

EAA Andrology Training Centre
Centre Report

2023



Florence EAA Center, University Hospital Careggi

CENTRE

REPORT

History of Centre

The official history of the Andrology Center in Florence started in 1983 under the guidance of Prof Mario Serio, who was one of the founders of the European Academy of Andrology (EAA) in 1992. The Florence Andrology center was established at the University Hospital of Careggi and its relevance and reputation was internationally recognized under the direction of prof Gianni Forti (president of the EAA between 1998-2006) and then Prof Mario Maggi who took over the direction of the Sexual Medicine and Andrology Unit up to 2018. Among the first major achievements of the Florence group the description of the rapid effects of progesterone on intracellular calcium accumulation, acrosome reaction and their relationship with sperm fertilizing capacity should be mentioned, as well as the development of the first structured interview for assessing erectile dysfunction (SIEDY) and male hypogonadism (ANDROTEST). Noteworthy, under Prof. Mario Maggi the Florence Unit became one of the biggest European center in terms of clinical and research activity in the field of male hypogonadism, sexual dysfunction and infertility. In particular the clinical group, with major contribution by Giulia Rastrelli and Giovanni Corona, both international experts in male hypogonadism, has progressively expanded knowledge on the complex interplay between male hypogonadism, metabolic diseases and cardiovascular risk, also actively participating to the European Male Aging Study. A strong preclinical and clinical research group lead by Linda Vignozzi unraveled important pathogenic mechanisms underlying the association between male hypogonadism and metabolic diseases, and their consequences such as erectile dysfunction, benign prostatic hyperplasia (BPH)/lower urinary tract symptoms (LUTS), non-alcoholic steatohepatitis (NASH) and visceral adipose tissue dysfunction. Since 2015, our center has been one of the two training centers for the EAA Ultrasound School, which is co-directed by F. Lotti and attracts numerous fellows from all over the world every year. F. Lotti and M. Maggi have led the EAA multicentre project on ultrasonography of male genital tract, achieving relevant publications on standardization of this method in Andrology and reporting for the first time evidence-based ultrasound “normative” parameters in the andrologic field. The centre also progressively expanded its clinical and research activities in the field of the genetics of male infertility and onco-andrology. Csilla Krausz (EAA President from 2014-2022)

initiated genetic studies in male infertility since 1995, starting from the role of Y chromosome in male infertility up to the latest discoveries of novel azoospermia genes through whole exome sequencing. From 2003, Florence also became the venue of three editions of the Florence-Utah International Symposium on “Genetics of Male Infertility: from Research to Clinic”. Since 2004, the Krausz laboratory has been the reference laboratory for the European Molecular Genetics Quality Network (EAA/EMQN Y chromosome scheme). The laboratory directed by Elisabetta Baldi has pioneered (since the end of 90ies) in the study of sperm DNA fragmentation (SDF) through the method developed by Monica Muratori and since then produced a large number of publications on the role of SDF in male reproduction. The laboratory also highly contributed in unraveling the role of metabolic syndrome in the pathogenesis of male infertility thanks to the preclinical and clinical activity developed by Sara Marchiani and Lara Tamburrino. In the laboratory a sperm bank was established in 1998 and it became the Regional Reference Centre for Semen Cryopreservation in 2002. A dedicated outpatient session with an annual follow up for oncological patients seeking sperm cryopreservation has been active since 2013 under the responsibility of Csilla Krausz. In 2015 a Sperm Donation service was started, recruiting donors from all over Italy. Under the direction of Mario Maggi, the Florence Unit also initiated important clinical activity dedicated to individuals presenting Gender Incongruence. In particular, Alessandra D. Fisher coordinates together with J. Ristori (endocrinologist and psychologist, respectively) the Gender Incongruence (GI) team which offers clinical support to children, adolescents and adults with gender identity issues. In 2008, an outpatient clinic for female sexual dysfunction was also initiated under the supervision of Linda Vignozzi, Elisa Maseroli and Sarah Cipriani.

Under the direction of Linda Vignozzi (from 2018), the hospital Unit of Andrology, Female endocrinology and Gender Incongruences achieved the following healthcare improvement. In particular, the project for developing a healthcare network dedicated to Gender Incongruence, started under the guide of Mario Maggi, was completed by obtaining the recognition as the Regional Center for the management of healthcare problems related to Gender Incongruence for adolescent and adulthood individuals, which is currently coordinated by Alessandra D Fisher and Jiska Ristori. The Unit also initiated a tight collaboration with the

Pediatric Hospital nearby which is one of the most famous and large Pediatric Hospitals in Italy (Meyer-Hospital). This collaboration is currently coordinated by Giulia Rastrelli and it is intended to have a continuous shared management of children and adolescents and to prepare a solid process of transition from pediatric to adult age care. Moreover, starting from September 2022 a service dedicated to testicular tissue preservation for pre-pubertal boys has been established under the supervision of Prof. Elisabetta Baldi and Dr. Lara Tamburrino in tight collaboration with the Urological Unit of the Pediatric Hospital -Meyer. Furthermore, since October 2022, the unit directed by Linda Vignozzi has expanded its laboratory activities to also include a clinical mass spectrometry service, currently dedicated to the dosage of steroids, supervised by Giovanna Danza. A new outpatient clinic service dedicated to lifestyle and nutrition was also developed to provide lifestyle intervention for improving reproductive and sexual outcomes (responsible for this part of the Project is Elisa Maseroli).

Finally, in march 2022 the Head of the Hospital created the Center for the Prevention, Diagnosis and therapy of infertility, connecting the Unit of Andrology, Female endocrinology and Gender Incongruences and the Unit dedicated to Assisted Reproduction Technology, entrusted its Direction to Linda Vignozzi. The new Center was also aimed at creating a network for the management of couple infertility with the healthcare territorial services (responsible for this part of the Project is Sarah Cipriani)

Organization of Centre

Educational activities

Since its establishment, the EAA center offers training in clinical andrology according to the EAA/ESAU Curriculum. A total of eight clinical fellows obtained the EAA Clinical Andrologist certificate.

The Center:

- is involved in the Residency Program of the School of Endocrinology for post-graduated in Medicine.
 - organizes a 24 months Master course (II level) in Andrology and Sexual Medicine with a period of 4 weeks of tutored training in the outpatient clinic.
 - organizes a 12 months Master course (II level) in Biology and Biotechnology of
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- Reproduction for biologists and biotechnologists with 4 weeks tutored training.
- offers training to psychotherapists interested in sexual medicine and gender identity disorders.
 - organizes a 12 months Master course (I level) in “clinical applications of Mass Spectrometry” for biologists, biotechnologists, chemists and laboratory technicians.
 - regularly organizes post-graduate courses on Sexual Medicine and Andrology addressed to specialists in endocrinology, urology, gynaecology, internal medicine and general practitioners.
 - includes Andrology topics in the Endocrinology courses of several University Degree courses including Medicine, Biology, Biotechnology, Psychology, and Sport Sciences
 - holds an optional course for Medical students in Sexual Medicine (16 hours)
 - holds an optional course for Biotechnology students in Biological Mechanisms of Sexual Function (24 hours)
 - among the practical activities of the Endocrinology course for medical students, includes the attendance in Andrology outpatient clinic
 - organizes the “EAA Courses in male genital tract and penile ultrasound” since its establishment under the guidance of F. Lotti. Fellows are international endocrinologists, andrologists and urologists attending a theoretical course and spending a period of 4 weeks for hands-on activity in ultrasound, finally undergoing an examination to get the “EAA ultrasound certification”.
 - is part of a PhD program addressed to PhD students with MS degree in biotechnology, biology or medicine. In the frame of the Marie Curie Network of the European Commission, entitled “Reproductive Early Research Training” (2011-2015) two ESR fellows were trained at the Molecular Genetic lab of our Centre under the supervision of C. Krausz
 - organizes free educational/informative activities for citizens
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Research activities

Basic and translational research

- Spermatology (PIs: E. Baldi, S. Marchiani, L. Tamburrino, S. Dabizzi)

1) Multilevel machine learning of toxicogenomic, molecular, endocrine, genotoxic and transgenerational effects of air pollution on reproduction (founded by Italian Ministry of Research). The project aims to evaluate the in vitro effect of benzo(a)pyrene on sperm functional parameters/DNA integrity/oxidative stress markers.

2) In collaboration with the Demetra ART center of Florence, we are currently evaluating the impact of some sperm characteristics (oxidative stress, chromatin compaction, level of hyperactivation) on reproductive outcomes and evaluation of microfluidic methods of sperm selection.

3) Implementation of a novel method to cryopreserve spermatozoa of Klinefelter and criptozoospermic men. The aim of this research project is the development of new methods of cryopreservation of very low sperm counts in existing or new devices, with an effective sperm recovery rate upon thawing. The initial results validated the effectiveness of the SpermVD device for the cryopreservation of a few tens of sperms. In addition, the current investigation of the micro-Tips vapour fast freezing method gives hope of preserving the fertility of severe oligozoospermic patients, instead of undergoing testicular biopsies

External Collaboration:

Timo Strunker (University of Munster)

Dr. Pellegrini e Benini (Demetra Center, Florence)

- AndroGenetics and Oncofertility (PI: C. Krausz)

1) Role of DNA repair genes and genes of Fanconi Anemia in non-obstructive azoospermia: genetic link between bone marrow failure and spermatogenic failure;

2) Whole exome analysis in patients affected by meiotic arrest. Development of genetic tools with potential pre-TESE predictive value

3) Whole exome analysis in patients affected by testis cancer: Discovery of novel genetic factors involved in the etiology of testis cancer and familial aggregation of cancers

4) Mosaic loss of Y chromosome and spermatogenesis (prior and after chemotherapy)

5) Analysis of *de novo* mutation rate in patients after oncological treatments

-Gender incongruence (PI: A. D. Fisher)

1) Clinical impact of Androgen receptor(CAG)_n polymorphism on gender-affirming hormonal treatment in assigned female at birth (AFAB) trans people

- Hypogonadism, erectile dysfunction, metabolic syndrome, and

gynecological endocrinology (PIs M. Maggi & L. Vignozzi; researchers: P. Comeglio; I. Cellai; S. Filippi):

- Pathophysiology of the erectile function and investigation of the metabolic derangements induced by metabolic syndrome (MetS) and obesity, by means of in-vitro studies in humans and in-vivo, ex-vivo and in-vitro studies in experimental animal models
- Effect of physical activity on erectile dysfunction induced by high-fat diet in an animal model of MetS
- Effects of testosterone on muscle fiber asset and exercise performance in a metabolic syndrome animal model
- Mechanisms regulating differentiation and function of gonadotropin-releasing hormone neurons in humans and MetS animal models
- Neuroprotective effects of sex steroids in human and animal experimental models
- Anti-inflammatory effects of androgens and intracrinology in the human and animal model vagina
- Facilitating effects of androgen signaling on sexual behavior in ovariectomized female rats primed with estradiol
- Sexual behaviour in a rat model of ovariectomy following several different treatments with sex steroids
- Hepatic, visceral adipose tissue, skeletal muscle and pulmonary dysfunctions in hypogonadic animal models, with particular focus on the underlying pathogenetic mechanisms

External Collaborations:

LIPOCINE INC. (USA) - Pharmaceutical Company

GALECTO INC. (Denmark) - Pharmaceutical Company

Sperm Biology (PI: M. Muratori. Researchers: C. Calamai; O. Ammar)

- Development of a novel flow cytometric technique to reveal oxidative stress in the viable sperm fraction of native semen samples: detection of oxidative stress in oncological patients and in infertile subjects. Building of reference values recruiting healthy donors.
- Comparison between the main techniques to reveal sperm DNA fragmentation: induction of damage by incubation and cryopreservation.
- Study of protective effects of a plant extract on sperm damage developed during in vitro incubation and cryopreservation
- Study on novel techniques (carriers, media, procedures) to cryopreserve human spermatozoa
- DNA fragmentation in viable spermatozoa: predictive power and effect of sperm selection.

External Collaborations:

Prof. Lisa Giovannelli, Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA)

Prof. Nadia Mulinacci, Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA)

Dr. Simone Palini, IVF Unit, Department of Reproductive Biology, Cervesi Hospital, Cattolica, Rimini, Italy.

Mass Spectrometry (Giovanna Danza, Sara Marchiani, Fabio Villanelli)

- development of new methods for quantitative steroid analysis by ID- LC-MS/MS) in different biological matrices
- analysis of steroid hormones in a longitudinal study on the effect of lifestyle and hormone concentration in women at Breast Cancer Risk.
- development of a quantitative GC-MS method for quantification of ketone bodies in different biological matrices

Clinical research:

- 1) **Erectile dysfunction and hypogonadism** (PIs M. Maggi, G. Rastrelli, L. Vignozzi, F. Lotti, C. Krausz) : the centre has been involved in carrying out epidemiological studies on the general population (in collaboration with the European Male Ageing Study group) and pathological populations with sexual dysfunction. Main research interest: late onset hypogonadism (predisposing factors and clinical correlates of the decline in testosterone levels during aging); role of obesity and metabolic derangements; development of markers for improving the diagnostic work up of hypogonadism; comorbidities in metabolic syndrome; the role of sex hormone binding globulin (SHBG) in the diagnosis of hypogonadism; assessment of cardiovascular (CV) risk in patients consulting for sexual dysfunction; the role of prolactin levels on male sexual function; the anti-inflammatory role of testosterone on the prostate of men with benign prostatic hyperplasia (BPH) through a randomized clinical trial; pubertal development in young boys and need of care for transitional age; the correlates of serum testosterone levels and/or testosterone treatment in population of men with inflammatory diseases; clinical and genetic investigation of hypogonadotropic hypogonadism; investigation of erectile and sexual dysfunction and hypogonadism in infertile men; investigation of erectile and sexual dysfunction and hypogonadism in men with endocrine disease (e.g. acromegaly, adrenocortical carcinoma, etc.)

External collaborations: 1) University of Manchester; 2) Katholieke Universiteit of Leuven; 3) Malmö University Hospital; 4) Santiago de Compostela University;

5) Albert Szent-György Medical University of Szeged; 6) Medical University of Łódź; 7) University of Tartu; 8) Imperial College London; 9) University of Glasgow; 10) Università degli Studi di Roma "La Sapienza"; 11) Università degli Studi di Padova; 12) Università degli Studi di Catania; 13) Università Politecnica delle Marche; 14) Università de L'Aquila.

- 2) **Male genital tract and penile ultrasound** (PIs F. Lotti and M. Maggi) A research area that has greatly developed with the study of clinical, seminal and biochemical correlates of male genital tract and penile ultrasound. The group led the European multicentre study for the assessment of normative ultrasound parameters of the male genital tract ("EAA ultrasound project", see at <https://www.andrologyacademy.net/ea-studies>). Main research interests:
1. Ultrasound characteristics of healthy, fertile men.
 2. Ultrasound characteristics of infertile men.
 3. Ultrasound characteristics of men with obesity/metabolic syndrome/diabetes.
 4. Ultrasound characteristics of men with different endocrinological diseases (e.g. acromegaly, thyroid diseases, prolactin levels, etc.).
 4. Ultrasound study of male sexual dysfunctions: erectile dysfunction, premature and delayed ejaculation, retrograde ejaculation.
 5. Ultrasound characteristics of men with chronic pelvic pain (including prostatitis, vesiculitis, epididymitis, orchitis).
 6. Ultrasound characteristics of men with testicular lesions/tumors.
 7. Male breast ultrasound evaluation.
 8. Thyroid ultrasound in men with premature ejaculation or metabolic syndrome.
- Diagnostic Therapeutic Assistance Pathways (DTAP) are available to study (i) erectile dysfunction (ED), (ii) male infertility and (iii) premature ejaculation (PE)/chronic pelvic pain (CPP). All DTAP include the evaluation, within the same day, of clinical, seminal, hormonal, biochemical and ultrasound parameters. Regarding the latter, the ED DTAP include flaccid or dynamic penile ultrasound evaluation and ultrasound assessment of carotid arteries to estimate the systemic cardiovascular risk; the male infertility DTAP include scrotal and transrectal ultrasound before and after ejaculation; the PE/CPP DTAP include scrotal and transrectal ultrasound as well as thyroid ultrasound. External collaborations: A. Main international societies: 1) European Society of Urogenital Radiology - Scrotal and Penile Imaging Working Group (ESUR-SPIWG; F. Lotti is a member of the Board). 2) Special Interest Group in Andrology of the European Society of Human Reproduction and Embryology (ESHRE-SIGA; F. Lotti is currently Senior Deputy) . 3) International and European Society for Sexual Medicine (ISSM and ESSM). B. Main University Centers: 1. Sapienza University of Rome, Italy; 2. University of Modena, Italy; 3. University of Trieste, Italy; 4. Polytechnic University of Marche, Ancona, Italy; 5. University of L'Aquila, Italy; 6. University of Padua, Italy; 7. University of Catania, Italy; 8. University of Naples, Italy; 9. Martin Luther University Halle-Wittenberg, Halle, Germany; 10. Münster University Hospital, Münster, Germany; 11. Justus Liebig University, Giessen, Germany; 12. Tartu University Hospital, Tartu, Estonia; 13. Fundació Puigvert, Universitat Autònoma de

Barcelona, Spain; 14.Cairo University, Cairo, Egypt; 15.King's College London, UK.

- 3) **Male infertility** (PIs F. Lotti, C. Krausz, L. Vignozzi, E. Baldi, M. Maggi) A research area that has greatly developed with the study of clinical, seminal and ultrasound (see above) characteristics of fertile and infertile men as well as spermatology, androgenetic and oncofertility (see above). In particular, research on fertile men to obtain normal seminal parameters has been performed by F. Lotti, M. Maggi and E. Baldi and led to a publication (Campbell MJ et al.. Distribution of semen examination results 2020 - A follow up of data collated for the WHO semen analysis manual 2010. *Andrology*. 2021 May;9(3):817-822) very relevant for the creation of the latest "WHO laboratory manual for the examination and processing of human semen". Research on infertile men include not only clinical, seminal and ultrasound evaluation but also association with sexual dysfunctions, lower urinary tract diseases, psychological burden, chronic illness, endocrine and metabolic diseases.
- 4) **Gender incongruence in adulthood and adolescence** (PI: A.D. Fisher, J. Ristori)
- European Network for the Investigation of Gender Incongruence, ENIGI: the endo adult part (Dr. Fisher, co-PI and member of the steering committee). The ENIGI project is aimed to evaluate the efficacy and safety of gender affirming hormonal treatment on metabolic parameters, bone density, anthropometric characteristics, as well as physical and psychological well-being;
 - European Network for the Investigation of Gender Incongruence, ENIGI: the endo adolescents part (Dr. Fisher, co-PI and member of the steering committee). The ENIGI project is aimed to evaluate the efficacy and safety of puberty suppression in adolescents with GI;
 - Italian Network on gender dysphoria, ItanGD (PI Dr A.D. Fisher and Dr. J. Ristori), an italian multicenter study is focused on the evaluation of psychobiological correlates of puberty suppression and gender affirming treatment in adolescents and adults with GI;
 - Italian Adolescents Gender Identity Research Group, IAGIR (PI Dr. J. Ristori and Dr Fisher)
 - the Estimate of transgender adult population in Italy (SPoT study. PI Dr. Fisher) in collaboration with the with the National Institute of Health and the National Office against the Discrimination in Italy aimed to evaluate the the size of the adult TGD population in Italy across ages;
 - The ENIGMA (Enhancing NeuroImaging Genetics through Meta Analysis) Gender Studies working group
 - Italian Transgender and Gender Diverse adult population: a voluntary sampling observational study (in collaboration with the National Institute of Health and the National Office against the Discrimination in Italy)

- Estimate of the intersex population in Italy (in collaboration with the with the National Institute of Health and the National Office against the Discrimination in Italy) aimed to evaluate the the size of the intersex people referring to specialized centers in Italy

5) **Androgenetics** (PI. C Krausz)

-Pharmacogenetic studies on three SNPs on FSH β (rs10835638 in position -211) and FSHR (rs6166 and rs1394205) in infertile patients under treatment with FSH with two different end-points (effect on sperm DNA fragmentation in the frame of an international multicentre study; effect on sperm maturation, improved hyaluronic acid binding capacity)

-Evaluation of the effect of cytostatic therapy on the male gamete genome. As "sentinels" of the genomic effects of cytostatic therapy we are analysing prior and after therapy sperm DNA fragmentation (SDF). The ultimate goal of the project is to define reproductive safety in oncological patients and thus provide evidence based information for decision making concerning the type of conception (pre-therapy frozen/thawed spermatozoa in the context of in vitro fertilization) or natural pregnancy (spermatogenesis is recovered in about 80% of patients after chemotherapy).

-Study of familial aggregation of neoplasms in testicular germ cell tumors (TGCT); identification of novel clinical risk factors of TGCT: the impact of anogenital distance.

-genetic screening in hypogonadotropic hypogonadism through NGS gene panel for diagnostic and research purposes.

6) **Women's sexual health** (PI L. Vignozzi)

-The main current research topics include: The role of endogenous androgens in women's sexual function; Female sexual health as a mirror of cardiovascular health: CARDIOSEX study, funded by a Grant of the International Society for Women's Sexual Health (ISSWSH); Objective assessment of Female Arousal Disorder by Doppler ultrasound of the clitoral arteries: our Center is the first designated Training Center of the EFUS, Female ultrasound school of the European Society for Sexual Medicine; Efficacy and safety of transdermal testosterone therapy in women with sexual dysfunction, and its effect on genital Doppler parameters compared to other treatments; Evaluation of sexual function in women with Polycystic Ovary Syndrome/Androgen Excess, as part of the multicenter PCOS Outcome study, promoted by the Italian Society of Endocrinology; Psychological evaluation of sexual inhibition and excitation as a tool for the prediction of therapeutic outcomes in women with sexual dysfunction.

External collaborations: Section of Endocrinology, Unit of Andrology, Reproductive Medicine and Male and Female Sexuality (FERTISEXCARES), Federico II University of Naples, Italy; Department of Experimental Medicine,

Sapienza University of Rome, Policlinico Umberto I Hospital, Rome, Italy; Department of Clinical, Surgical, Diagnostic and Pediatric Science, University of Pavia, Italy; Endocrinology and Medical Sexology (ENDOSEX), Department of Systems Medicine, University of Rome Tor Vergata, Italy.

Clinical activities

Male sexual dysfunctions

Referral and follow-up for male sexual dysfunction represent half of the clinical activity of the center. Most of them consult for erectile dysfunction (about 60%), premature ejaculation (30%), Peyronie's disease (5%), and delayed ejaculation (5%). During the initial clinical assessment, all patients undergo a standardized protocol that includes the evaluation of all the aspects of sexual response, including sexual desire, morning erection, masturbation activity; psychological aspects as well as couple relationship are taken into account. This allows the clinician to have a holistic view of the patient which is necessary to identify all the possible aspects contributing to the sexual symptom they are complaining about. This protocol is the result of the knowledge that we accrued from our clinical research in this field that now we translate in our clinical practice. Possible psychological and relational issues are treated by the referral to our psychiatric consultants that are well trained for behavioral couple therapy and use a pharmacologic approach if appropriate. If sexual dysfunction in the female partner are identified, a dedicated service is available in our center (see below). The organic pathogenic component of the sexual dysfunction is investigated by Diagnostic Therapeutic Assistance Pathways (DTAPs) to study erectile dysfunction (ED), or premature ejaculation (PE). Both DTAPs include the evaluation, during the same day, of hormonal, biochemical and ultrasound parameters (penile ultrasound evaluation, ultrasound assessment of carotid arteries, scrotal and transrectal ultrasound, thyroid ultrasound). When required, specific in-depth connections are available to go into detail through pituitary MRI, cardiologic visit, urologic visit or neurophysiological study of the pudendal nerve.

Male infertility

Since 2020, a collaboration between Careggi Hospital and the Local Health Authority (AUSL) Toscana Centro has been active, with the participation of the andrologists of our center in the "Aware fertility outpatient clinics" at Women's Center (Pistoia, Tuscany), Women's Health Center (Prato, Tuscany) and Piero Palagi Hospital (Florence, Tuscany), providing visits for the infertile couple with simultaneous andrological evaluation for the male partner and gynecological evaluation for the female one. Such a collaboration was definitively formalized thanks to an implementation agreement („Accordo Attuativo di Area Vasta per la gestione integrata del percorso clinico assistenziale della coppia infertile“ of 05/09/2022) between AUSL Toscana Centro and Careggi Hospital, which allows the movement of healthcare personnel between the two companies in relation to the clinical path of couple infertility. Furthermore, with the provision of the Careggi General Manager n ° 152 of 23/02/2022 the "Center for the prevention,

diagnosis and treatment of infertility" was created, which coordinates the personnel belonging to the Unit of Andrology, Women's Endocrinology and Gender Incongruence (directed by Prof. Linda Vignozzi) and the Unit of Assisted Reproductive Technology (ART) (directed by Prof. Maria Elisabetta Coccia). The center belongs to the Maternal-Infantile Department (directed by Prof. Felice Petraglia).

Thanks to the creation of the Centre, couples evaluated in the "Aware fertility outpatient clinics" of the AUSL Toscana Centro (since October 2022 and currently active at Palagi Hospital and SS. Cosma e Damiano Hospital in Pescia, Tuscany) can be sent directly to Careggi for the continuation of the therapeutic process. The constitution of the Center aims to manage infertility by looking at the couple desiring pregnancy in its entirety, analyzing the possible causes of infertility in both members of the couple, with the evaluation by the andrologist for the male partner and the gynecologist for the female partner.

At the end of the multidisciplinary couple visit, the two specialists, after a mutual comparison and based on the clinical picture of the two partners and the clinical history of the couple, agree on the most appropriate diagnostic-therapeutic course (biochemical/hormonal tests, seminal liquid analysis with evaluation of sperm DNA fragmentation and Interleukin-8 level, scrotal and prostate ultrasound tests for the male partner) to obtain pregnancy. Furthermore, a genetic analysis service was created for suspected genetic anomalies of the reproductive axis in collaboration with the Unit of Genetic Diagnostics of Careggi Hospital. In case of clinical suspicion of a genetic condition potentially interfering with fertility for one of the two partners (i.e. karyotype abnormalities, Y chromosome microdeletions, hypogonadotropic hypogonadism, primary ovarian insufficiency, etc.) a blood test can be carried out for the genetic analysis at the Unit of Andrology, Female Endocrinology and Gender Incongruence. Subsequently, a genetic evaluation is scheduled for the patient/couple concerned, carried out by the medical genetics specialists of the Unit of Genetic Diagnostics. If at the first visit or during the diagnostic-therapeutic process the couple presents a picture of untreatable infertility, in the unanimous opinion of both the gynecologist and the andrologist, they will be sent via a facilitated 'fast-track' path to the ART procedures.

Male genital tract and penile ultrasound

The clinical ultrasound activity of our Unit is mainly related to the study of 1. ultrasound characteristics and abnormalities of infertile men (secretive, obstructive or mixed infertility/azoospermia) 2. male genital tract (especially testicular and prostate) tumors and related risk factors (cryptorchidism, microlithiasis, infertility etc.) 3. chronic or acute pelvic or scrotal pain (prostatitis, vesiculitis, epididymitis, orchitis, varicocele, any acute scrotum, testicular torsion etc.) 4. men with sexual dysfunctions: erectile dysfunction, premature and delayed ejaculation, 5. men with penile diseases: erectile dysfunction, La Peyronie's disease, Mondor's disease, penile nodules etc., 6. lower urinary tract symptoms (LUTS), including BPH and prostate inflammation 7. Male breast

ultrasound evaluation. 8. Thyroid ultrasound in men with premature ejaculation. 9. Carotid ultrasound to estimate the cardiovascular risk. Diagnostic Therapeutic Assistance Pathways (DTAP) are available to study (i) erectile dysfunction (ED), (ii) male infertility and (iii) premature ejaculation (PE)/chronic pelvic pain (CPP). All DTAP include the evaluation, within the same day, of clinical, hormonal, biochemical parameters, seminal parameters for PE/CPP and male infertility DTAP and ultrasound parameters. Regarding the latter, the ED DTAP include flaccid or dynamic penile ultrasound evaluation and ultrasound assessment of carotid arteries to estimate the systemic cardiovascular risk; the male infertility DTAP include scrotal and transrectal ultrasound before and after ejaculation; the PE/CPP DTAP include scrotal and transrectal ultrasound as well as thyroid ultrasound.

Oncofertility

- outpatient clinic dedicated to men with malignancies that, before starting treatments for cancer, are referred to our Unit for sperm cryopreservation. Since 2013, the clinical andrological assessment, performed before sperm cryopreservation is aimed at providing a proper counseling about assessment of risk for infertility, eligibility for fertility preservation method, methods and indications for assisted reproductive technology that might be needed in the future and, finally, prognosis in terms of recovery of spermatogenesis after anti-cancer therapies. This is a service complimentary to sperm cryopreservation (that is active since 1998), activated for supporting patients in obtaining correct information on fertility consequences of cancer. See the specific paragraph below for further details. Oncological patients attending the clinic for cryopreservation of semen prior chemo/radiotherapy undergo to a complete andrological clinical workup which includes standardized questionnaire, physical exam, hormone dosage, Y chromosome deletion analysis in testis cancer patients and semen analysis. A yearly andrological follow up is performed with semen analysis up to 3 years. Patients who are affected by testis cancer, hematological malignancies are invited to participate at the research project (see in the dedicated paragraph in research section before) aimed to study the genotoxic effects of chemo/radiotherapy.

Gender incongruence multidisciplinary team is composed by different professionals including psychologists, endocrinologists, psychiatrists, gynecologists, plastic surgeons, urologists, as well as a child psychiatrist and a bioethicist with certified experiences in transgender health. The Centre operates in line with the World Professional Association for Transgender Health (WPATH) Standards of Care 8th version and Endocrine Society (ES) guidelines. The Unit provides clinical support for children, adolescents and adults with GI who refer for their gender-related health care needs and their families. Indeed, gender diverse pre-pubertal children receive a psychological assessment and support. During adolescents, if criteria are satisfied, puberty suppression with GnRH analogs and gender affirming hormonal treatment can be offered. The Centre provides counseling and services for fertility preservation procedures in Assigned male at birth (AMAB) and Assigned female at birth (AFAB) persons who ask for medical gender affirming

treatments.

Women's sexual health

In recent years, our center has developed and implemented its clinical activity in the field of Women's Endocrinology. Indeed, interpersonal factors are key to the work-up of all male sexual dysfunctions, and the assessment of sexual symptoms in the female partner is crucial for a successful process of care of the couple. Doppler ultrasound of clitoral arteries is performed routinely to assess the vascular component of Female Arousal Disorder. The main reasons for referral to our center include the following conditions: Hypoactive Sexual Desire Disorder in pre- and post-menopausal women; vaginismus, dyspareunia, Genito-pelvic pain and penetration disorder and vulvodynia; prevention and treatment of sexual dysfunction related to hormonal contraception; sexual dysfunction in patients with eating disorders, neurological conditions (i.e. multiple sclerosis) and cardiovascular disease; sexual dysfunction in natural and surgical menopause, gynecological cancer survivors, endometriosis; sexual dysfunction in women diagnosed with common endocrine disorders such as obesity, Diabetes Mellitus, alterations of thyroid function, hyperprolactinemia; sexual dysfunction in women with infertility.

Women's reproductive health

In a multidisciplinary approach, physicians of our Center have been collaborating with the Gynecology Unit and been involved in the diagnostic work-up and clinical management of women with primary amenorrhea, Premature Ovarian Insufficiency, Polycystic Ovary Syndrome, Congenital Adrenal Hyperplasia and other hyperandrogenic conditions with and impact on couple fertility.

Pediatric to adulthood care

In 2015, a pediatric to adulthood care transition service was established in the center. This service has been gradually empowered and the organization improved, being in its full activity since 2017. It is performed in close collaboration with the Auxoendocrinology Unit of the Meyer University Hospital which is one of the most important pediatric hospitals in Italy. Patients candidates for transition from the pediatric to the adulthood hospital setting are jointly visited by a pediatrician with specific auxoendocrinological training and an endocrinologist at the Meyer Hospital. After a variable number of joint visits, when the pediatrician and the endocrinologist deem the patient suitable to the adulthood care setting, a visit is scheduled at our Unit in Careggi where the most appropriate follow-up schedule is defined for each patient. Patients have endocrinological conditions, including andrological ones. Currently about 300 patients are routinely visited with 30% of them evaluated and treated for andrological conditions including pubertal disorders, congenital hypogonadotropic hypogonadism, Klinefelter syndrome, congenital anorchia, monorchidism, cryptorchidism, gynecomastia, hypopituitarism, consequences of pediatric neoplasia.

Nutritional and lifestyle intervention

Since 2020, our center has developed a focus on the potential benefits of weight loss on reproductive and sexual health in men and women with a poor metabolic state (i.e. overweight, obesity, metabolic syndrome). Indeed, this population is at higher risk for both sexual dysfunction and infertility. Patients are referred whenever reproductive or sexual consequences of metabolic disorders are identified; weight loss may be mandatory in obese women candidates for ART procedures. Bio-electrical impedance analysis (BIA) is routinely used for the accurate evaluation of body composition. Weight loss programs are individualized and include pharmacological treatment and lifestyle interventions, such as Very low calories ketogenic diet, Mediterranean diet, and monitored physical activity programs.

Sperm analysis and Cryobanking

The principal routine analysis of the semen laboratory are: Semen Analysis, Capacitation Tests, Interleukin 8 Elisa Assay, Semen Cryopreservation, evaluation of sperm DNA fragmentation.

The lab adheres to more than one external quality controls such UK NEQAS and VEQ-Regione Toscana since 2005, and recently participates in the development and distribution of a quality control for sperm motility dedicated to SIAMS-accredited laboratories.

The laboratory is a Regional Reference Centre for Semen Cryopreservation with over 4000 collections during almost 24 years of activity and more than 2000 samples currently cryopreserved. In 2021 it was accredited by the Italian National Transplant Centre (CNT) receiving the TE-code for sample distribution.

The banking activity has been gradually increasing and, despite the Covid period in 2020, the positive trend was maintained. Patients have access to semen cryopreservation for neoplastic disease, oligospermia or spinal cord injury.

Starting from September 2022 the bank initiated, in collaboration with Prof L. Masieri of the Pediatric Hospital Meyer, to collect testicular tissues from pre-pubertal boys undergoing potential gonadotoxic treatments.

Sperm donation

Possible donors of semen undergo a strict evaluation in our Unit: andrological and clinical workup, blood, urine and semen analysis, psychiatric consultation and genetic testing. If the possible candidate is suitable, his semen is cryopreserved in our Bank and available for use in ART (assisted reproduction technique). Additional and updated information can be added any time to our Register.

Mass Spectrometry

The routine analysis currently performed are: urinary free cortisol, serum 17-hydroxyprogesterone, Androstenedione. All these analyses are conducted using Laboratory tests internally developed, validated and adhering to the external quality control UK-NEQAS steroid hormones. The number of analytes will be progressively

increased to include testosterone and low concentration estrogens.

Diagnostic Molecular Genetics The diagnostic part of the molecular genetics laboratory performs analyses for : i) Y chromosome microdeletion analysis (AZF deletions and the g r/gr deletion which is a risk factor for oligozoospermia and TGCT). ii) search for mutations in 35 candidate genes of congenital hypogonadotropic hypogonadism. The laboratory is the reference laboratory for the European Molecular Genetics Quality Network (EAA/EMQN Y chromosome scheme) and provides the characterization of cell lines for Y chromosome microdeletions and annual validation of selected samples for external quality control.

Name and address of Centre

Andrology, Womens' Endocrinology and Gender Incongruence Centre,
 Materno-Infantile Department
 Azienda Ospedaliera Universitaria Careggi
 University of Florence
 Viale G. Pieraccini 6
 I-50139 Firenze, Italy
 Tel: +39 055 4271 414
 Fax: +39 055 4271 413

Type of Centre

University	<input type="checkbox"/>
University Hospital	<input checked="" type="checkbox"/>
Private Centre	<input type="checkbox"/>

Other (please specify) _____

1. Director

Linda Vignozzi

Academician Affiliated Member Clinical Andrologist

1. co-director of the EAA center

Csilla Krausz

Academician Affiliated Member Clinical Andrologist

2a. Clinical responsible

Francesco Lotti

Academician Affiliated Member Clinical Andrologist

2b. Clinical responsible

Giulia Rastrelli

Academician Affiliated Member Clinical Andrologist

2c. Clinical responsible

Sarah Cipriani

Academician Affiliated Member Clinical Andrologist

2d. Clinical responsible

Alessandra D. Fisher

Academician Affiliated Member Clinical Andrologist

2e. Clinical responsible

Elisa Maseroli

Academician Affiliated Member Clinical Andrologist

2f. Clinical responsible

Francesca Frizza

Academician Affiliated Member Clinical Andrologist

2g. Clinical responsible

Maria Torcia

Academician Affiliated Member Clinical Andrologist

3. Present Staff (*Senior Scientists*)

1) Name Jiska Ristori
 Degree Psy
 Speciality Psychologist Psychotherapist (Gender Incongruence Team)

Academician Affiliated Member Clinical Andrologist

2) Name Elisabetta Baldi
 Degree MSc, PhD
 Speciality Clinical Pathology

Academician Affiliated Member Clinical Andrologist

3) Name Sara Marchiani
 Degree MSc Biological Sciences, PhD, Specialist in clinical pathology and biochemistry
 Speciality Sperm biology, mass spectrometry

Academician Affiliated Member Clinical Andrologist

4) Name Sara Dabizzi
 Degree MSc
 Speciality Clinical Pathology and Biochemistry

Academician Affiliated Member Clinical Andrologist

5) Name Lara Tamburrino
 Degree MSc, PhD
 Speciality Clinical Pathology and Biochemistry

Academician Affiliated Member Clinical Andrologist

6) Name Monica Muratori
 Degree MSc, PhD
 Speciality Basic sciences

Academician Affiliated Member Clinical Andrologist

7) Name Giovanna Danza
 Degree MSc Chemistry
 Speciality Mass Spectrometry, steroidomics

Academician Affiliated Member Clinical Andrologist

Insert any additional staff below (if required)

MD/Biologists/Chemists

1) Name Ilaria Cellai
 Degree MSc, PhD
 Speciality Biology
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

2) Name Traini Giulia
 Degree PhD student
 Speciality Biotechnologists
 Full time/part time full time

Academician Affiliated Member Clinical Andrologist

3) Name Emanuela Ragosta
 Degree Assistant researcher
 Speciality Biotechnologist
 Full time/part time full time

Academician Affiliated Member Clinical Andrologist

4) Name Dimitri Yannas
 Degree MD
 Speciality Resident in Endocrinology
 Full time/part time Part time

Academician Affiliated Member Clinical Andrologist

5) Name Francesca Mazzoli
 Degree Psy
 Speciality Psychologist, Gender Incongruence
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

6) Name Carlotta Cocchetti
 Degree MD, Endocrinologist
 Speciality Endocrinology, Gender Incongruence team
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

7) Name Alessia Romani
 Degree MD
 Speciality Resident in Endocrinology
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

8) Name Teresa Angotti
 Degree Psy
 Speciality Psychologist, Gender Incongruence Team
 Full time/part time Par time

Academician Affiliated Member Clinical Andrologist

9) Name Matteo Vannucci
 Degree MD
 Speciality Endocrinology, oncofertility, infertility
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

10) Name Ginevra Farnetani
 Degree Bsc, MS
 Speciality PhD Student androgenetic-group
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

11) Name Serena Anna Ravelli
 Degree MD
 Speciality Resident in Endocrinology
 Full time/part time Part time

Academician Affiliated Member Clinical Andrologist

12) Name Chiara Alfaroli
 Degree MD
 Speciality Resident in Endocrinology
 Full time/part time Part time

Academician Affiliated Member Clinical Andrologist

13) Name Oumaima Ammar
 Degree MSc, PhD
 Speciality Biology
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

14) Name Costanza Calamai
 Degree PhD student
 Speciality Biotechnologist
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

15) Name Fabio Villanelli
 Degree MSc Biology
 Speciality mass spectrometry
 Full time/part time Full time

Academician Affiliated Member Clinical Andrologist

Insert any additional staff below (if required)

Specialists

- | | |
|---------|-------|
| 1) Name | _____ |
| 2) Name | _____ |
| 3) Name | _____ |
| 4) Name | _____ |
| 5) Name | _____ |

PhD Students

- | | |
|---------|------------------|
| 1) Name | Traini Giulia |
| 2) Name | Calamai Costanza |
| 3) Name | _____ |

Nurses

- | | |
|---------|-------|
| 1) Name | _____ |
| 2) Name | _____ |
| 3) Name | _____ |

Laboratory Technicians

- | | |
|---------|-----------------------------|
| 1) Name | Paolo Comeglio, MSc, PhD |
| 2) Name | Sandra Filippi, BSc, PhD |
| 3) Name | Selene Degl'Innocenti, TSLB |
| 4) Name | _____ |
| 5) Name | Maria Grazia Fino, TSLB |
| 6) Name | _____ |

Administrative Personnel

- | | |
|---------|-----------------|
| 1) Name | Anna Calandrone |
| 2) Name | _____ |
| 3) Name | _____ |

4. Clinical Activity

A. Outpatients: Consultations per year in the last 3 years

	2020	2021	2022
New patients	1354	1545	1477
Follow-up patients	3966	4837	4073

Type of patients in the last years (%)	2020	2021	2022
Infertility	572	676	655
Infertility evaluated in Hospitals or Outpatient Clinics outside Careggi	41	59	72
Erectile dysfunction	191	225	218
Hypogonadotropic Hypogonadism	30	41	39
Klinefelter	79	111	84
Gynaecomastia	32	47	40
Varicocele	80	93	109
Cryptorchidism	51	61	59
Male sex accessory gland infections	86	108	105
Testicular tumors (Firstly diagnosed by our center)	16	24	23
Gender Incongruence (endocrinology)	250	331	962
Gender Incongruence (psychology)		342	540
Intersex conditions	35	35	40
Oncofertility (first +follow-up visits)	120+150	121+245	118+250
Female sexual dysfunction (new patients)	25	40	44
Female endocrinological conditions related to fertility? (new patients)	/	/	175
Nutrition - males (new patients)	13	17	18
Nutrition - females (new patients)	54	67	72

B. Ultrasound (testis, penile, prostate, mammary, gynecological) *

	2020	2021	2022

Total	462	585	549
Controls	nv	nv	nv

** performed at the Department of Radiology*

C. Andrological surgery procedures THESE PROCEDURES ARE PERFORMED AT THE ART CLINIC AND AT THE UROLOGY DEPARTMENT

	2020	2021	2022
Testicular biopsies	2	2	2
Varicocele ligation	These are provided by the Urology Unit which is in close connection with our Unit		
Prostate biopsies			
BPH			
Prostate cancer			
Vasectomy			
Vaso-vasostomy			
Other			

5. A. Andrology laboratory activity

	2020	2021	2022
Semen analyses	1612	2220	2596
Sperm antibodies	1518	2122	2495
Seminal markers	63	243	245
Sperm DNA fragmentation	189	299	282

5. B. Andrology laboratory activity

Sperm banking donors	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Sperm banking cancer patients	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>

<i>If yes:</i>			
	2020	2021	2022
Number of samples	178	174	168

5. C. Histopathological evaluation of biopsies	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
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5. D. Reproductive Hormones Assays	Yes	<input type="checkbox"/>	No	<input checked="" type="checkbox"/>
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If yes please specify type of assays and number of samples in the last year

Reproductive Hormones Assays
(FSH, LH, testosterone, SHBG, prolactin)

5. D1. Steroid Hormones Assays	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
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<i>If yes:</i>			
	2020	2021	2022
free urinary cortisol	767	1022	1026
serum 17-OH progesterone	1970	2303	1209
serum Androstenedione	1490	1601	913

5. E. Y chromosome microdeletions according to EAA/EMQN guidelines Yes No

78

If yes number of tests in the past year

Participation to the EAA quality control scheme? Yes No

If no, specify if available in another lab of the same hospital Yes No

Blood karyotyping Yes No

If no, specify if available in another lab of the same hospital Yes No

Other genetic tests (please specify)

Gene panel for Congenital Hypogonadotrophic hypogonadism

Gene panel for Intersex Conditions

6. Collaborations with other Clinical Units of the University/Hospital

IVF Unit Yes No
If yes please specify: Children, Endocrinology, IVF, Urology, Genetics, Pathology

Urology Clinic	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Endocrine Clinic	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Genetics Lab/Unit	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Paediatric Unit	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Central Hospital Laboratory	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
Private Centres	Yes	<input type="checkbox"/>	No	<input checked="" type="checkbox"/>

Further collaborations are represented by Hospitals and Outpatients outside Careggi (Area Vasta Centro) performing visits for infertility

7. Clinical teaching activity

Duration of training (years):

	Number
A: Trainees in the last five years	60
B: Trainees who passed EAA-ESAU\exam for Clinical Andrologist in the last 5 yrs	3
C: Trainees working in the center preparing to pass the EAA-ESAU examination	
D: PhD Students	9
E: Medical Students	10 (attending the unit for elective clinical or research activity)
F: Other students (MSc)	

8. Formal Andrology teaching program Yes No
If yes: specify duration (years/months): Years Months

	Hours of formal teaching per year	Professional training (weeks/months)
Medical Students	12	2 weeks
PhD Students	12	9 months for 3 year
Post Graduate students	45	6 months
Trainees	45	6 months
Master students	84	4 weeks
Other degrees (please specify)		

9. Research Activity (maximum 1 page)

Please shortly describe the main research topics of the center and list the most relevant papers in peer review journals (with IF) related to these activities.

The full list of publications (years 2018 - 2023) are presented at the end of this report.

Basic research on metabolic derangements, hypogonadism, erectile dysfunction, and gynecological endocrinology by means of *in-vivo* and *ex-vivo* studies in animal models of metabolic syndrome (MetS), obesity, hypertension, hypogonadism and menopause, and *in-vitro* studies in humans. Selected recent publications:

- Comeglio et al. J Endocrinol Invest. 2021;44(10):2175 [IF 5.467]
- Cellai et al. J Endocrinol Invest. 2022 Jun;45(6):1161-1172 [IF 5.467]
- Guarnieri et al. Environ Pollut. 2023 Jan 15;317:120766 [IF 9.988]

Basic research on sperm biology and semen characteristics in fertile and infertile men. Evaluation of new advancement on cryopreservation. Impact of male gamete characteristics on ART outcomes.

- Traini G, et al. Front Endocrinol (Lausanne). 2022 Nov 22;13:1012416. (IF: 5.2)
- Marchiani S, et al. Sci Rep. 2021 Sep 28;11(1):19177. (IF: 4.6)
- Marchiani S, et al. J Endocrinol Invest. 2022 May;45(5):973-980. (IF:5.467)

Basic research on: sperm oxidative stress in oncological patients and building of reference values in healthy donors; cryopreservation: novel procedures and cryoprotectants; predictive ability of DNA fragmentation in viable and non viable spermatozoa.

- 1. Calamai C et al. Antioxidants (Basel). 2023 May 24;12(6):1145. IF= 7.675
- 2. Arciero V et al. Andrology. 2022 Sep;10(6):1123-1133. IF= 4.456
- 3. Muratori M et al. J Clin Med. 2020 May 4;9(5):1341. IF= 4.964

Translational research in androgenetics:

Whole Exome Sequencing (WES) studies reached to the discovery of late onset Fanconi anemia in SCOS patients; a number of novel autosomal (recessive) meiotic genes with potential predictive value for TESE. The first large multicenter study led by our center, analyzed all X chromosome genes in over 2000 NOA patients discovering 21 novel X linked genes.

- Krausz et al Genet Med. 2019 Jan;21(1):189-194. (IF: 8.86)
- Krausz et al Genet Med. 2020 Dec;22(12):1956-1966. (IF: 8.86)
- Riera-Escamilla et al. Am J Hum Genet. 2022 Aug 4;109(8):1458-1471. (IF 11.04)

Clinical research on

- the clinical correlates of testis dysfunction and its clinical correlates
- the testis physiopathology and its functional modifications in ageing men
- effectiveness and safety of testosterone therapy in adult men
- erectile dysfunction and clinical correlates, including metabolic disorders and cardiovascular risk
- the clinical correlates of change in serum prolactin levels in men
- clinical characteristics of boys with andrological conditions in the transition from pediatric to adult care

Selected recent publications:

- Rastrelli et al., Clin Endocrinol (Oxf). 2018 Oct;89(4):459-469 (IF 3.2)
- Rastrelli et al., Andrology. 2021 Jan;9(1):88-98 (IF 4.5)
- Rastrelli et al., J Endocrinol Invest. 2022 Jul;45(7):1413-1425 (IF 5.4)

-Ultrasound of the male genital tract

- Lotti et al. Andrology. 2022 Sep;10(6):1150-1171. (IF 4.5)
- Lotti et al. Andrology. 2021 Mar;9(2):559-576. (IF 4.5)
- Freeman S, Lotti F et al. Eur Radiol. 2020 Jan;30(1):11-25. (IF 7.034)

-Male infertility

- Campbell, Lotti et al. Andrology. 2021 May;9(3):817-822. (IF 4.5)
- Lotti et al. Andrology. 2020 Sep;8(5):1005-1020. (IF 4.5)
- Lotti et al. Int J Mol Sci. 2021 Feb 17;22(4):1988.(IF 5.4)

-Onco-andrology and oncofertility:

-The effect of cytotoxic therapies on sperm DNA integrity.

-The role of Y chromosome gr/gr deletions on the etiology of testis cancer

-Anogenital distance as novel biomarker for testis cancer

- Farnetani et al Andrology. 2023 Mar 17. ePubahead (IF: 4.45)
- Moreno-Mendoza et al Andrology. 2020 Nov;8(6):1770-1778. (IF: 4.45)
- Moreno-mendoza et al Eur J Hum Genet. 2019 Oct;27(10):1578-1588. (IF:5.35)

10. Research Funding

Please specify the amount of available funds in the last 3 years and their source (Government, European Union, University, Local Government, Pharmaceutical Industries, Banks, Foundations....)

Governmental funds (competitive)

Year: 2019-2023

Total amount (€): 150.000

Funding Source: PRIN Ministry of Research PI Krausz

Year: 2023-2025

Total amount (€):70.000

Funding Source: PRIN Ministry of Research PI Krausz

Year: 2020-2022

Total amount (€): 44.600

Funding Source: **Fondazione** Ente Cassa di Risparmio di Firenze PI Krausz

Year: 2019-2023

Total amount (€): 128.300

Funding Source: PRIN Ministry of Research PI Baldi

Year: 2023-2025

Total amount (€):180.000

Funding Source: PNRR Tuscany Health System PI Baldi

Year 2023

Total Amount: 235.000 euro

Funding Source (PRIN-PNRR 2022, PI: E. Baldi)(in collaboration with University of Rome La Sapienza e University of Teramo)

Year	2019-2023
Total amount (€)	250.000
Funding Source(s)	PRIN Ministry of Research PI Rastrelli

Year	2022
Total amount (€)	Funding for the recruitment of a researcher (3 year contract)
Funding Source(s)	PNRR Ministry of Research PI Maggi

Year	2023-25
Total amount (€)	235.000
Funding Source(s)	PNRR Ministry of Research PI Baldi (in collaboration with Paoli UniRoma e Loi UniTeramo)

Year	2023-2025
Total amount (€)	130.000
Funding Source(s)	PRIN-PNRR Ministry of Research PI Rastrelli

Year	2023-2025
Total amount (€)	40.000
Funding Source(s)	PRIN-PNRR Ministry of Research PI Vignozzi

Year	2020-2022
Total amount (€)	40.000
Funding Source(s)	Department of Excellence PI Lotti

Insert any additional funding below if required

Year: 2020

Total amount (€): 10,000.00

Funding Source: Pharmaceutical Industry

Year: 2020

Total amount (€): 68,000.00

Funding Source: Pharmaceutical Industry

Year: 2021

Total amount (€): 233,600.00

Funding Source: Pharmaceutical Industry

Year: 2022

Total amount (€): 12,500.00

Funding Source: Pharmaceutical Industry

Year: 2022

Total amount (€): 6,218.25

Funding Source: ISSWSH International Society for the Study Women's Sexual Health

ORGANIZATION CHARTS

Unit name
<p>Andrology, Women's Endocrinology and Gender Incongruence Materno-Infantile Department Azienda Ospedaliera Universitaria Careggi University of Florence Viale G. Pieraccini 6 I-50139 Firenze, Italy</p>

Organization charts legend: Department / Unit Structure

<p>Directors: Prof. Linda Vignozzi - Prof. Csilla Krausz Past Director: Prof. Mario Maggi</p>		
<p>Staff members</p>		
<p>Prof Elisabetta Baldi Prof Giulia Rastrelli Prof Francesco Lotti Dr Alessandra D Fisher Dr Elisa Maseroli Dr Sarah Cipriani Dr Francesca Frizza Prof Maria Torcia Dr Sara Dabizzi Dr Lara Tamburrino Dr Giovanna Danza</p>	<p>Dr Paolo Comeglio Dr Sandra Filippi Dr Ilaria Cellai Dr Monica Muratori Dr Sara Marchiani Dr Fabio Villanelli Dr Jiska Ristori</p>	<p>Dr Ginevra Farnetani Dr Giulia Traini Dr Emanuela Ragosta Dr Costanza Calamai Dr Oumaima Ammar Dr Matteo Vannucci Dr Carlotta Cocchetti Dr Alessia Romani Dr Dimitri Yannas Dr Chiara Alfarol Dr Serena Anna Ravelli</p>
	<p>r Francesca Mazzoli</p>	D
	<p>r Teresa Angotti</p>	D
<p>Clinical Services</p> <p>Outpatient Clinics for sexual medicine, couple infertility, psychopathology of sexual dysfunction, psychological counselling and behavioural therapy, gender incongruence, female sexual dysfunctions</p> <p>Ultrasound penile arteries, scrotal and internal male genital tract</p> <p>FNA/TESE</p> <p>IUI</p>		
<p>Contribution to EAA training program</p> <p>Diagnosis of infertility Ultrasound of male genital tract Doppler ultrasound of penile arteries Counselling of infertile couple Cryopreservation of sperm</p>		

CENTRE PHOTOS

Please, include at least one high resolution photos

FULL LIST OF PUBLICATIONS (with IF) of staff members from the last 5 years

Selected publications for each PI

Vignozzi/Maggi

For the entire publication list see:

<https://www.scopus.com/authid/detail.uri?authorId=7102422617>

and

<https://www.scopus.com/authid/detail.uri?authorId=6507526011>

- Cellai I, Filippi S, Comeglio P, Cipriani S, Maseroli E, Di Stasi V, Todisco T, Marchiani S, Tamburrino L, Villanelli F, Vezzani S, Corno C, Fambrini M, Guarnieri G, Sarchielli E, Morelli A, Rastrelli G, Maggi M, Vignozzi L. Testosterone positively regulates vagina NO-induced relaxation: an experimental study in rats. *J Endocrinol Invest.* 2022 Jun;45(6):1161-1172. doi: 10.1007/s40618-022-01743-4. Epub 2022 Jan 24. PMID: 35072927; PMCID: PMC9098587. [IF 5.467]
- Comeglio P, Cellai I, Mello T, Filippi S, Maneschi E, Corcetto F, Corno C, Sarchielli E, Morelli A, Rapizzi E, Bani D, Guasti D, Vannelli GB, Galli A, Adorini L, Maggi M, Vignozzi L. INT-767 prevents NASH and promotes visceral fat brown adipogenesis and mitochondrial function. *J Endocrinol.* 2018 Aug;238(2):107-127. doi: 10.1530/JOE-17-0557. PMID: 29945982. [IF 4.669]
- Comeglio P, Sarchielli E, Filippi S, Cellai I, Guarnieri G, Morelli A, Rastrelli G, Maseroli E, Cipriani S, Mello T, Galli A, Bruno BJ, Kim K, Vangara K, Papangkorn K, Chidambaram N, Patel MV, Maggi M, Vignozzi L. Treatment potential of LPCN 1144 on liver health and metabolic regulation in a non- genomic, high fat diet induced NASH rabbit model. *J Endocrinol Invest.* 2021 Oct;44(10):2175-2193. doi: 10.1007/s40618-021-01522-7. Epub 2021 Feb 13. PMID: 33586025; PMCID: PMC8421272. [IF 5.467]
- Guarnieri G, Becatti M, Comeglio P, Vignozzi L, Maggi M, Vannelli GB, Morelli A. Benzo[a]pyrene impairs the migratory pattern of human gonadotropin-releasing- hormone-secreting neuroblasts. *Eur J Histochem.* 2021 Aug 13;65(s1):3282. doi: 10.4081/ejh.2021.3282. PMID: 34459573; PMCID: PMC8419627. [IF 1.966]
- Guarnieri G, Becatti M, Squecco R, Comeglio P, Garella R, Tamburrino L, Marchiani S, Vignozzi L, Vannelli GB, Maggi M, Morelli A. Effects of benzo[a]pyrene on the reproductive axis: Impairment of kisspeptin signaling in human gonadotropin-releasing hormone primary neurons. *Environ Pollut.* 2023 Jan 15;317:120766. doi: 10.1016/j.envpol.2022.120766. Epub 2022 Nov 29. PMID: 36460192. [IF 9.988]
- Guarnieri G, Sarchielli E, Comeglio P, Herrera-Puerta E, Piaceri I, Nacmias B, Benelli M, Kelsey G, Maggi M, Gallina P, Vannelli GB, Morelli A. Tumor Necrosis Factor α Influences Phenotypic Plasticity and Promotes Epigenetic Changes in Human Basal Forebrain Cholinergic Neuroblasts. *Int J Mol Sci.* 2020 Aug

- 25;21(17):6128. doi: 10.3390/ijms21176128. PMID: 32854421; PMCID: PMC7504606. [IF 6.208]
- Maseroli E, Cellai I, Filippi S, Comeglio P, Cipriani S, Rastrelli G, Rosi M, Sorbi F, Fambrini M, Petraglia F, Amoriello R, Ballerini C, Lombardelli L, Piccinni MP, Sarchielli E, Guarnieri G, Morelli A, Maggi M, Vignozzi L. Anti-inflammatory effects of androgens in the human vagina. *J Mol Endocrinol.* 2020 Oct;65(3):109-124. doi: 10.1530/JME-20-0147. PMID: 32755990. [IF 4.869]
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