)	Fallopian tube	11 (24.4%)
Low	6 (10.0%)	Normal weight (18.5–24.9)	37 (61.7%)	Dual	14 (23.3)	Endometriosis	7 (15.6%)
Intermediate	18 (30.0%)	Overweight (25–29.9)	7 (11.7%)	Undefined	13 (21.7)	Other female	4 (8.9%)
High	36 (60.0%)	Obesity (>30)	11 (18.3%)	Diagnosis in progress	3 (5.0)	Unexplained	12 (25.6%)
Marital status (N=44)		***Self-Rated Physical Health***		***Type of ART Treatment***		***Procedures***	
Married	47 (78.3%)	Poor	0	IVF/ICSI	50 (82.3)	Cycle 1	11 (24.4%)
Partner	13 (21.7%)	Fair	1 (1.7%)	IUI	1 (2.1)	Cycle 2	16 (35.6%)
Place of residence		Neither good nor bad	13 (21.7%)	OI	2 (4.2)	Cycle 3	12 (26.7)
County seat	18 (30.0%)	Good	37 (61.7%)	HSG	2 (4.2)	Cycle 4	6 (13.3%)
City	27 (45.0%)	Excellent	9 (15.0%)	Examination in progress	5 (31.1)	Serum oestradiol - pmol/l	1692±2073
Village	15 (25.0%)	***Healthy Diet***		***Child-wish (months)***	Mean±SD	Progesterone - nmol/l	30.42±21.29
Income		Pay attention	56 (93.3%)	Mean (SD)	59.0±38.4	FSH* - IU	2493±2925
Low	2 (3.3%)	Not really / No attention	4 (6.7%)	***Relationship (years)***		Gonadotropin* - IU	0.86±0.19
Medium	34 (56.6%)	***Tobacco Use***		Mean (SD)	7.6±3.8	No. of oocytes	7.87±4.96
High	24 (40.0%)	Occasional	2 (3.3%)	***Gravidity (N=45)***	N (%)	No. of matured oocytes**	5.44±3.93
		Non-Smoker	58 (96.7%)	Nulligravid	25 (55.6)	No. of Grade 1 embryos	3.31±2.98
		Exercise		Multigravid	20 (44.4)	No of transferred embryos	1.46±0.84
		Regularly 4-7 days weekly	6 (10.0%)	***Parity(N=45)***		hCG on day 12 - IU	364.9±912.3
		Regularly1-3 days weekly	24 (40.0%)	Nulliparous	38 (84.4)	Chemical pregnancies	22 (48.89%)
		Not	30 (50.0)	Multiparous	7 (15.6)	Clinical pregnancies	13 (28.9%)

ART: Assisted Reproductive Therapy, BMI: Body Mass Index, HSG: Hysterosalpingogram, ICSI: Intracytoplasmic Sperm Injection, IUI: Intrauterine Insemination, IVF: In-Vitro Fertilization, OI: Ovulation Induction, *: Total dose administrated, ** Metaphase II)

General and infertility-related quality of life

Based on the WHOQOL-BREF which examines general QoL, 70.00% of the respondents self-reported good or very good health and 78.33% of them was satisfied or very satisfied with her QoL. Respondents were less satisfied with Psychological Domain (67.75±13.13) and most satisfied with Physical Health Domain (75.22±14.95) of their QoL. (Table 11.)

For the purpose of measuring the level of infertility related QoL, a more specific tool, the FertiQoL was applied. We found similar values with this specific scale like with WHOQOL-BREF. In the four Core subscales of the questionnaire we found lower QoL by the Emotional Scale (59.51±20.09) and the Mind-Body Scale (62.85±20.93), mediate QoL by the Social Scale (69.72±19.38) and moderately better values by the Relational Scale (77.22±17.70). Respondents already receiving ART treatment rated their QoL referring the interventions equally in both Treatment subscales: Environment Scale (67.31±18.27) and Tolerability Scale (66.70±23.83). Subscales were summarised and similar values were found by the Core Scale 67.33±15.75 and the Treatment Scale 67.07±17.50. (Table 11.)

Table 11.

Pre-treatment quality of life characteristics of women undergoing ART (N=45)

WHOQOL-BREF					
	Very poor	Poor	Neither poor nor good	Good	Very good
SRH (%)	0.00	6.67	23.33	60.00	10.00
	Very dissatisfied	Dissatisfied	Neither dissatisfied nor satisfied	Satisfied	Very satisfied
QoL (%)	0.00	1.67	20.00	65.00	13.33
Domains	Mean	SD	Median	IQR lower	IQR upper
Physical Health Domain	75.22	14.95	81.00	69.00	88.00
Psychological Domain	67.75	13.13	69.00	63.00	75.00
Social Relationships Domain	70.98	15.03	75.00	56.00	81.00
Environment Domain	71.90	12.68	75.00	63.00	81.00
FertiQol					
	Very poor	Poor	Neither poor nor good	Good	Very good
SRH (%)	1.67	3.3	16.7	66.7	11.7
	Very dissatisfied	Dissatisfied	Neither dissatisfied nor satisfied	Satisfied	Very satisfied
QoL (%)	0.00	6.67	16.67	58.33	18.33
Domains	Mean	SD	Median	IQR lower	IQR upper
Emotional Scale*	59.51	20.09	58.33	42.71	79.17
Mind-Body Scale*	62.85	20.93	62.50	50.00	79.17
Relational Scale*	77.22	17.70	79.17	67.71	91.67
Social Scale*	69.72	19.38	68.75	58.33	87.50
Environment Scale**	67.31	18.27	70.83	58.33	79.17
Tolerability Scale**	66.70	23.83	75.00	54.69	81.25
Core Scale	67.33	15.75	68.23	54.17	83.07
Treatment Scale	67.07	17.50	68.75	56.88	82.50
Total Scale	67.66	14.54	68.01	56.99	80.15

ART: Assisted Reproductive Therapy, FertiQol: Fertility Quality of Life Tool, IQR: Interquartile Range, QoL: Quality of Life, SRH: Self-Rated Health, WHOQOL-BREF: World Health Organization Quality of Life-BREF Questionnaire, *Core Scale, **Treatment Scale

General and infertility-related distress

The validated Hungarian short-form of the Beck Depression Inventory (BDI-13) was applied [79-82, 85, 86] to reflect on distress in general. 68.96% of the respondents scored less than 5 points, which indicates normal mood state; and 20.68% belonged to the category of mild depression (6-11 points). 2 patients reported severe depression.

For the purpose of measuring the level of infertility-related stress, FPI was applied and moderately high *Global stress* (183.33±28.19) was explored. In the five domains of the questionnaire we found similar values as in the pilot study: average stress by *Rejection of childfree lifestyle* (23.25±6.04), moderately high stress by *Social concern* (41.40±9.84) and very high stress level by *Sexual-* (38.62±7.77) and by *Relationship concern* (48.53±9.68). Stress related to *Need for parenthood* was low again, but markedly higher than in our first pilot study (31.68±8.35 vs 23.1±5.7). Table 12. shows these results.

Table 12.

Pre-treatment distress characteristics of women undergoing ART (N=45)

BDI					
	Mean	SD	Median	IQR lower	IQR upper
General Stress	4.92	4.82	4.00	1.00	8.00
FPI					
Domains	Mean	SD	Median	IQR lower	IQR upper
Social Concern	41.40	9.84	42.50	33.25	50.75
Sexual Concern	38.62	7.77	41.00	34.25	45.00
Relationship Concern	48.53	9.68	50.00	42.00	57.00
Rejection Concern	23.25	6.04	23.00	18.00	28.00
Need for Parenthood	31.68	8.35	31.00	28.00	37.00
Global Stress	183.33	28.19	179.50	165.00	202.50

Descriptive analysis of physical activity patterns

Pre-treatment physical activity patterns of women undergoing ART were summarised in Table 13. Intensity, frequency and mode of PA were described using the IPAQ-SFH, GPAQ-H questionnaires, and ActiGraph GT3X.

Regarding GPAQ-H respondents performed an average of 461.50±785.56 min/week moderate and 158.00±467.34 min/week vigorous PA in work and only 35.00±82.70 min/week vigorous activity in recreation/leisure time domain. However, medians (0.00) revealed, that

vigorous PA during work or leisure time are not common in the studied group. They preferred moderate-intensity recreational activities for 2 hours per week (124.80±339.56).

Nevertheless, they spent 268.75±521.77 min/week on average with active transportation, for example with walking or cycling, which covers 806.25±1565.30 MET energy expenditure. Means significantly differed in these relations also, as only 120 min transportation is characteristic. They spend 6.53 hours per day sedentary (2745.17±1755.39 min/week).

Analysing the data by intensity, we found that respondents spent 786.32±998.92 minutes (2910.65±3932.02 MET) with moderate to vigorous activities (MVPA). In total, considering all types and intensities of activities lasting more than 10 minutes, women performed around 16.98 hours (1018.95±1225.72 min/week) or 3716.90±4588.16 MET PA.

Regarding the ActiGraphs, light activity was the most characteristic with 1239.87±329.50 min/week, moderate (233.35±132.00 min/week) and vigorous activities (4.65±13.27 min/week) lag behind the subjective measures, very vigorous activity was almost negligible (3.70±15.73 min/week). They performed around 4 hours MVPA (241.70±145.10 min/week) and took in average 7060.28 steps daily (49422.73±16351.52 counts/week) based on objective measures.

Table 13.

Pre-treatment physical activity characteristics of women undergoing ART (N=45) based on accelerometer, self-administered IPAQ-SFH, GPAQ-H questionnaires and ActiGraph GT3X data

IPAQ-SFH						**GPAQ-H**					
Measure	Mean	SD	Median	IQR lower	IQR upper	Measure	Mean	SD	Median	IQR lower	IQR upper
Vigorous						**Work – VPA**					
min/week	193.71	464.05	0.00	0.00	120.00	min/week	158.00	467.34	0.00	0.00	0.00
MET	1162.25	2784.32	0.00	0.00	720.00	MET	948.00	2804.04	0.00	0.00	0.00
Moderate						**Work – MPA**					
min/week	255.50	523.65	40.00	0.00	240.00	min/week	461.50	785.56	75.00	0.00	630.00
MET	766.50	1570.95	120.00	0.00	720.00	MET	1384.50	2356.67	225.00	0.00	1890.00
Walking						**Transport**					
min/week	459.39	696.60	180.00	90.00	435.00	min/week	268.75	521.77	112.50	42.50	232.50
MET	1148.46	1741.51	450.00	225.00	1087.50	MET	806.25	1565.30	337.50	127.50	697.50
Sitting						**Recreation - VPA**					
min/week	2617.42	1551.98	2520.00	1365.00	3727.50	min/week	35.00	82.70	0.00	0.00	0.00
Total						MET	210.00	496.19	0.00	0.00	0.00
min/week	930.39	1349.96	360.00	190.00	990.00	**Recreation - MPA**					
MET	3173.20	4908.80	1140.00	555.00	2955.00	min/week	124.80	339.56	30.00	0.00	120.00
MVPA min/week	449.21	831.45	120.00	0.00	360.00	MET	368.15	1011.18	90.00	0.00	360.00
MVPA MET	1928.75	3721.82	390.00	0.00	1687.50	**Sitting**					
ActiGraph GT3X (N=30)						min/week	2745.17	1755.39	2940.00	1260.00	3780.00
Measure min/week	Mean	SD	Median	IQR lower	IQR upper	**PA by intensity**					
Sedentary	8598.43	401.84	8639.00	8345.17	8941.50	MPA min/week	594.12	847.16	240.00	0.00	720.00
Light	1239.87	329.50	1208.33	1053.83	1456.67	MPA MET	1752.65	2530.33	720.00	0.00	2122.50
Moderate	233.35	132.00	213.17	134.36	308.19	VPA min/week	193.00	478.26	0.00	0.00	120.00
Vigorous	4.65	13.27	1.00	0.33	1.75	VPA MET	1158.00	2869.56	0.00	0.00	720.00
Very Vigorous	3.70	15.73	0.00	0.00	0.17	MVPA min/week	786.32	998.92	300.00	90.00	1140.00
Total						MVPA MET	2910.65	3932.02	1260.00	355.50	3600.00
Total MVPA	241.70	145.10	214.67	134.36	310.14	Total PA min/week	1018.95	1225.72	470.00	210.00	1320.00
Steps counts/week	49422.73	16351.52	50675.33	34765.00	62113.00	Total MET	3716.90	4588.16	1605.00	639.75	5231.25

GPAQ: Global Physical Activity Questionnaire, IQR: Interquartile Range, MET: Metabolic Equivalent of Task, min: minute, MVPA: Moderate to Vigorous Physical Activity, PA: Physical Activity

Comparative analysis of physical activity patterns

Comparing the data of the three measurements, we found significant differences between the two subjective instruments and the objective measures in all of the marked scores except for moderate PA and MVPA means between Accelerometer and IPAQ-SFH (p=0.468, p=0.433 respectively) and vigorous means between Accelerometer and GPAQ-H (p=0.255). The GPAQ-H and IPAQ-HL questionnaires showed similar mean differences, but the overestimation of moderate activities and MVPA was higher in GPAQ-H, and of vigorous activities in IPAQ-SFH. (Table 14.)

Table 14.

Comparison of pre-treatment physical activity characteristics of women undergoing IVF based on accelerometer, self-administered IPAQ-HL, and GPAQ-H questionnaires and ActiGraph GT3X mean values difference

Intensity	**Measures**	**p**	**Mean Difference**
Sedentary	IPAQ-SFH - Accelerometer	.000	-6166.50
	GPAQ-H - Accelerometer	.000	-5980.21
Vigorous	IPAQ-SFH - Accelerometer	.001	333.10
	GPAQ-H - Accelerometer	**.255**	184.06
Moderate	IPAQ-SFH - Accelerometer	**.468**	151.97
	GPAQ-H - Accelerometer	.002	626.75
MVPA	IPAQ-SFH - Accelerometer	**.433**	481.37
	GPAQ-H - Accelerometer	.001	805.23

To validate subjective PA results, we examined the correlation between accelerometer and questionnaires according to moderate, vigorous, MVPA activities, and sitting time values.

By IPAQ-SFH, vigorous data showed significant moderate correlation with objectively measured Light (R=0.511, p=0.003), Moderate (R=0.376, p=0.037), Very Vigorous (R=0.428, p=0.016) PA and MVPA (R=0.381, p=0.034), but there were no significant results with Vigorous accelerometer (R=0.339, p=0.067) data. IPAQ-SFH walking min/week showed positive correlation with ActiGraph weekly steps (R=0.433, p=0.017) and Actigraph light PA (R=0.559, p=0.001) and negative correlation with ActiGraph sedentary behaviour (R=-0.538, p=0.002).

The GPAQ-H vigorous PA showed significant correlation with light accelerometer values (R=0.310, p=0.090). Time spent with transportation and the respective MET values showed a good correlation with light activities (R=0.506, p=0.004) a tendency-like relationship (R=0.349, p=0.055) with objectively measured weekly steps, yet strong negative correlation with sedentary time (R=-0.511, p=0.003).

However, several self-reported measures correlated with each other: Total PA (R=0.641, p<0.001), MVPA (R=0.414, p=0.001), moderate PA (R=0.416, p=0.001), walking (R=0.394, p=0.002 and sedentary behaviour (R=0.520, p<001).

PAQs scoring protocols are focusing on cumulative values of PA performed on average weeks or the week prior to the measurement. GPAQ categorises the level of physical activity as High, Moderate or Low by summing total PA [165], whereas the PA guidelines of PAGAC and ACOG focus on aerobe or exercise type PA in relation to health enhancing effects. Therefore, we decided to analyse our data using the recreational type of activities following the PAGAC and ACOG categories [64, 67, 118].

Inactive: lack of moderate- or vigorous-intensity physical activity except basic movement from daily life activities.
Insufficiently active: less than 150 minutes of MPA or 75 minutes of VPA or the equivalent combination of them per week.
Active I: equivalent of 150 minutes to 300 minutes of MPA per week.
Active II: exercising 240 minutes or more weekly**.**
Highly active: more than 300 minutes of MPA per week or equivalent.

Equivalent values were calculated through doubling by vigorous values and added to moderates.
We also combined these three categories with a new one, based on the results of Morris et al, who drew attention to unmet effects of PA. They concluded that regular exercise over 4 hours per week before IVF may negatively affect outcomes, hence we also included this cut-off into our study. Comparison of pre-treatment physical activity characteristics of women undergoing IVF by physical activity categories is presented in Table 15.

Table 15.

Comparison of pre-treatment physical activity characteristics of women undergoing IVF (N=45) by physical activity categories

	Physical Activity Categories				
	Inactive	**Insufficiently active**	**Active I**	**Highly active**	**Total**
Groups	0 min/week	≤149 min/week	150-299 min/week	≥300 min/week	
Non-pregnant	14	6	4	8	32
	43.75%	18.75%	12.50%	25.00%	100.00%
	77.78%	66.67%	44.44%	88.89%	71.11%
Pregnant	4	3	5	1	13
	30.77	23.08	38.46	7.69	100.00%
	22.22%	33.33%	55.56%	11.11%	28.88%
Total	18	9	9	9	45
	40.00%	20.00%	20.00%	20.00%	100.00%
	100.00%	100.00%	100.00%	100.00%	100.00%

If we categorise their performance, 27 women (60.00%) reported notable leisure time PA, and only 18 of them (40.00%) reached the 150 min/week RMPA recommendation. 9 (20.00%) persons spent more than 240 minutes/week with recreational type PA, just like in the PAGA Highly active category.

Relationship between quality of life aspects and PA

For detecting the relationship between pre-treatment physical activity patterns and quality of life of IVF patients (Table 16.), IPAQ-SFH and accelerometer data proved to be less informative. Regarding correlations between the IPAQ-SFH and any of the QoL's domains, relationship was only found with the following baseline factors: between age and amount of total PA in min/week (R=0.309, p=0.046) and expressed in METs (R=0.305, p=0.049), and between BMI and MVPA minutes and METs (R=0.331, p=0.032). Similar weak results were found in case of ActiGraph data. BMI was positively correlated with Light intensity activities (R=0.399, p=0.043), but no more relationship could be described. Amount of PA increased in line with years and also with BMI, suggesting more of a health-conscious behaviour by women exposed to higher risk.

With GPAQ-H more impressive finding could be described. Relationship between the same baseline biological factors and PA has been confirmed by GPAQ-H. Age strongly correlated with VPA minutes and METs (R=0.501, p=0.001), MVPA total min/week (R=0.371, p=0.015) and

MET (R=0.425, p=0.006) also with the cumulative values of all PA total minutes (R=0.415, p=0.007) and METs (R=0.440, p=0.004). BMI also correlated with Active transportation minutes (R=0.408, p=0.007), MVPA minutes (R=0.363, p=0.018) and METs (R=0.330, p=0.035) and also with total minutes (R=0.446, p=0.004) and total METs (R=0.436, p=0.004).

Regarding generic QoL scores, strong correlations were found by WHOQOL-BREF between Psychological Domain and time of vigorous recreational activities (R=0.484, p=0.001) and energy expenditure of recreational activities (R=0.428, p=0.006), and significant correlation with weekly time spent with recreational activity (R=0.319, p=0.039).

Similar correlations could be detected between the specific FertiQoL Core Scale's Mind-Body domain and Total METs (R=0.336, p=0.024). Tolerability Subscale also correlated with the total MET of active transportation (R=0.266, p=0.044). The most positive relationship was found between Total MET and the following subscales and scores of FertiQoL: weak correlation was found with Core Score (R=0.272, P=0.041) and more robust with Environment Scale (R=0.384, p=0.003), Tolerability Scale (R=0.371, p=0.004), Treatment Score (R=0.390, p=0.003) and Total Score (R=0.345, p=0.009).

Based on physical activity patterns, women were divided into PA groups as described above. Means of QoL generic questions and domains were compared regarding PA as the grouping variable. Significant difference cannot be described using PAGA categories or the 240 minutes cut off point.

Relationship between psychosocial distress aspects and PA

Relationship between generic PSD, measured with BDI and PA patterns cannot be described. Our results on GPAQ-H revealed, that recreational PA could counteract with some aspects of infertility related distress, since time spent with moderate RPA, total time and total MET of RPA negatively correlated with Social Concern (R=-0.378 p=0.013, R=-0.386 p=0.012 and R=-0.360 p=0.023 respectively) and Relationship Concern of FPI (R=-0.365 p=0.019, R=-0.368 p=0.018 and R=-0.342 p=0.033 respectively). However, time spent with vigorous RPA was also significantly correlated to 'Rejection of childfree lifestyle' (R=0.354 p=0.021). (Table 17.) A relationship similar to the above cannot be described by IPAQ-SFH or ActiGarph.

Table 16. Relationship between quality of life and pre-treatment physical activity undergoing IVF/ICSI (N=45)

	GPAQ-H		WVPA m/w	WMPA m/w	WTPA m/w	WTPA MET	TTPA m/w	TTPA MET	RVPA m/w	RMPA m/w	RTPA m/w	RTPA MET	Sitting m/w	VPA m/w	VPA MET	MPA m/w	MPA m/w	MVPA m/w	MVPA MET	TPA m/w	Total MET
WHOQOL-BREF,	Physical Health	R	-.029	-.099	-.060	-.047	.114	.206	.105	.060	.101	.173	-.006	.038	.038	-.091	-.102	-.023	-.010	.012	.165
		p	.857	.534	.704	.767	.471	.124	.507	.707	.525	.285	.965	.813	.813	.568	.524	.883	.953	.939	.225
	Psychological	R	.001	.094	.072	.065	-.055	-.006	**.484**	.159	**.319**	**.428**	-.081	.238	.238	.141	.141	.173	.206	.163	.256
		p	.995	.552	.650	.684	.729	.962	**.001****	.315	**.039***	**.006****	.551	.130	.130	.372	.378	.274	.196	.309	.055
	Social Relationships	R	-.013	.063	.081	.062	.033	.094	-.038	-.183	-.122	-.124	-.106	-.061	-.061	.059	.056	.084	.086	.131	.168
		p	.937	.690	.612	.694	.836	.486	.812	.245	.442	.445	.438	.699	.699	.710	.727	.596	.592	.413	.214
	Environment	R	-.169	-.163	-.172	-.181	-.123	.009	.281	.114	.243	.289	-.015	-.047	-.047	-.120	-.120	-.092	-.064	-.121	.079
		p	.285	.302	.277	.252	.439	.948	.071	.471	.121	.070	.914	.768	.768	.450	.455	.562	.691	.451	.559
FertiQoL	Emotional Scale	R	.089	.068	.045	.045	.095	.111	.040	-.137	-.130	-.136	.003	.103	.103	.058	.058	.051	.083	.118	.222
		p	.573	.670	.779	.775	.551	.406	.803	.386	.411	.404	.981	.516	.516	.714	.718	.746	.607	.462	.097
	Mind-Body Scale	R	.079	.129	.138	.143	.210	.197	.066	-.043	-.033	-.052	-.087	.079	.079	.121	.120	.143	.162	.242	**.303**
		p	.620	.414	.382	.365	.183	.138	.679	.788	.834	.748	.519	.617	.617	.445	.456	.366	.312	.128	**.022***
	Relational Scale	R	-.028	.128	.163	.145	-.228	-.088	-.007	-.006	-.018	.008	.007	-.096	-.096	.099	.109	.139	.128	.098	.131
		p	.858	.421	.303	.359	.147	.513	.963	.970	.912	.962	.960	.545	.545	.535	.496	.378	.427	.543	.332
	Social Scale	R	-.211	.117	.100	.066	-.144	-.022	-.039	-.280	-.224	-.231	-.197	-.201	-.201	.073	.064	.055	.020	.034	.106
		p	.181	.462	.530	.678	.364	.868	.806	.072	.154	.152	.141	.201	.201	.644	.692	.730	.899	.831	.431
	Environment Scale	R	-.150	.220	.183	.151	-.091	.181	.196	.049	.069	.100	-.031	-.050	-.050	.214	.226	.188	.179	.180	**.384**
		p	.344	.162	.245	.339	.567	.173	.213	.759	.663	.537	.818	.754	.754	.174	.155	.233	.262	.261	**.003****
	Tolerability Scale	R	.094	.121	.206	.207	.113	**.266**	-.083	-.125	-.189	-.209	.006	-.005	-.005	.084	.084	.160	.161	.241	**.371**
		p	.555	.446	.192	.188	.478	**.044***	.600	.432	.230	.195	.962	.973	.973	.597	.600	.312	.315	.128	**.004****
	Core score	R	.053	.158	.182	.174	.000	.079	.002	-.158	-.162	-.167	-.089	.010	.010	.133	.130	.168	.172	.209	**.272**
		p	.740	.318	.248	.271	.998	.553	.990	.317	.304	.303	.512	.949	.949	.401	.420	.287	.282	.189	**.041***
	Treatment score	R	-.088	.154	.172	.150	-.038	.207	.080	-.008	-.050	-.052	.042	-.080	-.080	.143	.149	.158	.150	.192	**.390**
		p	.580	.331	.277	.342	.812	.119	.616	.961	.753	.751	.759	.616	.616	.367	.352	.317	.348	.228	**.003****
	Total score	R	.018	.200	.222	.208	-.021	.130	.020	-.144	-.162	-.150	-.076	-.011	-.011	.161	.166	.188	.182	.235	**.345**
		p	.908	.203	.158	.186	.894	.330	.900	.362	.305	.355	.576	.946	.946	.307	.299	.233	.254	.138	**.009****

Table 17. Relationship between quality of life and pre-treatment physical activity undergoing IVF/ICSI (N=45)

	GPAQ-H		WVPA m/w	WMPA m/w	WTPA m/w	WTPA MET	TTPA m/w	TTPA MET	RVPA m/w	RMPA m/w	RTPA m/w	RTPA MET	Sitting m/w	VPA m/w	VPA MET	MPA m/w	MPA m/w	MVPA m/w	MVPA MET	TPA m/w	Total MET
BDI	General Stress	R	.135	.012	.035	.053	.038	-.045	-.140	.120	.031	-.044	.123	.071	.071	.028	.027	.028	.017	-.039	-.121
		p	.395	.938	.828	.740	.811	.739	.377	.451	.846	.790	.363	.654	.654	.862	.865	.860	.915	.808	.371
FPI	Social Concern	R	.125	.109	.155	.159	.026	-.006	-.146	**-.378**	**-.386**	**-.360**	-.088	-.075	-.075	.035	.037	.077	.073	.119	.088
		p	.430	.493	.326	.315	.870	.962	.357	**.013***	**.012***	**.023***	.516	.638	.638	.826	.819	.626	.650	.459	.516
	Sexual Concern	R	-.070	.171	.108	.095	-.166	-.047	.037	-.141	-.106	-.084	-.147	-.043	-.043	.130	.124	.075	.068	.026	.070
		p	.657	.279	.494	.549	.294	.729	.818	.373	.502	.605	.275	.786	.786	.413	.441	.637	.673	.870	.606
	Relationship Concern	R	.026	.090	.068	.060	-.071	.006	-.228	**-.365**	**-.368**	**-.342**	-.089	-.163	-.163	-.010	-.011	-.034	-.057	-.010	-.014
		p	.872	.575	.674	.710	.658	.967	.151	**.019***	**.018***	**.033***	.512	.310	.310	.952	.947	.831	.725	.953	.918
	Rejection Concern	R	.069	-.057	-.031	-.007	-.144	-.041	**.354**	-.097	.048	.158	-.194	.280	.280	-.137	-.143	-.051	.011	-.108	.095
		p	.665	.722	.847	.965	.362	.761	**.021***	.541	.764	.331	.149	.072	.072	.387	.373	.746	.948	.503	.480
	Need for Parenthood	R	.142	.063	.091	.105	.005	.107	.162	.029	.106	.114	-.151	.196	.196	.064	.055	.095	.137	.103	.219
		p	.369	.694	.567	.509	.977	.424	.305	.854	.504	.482	.263	.214	.214	.689	.732	.551	.393	.522	.102
	Global Stress	R	.106	.119	.136	.138	-.107	-.026	.005	-.302	-.250	-.193	-.189	.053	.053	.045	.042	.076	.097	.074	.119
		p	.511	.457	.395	.389	.504	.846	.976	.055	.115	.240	.163	.742	.742	.781	.795	.636	.553	.649	.382

Legend to Table 16 & Table 17

FertiQoL: Fertility Quality of Life Questionnaire, GPAQ: Global Physical Activity Questionnaire, BDI: Beck Depression Inventory, FPI: FPI: Fertility Problem Inventory, MET: metabolic equivalent of task, MPA: moderate physical activity, MVPA: moderate to vigorous physical activity, m/w: minutes/week, R: Recreation, T: Transport, TPA: total physical activity, VPA: vigorous physical activity, W: Work, *p≤0.05, **p≤0.01

Relationship between IVF outcomes and physical activity

If we divided IVF patients regarding the presence of clinical pregnancy as the primary outcome, we can conclude that PA patterns differ. Due to high SD, we could detect a significant difference only in case of GPAQ-H recreational PA MET means (p=0.048). Minutes spent with recreation per week also showed tendency-like difference, but a level of significance was not reached (p= 0.067). In both cases, means of the pregnant group were higher.

If we analyse the tendencies by all subjective and objective measures, we see that pregnant women spent more time and energy expenditure with recreational type- or with vigorous activities, which refers to exercise. In contrast, in the non-pregnant group cumulative values of PA were higher, but in relation with work or in total, we assume that this alone did not have a positive effect. Type and intensity of PA seems to be significant. (Table 18.)

Consistent with previous results, if the pre-treatment PA measures undergoing IVF/ICSI were analysed by secondary outcomes, correlations can only be found with time spent with recreation. Significant relationship was found with the number of retrieved oocytes (R=0.315, p=0.045), number of matured oocytes (R=0.339, p= 0.030) and tendency-like relationship with Grade 1 embryos (R= 0.294, p=0.062) by women who reached at least 150 minutes RPA measured by GPAQ-H.

Table 18.

Mean differences of pre-treatment physical activity measures undergoing IVF/ICSI (N=45) by primary outcome

		Non-pregnant		Pregnant*		Total			
		Mean	SD	Mean	SD	Mean	SD	Z	p
ActiGraph GT3X	Sedentary	**8294.74**	1388.92	8135.17	2445.36	8265.73	1555.60	-.341	.733
	Light	**1092.32**	396.67	1015.29	174.39	1078.32	364.21	-.170	.865
	Moderate	**211.65**	139.16	199.79	130.87	209.49	134.71	0.000	1.000
	Vigorous	1.24	1.66	**5.17**	9.68	1.95	4.24	-.429	.668
	Very Vigorous	0.05	0.08	**4.58**	6.29	0.87	2.98	-1.349	.177
	Total MVPA	**212.94**	140.51	209.54	140.15	212.32	137.08	-.085	.932
IPAQ-SFH	MPA m/w	**267.93**	538.57	101.82	135.85	222.25	467.57	-.505	.614
	MPA MET	**803.79**	1615.72	305.45	407.56	666.75	1402.71	-.505	.614
	VPA m/w	**198.97**	491.23	100.00	137.11	171.75	424.34	-.481	.630
	VPA MET	**1193.79**	2947.35	600.00	822.68	1030.50	2546.05	-.481	.630
	MVPA m/w	**466.90**	848.20	201.82	167.62	394.00	733.55	-.642	.521
	MVPA MET	**1997.59**	3831.81	905.45	823.42	1697.25	3310.47	-.657	.511
	Walking m/w	**497.76**	757.32	255.91	338.87	431.25	673.18	-.562	.574
	Walking MET	**1244.40**	1893.30	639.77	847.18	1078.13	1682.96	-.562	.574
	Sitting m/w	**2773.45**	1630.89	2119.09	1329.67	2593.50	1565.40	-1.235	.217
	Total m/w	**964.66**	1372.92	457.73	312.34	825.25	1196.17	-.045	.964
	Total MET	**3241.98**	5004.90	1545.23	975.83	2775.38	4337.83	-.106	.916
GPAQ-H	WMPA m/w	**532.76**	696.84	196.36	359.84	440.25	636.37	-1.387	.165
	WMPA MET	**1598.28**	2090.53	589.09	1079.52	1320.75	1909.12	-1.387	.165
	WVPA m/w	**221.38**	484.23	218.18	723.63	220.50	550.10	-.889	.374
	WVPA MET	**1328.28**	2905.37	1309.09	4341.76	1323.00	3300.60	-.889	.374
	WPA m/w	**754.14**	951.11	414.55	747.57	660.75	903.52	-1.043	.297
	WPA MET	**2926.55**	4016.62	1898.18	4280.15	2643.75	4061.58	-1.043	.297
	RMPA m/w	71.21	106.26	**83.18**	73.90	74.50	97.66	-1.059	.290
	RMPA MET	213.62	318.79	**249.55**	221.70	223.50	292.97	-1.059	.290
	RVPA m/w	25.86	54.81	**68.18**	104.00	37.50	72.77	-1.059	.289
	RVPA MET	155.17	328.84	**409.09**	624.01	225.00	436.65	-1.059	.289
	RPA m/w	97.07	129.67	**151.36**	108.26	112.00	125.22	-1.834	**.067**
	RPA MET	336.96	483.80	**658.64**	597.08	427.69	530.69	-1.975	**.048***
	TPA m/w	**299.14**	523.72	184.09	227.67	267.50	461.43	-.091	.927
	TPA MET	**897.41**	1571.16	552.27	683.01	802.50	1384.29	-.091	.927
	Sitting m/w	**3157.50**	1678.52	2252.73	1794.46	2902.31	1737.64	-1.598	.110
	VPA m/w	247.24	475.20	**286.36**	766.89	258.00	559.68	-.370	.711
	VPA MET	1483.45	2851.19	**1718.18**	4601.36	1548.00	3358.05	-.370	.711
	MPA m/w	**603.97**	738.65	279.55	350.13	514.75	666.83	-.901	.368
	MPA MET	**1811.90**	2215.94	838.64	1050.40	1544.25	2000.50	-.901	.368
	MVPA m/w	**851.21**	964.10	565.91	736.56	772.75	907.24	-.486	.627
	MVPA MET	**3295.34**	3985.60	2556.82	4387.30	3092.25	4056.06	-.395	.693
	Total m/w	**1150.34**	1230.55	750.00	728.43	1040.25	1120.71	-.409	.683
	Total MET	**4192.76**	4828.50	3109.09	4300.56	3894.75	4660.57	-.303	.762

Multivariate linear regression analysis

To define predicting factors of primary and secondary outcomes of IVF from pre-treatment habitual PA, psycho-socio-demographic variables, and baseline biomedical variables, we conducted a multivariate linear regression using the stepwise method.

We applied 3 models, which included women's age, education, BMI, child-wish, duration of infertility and number of cycles, QoL and PSD parameters, and PA values as covariates. In the first step, we adjusted for age, education, and BMI. In the second step child-wish, duration of infertility and number of cycles were additionally adjusted. In the third step, we adjusted subscales of WHOQOL-BREF, FertiQoL, BDI, and FPI as well, and finally, in the fourth step PA parameters as IPAQ-SFH, GPAQ-H and ActiGraph data were also included.

In Model 1 (R^2= 0.367) the number of oocytes, as the dependent variable was influenced positively by the GPAQ-H recreation MET (F=10.994, p=0.004; B=0.005, p=0.004, B Constant=4.604).

The number of Grade 1 embryos was also examined as a dependent variable in Model 2 (R^2=0.757, F=17.692, p<0.001, B Constant=1.342). Positive significant relationship was found with GPAQ-H recreational physical activity MET (B=0.004, p<0.001) and negative relationship with IPAQ sitting time (B= -0.001, p≤0.001) and BMI (B= -0.167, p=0.038).

When hCG levels on day 12 were considered as dependent variable, multivariate linear regression disclosed in Model 3 (R^2=0. 0.958, F=408.479, p<0.001) that higher Very Vigorous Activity level measured with ActiGraph was accompanied with higher hCG levels (B=63.703, p≤0.001).

Logistic regression analysis

On the basis of biomedical, psycho-socio-demographic and PA variables, logistic regression analysis was conducted to evaluate the effects of all the above parameters on livebirths. Contrary to our previous findings, the results indicated that time (min/week) spent with moderate PA measured with GPAQ (beta coefficient [B] = 0.002, standard error [SE] =0.001, Wald = 3.944, p = 0.047, OR = 1.002) significantly associated with livebirths.

Discussion of key findings

It was assumed that the abundance of pre-treatment PA will increase general and infertility related QoL and decrease psychosocial distress domains in ART patients and thereby enhance reproductive performance. To assess the effects of psychosocial and lifestyle factors with special regard to physical activity on course and success of ART an observational cohort study was conducted with a follow-up of primary and secondary outcomes.

Focusing on the QoL part of the study, it can be assumed, that participating women's self-rated general QoL and SRH was similar to that of the general population, but participants were less satisfied with their fertility related QoL. Around 70 % of the respondents reported normal mood state in general and moderately high infertility related stress. In the Hungarian validation study of the WHOQOL-BREF (Paulik et al). In this study women reported significantly lower values than men, except for the Social Relationship domain. Values scored between 13.82±2.19 (Environmental domain) to 14.15±3.02 (Social relationship domain) in the general female subsample. In the research of Paulik et al., data were also analysed by health status and age. If we compare our results (Psychological Domain 15.15±2.10, Environmental 15.74±2.00, Social Relationships 15.79±2.32, Physical Health 16.49±2.38) with the healthy matching age group (35-44 years) of the study of Paulik et al, we can find close similarities by Psychological, Social and Environmental domains (15.69±2.25, 15.87±2.76, 14.63±1.99 respectively). Healthy people estimated each aspect of QoL as significantly better, compared to respondents with health impairments. It is promising that women's results undergoing ART were closer to the healthy population [159].

In relation to general Qol, in our study positive correlation was found between WHOQOL-BREF Psychological Domain and recreational activities. Positive relationship was described between more domains of the Core Scale of FertiQoL and Total MET, and also between Treatment Scale's Tolerability Subscale and MET of active transportation. Relationship between generic PSD, measured with BDI and PA patterns cannot be described. Our results revealed by GPAQ-H, that recreational PA could counteract with some aspects of infertility related distress, RPA negatively correlated with Social Concern and Relationship Concern of FPI. Significant differences cannot be described using PAGA PA categories or the 240 minutes cut off point regarding QoL or PSD.

Comparison of fertility-specific and general questionnaires can be found in literature in relation to FertiQol-Hospital Anxiety and Depression (HADS) [104, 105], FertiQol – WHOQOL

[102]. Cserepes et. al conducted research using FertiQoL and Beck Depression Inventory on a Hungarian sample (126 couples). Female members of the couples reported poorer QoL than males. Subscales of the Core module scored between 69.01±16.33 (Emotional Scale) and 80.26±13.85 (Social scale), the total QoL was described as 77.27±12.05. These values were markedly higher than in our sample [103].

Domar et. al underline the role of improving mental health with psychological interventions in improved pregnancy rates among infertile women [107]. Other studies shift focus to lifestyle behaviours: Domar et al made surprising observations regarding interfering health behaviours as exhausting exercise, smoking, regular consumption of alcohol and caffeinated beverages and taking herbal supplements during IVF cycles [108]. In our sample more health-conscious lifestyle could be observed.

Porat-Katz and co-authors examined the associations between the use of complementary medicine, QoL, and lifestyle habits, i.a. PA among 323 women undergoing IVF and found that these variables are linked. Complementary-medicine users reported higher scores for the FertiQol Relational domain and lower for the Social domain ($p=0.005$, $p=0.010$), greater utilization of psychosocial support ($p<0.001$), and higher rates of PA ($p=0.004$) and consulting with dietitians ($p=0.050$) [175].

The Fertility Experiences Project examined 202 first IVF cycle patients to predict the influence of psychological distress on IVF treatment outcome and subsequent PSD, in a prospective cohort study over an 18-month period using the Epidemiologic Studies Depression Scale (CES-D) and the State Anxiety Subscale of the State-Trait Anxiety Inventory (STAI). In a binary logistic model including covariates (woman's age, ethnicity, income, education, parity, duration of infertility, and time interval), pre-treatment depression and anxiety were not significant predictors of the outcome measures. In linear regression models including covariates (woman's age, income, education, parity, duration of infertility, assessment point, time since last treatment cycle, and pre-IVF depression or anxiety), experience of a failed IVF were associated with higher post-IVF depression and anxiety, which draw attention to the support of patients to prepare for and cope with treatment and treatment failure [176].

Regarding the examination of PA patterns, PAQs routinely overestimated all types and intensity of PA, but showed relatively good correlation with objective values. Self-reported time spent sedentary was strongly correlated with questionnaires and accelerometer measures. Cumulative values of PA in average were analogous to the Hungarian general population, but medians demonstrated that most of these women completely avoided vigorous forms of PA and showed pre-treatment PA patterns like women during pregnancy.

60.00% reported notable leisure time PA, and only 40.00% reached the recommended level of 150 min/week recreational moderate physical activity. They spend 16.98 hours per week with all forms of activity and spent 6.53 hours per day sedentary. 50.00% of the women in the sample reported regular exercise, which could be discussed as a relatively active subpopulation in Hungary compared to previous national studies [177, 178]. However, Ács et al reported 10% improvement in PA habits based on representative Eurobarometer data from 2018: Hungarians' regular sport participation and physical activity is 33%, which is below the EU average (40%). Authors noted that 42% of Hungarian citizens spent more than 2.5 and less than 5.5 hours sedentary. With 6.53 hours daily sitting time (2745.17±1755.39 min/day), our results are slightly elevated but are in line with the above findings [53].

The amount of PA in our research increased unexpectedly in line with years and also with BMI, suggesting more of a health-conscious behaviour by women exposed to higher risk. The current study did not include questions on health literacy, so we can only assume that women had some supposed knowledge on the relationship between reduced conception rate and overweight/obesity, insulin resistance or amount of visceral fat. Lungren, Kiel and co-authors developed a study protocol to provide knowledge on the results of a high-intensity interval training before ART in subfertile overweight or obese women and include the program in regular fertility care [179]. Similarly to other studies emphasizing the importance of PA on BMI [180], in a randomised controlled pilot trial authors proved that the high-intensity interval training significantly improved insulin sensitivity, VO2 peak and abdominal fat. However, due to the low number of participants (intervention group N=8, control group N=10) they could not draw a conclusion on pregnancy rate [179].

"Walking the way to better health" general recommendations promote 10,000 steps daily [181, 182]. With 7060.28 steps per day measured with accelerometers, our respondents yet cannot be categorised as inactive compared to a Nature letter by Althoff et al. on worldwide activity inequality, which mentioned the average daily steps around 5,300 in Hungary, 5,000 Worldwide and 4,800 in the US, measured with smartphones [183]. In an updated published in ACSM's journal, Medicine & Science in Sports & Exercise authors revealed that 7,000-9,000 steps per day may trigger health benefits, which are associated with current public health guidelines' emphasis on minimal amounts of time spent in MVPA, the federally recommended amounts of 150 to 300 minutes per week [184].

Women were divided as per the abundance of clinical pregnancy. Pregnant women spent more time and energy expenditure with recreational type- or with vigorous activities, which refers to exercise. In contrast, in the non-pregnant group cumulative values of PA were higher, but in

relation with work or in total, we assume that this alone did not have a positive effect. Type and intensity of PA seems to be significant. Significant relationship could be described with the number of retrieved oocytes, number of matured oocytes and tendency-like relationship with Grade 1 embryos by women who reached at least 150 minutes RPA measured by GPAQ-H.

It could be claimed that the GPAQ-H measurement tool is a valid and reliable questionnaire to measure the healthy Hungarian general population's physical activity patterns [147]. By the validation study of GPAQ-H, Bland Altman plots revealed mean differences between the GPAQ-H and accelerometer data. The plots showed that GPAQ-H overestimates vigorous activities by 212.75 min/week (331.82-757.42) and MVPA values by 104.93 min/week (-1016.98-807.11). In our current study we observed similar overestimation of vigorous activities with 331.10 vs 184.06 minutes/week, and considerable overestimation of MVPA 481.37 vs 805.23 minutes/week in case of GPAQ-H and IPAQ-SFH. In the validation study a high difference, 6336.79 min/week (CI 3638.18-9035.40) was revealed regarding sitting, as GPAQ-H largely underestimated the time spent sedentary. [147]. Our study also revealed a difference in the measurement of sitting time between accelerometer and GPAQ-H, and IPAQ-SFH -5980.21 and -6166.50 min/week, respectively.

Regarding GPAQ, our respondents performed moderate intensity PA during work and preferred that during recreation. However, mean values showed some vigorous activity in work (158.00±467.34 min/week) and recreation (35.00±82.70 min/week). Medians demonstrated that most of these women completely avoided heavy forms of movement. Regarding female reproduction, there is a wide consensus on the beneficial effects of PA on gestation. Most studies draw attention to the risk of frequent vigorous PA on fertility [119, 120] and on success of ART [108, 121].

To describe PA levels, both instrumental and self-reported studies were published. Evenson et al discussed that the adjusted odds of intrauterine gestation are higher among IVF patients who had higher continuous active living (OR 1.96, 95% CI 1.09–3.50), sports/exercise (OR 1.48, CI 1.02–2.15), and total activity (OR 1.52, 95% CI 1.15–2.01) indices in the past year [141].

Regarding the benefits of pre-treatment activity, Moran et al. reported positive effect of lifestyle intervention including exercise and diet in conjunction with ART in overweight and obese women and described elevated successful pregnancy rate (12 ⁄ 18 vs 8 ⁄ 20) in the intervention group compared to controls (Moran, Tsagareli, Norman, & Noakes, 2011).

Palomba et al in their observational cohort study assessed the relationship between RPA and reproductive performance in connection with lifestyle interventions in obese infertile women who received ART (N=216). Number of pregnancies (16/41, 39.0% versus 28/175, 16.0%,

respectively; p= 0.002) and live births (10/41, 24.4% versus 13/175, 7.4%, respectively; p= 0.004) were significantly higher in 41 obese patients who did regular physical activity compared to 175 obese controls who did not. After adjusting for confounders, the relative risks for a clinical pregnancy and livebirth were 3.22 (95% CI 1.53–6.78;P= 0.002) and 3.71 (95% CI 1.51–9.11;P= 0.004) in active patients, and RPA significantly correlated with improved reproductive performance irrespective of bodyweight loss [131]. In our study we found significant difference between pregnant and non-pregnant groups by GPAQ-H recreational PA MET means (p=0.048), which underline the importance of leisure time activities (inter alia) against PA in general.

On the other hand, adverse effects of excessive PA are also demonstrated. Gudmundsdottir et al. found that women who are active on most days, tended to experience fertility problems 3.2 times more often. In this study exercising to exhaustion also led to 2.3 times more fertility impairments than low intensity PA [172]. Based on the data by Morris et al. on lifetime exercise (level of evidence: II-2), exercising 4 hours or more per week indicate 40% less likelihood of having a livebirth (OR 0.6, CI 0.4-0.8), it is 3 times more likely to lead to cycle cancellation, and 2 times more likely to lead to implantation failure or pregnancy loss (OR 2.8, CI 1.5-5.3; OR 2.0, CI 1.4-3.1; OR 2.0, CI 1.2-3.4 respectively) compared to non-exercise [121]. In the current research during the follow-up of IVF outcomes, particular attention was given to the women in our sample who reported at least 4 hours exercise weekly (18.2%). In our study neither negative nor positive effects can be concluded by exceeding 240 or even 300 minutes of activity per week. Significant relationship could be described in relation to reproductive performance (number of retrieved oocytes and number of matured oocytes) by women who reached at least 150 minutes pre-treatment RPA measured by GPAQ-H.

Positive effects were also concluded in the meta-analysis of eight published studies (N=3683 infertile couples) of Rao et al., which reported an increasing but not statistically significant trend in the implantation rate for physically active women when compared with physically inactive women (OR = 1.95, 95% CI 0.99–3.83, I2 = 77%). Rates of clinical pregnancy and live births in physically active women were significantly higher than those in physically inactive women (OR = 1.96, 95% CI 1.40, 2.73, I2 = 42% and OR = 1.95, 95% CI 1.06–3.59, I2 = 82%, respectively) [157].

Regarding PA immediately after IVF, Evenson et al could not find any association between accelerometer-measured activity or sedentary behaviour with IVF outcomes. They described that after embryo transfer women engaged only in light activity (ME 3.0 hour/day) and sedentary behaviours (ME 9.0 hour/day). Although the current research focused on pre-treatment habitual

PA, measurement of post-treatment PA in relation to QoL, PSD, and success rates could also offer research potential.

Espinós et al. reported in their meta-analyses based on 8 RCTs, that although lifestyle programmes improved pregnancy rates (RR: 1.43, CI: 95% 1.02 to 2.01; I2=60%; 8 RCTs; N=1098), they had no impact on live births (RR: 1.39, CI: 95% 0.90 to 2.14; I2=64%; 7RCTs; N=1034) and increased risk of miscarriage in obese infertile women [185]. In our sample positive association was found between moderate PA and live births and no relationship with the ratio of miscarriage.

An analysis of 121 744 women with failed first treatment revealed that female age is a key predictor of failure to have a livebirth following IVF as well as the risk of hindered performance, while increased duration of infertility is also associated with poorer outcomes at every stage [186]. Comparing our results to our models, we cannot confirm the emphasized importance of PSD and age on reproductive performance.

To define predicting factors of primary and secondary outcomes of IVF from the point of view of PA, QoL and PSD, we conducted a multivariate linear regression using the stepwise method. We applied 3 models, which included women's age, education, BMI, child-wish, duration of infertility and number of cycles, QoL and PSD parameters, and PA values as covariates. In Model 1 the number of oocytes was influenced positively by the GPAQ-H recreation MET, in Model 2 the number of Grade 1 embryos was positively correlated with GPAQ-H recreational physical activity MET and negatively with IPAQ sitting time and BMI. It was disclosed in Model 3 that higher Very Vigorous Activity level measured with ActiGraph was accompanied by higher hCG levels.

Gaskins and co-authors reported similar findings on maternal PA and sedentary behaviour in relation to ART’s reproductive outcomes. They found no association between MVPA time or total MET and outcomes as probability of implantation, clinical pregnancy or live birth. However, specific leisure time activities (aerobics, rowing, exercising with ski or stair machine) were positively associated with live birth (p-trend=0.02)

Conclusions

Infertility-specific and generic scales could also provide appropriate information on QoL and distress of ART patients. GPAQ-H could be used as a valid measurement tool for mapping PA habits of ART patients. Based on our results, recreation type of pre-treatment PA could positively influence domains of infertility related QoL and PSD during ART and improve reproductive performance. Existing differences in response to infertility due to PA suggest the need for development of a specific intervention.

Limitations

The limitations of the study include the sample's non-representative nature. To avoid potential confounders, patients were carefully selected, but made the study population modest. Objective measurement of PA patterns cannot be conducted by all patients and complete medical record was also missing in a portion of patients.

A post-hoc sample size estimation (using G*Power for Mac version 3.1.9.6) for the multivariate linear regression analysis (significance set at 5%, power set at 0.8, effects size at 0.15, and number of predictors at 2) showed that a total of 55 subjects would have been required to ensure adequate statistical power for analyses. The final sample of 45 subjects did not meet the sample requirements. Whereas the sample size was relatively suboptimal, given the limited study power, i.e 71.84%, to detect the difference in primary and secondary outcomes of ART.

Gaskins et al has been calling attention the use of intermediate outcomes of IVF as surrogates of women's reproductive performance [187]. Ongoing pregnancy has been considered as acceptable surrogate for live birth, as well as clinical pregnancy in or study. However, the major potential limitation of using ongoing pregnancies as the primary outcome of ART is the significant odds of pregnancy loss between the pregnancy confirmation and live birth.

For more impressive results on the effects of physical activity on the effectiveness of fertility programmes, a detailed objective assessment of physical activity, increased number of participants, and further examinations on outcome measures, with live birth's rate as end point are needed in a well-powered randomized controlled prospective study.

Clinical implication

Infertility-specific and generic scales could provide appropriate information on QoL and PSD of ART patients. Pre-treatment PA may positively influence domains of QoL and PSD during ART and reproductive performance.

Therefore, combined investigation of these factors is recommended to identify patients who could benefit from psychosocial interventions or lifestyle changes. After more detailed Randomized controlled trial (RCT)-based examinations, a routine screening protocol of ART patients can be developed for psychosocial and lifestyle screening. For promoting appropriate pre-treatment PA habits, development of a specific guideline for ART patients is recommended.

Recruiting patients in intervention groups, offering exercise sessions and facilitation to perform the needed RPA under the guidance of health professionals could be also favourable. These groups could also act as peer support groups, raising the positive effects of PA interventions with psychosocial benefits and would provide protection against medicalization. Exploration of patient experiences during ART could also help offset negative reactions to infertility and its treatment, to improve willingness to continue with the treatment, may improve patient outcomes, and, if the treatment is unsuccessful, may support to cope with the circumstances of remaining childless.

Parallel to the psychosocial support, a multi-centre study with the University of Novisad and the Karolinska Institutet on insulin resistance, physical activity and ART is under preparation.

Further perspectives

On the one hand we intend to start developing a dance intervention for IVF patients in collaboration with Dr Anna Duberg PhD (Health Science Research Centre, Örebro University, Sweden). In this project we attempt to adapt the methods of dance intervention for internalizing problems [188-191].

Infertility-specific and generic scales could provide appropriate information on QoL and PSD of ART patients. Pre-treatment PA may positively influence domains of QoL and PSD during ART and reproductive performance. After more detailed examinations of pre-treatment activities, measurement of post-treatment PA in relation to QoL, PSD and success rates could also offer research potential.

The relationship between psychosocial stress and the release of adrenal hormones in relation to success of IVF/ICSI is still moderately discussed [192]. We intend to expand the current research to gain understanding on the endocrine point of view beside the already studied factors. This will provide the opportunity to compare the role of self-reports with endocrine variables.

We attempt to combine psychosocial and biomedical methods to examine the associations between perceived (self-reported) and endocrine stress (measured by levels of the biomarkers of stress: adrenaline, noradrenaline, dopamine, cortisol and alpha-amylase) during fertility treatment, in order to investigate the hypothetic stress-reducing mechanism of self-reported and accelerometer monitored PA on the previously observed negative association of anxiety and depression with the outcome of IVF/ICSI.

Summary of novel findings

1.

Longitudinal analyses of the the utilization of assisted reproductive treatments was conducted based on International Classification of Health Interventions (WHO) codes in Hungary between 2010-2018 by number and weighting of cases, type of interventions, mean age of patients, financial categories and regional and territorial distribution on the National Health Insurance Fund's dataset to demonstrate the changing patterns and the importance of fertility interventions in Hungary. 61.39% expansion in the cumulative number of cases and 2.122 years increase in the mean age of patients was reported during this nine-year period.

Robust regional and territorial differences could be described. Most patients lived in Central Hungary (NUTS 1 region) and based on the number of cases per 10 000 inhabitants by counties, compared to the national mean value, utilization values of Baranya county (79.569) were significantly higher in 2018 (43.117), where cases doubled compared to 2010. In addition to Baranya, Hajdú-Bihar, Tolna, and Somogy counties had outstanding utilization values as well.

2.

Based on a cross-sectional, observational cohort pilot study on the relationship between self-reported frequency of exercise and success of assisted reproductive treatments, it was assumed that infertility-specific scales provide more appropriate description on mental status of ART patients than general scales and based on the results of these scales of the studied sample, by decreasing the level of infertility related distress, abundance of regular pre-treatment physical activity may increase the success rate of ART measured by clinical pregnancy ($p=0.036$).

3.

To select the most appropriate method of detailed measure of physical activity in the context of assisted reproduction, a systematic literature review was conducted following the PRISMA criteria and 398 related studies were explored. In the qualitative synthesis of the final nine studies it was concluded that the IPAQ-SF and GPAQ questionnaires combined with accelerometers assumed to be the most appropriate tools.

4.

To the best of our knowledge the main study of the thesis was the first in Hungary which gave a detailed description on the physical activity patterns of the specific cohort of patients undergoing assisted reproductive treatment using ActriGraph GT3X accelerometers, IPAQ-SF and GPAQ-H questionnaires. The study also presented the relationship between PA patterns and psycho-socio-demographic characteristics or primary and secondary outcomes of ART.

Respondents in the studied sample were less satisfied with the Psychological Domain of the Generic (WHOQOL-BREF) and Emotional Scale of the Infertility-related quality of life (FertiQoL). In general, 68.96% of them reported normal mood state (BDI-13), while they could be characterised by moderately high infertility-related distress (FPI), with moderately high level by Social-, and very high level by Sexual concern.

Compared to the general Hungarian population, the subpopulation of the studied women cannot be described as inactive, however only 60.00% reported notable leisure time PA, and 40.00% reached the 150-minute weekly moderate physical activity recommendation regarding recreational activities and the medians of all subjective and objective PA measures demonstrated that most of these women completely avoided vigorous forms of PA.

Questionnaires highly overestimated participants' physical activity values compared to the accelerometer measures, the robust mean difference between objective and subjective measures of PA highlight the need to improve physical literacy of women undergoing ART.

Based on our results, recreation type of pre-treatment PA could positively influence domains of infertility related QoL and PSD during ART and improve reproductive performance as follows:

GPAQ-H proved to be a more informative measurement tool for mapping PA habits of ART patients, because as a multidomain questionnaire, it describes not only the intensity but also the type of PA, pointing out strong correlations between the Psychological Domain of WHOQOL-BREF and time of vigorous recreational activities ($R=0.484$, $p=0.001$) and energy expenditure of recreational activities ($R=0.428$, $p=0.006$), and significant correlation with weekly time spent with recreational activity ($R=0.319$, $p=0.039$).

It was also revealed that recreational PA could counteract with some aspects of infertility related distress, since time spent with moderate RPA, total time and total MET of RPA negatively correlated with Social Concern (R=-0.378 p=0.013, R=-0.386 p=0.012 and R=-0.360 p=0.023 respectively) and Relationship Concern of FPI (R=-0.365 p=0.019, R=-0.368 p=0.018 and R=-0.342 p=0.033 respectively).

If IVF patients were divided regarding the primary outcome (presence of clinical pregnancy), it could be concluded that PA patterns differ; significant difference could be detected in case of GPAQ-H recreational PA MET means (p=0.048), minutes spent with recreation per week also showed tendency-like difference (p=0.067). In both cases, means of the pregnant group were higher. When the tendencies were analysed by all subjective and objective measures, it was apparent that pregnant women spent more time and energy expenditure with recreational type- or with vigorous activities, which refers to exercise. In contrast, in the non-pregnant group cumulative values of PA were higher, but in relation to work or in total, it was assumed that amount of PA alone did not have a positive effect. Type and intensity of PA seemed to be more significant.

By secondary outcomes, correlations can only be found by Spearman's rank correlation with time spent with recreation. Significant relationship could be described with the number of retrieved oocytes (R=0.315, p=0.045), number of matured oocytes (R=0.339, p= 0.030) and tendency-like relationship with Grade 1 embryos (R=0.294, p=0.062) by women who reached at least 150 minutes recreational PA measured by GPAQ-H.

To define predicting factors of primary and secondary outcomes by multivariate linear regression using the stepwise method in Model 1 (R^2= 0.367) the number of oocytes, as the dependent variable was influenced positively by the GPAQ-H recreation MET (F=10.994, p=0.004; B=0.005, p=0.004, B Constant=4.604). In Model 2 (R^2=0.757, F=17.692, p<0.001, B Constant=1.342) positive significant relationship was found with GPAQ-H recreational physical activity MET (B=0.004, p<0.001) and negative relationship with IPAQ sitting time (B= -0.001, p≤0.001) and BMI (B= -0.167, p=0.038) on the number of Grade 1 embryos. It was disclosed in Model 3 (R^2=0. 0.958, F=408.479, p<0.001), that higher Very Vigorous Activity level measured with ActiGraph was accompanied with higher hCG levels (B=63.703, p≤0.001).

Logistic regression analysis was conducted to evaluate the effects of all parameters on livebirths. Contrary to our previous findings, the results indicated that total time (min/week) spent with

moderate PA measured with GPAQ (beta coefficient [B] = 0.002, standard error [SE] =0.001, Wald = 3.944, p = 0.047, OR = 1.002) was significantly associated with livebirths.

Existing differences in response to infertility due to PA suggest the need for the development of a specific intervention.

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List of Publications

In extenso publications

Articles related to the thesis

Prémusz, V ; Makai, A ; Perjés, B ; Máté, O ; Hock, M ; Ács, P ; Koppán, M ; Bódis J ; Várnagy, Á[#] ; Lampek, K[#hűá].(# equally contributed)
Multicausal analyses on psychosocial and lifestyle factors undergoing assisted reproductive therapy – with special regard to self-reported and objective measures of pre-treatment habitual physical activity. BMC PUBLIC HEALTH S20, pp. 1-13. (2020)
In Press

Ács, P ; Betlehem, J ; Oláh, A ; Bergier, B ; Morvay-Sey, K ; Makai, A ; **Prémusz, V** . Cross-cultural adaptation and validation of the Global Physical Activity Questionnaire among healthy Hungarian adults. BMC PUBLIC HEALTH pp. 1-11. DOI : 10.1186/s12889-020-08477-z (2020)
In Press

Prémusz, V ; Makai, A ; Gács, B ; Nagy, Á ; Perjés, B ; Ács, P ; Lampek, K ; Várnagy, Á .
Preliminary study on pre-treatment physical activity and quality of life in infertility
EXERCISE AND QUALITY OF LIFE: JOURNAL OF SCIENCE IN SPORTS 11 : 2 pp. 5-17. , 12 p. (2019)

Prémusz, V; Makai, A; Nagy, Á; Perjés, Betarix ; Ács, Pongrác ; Lampek, Kinga ; Várnagy, Á .
Szisztematikus irodalmi áttekintés kvalitatív szintézise a fizikai aktivitás méréséről az asszisztált reprodukcióval összefüggésben
SPORT- ÉS EGÉSZSÉGTUDOMÁNYI FÜZETEK 3 : 4 pp. 1-13. (2019)

Prémusz, V ; Makai, A ; Gács, B ; Simon-Ugron, Á ; Ács, P ; Lampek, K ; Várnagy, Á .
Relationship between pre-treatment habitual physical activity and success of assisted reproduction
STUDIA UNIVERSITATIS BABES-BOLYAI EDUCATIO ARTIS GYMNASTICAE 58 : 3 pp. 41-58. (2018)

Prémusz, V ; Makai, A ; Melczer, C ; Perjés, B ; Ács, P ; Bódis, J ; Lampek, K ; Várnagy, Á .
Habituális fizikai aktivitás és életminőség összefüggése várandósság alatt a WHO Global Physical Activity Questionnaire alapján
MAGYAR NŐORVOSOK LAPJA 81 : 6 pp. 343-350. (2018)

Additional articles

Ács, P ; Betlehem, J ; Oláh, A ; Bergier†, J ; Melczer, Cs ; **Prémusz, V[#]** ; Alexandra Makai[#] .(# equally contributed)
Measurement of public health benefits of physical activity: Validity and reliability study of the International Physical Activity Questionnaire in Hungary.
BMC PUBLIC HEALTH, DOI : 10.1186/s12889-020-08508-9 pp. 1-12. (2020)
In Press

Rétsági, E ; **Prémusz, V** ; Makai, A ; Melczer, Cs ; Betlehem, J ; Lampek, K ; Ács, P ; Hock, M.
Association with subjective measured physical activity (GPAQ) and quality of life (WHOQoL-BREF) of ageing adults in Hungary, a cross-sectional study

BMC PUBLIC HEALTH DOI: 10.1186/s12889-020-08833-z, pp. 1-10. (2020)
In Press

Bódis, J ; Sulyok, E ; Kőszegi, T ; **Prémusz, V** ; Várnagy, Á ; Koppán, M .
Serum and follicular fluid levels of serotonin, kisspeptin, and brain-derived neurotrophic factor in patients undergoing in vitro fertilization : an observational study: Neurohormones in patients receiving IVF
JOURNAL OF INTERNATIONAL MEDICAL RESEARCH UNSP 0300060519879330 https://doi.org/10.1177/0300060519879330 pp 1-15. (2020)

Bódis, J ; Sulyok, E ; Kőszegi, T ; Gödöny, K ; **Prémusz, V ;** Várnagy, Á .
Serum and follicular fluid levels of sirtuin 1, sirtuin 6, and resveratrol in women undergoing in vitro fertilization: an observational, clinical study.
JOURNAL OF INTERNATIONAL MEDICAL RESEARCH 47 : 2 pp. 772-782. (2019)

Melczer, Cs ; Melczer, L ; Raposa, BL ; **Prémusz, V** ; Makai, A ; Ács, P .
Assessement the physical activity of heart failure patients by telemetry data
SPORT- ÉS EGÉSZSÉGTUDOMÁNYI FÜZETEK 3 : 3 pp. 25-38. (2019)

Nagy, AL ; **Premusz, V** ; Beatrix, Perjés ; Anna, Duberg ; Gabriella, Hegyi
Dance as Moderate Intensity Activity in the Stress Management among Teenage Girls
HEALTH EDUCATION AND PUBLIC HEALTH 2 : 2 pp. 181-186. (2019)

Moghaddam Hosseini, V ; Makai, A ; Varga, K ; Ács, P ; **Prémusz, V ;** Várnagy, Á .
Assessing fear of childbirth and its predictors among Hungarian pregnant women using Wijma Delivery Expectancy/Experience Questionnaire subscales
PSYCHOLOGY HEALTH & MEDICINE 24 : 7 pp. 879-889. (2019)

Várnagy, Á ; Kőszegi, T ; Györgyi, E ; Szegedi, S ; Sulyok, E ; **Prémusz, V ;** Bódis, J .
Levels of total antioxidant capacity and 8-hydroxy-2'-deoxyguanosine of serum and follicular fluid in women undergoing in vitro fertilization: focusing on endometriosis.
HUMAN FERTILITY pp. 1-9 (2019)

Ács, P ; **Prémusz, V ;** Melczer, Cs ; Bergier, J ; Salonna, F ; Junger, J ; Makai, A .
Nemek közötti különbségek vizsgálata a fizikai aktivitás vonatkozásában a V4 országok egyetemista populációjának körében
MAGYAR SPORTTUDOMÁNYI SZEMLE 19 : 74 pp. 3-9. (2018)
External citations: 2, Self citations: 0, Unhandled citations: 0, All citations: 2

Ács, P ; **Prémusz, V ;** Morvay-Sey, K ; Kovács, A ; Makai, A ; Elbert, G
A sporttal, testmozgással összefüggésben lévő mutatók változása Magyarországon és az Európai Unióban az elmúlt évek eredményeinek nyomán
SPORT- ÉS EGÉSZSÉGTUDOMÁNYI FÜZETEK 2 : 1 pp. 61-76. (2018)

Makai, A ; **Prémusz, V** ; Lampek, K ; Ács, P ; Simon-Ugron, Á ; Figler, M .
Sitting Time and Sport Participation of the Employed Population In Hungary and Europe
STUDIA UNIVERSITATIS BABES-BOLYAI EDUCATIO ARTIS GYMNASTICAE LVIII : 2 pp. 11-22. (2018)

Makai, A ; **Prémusz, V** ; Ács, P ; Figler, M

Fizikai aktivitás mértékének vizsgálata a magyarországi munkavállalók körében egy európai keresztmetszeti vizsgálat alapján
SPORT- ÉS EGÉSZSÉGTUDOMÁNYI FÜZETEK 2 : 2 pp. 3-16. (2018)

Bánkyné, PB ; **Prémusz, V** ; Nagy, Á ; Várnagy, Á ; Bódis, J .
Szülésfelkészítő tréning?: A várandósság alatt végzett rendszeres testedzés hatása a szülés kimenetelére – Irodalmi áttekintés
SPORT- ÉS EGÉSZSÉGTUDOMÁNYI FÜZETEK 1 : 2 pp. 3-17. (2017)

Szalai, M ; Szirmai, A ; Fuge, K ; Makai, A ; Erdelyi, G ; **Premusz, V[#] ;** Bodis, J[#] .
Special aspects of social support: Qualitative analysis of oncologic rehabilitation through a belly dancing peer support group.
EUROPEAN JOURNAL OF CANCER CARE 26 : 6 Paper: e12656 , 14 p. (2017)
External citations: 3, All citations: 3

Makai, A ; **Prémusz, V** ; Füge, K ; Figler, M ; Lampek, K .
Social Participation and Health among Ageing People in East-Central Europe
PRACTICE AND THEORY IN SYSTEMS OF EDUCATION 10 : 2 pp. 177-185. , 9 p. (2015)
External citations: 1, All citations: 1

Szalai, M ; Levay, B ; Szirmai, A ; Papp, I ; **Premusz, V** ; Bodis, J .
A Clinical Study to Assess the Efficacy of Belly Dancing As a Tool for Rehabilitation in Female Patients with Malignancies.
EUROPEAN JOURNAL OF ONCOLOGY NURSING 19 : 1 pp. 60-65. (2015)
External citations: 9, All citations: 10

Makai, A ; **Prémusz, V** ; Figler, M ; Lampek, K
Az idősödő népesség szubjektív életminősége és társas aktivitása
In: Ács, Pongrác (eds.) Tudományos szemelvények a Pécsi Tudományegyetem Egészségtudományi Kar Fizioterápiás és Sporttudományi Intézetének jelenéből : Jubileumi tanulmánykötet Kránicz János 70. születésnapja alkalmából
Pécs, Hungary : Pécsi Tudományegyetem Egészségtudományi Kar (PTE ETK), pp. 78-86. (2014)

Szalai, M ; Rektorovics, K R ; **Prémusz, V .**
Orientális tánc, mint rehabilitációs módszer a rosszindulatú daganatos megbetegedésekben
NŐVÉR 27 : 1 pp. 26-34. , 9 p. (2014)
External citations: 1, All citations: 1

Abstracts and oral presentations

Abstracts related to the thesis

Premusz, V ; Makai, A. ; Melczer, C. ; Gacs, B. ; Boncz, I ; Acs, P. ; Lampek, K. ; Varnagy, A.
Relationship between infertility related distress and pre-treatment moderate to vigorous physical activity in female patients
VALUE IN HEALTH 22 pp. S628-S628. (2019)

Prémusz, V ; Makai, A ; Perjés, B ; Kerner, Á ; Melczer, Cs ; Lampek, K ; Várnagy, Á ; Ács, P .
A habituális fizikai aktivitás hatása a reprodukciós potenciálra asszisztált reprodukciós kezelés esetén
Magyar Sporttudományi Szemle Különszám 82 : 5 p. 62 (2019)

Prémusz, V ; Makai, A ; Perjés, B ; Pálvölgyi, Á ; Bodor, AL ; Onchonga, DO ; Ács, P ; Lampek, K ; Várnagy, Á .
Fizikai aktivitási ajánlások összefüggése az életminőséggel és egészségi állapottal, keresztmetszeti vizsgálat a női reprodukció vonatkozásában
In: Németh, Katalin (szerk.) Tavaszi Szél Konferencia 2019 : Nemzetközi Multidiszciplináris Konferencia: Absztraktkötet
Budapest, Magyarország : Doktoranduszok Országos Szövetsége, (2019) p. 571 , 1 p.

Prémusz, V ; Lendvai-Emmert, D ; Makai, A ; Amrein, K ; Czeiter, E ; Sulyok, E ; Várnagy, Á .
Effects of pre-treatment habitual physical activity-induced oxidative stress on reproductive potential during assisted reproduction
In: 12TH INTERNATIONAL INSHS CHRISTMAS SPORT SCIENTIFIC CONFERENCE, Book of abstract
(2019) pp. 9-10. , 2 p.

Prémusz, V ; Lendvai-Emmert, D ; Makai, A ; Amrein, A ; Czeiter, E ; Sulyok, E ; Várnagy, Á .
The impact of oxidative stress on reproductive potential: Level of 8-hydroxy-2'-deoxyguanosine in saliva of patients undergoing in vitro fertilization
In: Csiszár, Beáta; Bódog, Ferenc (szerk.) Medical Conference for PhD Students and Experts of Clinical Sciences : Book of abstracts
Pécs, Magyarország : Pécsi Tudományegyetem Doktorandusz Önkormányzat, (2019) p. 72 , 1 p.

Prémusz, V ; Makai, A ; Meszlényi-Lenhart, E ; Oláh, A ; Betlehem, J ; Perjés, B ; Ács, P ; Várnagy, B ; Lampek, K
Physical Activity or Exercise During Pregnancy in Relation with Self-Reported Health and Quality of Life
In: F., Salonna (eds.) Abstract book for the ISBNPA 2019 Annual Meeting in Prague
Praha, Czech Republic : International Society of Behavioral Nutrition and Physical Activity, (2019) pp. 1122-1122. , 1 p.

Prémusz, V ; Makai, A ; Perjés, B ; Pálvölgyi, Á ; Bodor, AL ; Onchonga, DO ; Ács, P ; Lampek, K ; Várnagy, Á .
Fizikai aktivitási ajánlások összefüggése az életminőséggel és egészségi állapottal, keresztmetszeti vizsgálat a női reprodukció vonatkozásában
In: Németh, Katalin (eds.) Tavaszi Szél Konferencia 2019 : Nemzetközi Multidiszciplináris Konferencia: Absztraktkötet

Budapest, Hungary : Doktoranduszok Országos Szövetsége, p. 571. (2019)

Prémusz, V ; Makai , A ; Nagy , Á ; Ács , P ; Lampek, K ; Várnagy, Á.
An exploratory study to assess the impact of social support on quality of life of infertile women at a selected infertility clinic in Hungary
In: Klavdija, ČUČEK TRIFKOVIČ; Ines, MLAKAR - 11. Študentska konferenca s področja zdravstvenih ved z mednarodno udeležbo : Raziskovanje študentov zdravstvenih ved prispeva k zdravju in razvoju sodobne družbe
Maribor, Slovenia : University of Maribor Press, p. 17. (2019)

Prémusz, V ; Makai , A ; Gács , B ; Melczer, Cs ; Pálvölgyi , Á ; Lampek , K ; Ács , P ; Várnagy , Á.
Infertility related and general distress and quality of life in relation to pretreatment physical activity – Intervention opportunities in IVF
In: Bódog, Ferenc; Csiszár, Beáta (eds.) VIII. Interdiszciplináris Doktorandusz Konferencia 2019: absztraktkötet : 8th Interdisciplinary Doctoral Conference 2019: Book of Abstracts
Pécs, Hungary : Doctoral Student Association of the University of Pécs, p. 159. (2019)

Prémusz, V; Makai, A ; Melczer , Cs ; Ács, P ; Lampek, K ; Várnagy , Á.
Comparative analysis of measurement methods of pretreatment physical activity related to assisted reproduction
In: Bódog, Ferenc; Csiszár, Beáta (eds.) VIII. Interdiszciplináris Doktorandusz Konferencia 2019: absztraktkötet : 8th Interdisciplinary Doctoral Conference 2019: Book of Abstracts
Pécs, Hungary : Doctoral Student Association of the University of Pécs, (2019) p. 158 , 2 p.

Gács, B ; **Prémusz, V** ; Várnagy, Á.
A gyermekvállalás nehézségei: a meddőség-specifikus stressz pszichológiai velejárói. Pilot vizsgálat a PTE Reprodukciós Központjában
In: Dávid, Beáta; Feith, Helga Judit; Lukács, J Ágnes; Susánszky, Éva; Szabó, Ágnes (eds.) Ártó-védő társadalom konferencia 2.0
Budapest, Hungary : Semmelweis Egyetem Egészségtudományi Kar, (2018) pp. 17-18. , 2 p

Bánkyné Perjés, B ; **Prémusz, V** ; Nagy, Á ; Várnagy, Á ; Bódis, J.
Childbirth Preparation Training? Effects of Regular Physical Activity During Pregnancy on Delivery – Systematic Review
In: Ács, K; Bódog, F; Mechler, M; Mészáros, O (eds.) Book of Abstracts: Interdisciplinary Doctoral Conference 2017 = Absztraktkötet. Interdiszciplináris Doktorandusz Konferencia 2017
Pécs, Hungary : Pécsi Tudományegyetem Doktorandusz Önkormányzat, p. 94 (2017)

Additional abstracts

Prémusz, V ; Makai, A ; Lendvai-Emmert, D ; Amrein, K ; Czeiter, E ; Boncz, I ; Sulyok, E ; Várnagy, Á.
PNS209 consequences of physical activity-induced oxidative stress measured with 8-hydroxy-2'-deoxyguanosine as a biomarker on the outcome of assisted reproductive treatments
VALUE IN HEALTH 23 p. S322 (2020)

V, Premusz ; A, Makai ; J, Betlehem ; A, Olah ; Cs, Melczer ; Cs, Filo ; K, Lampek ; P, Acs
Comparison of the global physical activity questionnaire resultswith accelerometer data among healthy young adults
BMC SPORTS SCIENCE MEDICINE AND REHABILITATION 11 : Suppl 1 p. 32. (2019)

Meszlényi-Lenhart, E ; **Prémusz, V** ; Makai, A ; Vári, B ; Melczer, Cs ; Rétsági, E ; Oláh, A ; Betlehem, J ; Ács, P
Szubjektív és objektív eszközzel mért fizikai aktivitás, testtömeg-index és derék-csípő arány közötti összefüggések vizsgálata fiatal felnõttek körében
MAGYAR SPORTTUDOMÁNYI SZEMLE 20 : 2(79) p. 64. (2019)

Makai , A ; Cseh , AM ; Breitenbach , Z ; Füge , K ; Járomi , M ; **Prémusz , V** ; Ács , P ; Lampek, K ; Oláh , A ; Betlehem , J .
A web-based intervention to promote and increase physical activity level of Hungarian healthy adults
In: F., Salonna (eds.) ABSTRACT BOOK FOR THE ISBNPA 2019 ANNUAL MEETING IN PRAGUE
Praha, Czech Republic : International Society of Behavioral Nutrition and Physical Activity, pp. 1163-1163. (2019)

Makai , A ; **Premusz , V** ; Betlehem , J ; Olah , A ; Melczer , Cs ; Filo , Cs ; Lampek , K ; Figler , M ; Acs , P.
Special Eurobarometer on sport and physical activity versusInternational Physical Activity Questionnaire, comparison of twodifferent survey methods
BMC SPORTS SCIENCE MEDICINE AND REHABILITATION 11 : Suppl 1 Paper: P61 (2019)

Meszlényi-Lenhart, E ; **Prémusz, V** ; Makai, A ; Vári, B ; Melczer, Cs ; Rétsági, E ; Oláh, A ; Betlehem, J ; Ács, P.
Szubjektív és objektív eszközzel mért fizikai aktivitás, testtömeg-index és derék-csípő arány közötti összefüggések vizsgálata fiatal felnõttek körében
MAGYAR SPORTTUDOMÁNYI SZEMLE 79 : 2 p. 64. (2019)

Ács, P ; **Prémusz, V** ; Makai, A ; Junger, J ; Bergier, J.
Physical activity of university students according to IPAQ long questionnaires results
In: Potočníková, J; Bakalár, P (eds.) REKREAČNÝ ŠPORT, ZDRAVIE, KVALITA ŽIVOTA IV. : ZBORNÍK ABSTRAKTOV Z MED ZINÁRODNEJ VEDECKEJ KONFERENCIE
Kassa, Slovakia : Univerzita Pavla Jozefa Safárika v Kosiciach, p. 22. (2018)

Melczer , Cs ; Melczer , L ; **Prémusz , V ;** Raposa , BL ; Oláh , A ; Ács , P.
Analysis of telemetry data for characterization the physical activity of patients with heart failure
In: Bódog, Ferenc (eds.) VII. Interdiszciplináris Doktorandusz Konferencia 2018 absztraktkötet = = 7th Interdisciplinary Doctoral Conference 2018 book of abstracts
Pécs, Hungary : Pécsi Tudományegyetem Doktorandusz Önkormányzat, (2018) p. 180 , 1 p.

Makai, A ; **Prémusz, V** ; Ács, P ; Figler, M.
Ülő életmódot élők aránya az aktív korú munkavállalók körében magyarországon és Európában, egy keresztmetszeti kutatás eredményei
MAGYAR SPORTTUDOMÁNYI SZEMLE 19 : 75 pp. 62-63. , 2 p. (2018)

Prémusz, V ; Melczer, Cs ; Makai, A ; Bergier, J ; Ács, P.
A fizikai aktivítás mértéke a középiskolások körében a V4 országokban, egy keresztmetszeti kutatás eredményei
MAGYAR SPORTTUDOMÁNYI SZEMLE 19 : 75 pp. 77-77. , 1 p. (2018)

Prémusz, V ; Makai, A ; Várnagy, Á ; Ács, P.
Associations between HRQOL and PA in hungarian university students
In: Potočníková, J; Bakalár, P (eds.) REKREAČNÝ ŠPORT, ZDRAVIE, KVALITA ŽIVOTA IV. : ZBORNÍK ABSTRAKTOV Z MED ZINÁRODNEJ VEDECKEJ KONFERENCIE
Kassa, Slovakia : Univerzita Pavla Jozefa Safárika v Kosiciach, (2018) pp. 49-49. , 1 p.

Prémusz , V ; Makai , A ; Gács , B ; Perjés , B ; Ács , P ; Lampek , K ; Várnagy , Á.
Measurement of Physical Activity in Association with Assisted Reproduction (2017)
„5th International Scientific Conference on CIVILIZATION DISEASES AND LIFESTYLE", Janów Podlaski, 2017. május 19.-20., Country: Poland, oral presentation

Perjés, BB ; **Prémusz, V** ; Hegyi, G ; Moller, M ; Nagy, A ; Duberg, A
How can dance intervention become a way of stressmanagement between young girls?
THE EUROPEAN JOURNAL OF SPORTS MEDICINE 5 : 1 pp. 85-86. (2017)

Nagy, A ; Bobaly, V ; **Premusz, V** ; Hegyi, G
What is the role of dance in the stress management?
EUROPEAN JOURNAL OF INTEGRATIVE MEDICINE 8 : Suppl.1. p. 65 (2016)

Makai , A ; Füge , K ; Breitenbach , Z ; **Prémusz , V** ; Járomi , M ; Lampek , K ; Figler , M.
Physical activity and self-reported health of Hungarian adults: observation survey and elaboration of an educational intervention
In: International Society for Behavioral Nutrition; Physical Activity (ISBNPA)
(2015)

Prémusz, V ; Makai, A ; Füge, K ; Boncz, I ; Lampek, K
Comparative Analysis of Physical Activity, Sense of Control And Self-Reported Health of Elderly In Cee Countries.
VALUE IN HEALTH 18 : 7 pp. A564-A564. (2015)

Makai , A ; **Prémusz , V ;** Kata, Füge ; Mária, Figler ; Kinga, Lampek
Social participation and health among ageing people in East-Central Europe
In: Karlovitz, János Tibor (eds.) 2nd IRI Health Conference : Stúrovo, 2014. December 8-9. Slovakia. Program a abstrakty
Komárno, Slovakia : International Research Institute, p. 30. (2014)

Bobály, V ; **Prémusz, V** ; Győrfi, A ; Járomi, M ; Pusztafalvi, H.
Fogyatékkal élők mozgásképességeinek fejlesztése modern tánccal
In: Karlovitz, János Tibor (eds.) 2nd IRI Health Conference : Stúrovo, 2014. December 8-9. Slovakia. Program a abstrakty

Komárno, Slovakia : International Research Institute, p. 6. (2014)

Makai, A ; **Prémusz, V** ; Füge, K ; Figler, M ; Lampek, K.
Social activity and health among older adults
NÉPEGÉSZSÉGÜGY 92 : 2 pp. 122-123. , 2 p. (2014)

Nagy, A ; **Premusz, V** ; Lampek, K ; Tigyi, H ; Bobály, V
Dance for health and coping: A cross-sectional pilot study in Hungary
INTERNATIONAL JOURNAL OF BEHAVIORAL MEDICINE 21 : Suppl.1. p. S1 (2014)

Nagy, Á ; **Prémusz, V** ; Bobály, V ; Hegyi, G
Lifestyle change in the 21st century: the role of d ance in the therapy of chronic stress
In: Karlovitz, János Tibor (eds.) 2nd IRI Health Conference : Stúrovo, 2014. December 8-9. Slovakia. Program a abstrakty
Komárno, Slovakia : International Research Institute, (2014) pp. 32-32. , 1 p.

Prémusz, V ; Makai, A ; Füge, K ; Lampek, K.
Development of the social causation model by Ross and Wu systematic literature review
NÉPEGÉSZSÉGÜGY 92 : 2 , 1 p. (2014)

Prémusz, V ; Makai, A ; Bobály, V ; Füge, K ; Lampek, K.
Physical activity, sense of control and self-reported health of elderly in five transition countries
In: Karlovitz, János Tibor (eds.) 2nd IRI Health Conference : Stúrovo, 2014. December 8-9. Slovakia. Program a abstrakty
Komárno, Slovakia : International Research Institute, (2014) p. 35 , 1 p.

Prémusz, V ; Bobály, Viktória ; Lászikné, Nagy Ágnes ; Jill, Taube ; Tigyi, Zoltánné Pusztafalvi Henriette ; Lampek, Kinga
Coping és tánc (2013)
Fiatal Sporttudósok Országos Konferenciája, Szombathely, 2013.12.05., oral presentation

Bobály, V ; **Prémusz, V** ; Lászik, Á ; Lampek, K ; Pusztafalvi, H.
Tánc és megküzdés pp. 22-23.
In: Nagyházi, Bernadette (eds.) 7. Képzés és Gyakorlat Nemzetközi Neveléstudományi Konferencia : Innováció a neveléstudomány elméleti és gyakorlati műhelyeiben: Absztraktkötet
Kaposvár, Hungary : Kaposvári Egyetem Pedagógiai Kar, (2013)

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Ethical approval

PÉCSI TUDOMÁNYEGYETEM
Klinikai Központ
Regionális és Intézményi Kutatás-Etikai Bizottsága

Prémusz Viktória
PhD hallgató
PTE ETK Egészségtudományi Doktori Iskola
H-7621 Pécs, Vörösmarty út 4.
Vizsgálatvezető

Pécs, 2017. február 04.

Tisztelt Vizsgálatvezető!

A PTE-KK Regionális és Intézményi Kutatás – Etikai Bizottsága **2017.02.03.-ai ülésén megtárgyalta** az **Ön** által benyújtott dokumentumokat:

Cím: Fizikai aktivitás és stressz hatása az in vitro fertilizáció sikerességére

Témavezetők: dr. Várnagy Ákos egyetemi adjunktus
PTE KK Szülészeti és Nögyógyászati Klinika Édesanyák úti Reprodukciós Központ
dr. Lampek Kinga tanszékvezető főiskolai tanár
PTE ETK Egészségbiztosítási Intézet Egészségfejlesztési és Népegészségtani Tanszék

Mellékletek:
(1.) tudományos és irodalmi háttér angol nyelven;
(2.) igen részletes protokoll: a toborzási feltételek, kizárási okok;
(3.) Kérdőívek az általános állapottal, a fertilitással és az aktivitásssal kapcsolatos parameterek felmérésére;
(4.) Betegtájékoztató és (5.) beleegyező nyilatkozat a kutatásban való részvételről;
(6.) a PTE ETK Egészségtudományi Doktori Iskolának, a PTE KK Szülészet és Nögyógyászati Klinika igazgatójának, a témavezetőknek a támogató nyilatkozatai;

Döntés: a PTE KK RIKEB a **2017. február 03.-ai** ülésén **engedélyezte** a klinikai vizsgálatok protokoll szerinti kivitelezését. Ugyanakkor felhívja a tisztelt vizsgálatvezető figyelmét arra, hogy a **klinikai adatok felhasználása miatt** legyen szíves dr. Románcz Erzsébet jogtanácsos adatvédelmi előadóval felvenni a kapcsolatot: házi telefon: 33018. A klinikai vizsgálatok befejezése után **összefoglaló jelentést** legyen szíves készíteni Bizottságunk részére.

Ügyiratszám: 6533.

Szívélyes üdvözlettel

Dr. Kosztolányi György
egyetemi tanár, a Bizottság elnöke

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Data Availability Statement

The dataset, the questionnaires and the inform consent form are available from the author upon reasonable request.

Submission of the doctoral dissertation and declaration of the originality of the dissertation

The undersigned,
Name: Viktória Prémusz
Maiden name: Viktória Prémusz
Mother's maiden name: Gabriella Gombos
Place and time of birth: Dunaújváros, 03/10/1980

on this day submitted my doctoral dissertation entitled

EFFECTS OF PRE-TREATMENT HABITUAL PHYSICAL ACTIVITY
ON COURSE AND OUTCOME MEASURES OF
ASSISTED REPRODUCTIVE THERAPY

to the
PR-5. Human Reproduction Programme
of the Doctoral School of Health Sciences, Faculty of Health Sciences, University of Pécs.
Names of the supervisor(s): Dr. habil. Ákos Várnagy, Dr. habil. Kinga Lampek

At the same time, I declare that
- I have not submitted my doctoral dissertation to any other Doctoral School (neither in this country nor abroad),
- my application for degree earning has not been rejected in the past two years,
- in the past two years I have not had unsuccessful doctoral procedures,
- my doctoral degree has not been withdrawn in the past five years,
- my dissertation is independent work, I have not presented others' intellectual work as mine, the references are definite and full, on preparation of the dissertation I have not used false or falsified data.

Dated: 29/06/2020

.....
Viktória Prémusz
candidate

.....
Dr. habil. Ákos Várnagy, MD, Ph.D.
supervisor

.....
Dr. habil. Kinga Lampek, MSc, Ph.D.,
supervisor

References

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. The international committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary on ART terminology, 2009. Human Reproduction. 2009;24(11):2683-7.

2. WHO. Global recommendations on physical activity for health. Switzerland: Geneva: WHO; 2010.

3. WHO/EUROPE: Physical activity strategy for the WHO European Region 2016–2025. http://www.euro.who.int/__data/assets/pdf_file/0010/282961/65wd09e_PhysicalActivityStrategy_150474.pdf?ua=1 (2015). Accessed 11 06 2018.

4. WHO. Global action plan on physical activity 2018–2030: more active people for a healthier world. Switzerland: World Health Organization; 2018.

5. PAGAC. Physical activity guidelines for Americans. Chapter 7: Additional Considerations for Some Adults. Washington, DC: US Department of Health and Human Services; 2008.

6. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The Physical Activity Guidelines for Americans. Jama. 2018;320(19):2020-8.

7. UN. World population prospects 2019: Highlights. United Nations Econ Soc Aff. 2019.

8. Sobotka T. Postponement of childbearing and low fertility in Europe. Dutch University Press Amsterdam; 2004.

9. Sobotka T. Post-transitional fertility: the role of childbearing postponement in fuelling the shift to low and unstable fertility levels. Journal of Biosocial Science. 2017;49(S1):S20-S45.

10. KSH. Népesedési helyzetkép. Budapest: Központi Statisztikai Hivatal; 2016.

11. KSH. 120-year Interactive Population Pyramid [120 év interaktív korfája]. https://www.ksh.hu/interaktiv_korfa (2019). Accessed 29 07 2019.

12. KSH. STADAT: Main rates in vital statistics of Hungary (2001–2018) (2018) Accessed 08 06 2019

13. Eurostat: Fertility indicators: Total fertility rate. https://appsso.eurostat.ec.europa.eu/nui/submitViewTableAction.do (2017). Accessed 31 07 2019.

14. WHO. Reproductive health indicators: guidelines for their generation, interpretation and analysis for global monitoring. World Health Organization; 2006.

15. Kapitány B, Spéder Zs. Fertility. Demographic portrait of Hungary. 2018. 49-66.

16. Kapitány B, Spéder Zs. Fertility. Demographic portrait of Hungary. 2015. 41-55.

17. Eurostat. Mean age of women at childbirth and at birth of first child (2017) Accessed 06 06 2019.
18. ACOG. Female age-related fertility decline. Committee Opinion No. 589. Fertility and Sterility. 2014;101(3):633-4.
19. WHO. International statistical classification of diseases and related health problems: 11th revision (ICD-11). Geneva: World Health Organization; 2018.
20. WHO. Infecundity, infertility, and childlessness in developing countries. DHS Comparative Reports. 2004;9.
21. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Medicine. 2012;9(12):e1001356.
22. WHO. World report on disability. Geneva: World Health Organization; 2011.
23. McLaren JF. Infertility Evaluation. Obstetrics and Gynecology Clinics of North America. 2012;39(4):453-63.
24. ESHRE CWG. Social determinants of human reproduction. Human Reproduction. 2001;16(7):1518-26.
25. Bauquis C. The world's number of IVF and ICSI babies has now reached a calculated total of 5 million. Brussels: ESHRE. 2012.
26. Adamson GD, de Mouzon J, Chambers GM, Zegers-Hochschild F, Mansour R, Ishihara O, et al. International Committee for Monitoring Assisted Reproductive Technology: world report on assisted reproductive technology, 2011. Fertility and Sterility. 2018;110(6):1067-80.
27. De Geyter C, Calhaz-Jorge C, Kupka MS, Wyns C, Mocanu E, Motrenko T, et al. ART in Europe, 2014: results generated from European registries by ESHRE: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Human Reproduction. 2018;33(9):1586-601.
28. ESHRE. ART Fact Sheet 2016. ESHRE Grimbergen; 2017.
29. De Geyter C, Calhaz-Jorge C, Kupka MS, Wyns C, Mocanu E, Motrenko T, et al. ART in Europe, 2015: results generated from European registries by ESHRE. Human Reproduction Open. 2020;2020(1).
30. ESHRE. ESHRE Annual Report 2017. ESHRE Grimbergen; 2018.
31. Calhaz-Jorge C, de Geyter C, Kupka MS, de Mouzon J, Erb K, Mocanu E, et al. Assisted reproductive technology in Europe, 2012: results generated from European registers by ESHRE. Human Reproduction. 2016;31(8):1638-52.

32. Bernard A, Krizsa F. Generally about infertility. Modern diagnostic and therapy in infertility[A meddőségről általában In: Kaáli, S: A meddőség korszerű diagnosztikája és kezelése] Medicina Könyvkiadó, Budapest. 2006.
33. Boncz I, Evetovits T, Dozsa C, Sebestyen A, Gulacsi L, Agoston I, et al. The Hungarian Care Managing Organization Pilot Program. Value in Health Regional Issues. 2015;7:27-33.
34. Boncz I, Vajda R, Agoston I, Endrei D, Sebestyen A. Changes in the health status of the population of Central and Eastern European countries between 1990 and 2010. European Journal of Health Economics. 2014;15:S137-S41.
35. Endrei D, Molics B, Agoston I. Multicriteria Decision Analysis in the Reimbursement of New Medical Technologies: Real-World Experiences from Hungary. Value in Health. 2014;17(4):487-9.
36. Endrei D, Zemplenyi A, Molics B, Agoston I, Boncz I. The effect of performance-volume limit on the DRG based acute care hospital financing in Hungary. Health Policy. 2014;115(2-3):152-6.
37. Gulacsi L, Brodszky V, Pentek M, Varga S, Vas G, Boncz I. History of health technology assessment in Hungary. International Journal of Technology Assessment in Health Care. 2009;25:120-6.
38. Boncz I, Nagy J, Sebestyen A, Korosi L. Financing of health care services in Hungary. The European journal of health economics : HEPAC : Health Economics in Prevention and Care. 2004;5(3):252-8.
39. Boncz I, Sebestyen A. Financial deficits in the health services of the UK and Hungary. Lancet. 2006;368(9539):917-8.
40. Ponusz R, Endrei D, Kovacs D, Nemeth N, Schiszler B, Molics B, et al. Analysis of the utilization of one-day surgery in Hungary. Orvosi Hetilap. 2019;160(17):670-8.
41. Boncz I. Application of one-day procedures in gynaecology and obstetrics from the point of view of purchaser. Magyar Nőorvosok Lapja. 2002;65(6):453-8.
42. No. /2008. (XII. 30.) Government Decree on scope, method, place of publication, and control of the required statistical data on human reproductive procedures' performance in Hungary. Magyar Közlöny. 2008;191:25339-41.
43. No. 9/1993 (IV. 2.) Decree of the Ministry for National Economy on certain aspects of social security financing of healthcare. 1993.
44. No. 2/2020. (I. 30.) Regulation of the Minister of Human Resources amending certain ministerial decrees on health insurance. Magyar Közlöny. 2020;14:252-67.

45. No. 4/2020. (I. 31.) Government Decree on certain financing issues related to the management of infertility. Magyar Közlöny. 2020; 15:278-80.
46. Bódis J, Várnagy Á. Non-invazív vizsgálati lehetőségek az in vitro fertilizációs kezelés hatásfokának növelésére. Magyar Nőorvosok Lapja. 2015;78(5):226-31.
47. Várnagy Á, Györgyi E, Sulyok E, Prémusz V, Bódis J. Levels of total antioxidant capacity and 8-hydroxy-2'-deoxyguanosine of serum and follicular fluid in women undergoing in vitro fertilization: Focusing on endometriosis. Human Fertility. 2018; Nov 13:1-9.
48. Bódis J, Sulyok E, Kőszegi T, Gödöny K, Prémusz V, Várnagy Á. Serum and follicular fluid levels of Sirtuin 1, Sirtuin 6 and Resveratrol in women undergoing in vitro fertilization: an observational clinical study. Journal of International Medical Research 2018. Dec 16:772-82.
49. Szalai M, Lévay B, Szirmai A, Papp I, Prémusz V, Bódis J. A clinical study to assess the efficacy of belly dancing as a tool for rehabilitation in female patients with malignancies. European Journal of Oncology Nursing. 2015;19(1):60-5.
50. Szalai M, Szirmai A, Fuge K, Makai A, Erdelyi G, Premusz V, et al. Special aspects of social support: Qualitative analysis of oncologic rehabilitation through a belly dancing peer support group. European Journal of Cancer Care. 2017;26(6).
51. Perjés B, Prémusz V, Nagy Á, Várnagy Á, Bódis J. Szülésfelkészítő tréning?: a várandósság alatt végzett rendszeres testedzés hatása a szülés kimenetelére – irodalmi áttekintés. Sport- és Egészségtudományi Füzetek. 2017;1(2):3-17.
52. Nagy A, Premusz V, Lainpelc L, Tigyi T, Pusztafalvi H, Bobaly V. Dance for health and coping: a cross-sectional pilot study in Hungary. International Journal of Behavioral Medicine. 2014;21:S182.
53. Ács P, Prémusz V, Morvay-Sey K, Kovács A, Makai A, Elbert G. Changes of sport and physical activity indicators in Hungary and in the European Union according to the results from recent years (A sporttal, testmozgással összefüggésben lévő mutatók változása Magyarországon és az Európai Unióban az elmúlt évek eredményeinek nyomán). Sport- és Egészségtudományi Füzetek. 2018;2(1):61-76.
54. OGYEI: The Hungarian Diet and Nutritional Status Survey 2014 (Országos Táplálkozás és Tápláltsági Állapot Vizsgálat 2014). https://www.ogyei.gov.hu/otap_2014/ (2014). Accessed 10 10 2017.
55. Börjesson M, Hellénius M, Jansson E. FYSS - Physical Activity in the Prevention and Treatment of Disease. Swedish National Institute of Public Health. Stockholm: 2010.

56. Watson ED, Micklesfield LK, van Poppel MNM, Norris SA, Sattler MC, Dietz P. Validity and responsiveness of the Global Physical Activity Questionnaire (GPAQ) in assessing physical activity during pregnancy. PloS One. 2017;12(5).1-14
57. Chu AHY, Moy FM. Reliability and Validity of the Malay International Physical Activity Questionnaire (IPAQ-M) Among a Malay Population in Malaysia. Asia-Pacific Journal of Public Health. 2015;27(2):NP2381-9.
58. Bhola N, Kumari R, Bansal D. Pattern of physical activity and associated sociodemographic factors: A community based study using Global Physical Activity questionnaire. The Ceylon Medical Journal. 2018;63(4):159-68.
59. Ostojic SM, Stojanovic MD, Stojanovic V, Maric J, Njaradi N. Correlation between fitness and fatness in 6-14-year old Serbian school children. Journal of Health, Population and Nutrition. 2011;29(1):53-60.
60. Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants. The Lancet Global Health. 2018;6(10):e1077-e86.
61. Guthold R, Stevens GA, Riley LM, Bull FC. Correction to Lancet Glob Health 2018; 6: e1077-86. The Lancet Global Health. 2019;7(1):e36.
62. Resolution W. 66.10. Follow up to the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Disease. Sixty-fourth World Health Assembly, Geneva. 2013:20-7.
63. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet. 2012;380(9838):219-29.
64. HHS USDoHaHS. The Physical Activity Guidelines for Americans, 2nd edition,. Physical Activity Guidelines Advisory Committee; 2018.
65. Nemzeti Sportstratégia: Sport XXI. Nemzeti Sportstratégia (2007-2020). http://www.parlament.hu/irom37/18818/18818.pdf (2006). Accessed 11. 05. 2017.
66. Szmodis M, Bosnyák E, Bede R, Farkas A, Protzner A, Trájer E, et al. Az MSTT Mozgás= Egészség Programjának magyarországi tapasztalatai–A fiatal generációk fizikai teljesítményének háttérvizsgálata. Népegészségügy. 2013;91(2):141-9.
67. ACOG. Committee Opinion No. 650: Physical Activity and Exercise During Pregnancy and the Postpartum Period. Obstetrics and Gynecology. 2015;126(6):e135-42.

68. Davies GA, Wolfe LA, Mottola MF, MacKinnon C. Joint SOGC/CSEP clinical practice guideline: exercise in pregnancy and the postpartum period. Canadian Journal of Applied Physiology. 2003;28(3):330-41.
69. Aune D, Saugstad OD, Henriksen T, Tonstad S. Physical Activity and the Risk of Preeclampsia A Systematic Review and Meta-Analysis. Epidemiology. 2014;25(3):331-43.
70. Takito MY, Benicio MHD. Physical activity during pregnancy and fetal outcomes: a case-control study. Revista De Saude Publica. 2010;44(1):90-101.
71. Russo LM, Nobles C, Ertel KA, Chasan-Taber L, Whitcomb BW. Physical Activity Interventions in Pregnancy and Risk of Gestational Diabetes Mellitus A Systematic Review and Meta-analysis. Obstetrics and Gynecology. 2015;125(3):576-82.
72. Tendais I, Figueiredo B, Mota J, Conde A. Physical activity, health-related quality of life and depression during pregnancy. Cadernos De Saude Publica. 2011;27(2):219-28.
73. ACSM ACoSM. Impact of physical activity during pregnancy and postpartum on chronic disease risk. Medicine and Science in Sports and Exercise. 2006;38(5):989-1006.
74. Waxman A, World HA. WHO global strategy on diet, physical activity and health. Food and Nutrition Bulletin. 2004;25(3):292.
75. Borodulin KM, Evenson KR, Wen F, Herring AH, Benson AM. Physical Activity Patterns during Pregnancy. Medicine and Science in Sports and Exercise. 2008;40(11):1901-8.
76. Prémusz V, Makai A, Melczer C, Perjés B, Ács P, Bódis J, et al. Habituális fizikai aktivitás és életminőség összefüggése várandósság alatt a WHO Global Physical Activity Questionnaire alapján. Magyar Nőorvosok Lapja. 2018;81(6):343-50.
77. Lakatos E, Pápay N, Ádám S, Balog P. Paradigmák a meddőség értelmezésében. Pszichológia. 2014;34(3):261–87.
78. Goldberg DP, Blackwell B. Psychiatric Illness in General Practice: A Detailed Study Using a New Method of Case Identification. British Medical Journal. 1970;2(5707):439-43.
79. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Archives of General Psychiatry. 1961;4:561-71.
80. Beck AT, Steer RA, Carbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. Clinical Psychology Review. 1988;8(1):77-100.
81. Beck AT. Cognitive therapy of depression. Guilford Press; 1979.
82. Beck AT, Beck RW. Screening depressed patients in family practice. A rapid technic. Postgraduate Medicine. 1972;52(6):81-5.

83. Khademi A, Alleyassin A, Aghahosseini M, Ramezanzadeh F, Abhari AA. Pretreatment Beck Depression Inventory score is an important predictor for Post-treatment score in infertile patients: a before-after study. BMC Psychiatry. 2005;5(25):1-7.
84. Smeenk JM, Verhaak CM, Eugster A, van Minnen A, Zielhuis GA, Braat DD. The effect of anxiety and depression on the outcome of in-vitro fertilization. Human Reproduction. 2001;16(7):1420-3.
85. Kopp M, Fóris N. A szorongás kognitív viselkedésterápiája. Budapest: Végeken Sorozat. 1993.
86. Reynolds WM, Gould JW. A psychometric investigation of the standard and short form Beck Depression Inventory. Journal of Consulting and Clinical Psychology. 1981;49(2):306-7.
87. Newton CR, Sherrard W, Glavac I. The Fertility Problem Inventory: measuring perceived infertility-related stress. Fertility and Sterility. 1999;72(1):54-62.
88. Cserepes RE, Kollar J, Sapy T, Wischmann T, Bugan A. Effects of gender roles, child wish motives, subjective well-being, and marital adjustment on infertility-related stress: a preliminary study with a Hungarian sample of involuntary childless men and women. Archives of Gynecology and Obstetrics. 2013;288(4):925-32.
89. Oláh A. Psychological immunity: A new concept in coping with stress. Applied Psychology in Hungary. 2004;56:149-89.
90. Oláh A. Anxiety, Coping, and Flow: Empirical studies in interactional perspective. Trefort; 2005.
91. Freeman EW, Boxer AS, Rickels K, Tureck R, Mastroianni L. Psychological evaluation and support in a program of invitro fertilization and embryo transfer. Fertility and Sterility. 1985;43(1):48-53.
92. Reading AE, Chang LC, Kerin JF. Attitudes and anxiety levels in women conceiving through invitro fertilization and gamete intrafallopian transfer. Fertility and Sterility. 1989;52(1):95-9.
93. Hearn MT, Yuzpe AA, Brown SE, Casper RF. Psychological characteristics of invitro fertilization participants. American Journal of Obstetrics and Gynecology. 1987;156(2):269-74.
94. Greil AL. Infertility and psychological distress: a critical review of the literature. Social Science and Medicine. 1997;45(11):1679-704.
95. Magiakou MA, Mastorakos G, Webster E, Chrousos GP. The hypothalamic-pituitary-adrenal axis and the female reproductive system. In: Creatsas G, Mastorakos G, Chrousos GP, editors. Adolescent Gynecology and Endocrinology: Basic and Clinical Aspects. Annals of the New York Academy of Sciences. 1997;816:42-56.

96. Ferin M. Stress and the reproductive cycle. Journal of Clinical Endocrinology and Metabolism. 1999;84(6):1768-74.
97. Dobson H, Ghuman S, Prabhakar S, Smith R. A conceptual model of the influence of stress on female reproduction. Reproduction. 2003;125(2):151-63.
98. Dunkel-Schetter C, Lobel M. Psychological reactions to infertility. Infertility. Springer; 1991. 29-57.
99. Jacob MC, McQuillan J, Greil AL. Psychological distress by type of fertility barrier. Human Reproduction. 2006;22(3):885-94.
100. Domar AD, Broome A, Zuttermeister PC, Seibel M, Friedman R. The prevalence and predictability of depression in infertile women. Fertility and Sterility. 1992;58(6):1158-63.
101. Kee BS, Jung BJ, Lee SH. A study on psychological strain in IVF patients. Journal of Assisted Reproduction and Genetics. 2000;17(8):445-8.
102. Boivin J, Takefman J, Braverman A. The fertility quality of life (FertiQoL) tool: development and general psychometric properties. Human Reproduction. 2011;26(8):2084-91.
103. Cserepes RE, Korosi T, Bugan A. [Characteristics of infertility-specific quality of life in Hungarian couples]. Orvosi Hetilap. 2014;155(20):783-8.
104. Aarts JW, van Empel IW, Boivin J, Nelen WL, Kremer JA, Verhaak CM. Relationship between quality of life and distress in infertility: a validation study of the Dutch FertiQoL. Human Reproduction. 2011;26(5):1112-8.
105. Dural O, Yasa C, Keyif B, Celiksoy H, Demiral I, Yuksel Ozgor B, et al. Effect of infertility on quality of life of women: a validation study of the Turkish FertiQoL. Human Fertility. 2016;19(3):186-91.
106. Domar AD, Clapp D, Slawsby EA, Dusek J, Kessel B, Freizinger M. Impact of group psychological interventions on pregnancy rates in infertile women. Fertility and Sterility. 2000;73(4):805-11.
107. Domar AD, Gross J, Rooney K, Boivin J. Exploratory randomized trial on the effect of a brief psychological intervention on emotions, quality of life, discontinuation, and pregnancy rates in in vitro fertilization patients. Fertility and Sterility. 2015;104(2):440-51.e7.
108. Domar AD, Conboy L, Denardo-Roney J, Rooney KL. Lifestyle behaviors in women undergoing in vitro fertilization: a prospective study. Fertility and Sterility. 2012;97(3):697-701.
109. Domar AD, Rooney KL, Wiegand B, Orav EJ, Alper MM, Berger BM, et al. Impact of a group mind/body intervention on pregnancy rates in IVF patients. Fertility and Sterility. 2011;95(7):2269-73.

110. Salakari MRJ, Surakka T, Nurminen R, Pylkkanen L. Effects of rehabilitation among patients with advances cancer: a systematic review. Acta Oncologica. 2015;54(5):618-28.
111. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database of Systematic Reviews. 2012(8):CD008465.
112. Francisco Meneses-Echavez J, Gonzalez-Jimenez E, Ramirez-Velez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC Cancer. 2015;15.
113. Kimmel GT, Haas BK, Hermanns M. The Role of Exercise in Cancer Treatment: Bridging the Gap. Current Sports Medicine Reports. 2014;13(4):246-52.
114. Levine B, Land HM. A meta-synthesis of qualitative findings about dance/movement therapy for individuals with trauma. Qualitative Health Research. 2016 Feb;26(3):330-44.
115. Valoriani V, Lotti F, Vanni C, Noci MC, Fontanarosa N, Ferrari G, et al. Hatha-yoga as a psychological adjuvant for women undergoing IVF: a pilot study. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2014;176:158-62.
116. Pivarnik JM, Chambliss H, Clapp J, Dugan S, Hatch M, Lovelady C, et al. Impact of physical activity during pregnancy and postpartum on chronic disease risk. Medicine and Science in Sports and Exercise. 2006;38(5):989-1006.
117. Downs DS, Chasan-Taber L, Evenson KR, Leiferman J, Yeo S. Physical activity and pregnancy: past and present evidence and future recommendations. Research Quarterly for Exercise and Sport. 2012;83(4):485-502.
118. ACOG. Committee opinion. Number 267, January 2002: exercise during pregnancy and the postpartum period. Obstetrics and Gynecology. 2002;99(1):171-3.
119. Green BB, Daling JR, Weiss NS, Liff JM, Koepsell T. Exercise as a risk factor for infertility with ovulatory dysfunction. American Journal of Public Health. 1986;76(12):1432-6.
120. Wise LA, Rothman KJ, Mikkelsen EM, Sorensen HT, Riis AH, Hatch EE. A prospective cohort study of physical activity and time to pregnancy. Fertility and Sterility. 2012;97(5):1136-42.
121. Morris SN, Missmer SA, Cramer DW, Powers RD, McShane PM, Hornstein MD. Effects of lifetime exercise on the outcome of in vitro fertilization. Obstetrics and Gynecology. 2006;108(4):938-45.
122. Moran L, Tsagareli V, Norman R, Noakes M. Diet and IVF pilot study: short-term weight loss improves pregnancy rates in overweight/obese women undertaking IVF. The Australian & New Zealand Journal of Obstetrics and Gynaecology. 2011;51(5):455-9.

123. Ács P, Stocker M, Füge K, Paár D, Oláh A, Kovács A. Economic and public health benefits: the result of increased regular physical activity. European Journal of Integrative Medicine. 2016;8(2 Suppl.):8-12.
124. HHS USDoHaHS. Physical Activity Guidelines for Americans 2008 http://wwwhealthgov/paguidelines/. 2008. Accessed 20 01 2017
125. ACOG. Committee Opinion No. 650: Physical Activity and Exercise During Pregnancy and the Postpartum Period. Obstetrics and Gynecology. 2015;126(6):e135-42.
126. Calhaz-Jorge C, De Geyter C, Kupka MS, de Mouzon J, Erb K, Mocanu E, et al. Assisted reproductive technology in Europe, 2013: results generated from European registers by ESHRE. Human Reproduction. 2017;32(10):1957-73.
127. An Y, Sun ZZ, Li LA, Zhang YJ, Ji HP. Relationship between psychological stress and reproductive outcome in women undergoing in vitro fertilization treatment: Psychological and neurohormonal assessment. Journal of Assisted Reproduction and Genetics. 2013;30(1):35-41.
128. Prémusz V, Makai A, Gács B, Simon-Ugron Á, Nagy Á, Ács P, et al. Relationship between pre-treatment habitual physical activity and success of assisted reproduction. Studia Universitatis Babes-Bolyai, Educatio Artis Gymnasticae. 2018;63(3).
129. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Journal of Clinical Epidemiology. 2009;62(10):1006-12.
130. Kamarasi V, Mogyorosy G. [Support in diagnostics and therapy]. Orvosi Hetilap. 2015;156(38):1523-31.
131. Palomba S, Falbo A, Valli B, Morini D, Villani MT, Nicoli A, et al. Physical activity before IVF and ICSI cycles in infertile obese women: an observational cohort study. Reproductive Biomedicine Online. 2014;29(1):72-9.
132. Kucuk M, Doymaz F, Urman B. Assessment of the physical activity behavior and beliefs of infertile women during assisted reproductive technology treatment. International Journal of Gynecology and Obstetrics. 2010;108(2):132-4.
133. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. International Journal of Epidemiology. 1994;23(5):991-9.
134. Gaskins AJ, Williams PL, Keller MG, Souter I, Hauser R, Chavarro JE. Maternal physical and sedentary activities in relation to reproductive outcomes following IVF. Reproductive BioMedicine Online. 2016;33(4):513-21.

135. IPAQ RC: Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)–short and long forms. https://docs.google.com/viewer?a=v&pid=sites&srcid=ZGVmYXVsdGRvbWFpbnx0aGVpcGFxfGd4OjE0NDgxMDk3NDU1YWRlZTM (2005). Accessed 20 01 2017
136. Kucuk M, Doymaz F, Urman B. Effect of energy expenditure and physical activity on the outcomes of assisted reproduction treatment. Reproductive BioMedicine Online. 2010;20(2):274-9.
137. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Medicine and Science in Sports and Exercise. 2003;35(8):1381-95.
138. Ramezanzadeh F, Kazemi A, Yavari P, Nasr-Esfahani MH, Nejat S, Rahimi-Foroshani A, et al. Impact of body mass index versus physical activity and calorie intake on assisted reproduction outcomes. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2012;163(1):52-6.
139. Armstrong T, Bull F. Development of the World Health Organization Global Physical Activity Questionnaire (GPAQ). Journal of Public Health. 2006;14(2):66-70.
140. Calhoun KC, Steiner AZ, Wen M, Calingo A, Evenson K. Association of short-term and long-term physical activity on implantation in in vitro fertilization (IVF) cycles. Fertility and sterility. 2012;98(3):S31-2.
141. Evenson KR, Calhoun KC, Herring AH, Pritchard D, Wen F, Steiner AZ. Association of physical activity in the past year and immediately after in vitro fertilization on pregnancy. Fertility and Sterility. 2014;101(4):1047-U482.
142. Ainsworth BE, Sternfeld B, Richardson MT, Jackson K. Evaluation of the kaiser physical activity survey in women. Medicine and Science in Sports and Exercise. 2000;32(7):1327-38.
143. Janz KF. Physical activity in epidemiology: moving from questionnaire to objective measurement. British Journal of Sports Medicine. 2006;40(3):191-2.
144. Laeremans M, Dons E, Avila-Palencia I, Carrasco-Turigas G, Orjuela JP, Anaya E, et al. Physical activity and sedentary behaviour in daily life: A comparative analysis of the Global Physical Activity Questionnaire (GPAQ) and the SenseWear armband. PloS One. 2017;12(5):e0177765.
145. Oyeyemi AL, Umar M, Oguche F, Aliyu SU, Oyeyemi AY. Accelerometer-Determined Physical Activity and Its Comparison with the International Physical Activity Questionnaire in a Sample of Nigerian Adults. PloS One. 2014;9(1).

146. Sebastião E, Gobbi S, Chodzko-Zajko W, Schwingel A, Papini CB, Nakamura PM, et al. The International Physical Activity Questionnaire-long form overestimates self-reported physical activity of Brazilian adults. Public Health. 2012;126(11):967-75.
147. Ács P, Betlehem J, Oláh A, Bergier B, Morvay-Sey K, Makai A, et al. Cross-cultural adaptation and validation of the Global Physical Activity Questionnaire among healthy Hungarian adults. BMC Public Health. 2019;S20: DOI: 10.1186/s12889-020-08477-z
148. Ács P, Betlehem J, Oláh A, Bergier J, Melczer C, Prémusz V, et al. Measurement of public health benefits of physical activity: Validity and reliability study of the International Physical Activity Questionnaire in Hungary. BMC Public Health. 2020;S20: DOI: 10.1186/s12889-020-08508-9
149. Gaskins AJ, Williams PL, Keller MG, Souter I, Hauser R, Chavarro JE, et al. Maternal physical and sedentary activities in relation to reproductive outcomes following IVF. Reproductive Biomedicine Online. 2016;33(4):513-21.
150. WHO. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. Social Science & Medicine. 1995;41(10):1403-9.
151. Chachamovich JR, Chachamovich E, Zachia S, Knauth D, Passos EP. What variables predict generic and health-related quality of life in a sample of Brazilian women experiencing infertility? Human Reproduction. 2007;22(7):1946-52.
152. Rashidi B, Montazeri A, Ramezanzadeh F, Shariat M, Abedinia N, Ashrafi M. Health-related quality of life in infertile couples receiving IVF or ICSI treatment. BMC Health Services Research. 2008;8:186.
153. Lynch CD, Sundaram R, Maisog JM, Sweeney AM, Louis GMB. Preconception stress increases the risk of infertility: results from a couple-based prospective cohort studyuthe LIFE study. Human Reproduction. 2014;29(5):1067-75.
154. Boivin J, Takefman JE. Stress level across stages of in-vitro fertilization in subsequently pregnant and nonpregnant women. Fertility and Sterility. 1995;64(4):802-10.
155. Luppa P, Muller B, Jacob K, Kimmig R, Strowitzki T, Hoss C, et al. Variations of steroid-hormone metabolites in serum and urine in polycystic-ovary-syndrome after nafarelin stimulation - evidence for an altered corticoid excretion. Journal of Clinical Endocrinology and Metabolism. 1995;80(1):280-8.
156. Smeenk JM, Verhaak CM, Vingerhoets AJ, Sweep CG, Merkus JM, Willemsen SJ, et al. Stress and outcome success in IVF: the role of self-reports and endocrine variables. Human Reproduction. 2005;20(4):991-6.

157. Rao M, Zeng Z, Tang L. Maternal physical activity before IVF/ICSI cycles improves clinical pregnancy rate and live birth rate: a systematic review and meta-analysis. Reproductive biology and endocrinology : Reproductive Biology and Endocrinology. 2018;16(11):1-8.
158. Rich-Edwards JW, Spiegelman D, Garland M, Hertzmark E, Hunter DJ, Colditz GA, et al. Physical activity, body mass index, and ovulatory disorder infertility. Epidemiology. 2002;13(2):184-90.
159. Paulik E, Belec B, Molnár R, Müller A, Belicza É, Kullmann L, et al. Applicability of the brief version of the World Health Organization's quality of life questionnaire in Hungary. Orvosi Hetilap. 2007;148(4):155-60.
160. WHO WHO. The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. Social Science and Medicine. 1998;46(12):1569-85.
161. www.ipaq.ki.se https://sites.google.com/site/theipaq/ Accessed 02 03 2015.
162. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. International Journal of Behavioral Nutrition and Physical Activity. 2011;8.
163. van Poppel MN, Chinapaw MJ, Mokkink LB, van Mechelen W, Terwee CB. Physical activity questionnaires for adults: a systematic review of measurement properties. Sports Medicine. 2010;40(7):565-600.
164. Nash L, Rocha P, Whiting S, Organization WH. Development of a standardized physical activity and sport monitoring system for the European Union. Public Health Panorama. 2018;4(03):481-4.
165. WHO: Global Physical Activity Questionnaire (GPAQ) Analysis Guide V2. https://www.who.int/ncds/surveillance/steps/GPAQ%20Instrument%20and%20Analysis%20Guide%20v2.pdf (2012). Accessed 02.03. 2018.
166. Herrmann SD, Heumann KJ, Der Ananian CA, Ainsworth BE. Validity and Reliability of the Global Physical Activity Questionnaire (GPAQ). Measurement in Physical Education and Exercise Science. 2013;17(3):221-35.
167. Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF, Tully MA. Validity of the Global Physical Activity Questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health. 2014;14.
168. Bull FC, Maslin TS, Armstrong T. Global Physical Activity Questionnaire (GPAQ): Nine Country Reliability and Validity Study. Journal of Physical Activity and Health. 2009;6(6):790-804.

169. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. Medicine and Science in Sports and Exercise. 2002;34(12):1996-2001.
170. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Medicine and Science in Sports and Exercise. 1998;30(5):777-81.
171. Matthews CE, Ainsworth BE, Thompson RW, Bassett DR, Jr. Sources of variance in daily physical activity levels as measured by an accelerometer. Medicine and Science in Sports and Exercise. 2002;34(8):1376-81.
172. Gudmundsdottir SL, Flanders WD, Augestad LB. Physical activity and fertility in women: the North-Trondelag Health Study. Human Reproduction. 2009;24(12):3196-204.
173. Gödöny K, Laki K, Várnagy Á, Kovács K, Sulyok E, Berenténé Bene J, et al. Az in vitro fertilizáció sikerességét befolyásoló biomarkerek vizsgálata: a karnitin jelentősége. Egészség-Akadémia. 2014;5(4):247-53.
174. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods. 2007;39(2):175-91.
175. Porat-Katz A, Paltiel O, Kahane A, Eldar-Geva T. The effect of using complementary medicine on the infertility-specific quality of life of women undergoing in vitro fertilization. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2016;135(2):163-7.
176. Pasch LA, Gregorich SE, Katz PK, Millstein SG, Nachtigall RD, Bleil ME, et al. Psychological distress and in vitro fertilization outcome. Fertility and Sterility. 2012;98(2):459-64.
177. Bácsné Bába É, Fenyves V, Szabados G, Pető K, Bács Z, Dajnoki K. Sport Involvement Analysis in Hungary, in the North Great Plain Region. Sustainability. 2018;10(5):1629.
178. Gabnai Z, Müller A, Bács Z, Bácsné Bába É. The economic burden of physical inactivity at national level [A fizikai inaktivitás nemzetgazdasági terhei]. Egészségfejlesztés. 2019;60(1):20-30.
179. Lundgren KM, Romundstad LB, von During V, Morkved S, Kjotrod S, Moholdt T. Exercise prior to assisted fertilization in overweight and obese women (FertilEX): study protocol for a randomized controlled trial. Trials. 2016;17(268): 1-7
180. Ruiz-Montero PJ, Castillo-Rodriguez A, Mikalacki M, Nebojsa C, Korovljev D. 24-weeks Pilates-aerobic and educative training to improve body fat mass in elderly Serbian women. Clinical Interventions in Aging. 2014;9:243-8.

181. Duncan MJ, Brown WJ, Mummery WK, Vandelanotte C. 10,000 Steps Australia: a community-wide eHealth physical activity promotion programme. British Journal of Sports Medicine. 2018;52(14):885-6.
182. HHS USDoHaHS. The Physical Activity Guidelines for Americans, 2nd edition, Date Accessed 08/06, 2019, from Physical Activity Guidelines Advisory Committee; 2018.
183. Althoff T, Sosič R, Hicks JL, King AC, Delp SL, Leskovec J. Large-scale physical activity data reveal worldwide activity inequality. Nature. 2017;547(7663):336-9.
184. Tudor-Locke C, Craig CL, Brown WJ, Clemes SA, De Cocker K, Giles-Corti B, et al. How many steps/day are enough? for adults. International Journal of Behavioral Nutrition and Physical Activity. 2011;8(1):79.
185. Espinós JJ, Solà I, Valli C, Polo A, Ziolkowska L, Martínez-Zapata MJ. The effect of lifestyle intervention on pregnancy and birth outcomes on obese infertile women: a systematic review and meta-analysis. International Journal of Fertility and Sterility. 2020;14(1):1.
186. Bhattacharya S, Maheshwari A, Mollison J. Factors associated with failed treatment: an analysis of 121,744 women embarking on their first IVF cycles. PloS One. 2013;8(12):e82249.
187. Messerlian C, Gaskins AJ. Epidemiologic Approaches for Studying Assisted Reproductive Technologies: Design, Methods, Analysis and Interpretation. Current Epidemiology Reports. 2017;4(2):124-32.
188. Duberg A. Something about the dance. Archives of Pediatrics and Adolescent Medicine. 2012;166(11):1037-44.
189. Duberg A, Hagberg L, Sunvisson H, Möller M. Influencing self-rated health among adolescent girls with dance intervention: a randomized controlled trial. JAMA Pediatrics. 2013;167(1):27-31.
190. Duberg A, Moller M, Sunvisson H. "I feel free": Experiences of a dance intervention for adolescent girls with internalizing problems. International Journal of Qualitative Studies on Health and Well-Being. 2016;11(31946):1-14.
191. Philipsson A, Duberg A, Möller M, Hagberg L. Cost-utility analysis of a dance intervention for adolescent girls with internalizing problems. Cost Effectiveness and Resource Allocation. 2013;11(4):1-16.
192. Boivin J, Takefman JE. Stress level across stages of in-vitro fertilization in subsequently pregnant and nonpregnant women. Fertility and Sterility. 1995;64(4):802-10.