Master Thesis

Gender in biobanking

Submitted by

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Statutory declaration

I declare on my own honour that I have written this dissertation independently and without other assistance, that no sources other than those cited were used and that the sources used verbatim or in substance have been marked as such.

Graz, June the 25th 2022

Clara Benna eh

To participants, without whom no biobank would be possible and not even this thesis, and to volunteers who donate their time, one of the few things in the world that is not refundable.

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ABBREVIATIONS

- ABNA Australasian Biospecimen Network Association
- AI/AN American Indian/Alaskan Native
- BBMRI-ERIC Biobanking and Biomolecular Resources Research Infrastructure-European Research Infrastructure Consortium
- BBMRI.IT Biobanking and BioMolecular resources Research Infrastructure - Italian node
- CATA Check All That Apply
- CATI Computer Assisted Telephone Interview
- CTRNet Canadian Tissue Repository Network
- EBW Europe Biobank Week
- GASV Gender as a Sociocultural Variable
- GBA German Biobank Alliance
- GEP Gender Equality Plan
- GGT Gender Gap Tracker
- GWAS Genome Wide Association Study)
- LGBT Lesbian, gay, bisexual, and transgender
- RORA Retinoic acid-related Orphan Receptor Alpha
- SABV Sex As Biological Variable
- WHO WORLD HEALTH ORGANIZATION
- WMA World Medical Association

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ABSTRAKT

Hintergrund

Umfangreiche Daten über die Ungleichheit der Geschlechter in Wissenschaft und Medizin haben zu dem Schluss geführt, dass sich die Diskriminierung aufgrund des Geschlechts weltweit negativ auf die öffentliche Gesundheit auswirkt. Biobanking wurde als Instrument für die Gesundheitsforschung entwickelt. Die Bedingungen für Frauen im Bereich des Biobankings wurde noch nie untersucht. Es wurde über geschlechtsspezifische Unterschiede bei der Teilnahme an Biobank-Projekten berichtet, was zu einer Fehlinterpretation der Daten führen kann. In zahlreichen Umfragen wurde die Bereitschaft zur Teilnahme an Biobanken untersucht, aber in keiner wurden geschlechtsspezifische Verzerrungen berücksichtigt. Ziel dieser Studie ist es, die Beziehung zwischen Geschlecht und Biobanking zu beschreiben, indem die Sichtweise der Mitarbeiter*innen von Biobanken und die Bereitschaft der Spender*innen zur Teilnahme in Bezug auf das Geschlecht untersucht werden.

Methoden

Biobanken wurden befragt, um die Arbeitsbedingungen der Mitarbeiter*innen zu beurteilen; Biobank-Websites wurden durchsucht, um das Geschlechterverhältnis in der Leitung zu bewerten. Die Teilnahmebereitschaft der Spender*innen wurde durch eine systematische Durchsicht der Literatur über die Bereitschaft zur Teilnahme an Biobanken zwischen 2018 und 2022 ermittelt.

Ergebnisse

Insgesamt füllten 212 (21,9 %) Biobanker den Fragebogen aus. Die meisten Befragten stammten aus Europa, in leitender Position n=85 (40,3 %) und in einem öffentlichen Umfeld n=164 (77,4 %). 69,8 % der Befragten waren weiblich, 33 % von ihnen waren Führungskräfte; von den 28,3 % männlichen Befragten waren 57 % Führungskräfte. Es wurden keine geschlechtsspezifischen Unterschiede bei der vertraglichen

Wochenarbeitszeit, den monatlichen Überstunden und der allgemeinen Arbeitszufriedenheit und -unzufriedenheit festgestellt. Ein hochsignifikanter Unterschied wurde bei der Wahrnehmung von Diskriminierung festgestellt. Frauen fühlten sich bei Einstellungsmöglichkeiten, Karrierechancen und dem Verhalten der Vorgesetzten ihnen gegenüber in Bezug auf die Berücksichtigung von Ideen/Vorschlägen und Bedürfnissen/Beschwerden diskriminiert.

Bei der systematischen Überprüfung wurden 18 Studien analysiert. Die Mehrheit der Befragten waren Frauen (60,5 %), und die durchschnittliche Spendenbereitschaft lag bei 73 %. Neun Studien (50 %) berichteten über aussagekräftige Zusammenhänge zwischen dem Geschlecht und dem spezifischen Ergebnis der Studie in engem Zusammenhang mit der Bereitschaft zur Probenspende. In fast allen diesen Studien waren Männer eher bereit, Proben zu spenden.

Schlussfolgerungen

Diese Ergebnisse stützen die Hypothese, dass es geschlechtsspezifische Verzerrungen in Biobanken gibt; allerdings sollte diese Arbeit als Pilotstudie betrachtet werden, die bei der Konzeption einer möglichen zukünftigen Hauptstudie helfen könnte.

ABSTRACT

Background

Extensive data on gender inequality in science and medicine has led to the conclusion that gender discrimination is negatively affecting public health worldwide. Biobanking was born as a tool for health research. The conditions of women in the biobanking field have never been studied. Gender biases have been reported in participation in biobank-related projects, potentially leading to misinterpretation of data. Numerous surveys explored the willingness to participate in biobanks but none looked at gender biases. The purpose of this study is to describe the relationship between gender and biobanking by assessing the views of biobank employees and the donors' willingness to participate in relation to gender.

Methods

Biobanks were surveyed to appraise employees' working conditions; biobank websites were searched to evaluate gender ratios in the leadership. Donors' willingness to participate was assessed via a systematic review of the literature regarding willingness to participate in biobanks between 2018 and 2022.

Results

Overall, a total of 212 (21.9%) biobankers completed the questionnaire. The main respondents were from Europe, in leadership n=85 (40.3%), and in a public setting n=164 (77.4%). Females accounted for 69.8% of the respondents with 33% of them being managers; of the 28.3% male responders, 57% were managers. No gender differences were identified in the contractual working hours per week, the monthly overtime hours, and the overall job satisfaction and dissatisfaction. A highly significant difference was identified in the perception of discrimination. Women felt negatively discriminated against in hiring opportunities, career opportunities, and the superiors' behavior toward them in how ideas/proposals, and needs/complaints were taken into consideration.

In the systematic review, 18 studies were analyzed. The majority of the respondents were women (60.5%) and the average willingness to donate was 73%. Nine studies (50%)

reported meaningful associations between gender and the specific outcome of the study in close relation to the willingness to donate specimens. Men were found more willing in nearly all those studies.

Conclusions

These results support the hypothesis that there are gender biases in biobanks; however, this thesis should be considered a pilot study, which might help design a possible future main study.

INTRODUCTION

Gender equality in science, medicine, and global health

A gender disparity exists worldwide in science and medicine. Many authors described, analyzed, and reported data on gender inequality and concluded that gender discrimination at different levels is negatively affecting public health (Clark et al., 2017; Shannon et al., 2019; Tricco et al., 2020).

According to the High-Level Commission on Health Employment and Economic Growth, gender biases in the health sector "*undermine inclusive economic growth, full employment, decent work and the achievement of gender equality. They also create inefficiencies in health systems by limiting the productivity, distribution, motivation and retention of female workers, who constitute the majority of the health workforce*" (WHO, 2016). Low morale, low self-esteem, and decreased productivity are all related to gender discrimination (Newman, 2014). There is the potential for significant improvements in health, society, and the economy as a result of gender equality in science, medicine, and global health. Additionally, there is evidence that gender-diverse workplaces increase productivity, innovation, decision-making, employee retention, and satisfaction, mainly in the business and management sectors. Institutions with a greater gender diversity are more likely to perform better (Hunt et al., 2015). The same may be true in science, medicine, and global health. A more varied research team may provide more complex and pertinent research questions, leading to research that is applicable (and helpful) to a larger community. Improved patient outcomes could result from a more gender-diverse medical workforce. Records suggest that various patients prefer to be treated by a particular gender of doctor, which is crucial for ensuring that everyone has access to care (Cooper-Patrick et al., 1999). According to a study, women treated by male doctors had greater fatality rates than women treated by female doctors for acute myocardial infarction. If male doctors were exposed to more female patients and medical colleagues, the effect was lessened (Greenwood et al., 2018).

Gender equality in academia

In the academic setting, for example, the number of females enrolled in university in science and medicine exceeds the number of males; nevertheless, 72% of the scientific work positions are occupied by males (UNESCO, 2015). In 2013, only 36% of European mid-ranking professors and 18% of full professors were women. In health, the situation is comparable, the workforce is constituted prevalently by females (75%), but the proportion of women in apical positions is not representative of the number of employees (Vernos, 2013). Moreover, according to a UK research, female doctors' earnings are 40% less compared to their male colleagues (Rimmer, 2016). The situation is worse for some disciplines, as surgery (Lucidi et al., 2022). Women are typically given smaller research grants than men and only 12% of members of national science academies are female, according to UN statistics (United Nations, 2022). This concept is summarized in the metaphor of the "glass ceiling", *an unrecognized barrier to the advancement of a profession, which mainly affects women and minorities* (Oxford Languages, 2022).

In my institution, University of Padua, the first woman in the world was graduated in philosophy (1678), Elena Lucrezia Cornaro Piscopia. In 2021, the first female rector in the 800-hundred-year history of the University of Padua was elected. Regarding gender equality, the situation is improving over the years. The photograph of the employees of the University of Padua as of December 31st, 2019 displays a situation of substantial numerical parity between male and female presences, albeit with a slight prevalence of the latter. However, it still confirms disparities in both career tracks in university and academia. The female presence among the teaching staff shows a slight increase thanks to recent recruitments (women are 39% of the new teachers), and continues to taper off at higher academic career levels (female full professors are 23.8%). The same dynamic manifests at the level of the administrative and technical staff, compared to a female majority in all categories except in the top one. A look at the registrations highlights one uneven distribution of the population of students with respect to the subject areas. It confirms the phenomenon of horizontal segregation in university careers. The students in scientific disciplines and technology are mostly males, while students in the fields of education, social, medical-health and humanities disciplines are mostly females. This trend persists in doctoral programs and academic careers as well (University of Padua, 2020).

Transgender and gender-diverse persons in science and health

So far, there are only a few data on transgender persons in science. However, according to a study on nonbinary transgender people in the workplace, analyzing outcomes from the US National Transgender Discrimination Survey, transgender people suffer from higher levels of prejudice in employing and experience differential treatment after being hired (Davidson, 2016). Lesbian, gay, bisexual, and transgender (LGBT) people report barriers to healthcare access, according to the European survey FRA 2013 study. Due to their reports of being disregarded and real or anticipated negative reactions, 30% of LGBT women and 23% of LGBT men reported difficulty using or receiving healthcare services (FRA, 2013; FRA, 2016). Lesbian, gay, and bisexual people are 1.5 times more likely to report having had a negative experience with primary care than the overall population, according to the Health4LGBTI survey from 2017 (Franklin et al., 2021).

Promotion of gender equality in science, medicine, and global health

Many organizations are promoting gender equality in science, medicine, and global health and this trend has increased over the years. The WMA (World Medical Association) Statement on the access of women and children to health care was adopted by the 49th WMA General Assembly (Hamburg, Germany) in 1997 and revised twice in 2008 and 2019. The WHO selected a set of tools for gender analysis in health and criteria for assessing programs and policies (WHO, 2002; WHO, 2011).

The European Commission's Gender Equality Strategy 2020-2025 set out the Commission's broader commitment to equality across all EU policies. Because of the peculiarities of the research sector, specific actions were developed to overcome persisting gender gaps. The European Commission addressed these barriers through the main funding instrument (2014-2020) within the European Research Area in collaboration with member countries and research organizations. Therefore, in Horizon Europe gender equality is taken into consideration on three main levels (quoting verbatim) (EU Commission, 2022):

- *having a Gender Equality Plan (GEP) in place becomes an eligibility criterion for certain categories of legal entities from EU countries and associated countries;*
- *the integration of the gender dimension into research and innovation content is a requirement by default, an award criterion evaluated under the excellence criterion, unless the topic description explicitly specifies otherwise;*
- *increasing gender balance throughout the programme is another objective, with a target of 50% women in Horizon Europe related boards, expert groups and evaluation committees, and gender balance among research teams set as a ranking criterion for proposals with the same score*.

The Biobanking and Biomolecular Resources Research Infrastructure-European Research Infrastructure Consortium BBMRI-ERIC very recently published a gender equality plan and appointed a gender equality and diversity specialist. Quoting verbatim: "*BBMRI-ERIC believes that gender equality benefits research and innovation by improving the quality and relevance of the research process, by attracting and retaining more talent, and by ensuring that everyone can maximize their potential. As a result, BBMRI-ERIC aims at embedding gender equality principles in its organisational culture. Our goal is to make new treatments possible in the most inclusive way possible, making sure that women, men, nonbinary people, and the entire diversity spectrum are equally taken into account*" (Cano Abadia, 2022).

The highest-rated scientific journals have addressed this topic: an example is the "call for papers" for the journal The Lancet in 2017 (Clark et al., 2017) regarding "Women in science, medicine, and global health". In this call, the editors stated that gender prejudice is pervasive and sneaky. It is a manifestation of the unequal distribution of power in nations as well as the low regard in which women are held for their labor and contributions to public life. Women are perceived as less valuable and competent than men for a variety of reasons, including innovation, entrepreneurship, and leadership, and both male and female raters exhibit these biases. Noteworthy is the Frontiers Forum "Women in Science" (#WomeninScience, 2022) which features a selection of research and interviews by leading female scientists.

Women are quoted far less frequently than men in the news media. Since October 2018, seven Canadian news websites have been monitored by the Gender Gap Tracker (GGT), an automated technology developed by a team at Simon Fraser University in Burnaby, Canada. The GGT discovered that 71% of interviewees quoted in articles were men (Asr et al., 2021). Additionally, the Global Media Monitoring Survey stated that only 25% of news sources and subjects in 2020 were female, an increase from only 17% in 1995, when the project first started (Nature Editorial, 2021). The editorial of June 24th 2021 in the journal Nature was dedicated to gender bias in Nature's journalism (Nature Editorial, 2021). Men made up over 69% of the direct quotes (excluding paraphrased comments) in Nature's journalistic pieces, according to a software study of the gender of individuals cited in over 16,000 articles in the Nature News, Features, and Careers sections between 2005 and 2020. Generally speaking, the proportion of men being quoted in Nature's journalism has been decreasing. Before 2017, it was around 80%, and it was 87% in 2005 (Nature Editorial, 2021). However, according to Squazzoni and colleagues, who examined gender bias in peer review with data for 145 journals in various research fields, including approximately 1.7 million authors and 740,000 reviewers, peer review and editorial processes do not penalize women's manuscripts (Squazzoni et al., 2021).

Why stratifications by sex and gender matter in science

Gender is a social construct that intersects with, but differs from, biological sex. It refers to the socially constructed norms, roles, behaviours, attributes and relations that a given society considers appropriate for women and men. Sex refers to the biological characteristics of an individual (Madsen et al., 2017).

The U.S. Institute of Medicine (IOM, now the Academies of Science) acknowledged nearly 20 years ago that gender interacts with sex to influence health and disease processes throughout the lifespan in addition to the biological importance of sex in determining health outcomes (Klein et al., 2015; Wizemann and Pardue, 2001). The US National Institutes of Health (NIH) has mandated the inclusion of sex as a biological variable (SABV-2016) (Nielsen et al., 2021), and both the Canadian Institutes of Health Research (2010) (CIHR, 2018) and the European Commission (2014) have endorsed integrating sex and gender (typically expressed as male/female binaries) into health research in the past

ten years (Nielsen et al., 2021). However, gender is rarely taken into account in biological literature today (Madsen et al., 2017) and sex and gender are frequently improperly combined. Very recently, it has been proposed to add Gender as a Sociocultural Variable (GASV) as a complement to SABV (sex as biological variable) (Nielsen et al., 2021).

In mice, for decades the belief that females are inherently more variable than males and must be evaluated at each of the four stages of the estrous cycle in order to produce trustworthy data caused the underrepresentation of female mice in neuroscience and biomedical research (Prendergast et al., 2014). Prendergast and colleagues in 2014 discovered that, for all endpoints, variability was not significantly higher in females than in males, although it was significantly higher in males for a number of features (Prendergast et al., 2014). Therefore, female mice were more frequently employed in research; an example is a recent study by Poley and colleagues, which showed that chemotherapeutic nanoparticles accumulate in the female reproductive system during ovulation affecting fertility and anticancer activity (Poley et al., 2022). Furthermore, it was shown that the sex of the researcher performing the experiments is relevant as the rodents exhibited different behaviors with the sex of the researcher. Sorge and colleagues found that exposure of rodents to male but not female experimenters produced pain inhibition. Indeed, olfactory exposure to male-related stimuli, including the presence of men, causes stress and related analgesia (Sorge et al., 2014). The inclusion of both sexes in animal experiments helped unveil seemingly inconsistent results on pain management. After decades of assuming that pain processing is equivalent in all sexes, scientists found that different biological pathways can produce pain (Dance, 2019). The study might pave the way for fresh medicinal developments. These are desperately needed because 20% of the global population face chronic pain and the majority are women. The pharmaceutical industry currently provides the same painkillers to everyone. However, if each person's pain has a unique set of causes, some medications may perform better for some than others (Dance, 2019).

Gender and sex interaction should be taken into consideration. Pain is experienced differently by males, women, and people of different genders (Schiebinger, 2022). They frequently communicate pain in different ways and could get different treatments. Better health outcomes might result from a deeper comprehension of sex and gender

differences in pain. The way that pain is seen, a patient's willingness to report discomfort, and how medical personnel handles pain can all be impacted by gender stereotypes. For instance, compared to men, certain healthcare professionals categorize pain in women as psychological discomfort more frequently (Schiebinger, 2022).

Communication should also be considered as a sex and gender interaction that might improve patient outcome. In a meta-analysis on the gender effect on medical communication, female primary care physicians had a more patient-centered communication style and had longer visits, but there was no gender difference in the quality of information conveyed to patients (Roter et al., 2002).

The use of digoxin is a historical example from the 1990s of how not considering sex as a variable in studies has led to serious public health consequences. In fact, the Digitalis Investigation Group trial provided for a disproportionate number of males to limit the effects of hormonal cycles on research topics (Rathore et al., 2002). Digoxin medication did not lower overall mortality rates among patients with heart failure and reduced left ventricular systolic function, according to the Digitalis Investigation Group trial, but it did marginally lower hospitalizations. Sex-based differences in the impact of digoxin were not considered, despite the fact that the epidemiologic characteristics, etiology, and prognosis of heart failure differ between men and women. In early 2000, digoxin therapy was found to have different effects on males and females (Rathore et al., 2002). In women, but not in men, with heart failure and impaired left ventricular systolic function, digoxin medication was associated with an increased risk of death from any cause. In particular, women who received digoxin by random assignment had a greater death rate than women who received a placebo (Rathore et al., 2002).

The long-held belief that osteoporosis affects mostly post-menopausal women has influenced how it is detected, diagnosed, and treated. After the age of 75, males account for one-third of all hip fractures caused by osteoporosis, and when they break their hips, they die more frequently than women (Franklin et al., 2021). Although there are a lot of men who have osteoporosis, the early diagnostics for the condition were created on young, white women (aged 20-29 years) and criteria to identify risk in men are not well established (Szulc et al., 2012). Men are still diagnosed using the female diagnostic cut-off

rate, this has not yet been updated, despite the fact that a reference population for men has been established (Looker et al., 1997). The diagnosis of osteoporosis in various populations of women and men is still under investigation. Overall, osteoporosis is a condition that affects both men and women equally, as bones are produced by both biology and culture, including activity levels, diet, and general lifestyle. The variations in osteoporosis rates between ethnic groups could be explained by these lifestyle variations (Schiebinger, 2022).

Finally, in addition to male osteoporosis, late diagnosis is common in females for bladder cancer and hematuria, often treated as cystitis, and for asthma where symptoms are different in males and females, wheezing more frequent in young males, dry nocturnal cough in young women (Oertelt-Prigione, 2014). For multiple sclerosis, males are more likely to be referred to an orthopedic surgeon and females to a psychiatrist, if not diagnosed correctly (Oertelt-Prigione, 2014).

A very recent example affecting world health is the COVID-19 pandemic. Although sex and gender differences affect the incidence of SARS-CoV-2 infection and COVID-19 mortality and, furthermore, sex differences affect the frequency and severity of drug side effects, a serious lack of consideration of sex and gender in clinical trials of COVID-19 persists. During 2020, of the 4,420 SARS-CoV-2/COVID-19 studies registered, 935 (21.2%) dealt with sex/gender exclusively in the context of recruitment, 237 (5.4%) planned gender-matched samples or representatives or emphasized sex/gender ratios and only 178 (4%) explicitly reported a plan to include sex/gender as an analytic variable. Only eight (17.8%) of the 45 clinical trials related to COVID-19 published in scientific journals reported sex-disaggregated results or subgroup analyses (Brady et al., 2021).

I personally experienced the importance of sex/gender subgroups in a recent study regarding genetic variants of circadian clock genes that influence melanoma susceptibility. The pooled data revealed no significance and most likely the effect was masked. Only after subgrouping by age and sex, we found significant effects of two genetic variants of the RORA clock gene, which could influence the predisposition to develop cutaneous melanoma in a gender-specific way. In particular, one variant was statistically significantly associated only in women, the other only in men (Benna et al., 2021).

Sex and gender are also relevant to new approaches and challenges to personalized medicine, such as in kidney transplantation using 3D bio-printed kidneys or in biomedicine and artificial intelligence healthcare. Gender and sex considerations should be included at every stage of development and use of 3D bioprinted kidneys: in the choice of design, cells, biomaterials and X-activated cells (Cirillo et al., 2020; van Daal et al., 2020).

Why stratifications by sex and gender matter in biobanking

Biobanking was born as a tool for health research. The term "biobank" was used for the first time in 1996 by Loft and Poulsen (Loft and Poulsen, 1996) in a publication regarding oxidative DNA damage in cancer. Nevertheless, the collection of human biological material with the purpose of a specific research, taking advantage of "left-over" material in clinical practice, began far before (Eiseman and Haga, 1999). Laboratories in which the researcher stored human samples in freezers were set up in the vicinity of the surgery rooms and associated data were annotated in notebooks. Biobanks evolved over time following stakeholders' needs and local regulations and today a large part of them are institutions with independent management. However, there is a tight and long-established connection between biobanking and clinical practice. While the work conditions of women in health care have been studied lately from different points of view, as students, workers, residents, and patients, the conditions of women in biobanking, to the best of my knowledge, have never been assessed.

Gender biases have been reported in participation in biobanks. A recent study included 3.3 million participants and was one of the largest GWAS (Genome Wide Association Study) so far. It was conducted by an international collaboration involving researchers and biobank cohorts from Denmark (iPSYCH), Finland (FinnGen), Japan (Biobank Japan), United Kingdom (UK Biobank), and United States (23andMe), and identified a widespread sex-differential participation bias (Pirastu et al., 2021). Researchers concluded that biases could potentially lead to misinterpretation of data when inferring results in downstream analyses and proposed two statistical methods to overcome this issue. GWAS was employed for the first time to detect participation biases, which may correlate with the complex trait being analyzed. They reported an example: "*females with higher genetic susceptibility to obesity are less likely to participate in studies than their male*

equivalents (or that genetically lean males are more likely to)" (Pirastu et al., 2021). In this view, it is worth analyzing the gender differences in the willingness to participate in biobanks. Several surveys explored the willingness to participate in biobanks, from different perspectives but none, as far as I know, specifically on gender bias.

Biobanks generally do not collect demographic data on transgender and gender-diverse people (TGDs), so research on cancer risk and the biological impact of gender-affirming therapies could be hampered. In a recent survey delivered to principal investigators in biobanks regarding the knowledge, attitudes, and research behaviors about transgender and gender-diverse patients (Jones et al., 2020), it was reported that among the 47 respondents, there was a high agreement (77%) on the importance of collecting TGD identities and gender-affirming treatment histories with biological samples. However, respondents self-reported low rates of biorepositories allowing for the entry of TGD identities (14.9%) and histories of gender-affirming interventions (8.5%).

It should also be taken into account that humans are not so absolutely dimorphic with regard to the composition of the sex chromosomes, the structure of the gonads, the hormonal levels and the structure of the internal genital duct and external genital systems. According to a systematic review of the medical literature from 1955 to 2000, including studies on the frequency of deviation from the ideal male or female, the frequency can be as high as 2% of live births. The frequency of individuals undergoing "corrective" genital surgery, however, is likely to be between 1 and 2 in every 1,000 live births (Blackless et al., 2000). Additionally, age-related monosomy has been reported in peripheral cells during life in which XX cells tend to lose an X, a phenomenon that can increase the risk of autoimmune diseases (Blackless et al., 2000).

There are additional pre-analytical factors to be considered in the context of sex when collecting samples. Here is an example. There are not many blood biomarker tests used in clinical practice, and recent revelations about the low reproducibility of biomarker research have raised concern. Ramsey and colleagues examined the potential contributions of women's sex and hormonal status to this pervasive irreproducibility. In 1,676 patients in the Dutch Depression and Anxiety Study, 171 serum proteins and small molecules were analyzed. Concentrations of 66 molecules varied among oral contraceptive pill users, postmenopausal women, and women in the follicular and luteal

phases of the menstrual cycle, and concentrations of 96 molecules varied with sex (Ramsey et al., 2016).

All of these examples underscore the relevance of including a representative sample in clinical trials and of offering disaggregated data analyzing sex, gender and sex-gender interactions in clinical research and thus in biobanks.

Aim of the study

The purpose of this study is to describe the relationship between gender ad biobanking. The overarching points are:

- ✓ to assess the views of biobank employees, including their work organization, personal satisfaction and dissatisfaction in the workplace, work-life balance, gender balance, and their perception of discrimination. A questionnaire was sent to biobanks and biobankers to appraise employees' working conditions, and biobank websites were searched to evaluate gender ratios in the leadership;
- ✓ to assess the donors' willingness to participate or to withdraw participation in relation to gender via a systematic review of the literature on studies regarding biobank awareness and willingness to participate in biobanks between 2018 and 2022.

METHODS

Survey

The delivered survey was designed to assess the working conditions of employees working in biobanks with special attention to gender equality. It was completely anonymous unless the respondent voluntarily wrote personal or contact information in the comment field. The questionnaire was coded in English via Google Forms and delivered by email directly to personnel working in the biobanking field at any level or to the different biobanks through the "contact" email address. To maintain the anonymity of the interviewees, I took advantage of several Google Forms options, therefore: I could not trace who filled out the questionnaire, it was not necessary to register on Google, and it would have been possible to fill in the questionnaire an infinite number of times. The survey was initiated on the 22nd of January 2022 and closed on the 22nd of March 2022 for a total of 8 weeks. A reminder was sent two weeks before the closure.

It was structured in 25 items divided into 7 sections: Demographic assessment, Biobank characteristics, Job organization, Personal satisfaction, Work-life balance, and gender balance, Discrimination, and Comments. A supplementary section with three questions was delivered only to managers to assess the presence of females in the management area and called Gender balance of the biobank. The questions were either multiple choice with only one possible answer or with all the possible answers with the "check all that apply" (CATA) format. In the majority of the questions, there was also the possibility to freely write. All questions were mandatory and could not be skipped; however, the answers "I am not sure" and/or "Other" were provided. The definition of gender was taken from The Center for Diversity and Inclusion (American University, 2022). For the Questionnaire Table see appendix.

Participants search

E-mail addresses were searched among the lecturers and the participants to the: BIKE Summer School - Fundamentals of Biobanking and Cohort Research (Groningen, Netherlands, 2017); Advanced Course - How to Operate a Biobank Sustainably Successful, Medical University of Graz (Graz, Austria, 2020); MSc Biobanking, Medical University of Graz (Graz, Austria, 2020); Europe Biobank Week 2021 (EBW virtual

edition). Moreover, the biobank locators of different biobank networks and societies were interrogated. They were:

- The Central Executive Management Office of BBMRI.ERIC (Biobanking and BioMolecular resources Research Infrastructure – European research Infrastructure Consortium) (BBMRI-ERIC Staff, 2022)
- Directory of the Italian node of BBMRI.ERIC, BBMRI.IT (Biobanking and BioMolecular resources Research Infrastructure - Italian node) (BBMRI.it, 2022)
- The Biobank Locator of the Biobank Resource Center (Biobank Resource Center, 2022) developed by The University of British Columbia (UBC) Office of Biobank Education and Research (OBER) and CTRNet (Canadian Tissue Repository Network)
- The registry of the Finnish biobanks, Suomen Biopankit (Finnish Biobanks, 2022)
- The Australasian member biobanks of ABNA (Australasian Biospecimen Network Association) (ABNA Australasian Biobanks, 2022)
- German Biobank Alliance (GBA) of The German Biobank Node – GBN (BBMRI.DE, 2022)

Further contacts were found among the corresponding authors of the papers included in the systematic review section of the present thesis and in the cited references regarding the biobanking activity. The social networking site for the business community LinkedIn was also employed to find contacts. Finally, the biobanks employed for the websites search and the corresponding governance were directly contacted.

Statistical analysis

Descriptive statistics were employed to summarize participants' characteristics, frequencies and percentages. All study variables are described in Questionnaire Table, see appendix. The "check all that apply" (Hopper, 2019) questions were analyzed as follows. The raw data were downloaded from Google Forms as an Excel dataset. All the options chosen for each of the CATA questions were in the same column. After assigning a column per option, each option was dichotomized in a binary variable. When possible, two options were combined to create a categorical variable with three categories. For

example, referring to the question “Which of the following issues do you think makes your job difficult?” the answers “I am often ignored by my team” and “My colleagues do not support me” were combined to create the “team_coll_consider” variable. For analysis purposes, categorical variables with more than three categories were collapsed and recoded into binary variables. Stratification analyses were made by gender, age, area of employment, biobank type, biobank age, and country. Rcmdr: R Commander - R package version 2.7-2 was employed for the descriptive analyses of the data (Fox and Bouchet-Valat, 2021). The Fisher’s exact test and Pearson’s Chi-square test were used for statistical hypothesis testing to determine whether there was a statistically significant difference between the expected frequencies and the observed frequencies in one or more categories of the contingency tables obtained with the “Graphs and Tables” tools. For continuous variables, Kolmogorov-Smirnov test was employed to assess whether the data were well-modeled by a normal distribution. A p-value inferior to 0.05 was considered significant.

Biobanks website search

The objectives of the biobanks website search were to assess the presence of women in a leadership position in the biobanking field, the hiring policy of employees in terms of options offered to manage the employees’ life-work balance, and career opportunities.
The selection of the biobanks was made including “the 10 largest biobanks in the world”, according to the biobanking industry web portal Global Biobank Directory (Global Biobank Directory, 2022) and to the website “Global Engage” (Williams, 2018). Overall, they are:

1. Biobank Graz
2. Shanghai Zhangjiang Biobank
3. “All of Us” Biobank
4. The International Agency for Research on Cancer (IARC) Biobank (IBB)
5. China Kadoorie Biobank
6. UK Biobank
7. FINNGEN biobanks
8. Canadian Partnership for Tomorrow Project Biobank
9. Estonian Biobank
10. EuroBioBank network
11. BioBank Japan

12. CTB (Chernobyl Tissue Bank)
13. Victorian Cancer Biobank (Australia)

The data extracted were: country, year of foundation, governance (Steering Committee, and whenever present the Scientific Advisory Committee and the Ethics Committee), ratio between females/males in the committees inferred from the photos of each member, the advertising of a gender equality plan, the options to manage life-work balance and the opportunities for professional development.

For analysis purposes, the search was initiated on the 5th of January 2022 and closed on the 15th of April 2022.

Systematic review of the literature

The "*PRISMA 2020 statement: an updated guideline for reporting systematic reviews*" was followed and the PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only (Page et al., 2021) employed.

I considered eligible all the studies concerning the patients' engagement in biobanking, in particular, surveys on biobank awareness and willingness to participate in biobanks. Exclusion criteria were: papers written in a language other than English, records not reporting original data as reviews, surveys directed to biobanks not to hypothetical participants or actual participants, studies not clearly reporting the outcome of interest, studies with only one gender, and studies with overlapping datasets. A database search of original articles analyzing the patients' engagement in biobanking was conducted via the PubMed gateway and the portal Google Scholar. The search included the following two groups of keywords: biobank OR biobanking OR bioresource AND willingness OR participation AND awareness. The data extracted from eligible studies were: authors, title, journal, year of publication, aim of the study, region or country where the study was conducted, sample size, type of questionnaire, age, gender, ethnicity, inclusion criteria, education, number questions/items, and results. For analysis purposes, the search was restricted to the scientific papers published between 2018 and 2022 and closed on the 15th of April 2022.

RESULTS

Overall results of the survey

Overall, 893 biobankers and 117 biobanks were contacted for a total of 1010 e-mails sent. The distribution of the countries involved is summarized in the map in Figure 1, and the list in Table 1. 41 (4.1%) e-mails were undelivered, while 31 persons (3.1%) replied offering comments.

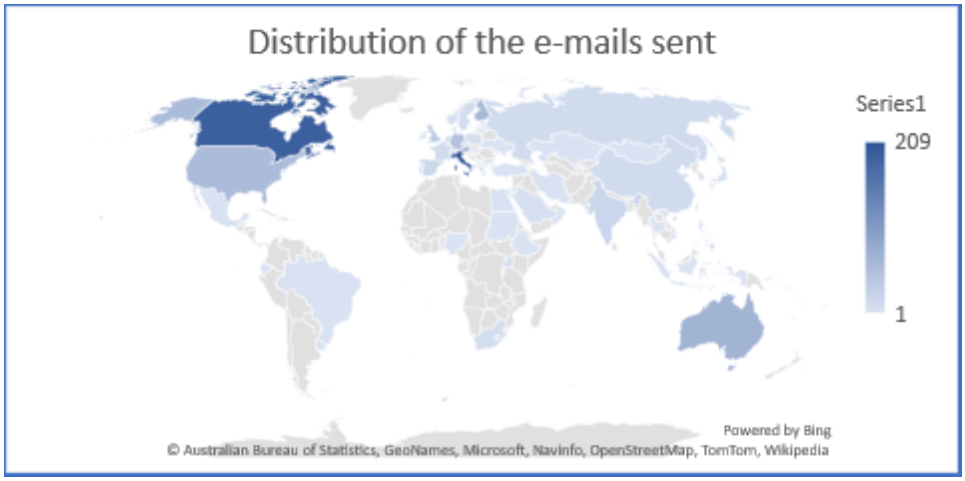

FIGURE 1. MAP OF THE COUNTRY DISTRIBUTION OF STAFF CONTACTED BY E-MAIL

Country	*n (%)*	*Country*	*n (%)*	*Country*	*n (%)*
Australia	70 (6.9)	*India*	20 (2.0)	*Saudi Arabia*	6 (0.6)
Austria	76 (7.5)	*Indonesia*	3 (0.3)	*Singapore*	3 (0.3)
Belgium	15 (1.5)	*Iran*	2 (0.2)	*Slovenia*	1 (0.1)
Brazil	2 (0.2)	*Ireland*	1 (0.1)	*South Africa*	9 (0.9)
Bulgaria	2 (0.2)	*Italy*	209 (20.7)	*South Korea*	1 (0.1)
Canada	193 (19.1)	*Japan*	8 (0.8)	*Spain*	19 (1.9)
China	13 (1.3)	*Jordan*	2 (0.2)	*Sudan*	1 (0.1)
Costa Rica	1 (0.1)	*Kazakhstan*	2 (0.2)	*Sultanate of Oman*	1 (0.1)
Cyprus	1 (0.1)	*Latvia*	1 (0.1)	*Sweden*	11 (1.1)
Czech Republic	3 (0.3)	*Lithuania*	1 (0.1)	*Switzerland*	6 (0.6)
Denmark	3 (0.3)	*Malta*	2 (0.2)	*Thailand*	1 (0.1)
Ecuador	1 (0.1)	*Mexico*	3 (0.3)	*The Netherlands*	36 (3.6)
Egypt	3 (0.3)	*Mongolia*	1 (0.1)	*Trinidad and Tobago*	1 (0.1)
Estonia	2 (0.2)	*Nigeria*	1 (0.1)	*Turkey*	2 (0.2)
Ethiopia	1 (0.1)	*Norway*	5 (0.5)	*Uganda*	5 (0.5)
Finland	63 (6.2)	*Philippines*	1 (0.1)	*UK*	39 (3.9)

Country	*n (%)*	*Country*	*n (%)*	*Country*	*n (%)*
France	13 (1.3)	*Poland*	7 (0.7)	*Ukraine*	2 (0.2)
Gambia	1 (0.1)	*Portugal*	2 (0.2)	*Uruguay*	1 (0.1)
Germany	50 (5.0)	*Puerto Rico*	1 (0.1)	*USA*	58 (5.7)
Greece	2 (0.2)	*Qatar*	2 (0.2)	*Vietnam*	3 (0.3)
Hungary	2 (0.2)	*Russia*	13 (1.3)		

TABLE 1. LIST OF THE COUNTRY DISTRIBUTION OF STAFF CONTACTED BY E-MAIL; N: NUMBER OF BIOBANKERS OR BIOBANKS CONTACTED BY E-MAIL

A total of 212 (21.9%) completed questionnaires were retrieved. The map of the distribution of the completed questionnaires is depicted in Figure 2.

FIGURE 2. MAP OF THE COUNTRY DISTRIBUTION OF THE COMPLETED QUESTIONNAIRES

The summary table of the respondents' characteristics is displayed in Table 2.

Characteristics of the respondents		*Overall, n=212*
Age, n (%)	Below 24	3 (1.4)
	25-34	42 (19.8)
	35-44	63 (29.7)
	45-54	56 (26.4)
	55-64	40 (18.9)
	Above 64	8 (3.8)
Gender, n (%)	Female	148 (69.8)
	Male	60 (28.3)
	Mixed	4 (1.9)
Area of employment, n (%)	Management	85 (40.3)
	Biologist	32 (15.2)
	Laboratory technician	27 (12.8)

Characteristics of the respondents		*Overall, n=212*
	Project/Data management	24 (11.4)
	Quality/Risk management	11 (5.2)
	Multiple areas	8 (3.8)
	Administration	4 (1.9)
	Principal Investigator	4 (1.9)
	Study nurse	4 (1.9)
	Training and education personnel	4 (1.9)
	ELSI	3 (1.4)
	Medical Doctor	3 (1.4)
	Information Technology (IT)	2 (0.9)

TABLE 2. SUMMARY TABLE OF THE RESPONDENTS' CHARACTERISTICS

Females were the majority accounting for 69.8% of the respondents and males were 28.3%. Four employees were either Gender Variant/Non-Conforming or preferred to describe themselves or not to answer. Referring to the area of employment, managers represented the vast majority of the respondents n=85 (40.3%) followed by biologists n=32 (15.2%) and laboratory technicians n=27 (12.8%). The least represented category was Information Technology with only two respondents (0.9%). Eight persons (3.8%) declared to work in more than one area embodying multiple professional figures.

In Table 3 the characteristics of the correspondent biobanks are summarized.

Characteristics of the Biobanks		
Biobank age, n (%)	Below 1 year	6 (2.8)
	1-5 years	44 (20.8)
	6-10 years	49 (23.1)
	11-15 years	57 (26.9)
	16-20 years	19 (9.0)
	More than 20 years	31 (14.6)
	I am not sure	6 (2.8)
Biobank type, n (%)	Public (Hospital and/or University-based)	164 (77.4)
	Private company/stand-alone	25 (11.8)
	Mixed	23 (10.8)
Country, n (%)	Italy	56 (26.4)
	Canada	22 (10.4)
	Australia	21 (9.9)
	Austria	13 (6.1)
	United States of America	11 (5.2)
	France	10 (4.7)
	Germany	8 (3.8)

Characteristics of the Biobanks

Norway	8 (3.8)
Russia	7 (3.3)
Sweden	6 (2.8)
Netherlands	5 (2.4)
Spain	5 (2.4)
Belgium	4 (1.9)
Cyprus	4 (1.9)
Denmark	4 (1.9)
Finland	4 (1.9)
Poland	3 (1.4)
United Kingdom	3 (1.4)
Lithuania	2 (0.9)
Philippines	2 (0.9)
Switzerland	2 (0.9)
China	1 (0.5)
Costa Rica	1 (0.5)
Ecuador	1 (0.5)
Gambia	1 (0.5)
India	1 (0.5)
Kazakhstan	1 (0.5)
New Zealand	1 (0.5)
Oman	1 (0.5)
Qatar	1 (0.5)
South Africa	1 (0.5)
Uganda	1 (0.5)
Ukraine	1 (0.5)

TABLE 3. SUMMARY TABLE OF THE SAMPLE BIOBANKS CHARACTERISTICS

The majority of the biobanks were public (Hospital and/or University-based) n=164 (77.4%) being the rest either owned by private companies (stand-alone) n=25 (11.8%) or mixed n=23 (10.8%). The mixed category included, for example, private university biobanks, biobanks in private hospitals, and biobanks of foundations.

For analysis purposes, the categories of categorical variables were reduced or recoded into binary variables. For gender analysis, only females and males were considered, being the mixed category underrepresented. In Table 4 a summary of the cohort's and the biobanks' characteristics used for the analyses is reported.

Respondent and biobank characteristics		*Overall, n=212*
Age, n (%)	Young (below 24 - 44 years)	108 (50.9)
	Senior (45 - above 64 years)	104 (49.1)
Gender, n (%)	Female	148 (69.8)
	Male	60 (28.3)
Area of employment, n (%)	Management	85 (40.3)
	Quality/Risk/Project/Data	35 (16.6)
	Biologist	32 (15.2)
	Multiple areas	32 (15.2)
	Laboratory technician	27 (12.8)
Biobank age, n (%)	Recent (less than 1 - 10 years)	99 (48.1)
	Long-lasting (11 - more than 20 years)	107 (51.9)
Biobank type, n (%)	Public (Hospital and/or University-based)	164 (77.4)
	Private company/stand-alone	25 (11.8)
	Mixed	23 (10.8)
Country, n (%)	Europe	81 (38.2)
	Italy	56 (26.4)
	Mixed	32 (15.1)
	Canada	22 (10.4)
	Australia	21 (9.9)

TABLE 4. SUMMARY OF THE COHORT'S AND THE BIOBANKS' CHARACTERISTICS

Job organization

In Figure 3 and Figure 4 are the pie charts representing the hours worked per week by contract and overtime hours per month are presented. The majority of the respondents (69.8%) worked 31-40 hours per week and worked overtime less than 5 hours per month (42.9%).

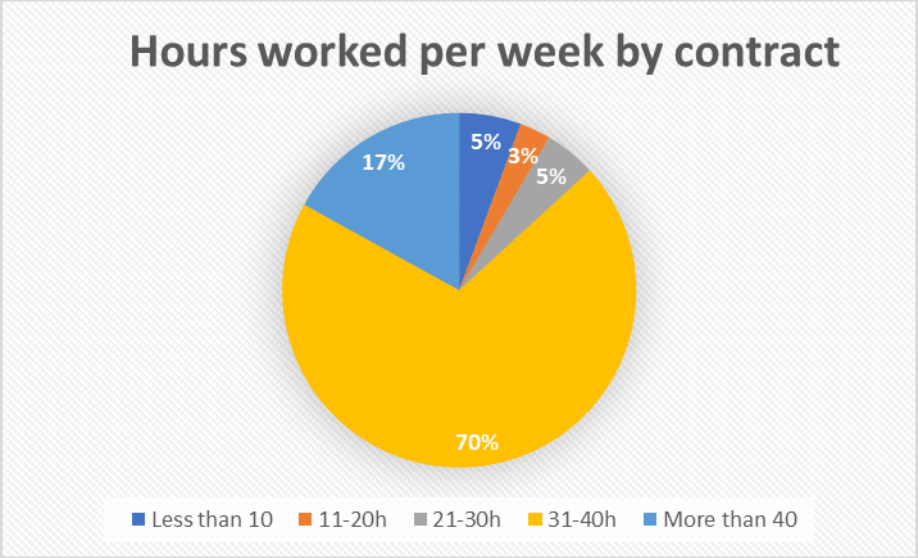

FIGURE 3. PIE CHART REPRESENTING THE HOURS WORKED PER WEEK BY CONTRACT

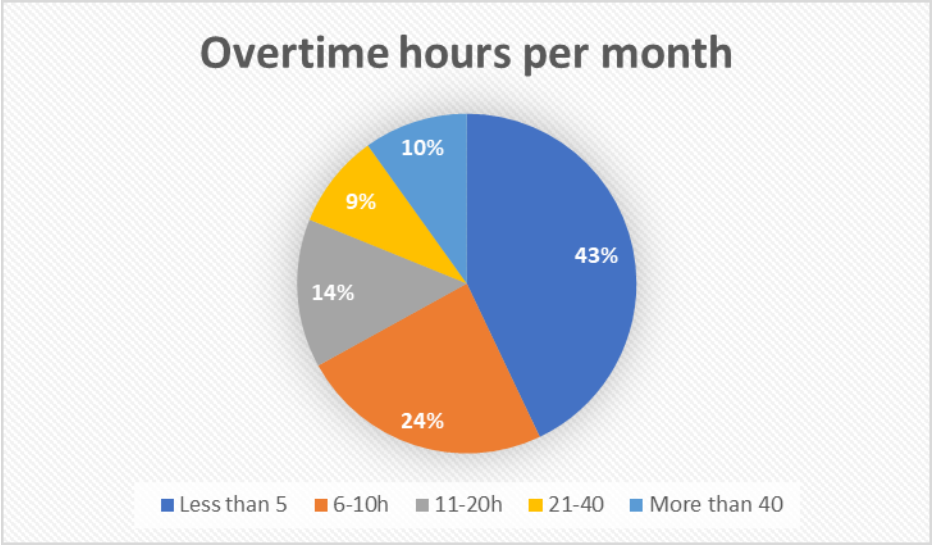

FIGURE 4. PIE CHART REPRESENTING THE OVERTIME HOURS PER MONTH

The majority of the respondents n=131 (62.4%) declared they have no particular issues in the workplace that make their job difficult, while the rest n=79 (37.6%) had issues at different levels.

In Table 5 the summary of the issues pinpointed by the biobankers of the present sample is reported.

Topic	*Answers*	*Overall, n=212 (%)*
Organizational and communication	Option not chosen	191 (91.0)
	Unsatisfactory (e.g. unclear roles, high workload)	14 (6.7)
	Lack of awareness of the importance of biobanking	5 (2.4)
Resources	Option not chosen	195 (92.9)
	Lack of resources (mainly personnel)	15 (7.1)
Superiors' qualification and careers opportunity	Option not chosen	179 (85.2)
	My superiors are less trained/qualified than me	18 (8.6)
	My superiors do not allow me to professionally grow	13 (6.2)
Superiors' consideration	Option not chosen	195 (92.9)
	I am often ignored by my superiors	15 (7.1)
Team and colleagues' consideration	Option not chosen	201 (95.7)
	My colleagues do not support me	6 (2.9)
	I am often ignored by my team	3 (1.4)
Physical strength and equipment	Option not chosen	190 (90.5)
	Insufficient physical strength	15 (7.1)
	Incorrect size/proportion of the equipment	5 (2.4)

TABLE 5. SUMMARY OF THE ISSUES CHOSEN BY THE BIOBANKERS. THE QUESTION WAS: "WHICH OF THE FOLLOWING ISSUES DO YOU THINK MAKES YOUR JOB DIFFICULT? CHECK ALL THAT APPLY"

The respondents identified issues in job organization and in communication, in particular, they found that unclear role definitions and high workload were the main reasons. Five respondents pinpointed that a lack of awareness of the importance of the biobanking field makes their job difficult. Lack of resources, mainly lack of personnel was an issue for 15 biobankers. Superiors' consideration, qualification, and career opportunities represented issues. In particular, 8.6 % of the respondents thought that superiors were not enough trained or qualified for the position and 6.2% that superiors did not allow a professional growth. Finally, 7.1% felt to be often ignored by superiors. Team and colleagues' considerations did not seem to be a major issue. On the other end, physical strength and equipment were chosen by 20 biobankers, insufficient physical strength being the most selected (7.1%).

Personal satisfaction

As displayed in the pie chart in Figure 5, 79% of the respondents were always or often satisfied with their job, the rest being satisfied sometimes. 3% were rarely or never

satisfied. The biobankers were satisfied or very satisfied with the tasks assigned (77%), outnumbering the biobankers who were neutral (19%) or unsatisfied (4%) as shown in Figure 6.

FIGURE 5. PIE CHART REPRESENTING THE OVERALL JOB SATISFACTION

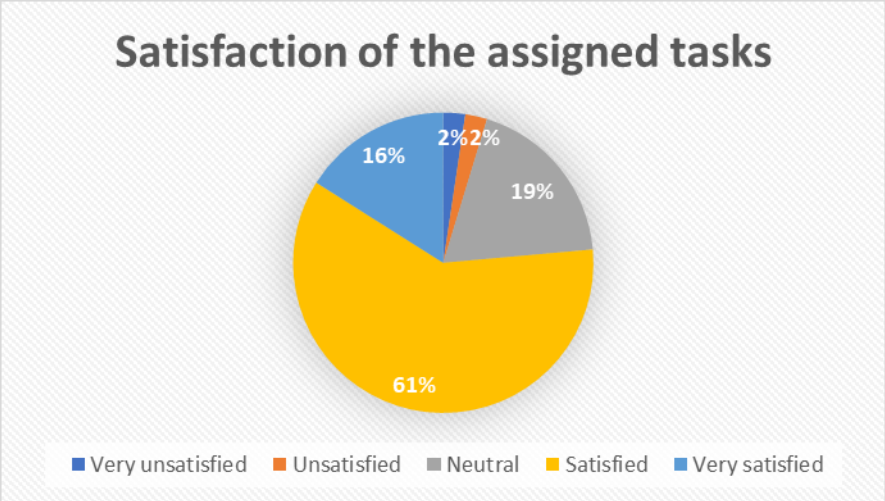

FIGURE 6. PIE CHART REPRESENTING THE SATISFACTION OF THE ASSIGNED TASKS

In Table 6 the reasons for satisfaction in the workplace are summarized. Most of the respondents n=199 (93.9%) felt satisfied with contributing to research, therefore only 13 individuals did not choose this answer.

Satisfaction reason	*Overall, n=212*
Contribution to research	199 (93.9)
Salary	65 (30.7)
Publications and scientific awards	57 (26.9)
Social prestige	38 (17.9)
Self-development	30 (14.2)
Teamwork and colleagues	20 (9.4)

TABLE 6. REASONS FOR SATISFACTION IN THE WORKPLACE. THE QUESTION WAS: "WHAT MAKES YOU SATISFIED WITH YOUR JOB? CHECK ALL THAT APPLY"

The second most frequent answer was "Salary", followed by "Publications and scientific awards". Although "Self-development" and "Teamwork and colleagues" were not offered in the original list of answers proposed in the survey, these two categories were added by combining answers written in the "Other [please specify]" field. In particular, "Self-development" includes "Participation in stimulating projects", "Patient assistance", "Training of young collaborators", "Recognition from supervisors" and similar.

In Table 7 the reasons for dissatisfaction in the workplace are summarized.

Dissatisfaction reasons	*Overall, n=201*
Too much bureaucracy	96 (47.8)
Few opportunities for career advancement	72 (35.8)
High workload	69 (34.3)
Salary too low	64 (31.8)
Life-work imbalance	49 (24.4)
Inadequate training	23 (11.4)
Overqualification for the job	17 (8.5)
Lack of awareness of the importance of biobanking and resources	17 (8.5)
Demotion	9 (4.5)

TABLE 7. REASONS FOR DISSATISFACTION IN THE WORKPLACE. THE QUESTION WAS: "WHAT MAKES YOU DISSATISFIED WITH YOUR JOB? CHECK ALL THAT APPLY"

201 (94.8%) employees experienced dissatisfaction in the workplace for different reasons, only 11 did not. Nearly half of the respondents, n=96, suffered from the level of bureaucracy, followed by the opportunities for career advancement considered scarce by 72 individuals, and the high workload, n=69. The least chosen option was demotion,

experienced by 9 individuals. The lack of awareness of the importance of biobanking and resources, deemed as issues in the previous section, was also a cause of dissatisfaction.

Life-work balance and gender balance

Just over half (56%) of the biobankers in this cohort was satisfied or very satisfied with the life-work balance, being the remaining neutral or unsatisfied, see Figure 7.

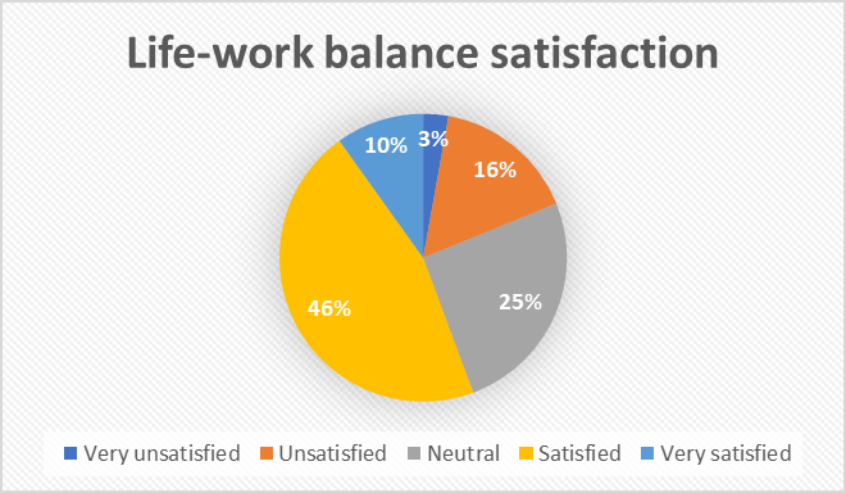

FIGURE 7. PIE CHART REPRESENTING THE SATISFACTION OF THE LIFE-WORK BALANCE

The options offered by the biobanks to the employees for achieving a sustainable work-life balance are listed in Table 8.

Options for achieving a sustainable work-life balance	*Overall, n (%)*
Flexible working hours	159 (82.0)
Maternity leave	145 (75.1)
Home office	100 (51.5)
Paternity leave	95 (49.0)
Part-time job	72 (37.1)
Smart working	49 (25.3)
Kindergarten on-site	22 (11.3)
No opportunities or I am not sure	18 (8.5)

TABLE 8. OPTION OFFERED FOR LIFE-WORK BALANCE. THE QUESTION WAS: "WHAT OPTIONS DOES YOUR BIOBANK OFFER TO ACHIEVE A SUSTAINABLE WORK-LIFE BALANCE? CHECK ALL THAT APPLY"

In Table 9 the actions taken by the biobanks to manage gender balance are listed.

Actions	*Overall, n (%)*
There is an "Equal Opportunity" plan, n (%)	57 (26.9)
There is a gender equality training for employees, n (%)	34 (16.0)
A gender balance report is periodically made, n (%)	11 (5.2)

TABLE 9. ACTIVITIES TO MANAGE GENDER BALANCE. THE QUESTION WAS: "HOW IS GENDER BALANCE TAKEN INTO CONSIDERATION IN YOUR BIOBANK? CHECK ALL THAT APPLY"

Figure 8 displays the distribution of the activities that the employees were offered to achieve a gender balance in their biobanks. For 31% (n=65) gender balance was not taken into consideration, while 24% (n=52) were not sure. 27% (n=58) were offered one of the activities listed in Table 8, 9% (n=19) were offered two activities, and 1% (n=2) all the three activities. The remaining 8% (n=16) declared that there was no need for different reasons or were offered different options such as, for example, a "Gender Unit" in place, an "Equal Opportunity Chairman" or the policy to use a gender-neutral language. Among the motivations for not needing gender balance actions was that gender balance was already in place or that there was no discrimination and all team members were treated with equal respect.

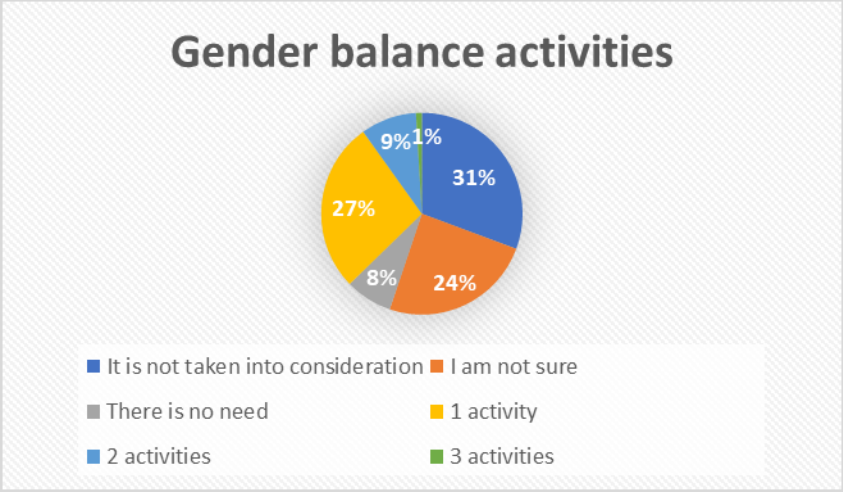

FIGURE 8. PIE CHART REPRESENTING THE DISTRIBUTION OF ACTIVITIES OFFERED TO EMPLOYEES TO ACHIEVE A GENDER BALANCE IN THEIR BIOBANKS.

Discrimination

In Table 10 the answers of the section dedicated to the discrimination assessment are summarized. Around 80% of the respondents did not feel discriminated against because

of their gender neither in hiring opportunities nor in superiors' behaviour, including how ideas/proposals or needs/complaints were taken into consideration. Nearly 86% did not feel discriminated by colleagues, while about 72% did not feel discriminated in career opportunities. Overall, the respondents who felt gender had an impact on those themes, thought it had a negative effect. The remaining felt it had a positive effect or, at times, had an influence on their lives both positive and negative.

		Overall, n=212 (%)
Hiring opportunities, n (%)	No	172 (81.1)
	Yes, negatively	30 (14.2)
	Yes, positively	7 (3.3)
	Sometimes, Maybe	3 (1.4)
Career opportunity, n (%)	No	152 (71.7)
	Yes, negatively	48 (22.6)
	Yes, positively	7 (3.3)
	Sometimes, Maybe	5 (2.4)
Colleagues' behaviour, n (%)	No	182 (85.8)
	Yes, negatively	17 (8.0)
	Yes, positively	4 (1.9)
	Sometimes, Maybe	9 (4.2)
Superiors' behaviour, n (%)	No	171 (80.7)
	Yes, negatively	21 (9.9)
	Yes, positively	11 (5.2)
	Sometimes, Maybe	9 (4.2)
Ideas/proposals consideration, n (%)	No	175 (82.5)
	Yes, negatively	19 (9.0)
	Yes, positively	7 (3.3)
	Sometimes, Maybe	11 (5.2)
Needs/complaints consideration, n (%)	No	172 (81.1)
	Yes, negatively	27 (12.7)
	Yes, positively	7 (3.3)
	Sometimes, Maybe	6 (2.8)

TABLE 10. DISCRIMINATION ASSESSMENT SUMMARY. THE QUESTIONS WERE: "DO YOU FEEL THAT YOUR GENDER AFFECTS YOUR HIRING OPPORTUNITIES? DO YOU FEEL THAT YOUR GENDER AFFECTS YOUR CAREER OPPORTUNITIES? DO YOU FEEL THAT YOUR GENDER AFFECTS YOUR COLLEAGUES' BEHAVIOUR TOWARDS YOU? DO YOU FEEL THAT YOUR GENDER AFFECTS YOUR SUPERIORS' BEHAVIOUR TOWARDS YOU? DO YOU FEEL THAT YOUR GENDER AFFECTS HOW YOUR IDEAS/PROPOSALS ARE TAKEN INTO CONSIDERATION BY YOUR SUPERIORS? DO YOU FEEL THAT YOUR GENDER AFFECTS HOW YOUR NEEDS/COMPLAINTS ARE TAKEN INTO CONSIDERATION BY YOUR SUPERIORS?"

Gender balance of the biobank

From the questionnaire delivered exclusively to the management level (n=85), it has been calculated that in the corresponding biobanks the median of employees was 7 [min 1, max 105], the median of women as employees was 5 [0, 53] and the median of women in a leadership position was 2 [0, 13]. The mean percentage of women was 67% ± 23% and the mean percentage of women in a leadership position was 23% ± 18%.

Results of the stratification analysis

There were no significant differences in the gender stratification of the occupational areas, as reported in Table 11, although it was possible to identify a trend. The low p-value was probably due to the difference in the management area where the percentage of males (56.7%) far exceeded that of females (33.3%).

		Females, n=148	*Males, n=60*	*p-value*
Area of employment, n (%)	Biologist	26 (17.7)	6 (10.0)	0.053
	Laboratory technician	19 (12.9)	6 (10.0)	
	Management	49 (33.3)	34 (56.7)	
	Multiple areas	25 (17.0)	7 (11.7)	
	Quality/Risk/Project/Data	28 (19.0)	7 (11.7)	

TABLE 11. AREA OF EMPLOYMENT: STRATIFICATION BY GENDER

Upon stratification by age, biobank age, and biobank type, there were no statistically significant differences, while when subgrouping by country, a significant difference was found, see Table 12. This was probably caused by a prevalence of males (48.3%) in the present cohort in Europe, nevertheless no further comparison was performed.

		Females, n=148	*Males, n=60*	*p-value*
Country, n (%)	Australia	16 (10.8)	5 (8.3)	0.012
	Canada	15 (10.1)	7 (11.7)	
	Europe	51 (34.5)	29 (48.3)	
	Italy	49 (33.1)	7 (11.7)	
	Mixed	17 (11.5)	12 (20.0)	

TABLE 12. COUNTRY: STRATIFICATION BY GENDER

Job organization

Although there were no gender differences in the number of hours worked per week by contract nor in the overtime hours per month, differences were detected when subgrouping by area of employment and by country, see Table 13 and Table 14.

		Biologist, n=32	*Laboratory technician, n=27*	*Management, n=85*	*Multiple areas, n=32*	*Quality Risk Project Data, n=35*	*p-value*
Overtime hours per month, n (%)	Less than 5	9 (28.1)	21 (77.8)	27 (31.8)	15 (46.9)	18 (51.4)	0.004
	6-10h	9 (28.1)	6 (22.2)	24 (28.2)	5 (15.6)	7 (20.0)	
	11-20h	7 (21.9)	0 (0.0)	17 (20.0)	2 (6.2)	4 (11.4)	
	21-40h	3 (9.4)	0 0.0)	6 (7.1)	5 (15.6)	5 (14.3)	
	More than 40	4 (12.5)	0 (0.0)	11 (12.9)	5 (15.6)	1 (2.9)	

TABLE 13. JOB ORGANIZATION: STRATIFICATION BY AREA OF EMPLOYMENT

		Australia, n=21	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Overtime hours per month, n (%)	Less than 5	9 (42.9)	17 (77.3)	38 (46.9)	12 (21.4)	15 (46.9)	0.008
	6-10h	8 (38.1)	4 (18.2)	19 (23.5)	14 (25.0)	6 (18.8)	
	11-20h	2 (9.5)	1 (4.5)	12 (14.8)	12 (21.4)	3 (9.4)	
	21-40h	1 (4.8)	0 (0.0)	4 (4.9)	10 (17.9)	4 (12.5)	
	More than 40	1 (4.8)	0 (0.0)	8 (9.9)	8 (14.3)	4 (12.5)	

TABLE 14. JOB ORGANIZATION: STRATIFICATION BY COUNTRY

No statistically significant difference was found in identifying issues when subgrouping by age, area of employment, biobank age, country, and gender. Nevertheless, a tendency could be seen in the stratification by gender of the topic “Superiors’ consideration”. The percentage of females (9.6%) that chose the answer “I am often ignored by my superiors” outnumbered that of the males (1.7%) and the p-value was 0.072.

Personal satisfaction

With regard to the overall satisfaction with the job, the subgroup analysis failed to detect any meaningful difference. On the other end, although there were no gender differences in satisfaction regarding the tasks assigned, the subgroup analysis by age, biobank age, and country revealed statistically significant differences, as shown in Table 15, Table 16, and Table 17.

Satisfaction with the assigned tasks	*Young, n=108*	*Senior, n=104*	*p-value*
Very unsatisfied, n (%)	0 (0.0)	5 (4.8)	0.019
Unsatisfied, n (%)	4 (3.7)	1 (1.0)	
Neutral, n (%)	23 (21.3)	17 (16.3)	
Satisfied, n (%)	69 (63.9)	59 (56.7)	
Very satisfied, n (%)	12 (11.1)	22 (21.2)	

TABLE 15. SATISFACTION WITH THE ASSIGNED TASKS: STRATIFICATION BY AGE

Satisfaction with the assigned tasks	*Recent, n=99*	*Long-lasting, n=107*	*p-value*
Very unsatisfied, n (%)	2 (2.0)	3 (2.8)	0.007
Unsatisfied, n (%)	5 (5.1)	0 (0.0)	
Neutral, n (%)	25 (25.3)	13 (12.1)	
Satisfied, n (%)	51 (51.5)	74 (69.2)	
Very satisfied, n (%)	16 (16.2)	17 (15.9)	

TABLE 16. SATISFACTION WITH THE ASSIGNED TASKS: STRATIFICATION BY BIOBANK AGE

Satisfaction with the assigned tasks	*Australia, n=21*	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Very unsatisfied, n (%)	0 (0.0)	3 (13.6)	1 (1.2)	0 (0.0)	1 (3.1)	0.033
Unsatisfied, n (%)	1 (4.8)	1 (4.5)	1 (1.2)	1 (1.8)	1 (3.1)	
Neutral, n (%)	3 (14.3)	0 (0.0)	14 (17.3)	12 (21.4)	11 (34.4)	
Satisfied, n (%)	15 (71.4)	13 (59.1)	50 (61.7)	35 (62.5)	15 (46.9)	
Very satisfied, n (%)	2 (9.5)	5 (22.7)	15 (18.5)	8 (14.3)	4 (12.5)	

TABLE 17. SATISFACTION WITH THE ASSIGNED TASKS: STRATIFICATION BY COUNTRY

In Figure 9 a bar graph of the subgroup analysis by gender of the reasons for satisfaction is displayed. There was a statistically significant difference in respect to the category “Self-development”. The percentage of females that considered self-development (17.6%) a satisfaction motivation for being a biobanker doubled that of their male colleagues (6.7%) with a p-value of 0.05.

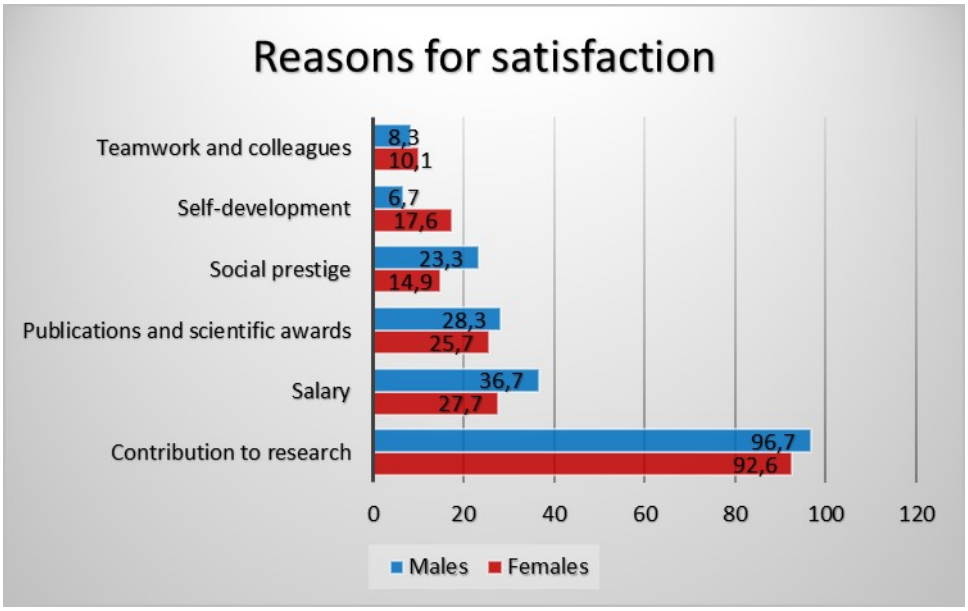

FIGURE 9. BAR GRAPH REPRESENTING THE REASONS FOR SATISFACTION: STRATIFICATION BY GENDER

With respect to "Salary" as a satisfaction motivation there were statistically significant differences upon stratification by area of employment and by country, see Table 18 and Table 19. No more differences were revealed in the satisfaction section of the survey nor subgrouping by age or biobank age.

Satisfaction reason		*Biologist, n=32*	*Laboratory technician, n=27*	*Management, n=85*	*Multiple areas, n=32*	*Quality Risk Project Data, n=35*	*p-value*
Salary, n (%)	Not chosen	28 (87.5)	17 (63.0)	49 (57.6)	26 (81.2)	26 (74.3)	0.009
	Chosen	4 (12.5)	10 (37.0)	36 (42.4)	6 (18.8)	9 (25.7)	

TABLE 18. REASONS FOR SATISFACTION: STRATIFICATION BY AREA OF EMPLOYMENT

Satisfaction reason		*Australia, n=21*	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Salary, n (%)	Not chosen	11 (52.4)	11 (50.0)	53 (65.4)	52 (92.9)	20 (62.5)	<0.001
	Chosen	10 (47.6)	11 (50.0)	28 (34.6)	4 (7.1)	12 (37.5)	

TABLE 19. REASONS FOR SATISFACTION: STRATIFICATION BY COUNTRY

In Figure 10 a bar graph of the subgroup analysis by gender of the reasons for dissatisfaction is displayed. There was no statistically significant difference between the

two categories, although a tendency could be inferred. The answer “Few opportunities for career advancement” was chosen by 39.3% of women (n=55) and 24.6% of men (n=14) with a p-value of 0.069. Upon stratification by country, as shown in Table 20, there were differences due to life-work imbalance and overqualification for the job answers.

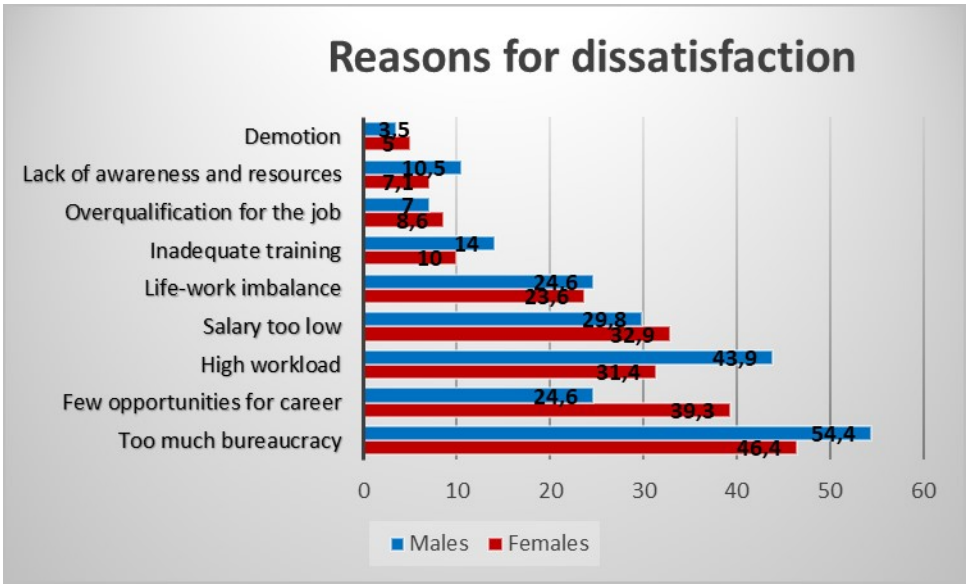

FIGURE 10. BAR GRAPH REPRESENTING THE REASONS FOR DISSATISFACTION: STRATIFICATION BY GENDER

Dissatisfaction reason		*Australia, n=21*	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Life-work imbalance, n (%)	Not chosen	20 (95.2)	17 (89.5)	60 (77.9)	37 (66.1)	18 (64.3)	0.023
	Chosen	1 (4.8)	2 (10.5)	17 (22.1)	19 (33.9)	10 (35.7)	
Overqualification for the job, n (%)	Not chosen	16 (76.2)	17 (89.5)	69 (89.6)	55 (98.2)	27 (96.4)	0.027
	Chosen	5 (23.8)	2 (10.5)	8 (10.4)	1 (1.8)	1 (3.6)	

TABLE 20. REASONS FOR DISSATISFACTION: STRATIFICATION BY COUNTRY

In subgrouping by area of employment, differences were found in the “Too much bureaucracy” category as shown in Table 21.

Dissatisfaction reason		*Biologist, n=32*	*Laboratory technician, n=27*	*Management, n=85*	*Multiple areas, n=32*	*Quality Risk Project Data, n=35*	*p-value*
Too much bureaucracy, n (%)	Not chosen	19 (59.4)	19 (73.1)	38 (47.5)	18 (58.1)	11 (34.4)	0.034
	Chosen	13 (40.6)	7 (26.9)	42 (52.5)	13 (41.9)	21 (65.6)	

TABLE 21. REASONS FOR DISSATISFACTION: STRATIFICATION BY AREA OF EMPLOYMENT

When subgrouping by age, differences were found in the "Too much bureaucracy" answer as well. Moreover, young biobankers are more likely dissatisfied feeling to be overqualified for the job, as displayed in Table 22.

Dissatisfaction reason		*Young, n=108*	*Senior, n=104*	*p-value*
Too much bureaucracy, n (%)	Not chosen	61 (59.8)	44 (44.4)	0.034
	Chosen	41 (40.2)	55 (55.6)	
Overqualification for the job, n (%)	Not chosen	89 (87.3)	95 (96.0)	0.040
	Chosen	13 (12.7)	4 (4.0)	

TABLE 22. REASONS FOR DISSATISFACTION: STRATIFICATION BY AGE

Finally, upon stratification by biobank type, a statistically significant difference was found in the "Demotion" reason for dissatisfaction, as can be seen in Table 23.

Dissatisfaction reason		*Public, n=164*	*Private, n=25*	*Mixed, n=23*	*p-value*
Demotion, n (%)	Not chosen	151 (96.8)	20 (83.3)	21 (100.0)	0.007
	Chosen	5 (3.2)	4 (16.7)	0 (0.0)	

TABLE 23. REASONS FOR DISSATISFACTION: STRATIFICATION BY BIOBANK TYPE

Life-work balance and gender balance

No dissimilarity was found in the satisfaction with life-work balance of the biobankers in this cohort in any of the subgroup analyses, except when performing stratification by age, as reported in Table 24.

Satisfaction with the life-work balance	*Young, n=108*	*Senior, n=104*	*p-value*
Very unsatisfied, n (%)	1 (0.9)	5 (4.8)	0.026
Unsatisfied, n (%)	13 (12.0)	21 (20.2)	
Neutral, n (%)	30 (27.8)	24 (23.1)	
Satisfied, n (%)	48 (44.4)	49 (47.1)	
Very satisfied, n (%)	16 (14.8)	5 (4.8)	

TABLE 24. LIFE-WORK BALANCE SATISFACTION: STRATIFICATION BY AGE

Each biobank in the diverse countries of the present cohort offered various options to achieve a sustainable life-work balance as displayed in Table 25.

Options		*Australia, n=21*	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Flexible working hours, n (%)	Not chosen	2 (9.5)	1 (4.5)	16 (20.8)	9 (19.1)	7 (25.9)	0.257
	Chosen	19 (90.5)	21 (95.5)	61 (79.2)	38 (80.9)	20 (74.1)	
Maternity leave, n (%)	Not chosen	2 (9.5)	4 (18.2)	14 (18.2)	15 (32.6)	13 (48.1)	0.006
	Chosen	19 (90.5)	18 (81.8)	63 (81.8)	31 (67.4)	14 (51.9)	
Home office, n (%)	Not chosen	6 (28.6)	4 (18.2)	26 (33.8)	43 (91.5)	15 (55.6)	<0.001
	Chosen	15 (71.4)	18 (81.8)	51 (66.2)	4 (8.5)	12 (44.4)	
Paternity leave, n (%)	Not chosen	6 (28.6)	9 (40.9)	31 (40.3)	35 (74.5)	18 (66.7)	<0.001
	Chosen	15 (71.4)	13 (59.1)	46 (59.7)	12 (25.5)	9 (33.3)	
Part-time job, n (%)	Not chosen	8 (38.1)	12 (54.5)	45 (58.4)	37 (78.7)	20 (74.1)	0.01
	Chosen	13 (61.9)	10 (45.5)	32 (41.6)	10 (21.3)	7 (25.9)	
Smart working, n (%)	Not chosen	13 (61.9)	18 (81.8)	61 (79.2)	32 (68.1)	21 (77.8)	0.346
	Chosen	8 (38.1)	4 (18.2)	16 (20.8)	15 (31.9)	6 (22.2)	
Kindergarten on-site, n (%)	Not chosen	19 (90.5)	21 (95.5)	65 (84.4)	43 (91.5)	24 (88.9)	0.586
	Chosen	2 (9.5)	1 (4.5)	12 (15.6)	4 (8.5)	3 (11.1)	
No opportunities and I am not sure, n (%)	Not chosen	21 (100.0)	22 (100.0)	77 (95.1)	47 (83.9)	27 (84.4)	0.021
	Chosen	0 (0.0)	0 (0.0)	4 (4.9)	9 (16.1)	5 (15.6)	

TABLE 25. OPTION OFFERED FOR ACHIEVING A SUSTAINABLE LIFE-WORK BALANCE: STRATIFICATION BY COUNTRY

There are no dissimilarities subgrouping by biobank age or biobank type with the exception of paternity leave, as summarized in Table 26.

Option		*Public, n=164*	*Private, n=25*	*Mixed, n=23*	*p-value*
Paternity leave, n (%)	Not chosen	68 (45.9)	18 (75.0)	13 (59.1)	0.022
	Chosen	80 (54.1)	6 (25.0)	9 (40.9)	

TABLE 26. OPTION OFFERED FOR ACHIEVING A SUSTAINABLE LIFE-WORK BALANCE: STRATIFICATION BY TYPE OF BIOBANK

The actions taken by the biobanks to manage gender balance are similarly distributed when stratifying by country, biobank age, or biobank type.

Discrimination

In Table 27 the answers of the discrimination section of the survey when subgrouping by gender are summarized. There are statistically significant differences in all categories with the exception of the colleagues' behavior. Women felt negatively discriminated against in hiring opportunities, in career opportunities, in the superiors' behavior towards them in how ideas/proposals are taken into consideration, and in how needs/complaints are taken into consideration in comparison with their male colleagues.

		Females, n=148	*Males, n=60*	*p-value*
Hiring opportunities, n (%)	No	115 (77.7)	54 (90.0)	<0.001
	Yes, negatively	30 (20.3)	0 (0.0)	
	Yes, positively	2 (1.4)	4 (6.7)	
	Sometimes, Maybe	1 (0.7)	2 (3.3)	
Career opportunity, n (%)	No	96 (64.9)	53 (88.3)	<0.001
	Yes, negatively	47 (31.8)	1 (1.7)	
	Yes, positively	1 (0.7)	5 (8.3)	
	Sometimes, Maybe	4 (2.7)	1 (1.7)	
Colleagues' behaviour, n (%)	No	126 (85.1)	52 (86.7)	0.786
	Yes, negatively	12 (8.1)	5 (8.3)	
	Yes, positively	4 (2.7)	0 (0.0)	
	Sometimes, Maybe	6 (4.1)	3 (5.0)	
Superiors' behaviuor, n (%)	No	116 (78.4)	51 (85.0)	0.01
	Yes, negatively	20 (13.5)	1 (1.7)	
	Yes, positively	5 (3.4)	6 (10.0)	
	Sometimes, Maybe	7 (4.7)	2 (3.3)	
Ideas/proposals consideration, n (%)	No	121 (81.8)	50 (83.3)	<0.001
	Yes, negatively	19 (12.8)	0 (0.0)	
	Yes, positively	2 (1.4)	5 (8.3)	
	Sometimes, Maybe	6 (4.1)	5 (8.3)	
Needs/complaints consideration, n (%)	No	117 (79.1)	51 (85.0)	0.003
	Yes, negatively	25 (16.9)	2 (3.3)	
	Yes, positively	2 (1.4)	5 (8.3)	
	Sometimes, Maybe	4 (2.7)	2 (3.3)	

TABLE 27. DISCRIMINATION ASSESSMENT SUMMARY: STRATIFICATION BY GENDER

All other stratifications failed to reveal any statistically significant difference with the exception of career opportunities, as reported in Table 28 and Table 29, when stratifying by area of employment and by country.

		Biologist, n=32	*Laboratory technician, n=27*	*Management, n=85*	*Multiple areas, n=32*	*Quality Risk Project Data, n=35*	*p-value*
Career opportunity, n (%)	No	22 (68.8)	25 (92.6)	65 (76.5)	20 (62.5)	20 (57.1)	0.026
	Yes, negatively	10 (31.2)	2 (7.4)	15 (17.6)	10 (31.2)	10 (28.6)	
	Yes, positively	0 (0.0)	0 (0.0)	3 (3.5)	0 (0.0)	4 (11.4)	
	Sometimes, Maybe	0 (0.0)	0 (0.0)	2 (2.4)	2 (6.2)	1 (2.9)	

TABLE 28. DISCRIMINATION ASSESSMENT SUMMARY: STRATIFICATION BY AREA OF EMPLOYMENT

		Australia, n=21	*Canada, n=22*	*Europe, n=81*	*Italy, n=56*	*Mixed, n=32*	*p-value*
Career opportunity, n (%)	No	15 (71.4)	19 (86.4)	58 (71.6)	32 (57.1)	28 (87.5)	0.002
	Yes, negatively	2 (9.5)	3 (13.6)	20 (24.7)	21 (37.5)	2 (6.2)	
	Yes, positively	1 (4.8)	0 (0.0)	3 (3.7)	2 (3.6)	1 (3.1)	
	Sometimes, Maybe	3 (14.3)	0 (0.0)	0 (0.0)	1 (1.8)	1 (3.1)	

TABLE 29. DISCRIMINATION ASSESSMENT SUMMARY: STRATIFICATION BY COUNTRY

Results of the website search

The selection of the biobank websites to be analyzed was made including “the 10 largest biobanks in the world”, according to the biobanking industry web portal Global Biobank Directory (2022) and adding them to those described on the "Global Engage" website (Williams, 2018). Overall, the number of biobanks included was 13. The most recently established biobank was the FINNGEN biobank (2017) while the most enduring was Chernobyl Tissue Bank (CTB), founded in 1998. The Shanghai Zhangjiang Biobank website was not available in English, so this biobank was excluded from further analysis. The aims were to assess the presence of women in a leadership position in the biobanking field, the hiring policy of employees in terms of options offered to manage the employees’ life-work balance, and career opportunities.

For 10 out of 12 biobanks, there was a description of governance either with a scheme or with the list of members of the various committees. The steering committee was the main body of the leadership. BioBank Japan, CTB (Chernobyl Tissue Bank), and Victorian Cancer Biobank (Australia) had the list of the members of the steering committee without photos; therefore, the gender of the members was not inferred. The analysis was possible for 7 biobanks. The number of members ranged from 6 to 24. One biobank had a leadership that had a share of women of 58%, the other 6 biobanks had a leadership in which the female share was less than 50% ranging from 13% to 42%. The median was 33%, meaning that males were twice as much present in leadership positions compared to females. The scientific advisory committee was available for four biobanks and the percentages of women were 53%, 44%, 33%, and 21%. The number of members ranged from 18 to 80. No subgroups per continent/country were performed due to sample size.

Two out of 12 biobanks promoted explicitly gender equality on their website, one, in particular, declared to have a “Gender Unit” in place.

Three out of 12 biobanks advertised the activities for employees to achieve a sustainable life-work balance as flexible working hours, family leave, paternity leave, training, kindergarten on site, and care for dependents.

Regarding career advancement, three out of 12 biobanks advertised opportunities as research, scientific writing, teaching, and didactics. In particular, videos of women telling their careers stories were made available, to be taken as role models.

Results of the systematic review of the literature

Overall, the process of the literature search is portrayed in the flowchart in Figure 11.

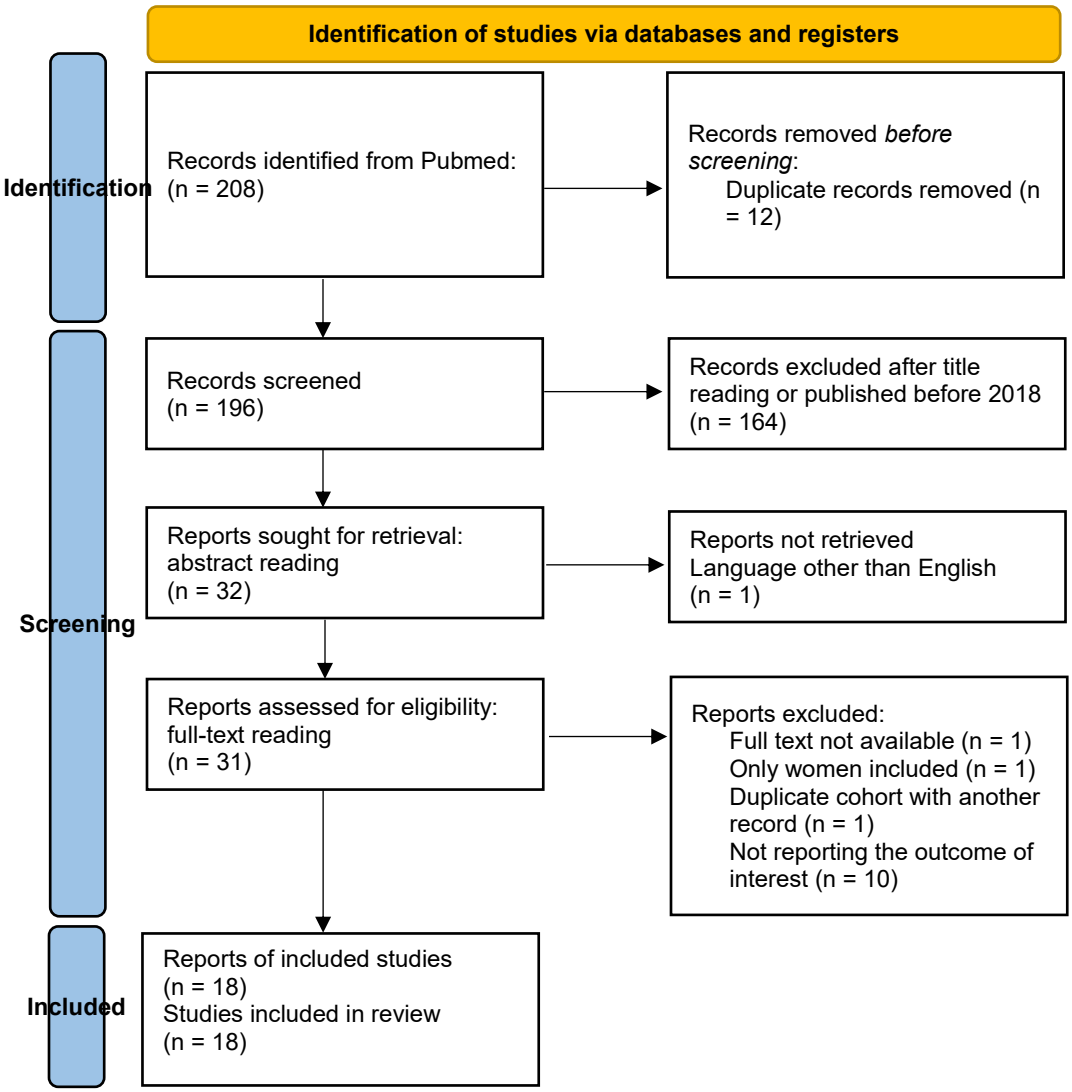

FIGURE 11. PRISMA 2020 FLOW DIAGRAM FOR SYSTEMATIC REVIEWS REPRESENTING THE PROCESS OF LITERATURE SEARCH WHICH INCLUDED SEARCHES OF DATABASES AND REGISTERS ONLY

A total of 196 citations were screened for inclusion. After excluding citations based on the screening of titles and abstracts, 32 were deemed potentially relevant for further evaluation and assessed for eligibility. Of these, 18 met the inclusion criteria and were included in the present systematic review. The studies of Kong et al., Behar-Horenstein et al., Mosavel et al., Mohanty et al., Bosisio et al., Beskow et al., Barnes et al., Rangel et al., Labib et al., Antonova et al. (Antonova and Eritsyan, 2022; Barnes et al., 2020; Behar-

Horenstein et al., 2020; Beskow et al., 2020; Bosisio et al., 2021; Kong et al., 2021; Labib et al., 2017; Mohanty et al., 2021; Mosavel et al., 2019; Rangel et al., 2019) were excluded because they were not clearly reporting the outcome of interests. Broekstra et al. (Broekstra, Reinder et al., 2021) employed a dataset already included. The study of Serrano et al. (Serrano et al., 2018) was available only in Spanish, while Savich et al. (Savich et al., 2020) employed a dataset with only women. The full-text of Cordeiro et al. (Cordeiro et al., 2021) was not available.

The characteristics of the included studies are reported in Table 30.

First Author and Year	Journal	Title	Country
(Broekstra, R. et al., 2022)	Eur J Hum Genet	Motives for withdrawal of participation in biobanking and participants' willingness to allow linkages of their data	Netherlands
(Pawlikowski et al., 2022)	Int J Environ Res Public Health	Associations between the Willingness to Donate Samples to Biobanks and Selected Psychological Variables	Poland
(Khatib et al., 2021)	BMC Med Ethics	Views of university students in Jordan towards Biobanking	Jordan
(Critchley, Christine R. et al., 2021)	Eur J Hum Genet	Identifying the nature and extent of public and donor concern about the commercialisation of biobanks for genomic research	Australia
(Gao et al., 2022)	Biopreserv Biobank	Willingness to Donate Remnant Human Biospecimens in the Context of the COVID-19 Pandemic	China
(Sinclair et al., 2021)	Prev Med Rep	Increasing health equity through biospecimen research: Identification of factors that influence willingness of Native Americans to donate biospecimens	USA
(Brall et al., 2021)	PLoS One	Public willingness to participate in personalized health research and biobanking: A large-scale Swiss survey	Switzerland
(Critchley, Christine et al., 2020)	Public Underst Sci	Examining diversity in public willingness to participate in offshore human biobanking: An Australian mixed methods study	Australia
(Lhousni et al., 2020)	Biopreserv Biobank	Patients' Knowledge and Attitude Toward Biobanks in Eastern Morocco	Morocco
(Mezinska et al., 2020)	BMC Med Ethics	Public awareness of and attitudes towards research biobanks in Latvia	Latvia
(Hathcock et al., 2020)	Front Public Health	Characteristics Associated With Recruitment and Re-contact in Mayo Clinic Biobank	USA
(Ewing et al., 2019)	J Community Genet	Factors associated with willingness to provide biospecimens for genetics research among African American cancer survivors	USA
(Makhlouf et al., 2019)	Pharmgenomics Pers Med	Population's perspectives toward biobanks in scientific research: a study from Jordan	Jordan
(Fradgley et al., 2019)	Asia Pac J Clin Oncol	Patients' experiences and preferences for opt-in models and health professional involvement in biobanking consent: A cross-sectional survey of Australian cancer outpatients	Australia

First Author and Year	Journal	Title	Country
(Obeid et al., 2018)	JAMIA Open	Research participation preferences as expressed through a patient portal: implications of demographic characteristics	USA
(Bossert et al., 2018)	Front Genet	The Public's Awareness of and Attitude Toward Research Biobanks - A Regional German Survey	Germany
(Antommaria et al., 2018)	AJOB Empir Bioeth	Parents' attitudes toward consent and data sharing in biobanks: A multisite experimental survey	USA
(Richter et al., 2018)	Genet Med	Broad consent for health care-embedded biobanking: understanding and reasons to donate in a large patient sample	Germany

TABLE 30. CHARACTERISTICS OF THE INCLUDED STUDIES.

The majority of the studies were carried out in USA (n=5), followed by Australia (n=3), Germany and Jordan (n=2).

As depicted in Table 31, the dataset comprised 103,893 subjects, 62,829 (60.5%) women and 41,064 (39.5%) men. All participants were adults and older than 18 years, except for the participants in the Khatib et al. (Khatib et al., 2021) dataset who were all university students aged 17-24.

Study	Questionnaire			Participants				Education		
First Author	*Type*	*Location*	Pay	*Sample Size*	*Female %*	*Male %*	*Ethnicity, Race, Language*	*Low*	*Mod.*	*High*
Broekstra R	self-administered	on-line	no	2615	49.5	50.5	not assessed	559	938	1083
Pawlikowski J	interview	in-person	no	1100	52.3	47.7	not assessed	79	596	425
Khatib F	self-administered	on-line	no	435	72.0	28.0	not assessed	0	435	0
Critchley CR 2021	interview	CATI	no	800	66.0	34.0	Australian born (83.2%)	n/a	n/a	n/a
Gao L	self-administered	on-line	no	721	62.1	37.9	Asian (80.3%)	94	345	282
Sinclair KA	self-administered	in-person	yes	278	62.0	38.0	(AI/AN) Native Americans	47	135	96
Brall C	self-administered	mixed	no	5086	51.8	48.2	German (70.6%) French (24.5%)	385	3394	1283
Critchley CR 2020	interview	CATI	no	750	52.4	47.6	Australian born (82.1%)	n/a	n/a	362
Lhousni S	interview	in-person	no	1133	69.0	31.0	not assessed	837	237	58
Mezinska S	interview	in-person	no	1017	52.8	47.2	Latvian (59%), Russian (32%)	116	631	270
Hathcock MA	mixed	mixed	yes	57041	59.0	41.0	White (92%)	9137	18464	28216
Ewing AT	self-administered	on-line	no	200	73.0	27.0	African American	77	20	101

Study	Questionnaire			Participants				Education		
First Author	*Type*	*Location*	Pay	*Sample Size*	*Female %*	*Male %*	*Ethnicity, Race, Language*	*Low*	*Mod.*	*High*
Makhlouf H	self-administered	on-line	no	476	52.0	48.0	not assessed	33	310	122
Fradgley EA	self-administered	in-person	no	113	71.7	28.3	English, Aboriginal	0	78	35
Obeid JS	self-administered	on-line	no	25768	64.4	35.6	White (84.9%), African American (11%)	n/a	n/a	n/a
Bossert S	self-administered	postal	no	204	58.4	41.6	German (92%)	28	47	116
Antommaria AHM	self-administered	postal	yes	5737	73.6	26.4	White (52.5%), Asian (18.35), Black (11.7%)	739	2929	1902
Richter G	self-administered	in-person	no	760	55.8	44.2	not assessed	n/a	n/a	n/a

TABLE 31. CHARACTERISTICS OF INCLUDED STUDIES: TYPE OF QUESTIONNAIRE AND PARTICIPANTS (N=103,893). CATI, COMPUTER ASSISTED TELEPHONE INTERVIEW; AI/AN, AMERICAN INDIAN/ALASKAN NATIVE

Five out of 18 studies collected data via interview, two of which were Computer Assisted Telephone Interviews (CATI), the rest being in person in different locations including the participant's home, the biobank site, and fairs. 13 surveys were self-administered by the participant employing both on-line tools (delivered by email, social networks, and hospital portals) and postal paper-based questionnaires delivered by mail. In three studies, participants received a reimbursement or a gift card for their time. Considering the 80-90% of the ethnicity, race and language included in each dataset, the majority of participants declared themselves White (or Caucasian). Education data was recovered for 75,070 subjects, 16.2% with low education, 38.0% with moderate education and 45.8% with high education.

In Table 32 the inclusion criteria of the included studies, the percentage of people willing to donate to biobanks, and whether associations have been found between willingness to donate with gender, age, and education are summarized.

First Author	Inclusion Criteria	Willingness to donate	Gender	Age	Education
Broekstra R	Active participants of Lifelines biobank, not withdrawn their participation at the time of the survey	n/a	yes	yes	yes
Pawlikowski J	Representative structure of the Polish population in: sex, age, number of respondents in a given voivodship, place of residence, and level of education	48%	no	no	no

First Author	Inclusion Criteria	Willingness to donate	Gender	Age	Education
Khatib F	All undergraduate students of all academic schools at the University of Jordan, second-year and higher students, and students with any grade point average	95%	no	n/a	n/a
Critchley CR 2021	Australians over the age of 18 years and who could speak English	n/a	yes	yes	n/a
Gao L	All walks of life in China	86%	no	no	yes
Sinclair KA	Individuals self-identified as AI/AN Native Americans and 18 years of age or older	43%	no	yes	no
Brall C	Swiss resident over 18 years of age	54%	no	yes	yes
Critchley CR 2020	Australians over the age of 18 years who could speak English	94%	yes	no	no
Lhousni S	Hospital outpatient and inpatient four health care centers in Eastern Morocco	81%	yes	yes	no
Mezinska S	Latvian residents aged 18 to 75 years	45%	no	no	no
Hathcock MA	Mayo Clinic Patients 18 or older, residents of the United States, and able to provide informed consent	n/a	yes	yes	no
Ewing AT	African American adults, 18 years of age and older, with a medical history of breast, colon, or prostate cancers	79%	yes	no	no
Makhlouf H	Aged ≥18 years reflecting the socioeconomic and demographic distribution of Jordanian people	85%	no	no	yes
Fradgley EA	English-speaking; 18 years or older; receiving adjuvant chemotherapy; had a confirmed diagnosis of breast, gastrointestinal, lung, or ovarian cancer; and had cancer-related surgery (i.e. curative resection) from March 2014 to the time of recruitment (up to February 2016)	89%	no	no	yes
Obeid JS	Adults (18 years of age or older) with an active account in the patient portal of South Carolina from December 2014 and May 2016	77%	yes	yes	n/a
Bossert S	Hannover registration office, register of all residents (age 18 or older)	70%	yes	no	no
Antommaria AHM	Participants or their minor child (1) were a patient at 1 of the 11 Electronic Medical Records and Genomics (eMERGE) Network sites between October 2013 and September 2014, (2) had an address that could be geocoded, and (3) had their age and sex documented in the electronic medical record; also (4) reported that they were the parent or guardian of a child under 18 years old	76%	no	no	no
Richter G	Adult patients at the Comprehensive Center for Inflammation Medicine (CCIM) in Kiel, Germany, in September 2015 and in February 2016	n/a	yes	yes	yes

TABLE 32. CHARACTERISTICS OF INCLUDED STUDIES: INCLUSION CRITERIA AND WILLINGNESS TO PARTICIPATE IN BIOBANK

The average willingness to donate was 73%, with a minimum of 43% and a maximum of 95%, while in four studies the percentage was not assessed. In nine out of 18 studies, the authors found an association with gender, in eight studies with age, in six studies with

education and the specific outcome of the study in close relation to the willingness to donate.

Broekstra et al. (2022) (Broekstra et al., 2022) examined the "*Motives for withdrawal of participation in biobanking and participants' willingness to allow linkages of their data*" and found that gender had a significant effect on the relevance of specific motives. Individual benefit was a motive for participating, which was less relevant for women than for men, on the other end societal and individual harm were motivations for withdrawal of participation, which were more frequent in women. In assessing respondents' intention to allow their data to be linked to a large-scale dataset, the authors found that being younger and being male were predictors of participants' willingness.

Critchley et al. (2021) (Critchley et al., 2021) studied the nature and extent of public and donor concern about the commercialization of biobanks for genomic research in Australia and pinpointed the majority opposing all aspects of commercialization, a minority supporting all, one quarter opposing some (sharing and selling tissue) but not others (research locations and funding), and a group who were unsure about most aspects but opposed selling tissue. In respect to gender, males and people with disabilities were more likely to support rather than oppose all forms of commercialization, with males 75% more than females and people with disabilities more than twice as likely.

Critchley et al. (2020) (Critchley et al., 2020) examined the diversity in public willingness to participate in offshore human biobanking in Australia and concluded that the majority of the participants were willing to donate samples to an Australian biobank employed by Australian researchers (94%). The percentage dropped dramatically when hypothesizing the biobank to be located overseas (62.5%). The major concerns were about privacy and foreign ethical and regulatory standards. Age, education and ethnicity were not significantly associated with the prediction to have a specific set of concerns. Men were found to be significantly more likely than women to manifest no concerns.

Lhousni et al. (2020) (Lhousni et al., 2020) investigated the "*Patients' Knowledge and Attitude Toward Biobanks in Eastern Morocco*" and found that 97% of the respondent had never heard of the term biobank, nevertheless, 80.7% of the participants were willing to donate biospecimens. Males were more likely to be a hypothetical donors (OR 1.77 95%CI 1.25-

2.52) as were people aged 18-40 years. No significant association was found with the level of education.

Hathcock et al. (2020) (Hathcock et al., 2020) scrutinized the “Characteristics Associated With Recruitment and Re-contact in Mayo Clinic Biobank” in the USA and identified a significant interaction between age and gender. Up until the age of 65, more women gave their consent than men did; beyond that, males gave their consent at a higher rate. Consent rates in patients who self-reported their race as white were the highest followed by American Indian/Alaskan Native and Asian. Black/African Americans consented at the lowest rate. No meaningful difference upon gender was recorded in consenting to follow-up studies.

Ewing et al. (2019) (Ewing et al., 2019) analyzed the “*Factors associated with willingness to provide biospecimens for genetics research among African American cancer survivors*” and inferred that 79% of participants were willing to donate a biospecimen for cancer genetic research. Men with a higher income and without government insurance were more likely to be willing to be engaged in biobanking. Associations were found with individuals who thought it is important to participate in genetics research, those who believed in the relevance of genetic causes of cancer, and those who stated they would participate in genetics research to help future generations.

Obeid et al. (2018) (Obeid et al., 2018) surveyed the participation preferences of patients at the Medical University of South Carolina (MUSC) and the implication of demographic characteristics and calculated that 76.5% agreed to participate. Based on gender stratification, males were statistically significantly more likely to agree on biobank participation (OR 1.18 95% CI 1.06-1.33). Race showed an impact with white being different from all the other categories and more likely to agree. Age showed an interaction with race being over 65 in agreement to biobank preference for both white and African American.

Bossert et al. (2018) (Bossert et al., 2018) researched on the public's awareness of and attitude toward research biobanks in the region of Hannover (Germany) and showed that 70.4% of the cohort expressed the intention to participate in biobanks during a hypothetical hospitalization. The authors found two significant independent variables

explaining the variation in participants' assessment of biobanks: their assessment of genetic research, and gender. Male respondents and persons who somewhat or definitely approved genetic research were more likely to be willing to donate to biobanks. Moreover, men were significantly more likely to make a definite assessment of biobanks (e.g. answering clearly "yes" or "no").

Richter et al. (2018) (Richter et al., 2018) explored the reasons to donate in a large patient cohort in Germany, focusing on broad informed consent. Respondents who were in favor of broad consent for health care-embedded biobanking were 86.9%. Motivations to give broad consent were mainly for prosocial reasons, including altruism, solidarity, reciprocity, and gratitude. In order to determine which individual-specific factors might potentially explain the motivations, the authors performed further analyses including sex, age, education level, and other categories (as past experience with medical research, objective understanding, expectation of personal benefit, and opposition to the nonreporting policy) in the model. Women resulted to be more inclined to state the support of research as a motivation (altruism) and the elderly being more inclined to donate out of gratitude to their physicians.

DISCUSSION

The present thesis describes the findings of the first comprehensive research on gender in biobanking. I dissected this topic from two different perspectives: the employees' view, delivering a survey on their working conditions, and the participants' view reviewing the literature on the willingness to participate and motives to withdraw. The results might argue in favor of the persistence of gender biases also in the biobanking field for both the assessed outcomes.

Survey

Overall, a total of 212 (21.9%) biobankers completed the questionnaire. The main respondents were from Italy, Canada, and Australia with a proportion corresponding approximately to the number of emails sent. They were, in fact, the countries with the greatest number of contacts. The search for potential participants was supported by the presence of a strong networking in the correspondent countries. For instance, the biobank locator of BBMRI.IT provides a list of all the member biobanks with the contact details of the reference person and of the responsible person. This was similarly true for the Canadian CTRNet and the Australasian ABNA. However, a peak of responses was reached after sending the survey to the EBW (European Biobank Week) 2021 participants, probably because this category of biobankers is prone to discuss biobanking at different levels. Consequently, after combining the countries with a location logic (e.g. UK responses were considered Europe), Europe was the most represented area. Most of the biobanks were in the public sector (77.4%), while with reference to the year of establishment, the recent biobanks were equal to the long-term ones. Finally, the most represented occupational area was the managerial one.

What was not found to be different by gender

As regards the organization of work, no gender differences were identified in the number of contractually worked weekly hours or in monthly overtime. Furthermore, no statistically significant difference was found in identifying problems that make daily work difficult. Although the majority of the interviewees stated that they did not have any major problems, the relationship with superiors appeared as one of the main reasons for difficulty. In particular, the consideration and qualification of the superiors were

considered inadequate together with the lack of opportunities for professional growth due to the ostracism of the superiors. Many respondents were unsatisfied with some organizational aspects of their biobanks such as unclear roles or high workload. Among the answers freely written, the lack of resources (mainly personnel) was ascertained by quite a few biobankers, and probably this issue was underestimated because it was not present in the list of possible choices. Eventually, the lack of awareness of the importance of biobanking is particularly relevant, written by five respondents and probably underestimated for the same reason as the previous issue. This lack of culture has often been considered by various authors (Mohanty et al., 2021; Rangel et al., 2019) to be a problem relating to the willingness of hypothetical participants to donate and therefore affecting the operation of the biobank, while in this context it emerged that it makes the work of biobanks even more difficult.

No gender diversity was identified in the overall job satisfaction, or satisfaction reasons as a contribution to research, salary, scientific publications and awards, social prestige, teamwork and colleagues, with the exception of self-development. Symmetrically, the reasons for dissatisfaction were not gender-driven, being the most selected: too much bureaucracy, few opportunities for career advancement and high workload. The work-life imbalance caused dissatisfaction in 24% of the cohort and consistently just over half (56%) of the biobankers in this cohort were overall satisfied with the work-life balance, while the rest remained neutral or dissatisfied.

What was found to be different by gender

Women responded more frequently to surveys, both in the present and systematic review, therefore their responses could be analyzed more thoroughly.

Women in the management area

Essentially, I collected three types of information: the percentage of female managers in the cohort of interviewees, the percentage of women in leadership referred to the section of the questionnaire delivered to management only, and the percentage of women in leadership deduced from the research on websites. The results of the stratification analysis, concerning the occupational area of the respondents of the present survey, were not statistically significant (p-value = 0.053), although a meaningful difference emerged

in the management area: 57% of men were managers compared to 33% of their female colleagues. While referring to the gender balance of biobanks, no comparison between gender in the leadership position was possible, mainly because of the high heterogeneity of the surveyed biobanks. They ranged from one to a hundred employees and there was no precise definition of the governance, which is organized in a specific fashion for each biobank. Nonetheless, from the answers obtained in the section for management only relating to women in leadership positions, it can be inferred that females are the most represented gender in the workforce of biobanks (67%) of whom 23% work in a leadership position. From the results of the website search it can be deduced that the majority of biobanks had a leadership in which females were less than 50% ranging from 13% to 42%. The median was 33%, meaning that males were twice as much compared to females. The variability can be explained by the sample size. The managers interviewed were 85, referring to 85 biobanks (or less, because it would have been possible that they referred to the same biobank). Those biobanks were heterogeneous in many ways. The research on the websites covered 13 biobanks, of which only 7 could be analyzed for the gender balance of leadership.

With respect to personal satisfaction, females (17.6%), significantly more than males, considered self-development a satisfaction motivation for being a biobanker. This answer was also a merge of different answers comprising “Participation in stimulating projects”, “Patient assistance”, “Training of young collaborators”, “Recognition from supervisors”, “Fulfilling my goals in science and research”, and similar. On the other hand, “Superiors’ consideration” and “Few opportunities for career advancement” were not statistically significant (p-value= 0.07), but a trend could be identified, being females the most dissatisfied.

The most dramatically significant difference was in the perception of discrimination. Women felt negatively discriminated against in hiring opportunities, in career opportunities, in the superiors’ behavior toward them in how ideas/proposals are taken into consideration, and in how needs/complaints are taken into consideration in comparison with their male colleagues. The only exception was the colleagues' behavior which did not show to be affected by gender. All other subgroups were not significantly

different, probably implying that this perception did not belong to academia, the private sector or the country, but was a widespread view.

Life-work balance

Just over half of the biobankers in this cohort were satisfied with their life-work balance. Coherently, a quarter of the respondents cited the life-work imbalance as a reason for workplace dissatisfaction. For the latter, the percentage of women and men who chose this answer was almost identical (around 24%), while there was a difference in the subgroups by country with Australians and Canadians being the least dissatisfied. However, a meaningful difference was found in the satisfaction with the life-work balance sub-grouped by age: senior biobankers were far more unsatisfied than the younger colleagues were. This could be due to increased duties in the workplace or increased family needs over the years.

Several options have been offered by biobanks to achieve a sustainable life-work balance, with flexible working hours being the most widespread. Maternity and paternity leave are options used for a particular period of a person's life and do not take into account maintaining a sustainable life-work balance over a long period. Therefore, excluding maternity and paternity leave and considering the number of options offered to each employee, it was found that most biobankers are offered two options (among flexible working hours, home office, part-time job, smart working, and kindergarten on-site) and this probably explains the dissatisfaction. With regard to the website search, three out of the 12 examined biobanks advertised the activities for employees to achieve a sustainable life-work balance as flexible working hours, family leave, paternity leave, training, kindergarten on-site, and care for dependents. This data does not imply that others do not necessarily have options in place, but that this is not considered a reason for advertising. Paternity leave is the only action that was found statistically significantly different when subgrouping by biobank type. Some authors argue that, whenever paternity leave is present, it is an option rarely exploited by families due to cultural norms and perceptions about gender roles in child rearing and because males on paternity leave fear that they could be discriminated against (Janta and Stewart, 2018; van Belle, 2016).

According to a respondent's comment, a biobank of this cohort recommends employees two hours of physical exercise per week. This benefit is far-sighted considering that 7% of the surveyed mentioned insufficient physical strength as an issue that made work difficult. Furthermore, the scarcity of physical strength was not specific to a gender or area of employment but was widespread among employees.

Gender balance

Actions taken by biobanks to manage gender balance are ignored by 24% of interviewed biobankers. Furthermore, according to 31% of employees, their biobanks did not take gender balance into account. There is a lack of culture of the importance of gender equality despite the fact that specific actions have been developed by many organizations such as the European Commission to overcome persistent gender gaps. For instance, having a Gender Equality Plan (GEP) is an eligibility criterion for certain categories of legal entities from EU and associated countries. Furthermore, BBMRI-ERIC very recently (March 30th, 2022) published a plan for gender equality and appointed a specialist in gender, equality and diversity.

Significant differences in non-gender stratifications: Salary and Bureaucracy

Although the percentage of men who found salary a reason for satisfaction was 10% higher than that of women, this difference was not significant. In this regard, significant differences were found among areas of employment and countries. Biologists have selected this motivation to a lesser extent than in other areas besides the Italians. The level of bureaucracy was an issue for all categories, in particular, quality / risk / project / data managers had the highest dissatisfaction in the workplace as did senior biobankers.

Comments from the survey participants

Among the numerous comments that I received and to which authors I am extremely grateful, I selected few of them that I consider meaningful.

"I do not believe in gender or in age discrimination. I believe in skills, and qualifications (my own as well as my employees) and I expect that upper management listen to me because of my qualifications rather than my gender."

The author of this comment reached exactly the core of the discussion, which is to give relevance to skills and qualifications rather than different aspects of the hypothetical applicant.

"My current biobank is my ideal workplace, but my previous one (within the same institution) was the total opposite. There, I felt that my gender had a negative impact on my experience and how I was respected by my colleagues – including my supervisor. I was the only male who was able to remain at that previous biobank for longer than 2 years, and today that biobank happens to be employing 100% females."

I chose this comment because it gives the idea that gender equality makes employees work in a better environment despite gender.

"I believe that even the work force are mostly women, men are still giving more opportunities."

This comment summarizes the results obtained in the perception of discrimination section of this thesis and goes under the umbrella of the *glass ceiling* definition: *an unrecognized barrier to the advancement of a profession, which mainly affects women and minorities* (Oxford Languages, 2022).

"Our biobank is inside a larger organisation. I work alone but with other departments as a collaborative. I work in a great organisation and there is good opportunities but I do know that as a mid-40 female, there is less career options available to me and I am over looked unless I ask for it directly. I know the men, with less experience and qualifications, get headhunted. I love my colleagues but I often get asked to do female assumed duties, e.g. organise the social event. It is partly because I am actually pretty good at organising stuff but also, I believe, because I am female."

This comment deals with gender stereotypes, in which female are "more suitable" for some kind of tasks.

"As a gay man, it has been very difficult over the years struggling with institutional homophobia."

A further stratification of discrimination that must be taken into consideration in policy making.

Systematic review

In the present systematic review, 18 studies, published between 2018 and 2022, were analyzed to assess whether donors' willingness to participate or withdraw participation was associated with gender, among other factors. Overall, the majority of the respondents were women (60.5%) and the average willingness to donate was elevated (73%). Nine studies (50%) reported meaningful associations between gender and the specific outcome of the study in close relation to the willingness to donate specimens to biobanks. Interestingly, men were found more willing to donate in nearly all those studies (Bossert et al., 2018; Broekstra et al., 2022; Critchley et al., 2020; Critchley et al., 2021; Ewing et al., 2019; Lhousni et al., 2020; Obeid et al., 2018; Richter et al., 2018). Women resulted to be more inclined to state support of research for altruism as a motivation (Richter et al., 2018), moreover individual benefit was a purpose less relevant for women t(Broekstra et al., 2022)(Broekstra et al., 2022). In two Australian studies, men were found more likely to support all forms of commercialization of biospecimens (Critchley et al., 2021) and to express no concern about participating in human offshore biobanks rather than in Australian biobanks employed by Australian researchers (Critchley et al., 2020). Men were more likely to agree in the biobank participation at the Medical University of South Carolina (USA), although race had an impact according to Obeid and colleagues (Obeid et al., 2018) with the respondents, who self-reported as white, accepting to donate more frequently. With respect to race, a similar result was reported by Hathcock and colleagues (Hathcock et al., 2020) in the consent rate at the Mayo Clinic Biobank (USA). Men were willing to provide biological samples for genetic research to a greater extent than women even among African-American cancer survivors (Ewing et al., 2019). Of note is a significant interaction between age and gender identified by Hathcock and colleagues (Hathcock et al., 2020). Women consented at a higher rate until the age of 65, at which time the consent rate became higher in men. In general, the results of the association between age and willingness to donate in the analyzed datasets were quite heterogeneous, in fact some authors (Brall et al., 2021; Broekstra et al., 2022; Lhousni et al., 2020) found that younger age was a predictor of patients' willingness to donate, while others argued that it was older age (Obeid et al., 2018; Richter et al., 2018; Sinclair

et al., 2021). In particular, Richter and colleagues (Richter et al., 2018) reported that elderly were more prone to donate out of gratitude to their practitioners.

Strength and limitations

To the best of my knowledge, the present thesis represents the first study on gender equality in biobanking for both employees and participants as well as the first field synopsis dedicated to the willingness to donate in the context of gender. Nevertheless, there are several limitations that must be discussed.

Limitations of the survey

The survey was delivered in English only, therefore this language barrier may have caused an under-representation of non-English speaking biobankers. Henderson and colleagues (Henderson et al., 2019) had their survey of biobanks business planning translated into four different languages in addition to English: French, Spanish, German, and Chinese and involved 276 biobanks and the most represented country was China. On the other hand, it was difficult to access the contact information of biobanks whose websites were not translated into English. The gender-variant/non-conforming and transgender were also probably underrepresented in this cohort; however, data on the proportion of gender-variant/non-conforming and transgender among biobankers are missing.

The sample size was not assessed. Calculating the sample size is essential to test the hypothesis effectively and to dimension the cost of a study appropriately. However, pilot studies are needed to calculate a sample size and to estimate the expected outcomes and all the other aspects of the main study. Some authors proposed different rules of thumb, for example Browne in 1995 (Browne, 1995) proposed a general flat rule for a pilot trial to “use at least 30 subjects or greater to estimate a parameter”. In general, the sample size for a pilot study is between 30 and 50. For basic surveys, most statisticians accept a minimum sample size of 100 to achieve meaningful results, and a maximum of 10% of the population as long as it does not exceed 1000 (Bisits Bullen, 2013). For structured and complex surveys, such as national household surveys, the calculation should consider different parameters (Conroy, 2018). An example can be found among the included studies of the present systematic review. Lhousni and colleagues (Lhousni et al., 2020) made a calculation accounting for the estimate of the population of the studied regions of Eastern

Morocco, the estimate of the participants that would have a positive opinion toward biobanking, a confidence level of 95%, an error margin of 2.5% and assuming a nonresponse rate of 10%. This thesis represents a pilot study of its kind by means of a basic survey. So far, the population of biobankers in the world is not precisely known, nevertheless, a cohort of 212 employees was engaged, a sample that should be considered appropriate for the purpose of this study.

For the same reasons, the p-value threshold was set at the level of 0.05, and was not corrected for multiple tests, as were the stratifications by age, gender, biobank age, biobank type, and country.

Self-reported data hold intrinsic bias and the debate on the reliability of such data is still ongoing (Brenner and DeLamater, 2016; Telnes Instanes, 2021). “Social desirability”, the interviewee's attitude of giving what is considered the most socially acceptable answer, is one of them and occurs in both interviews and self-administered surveys. Nevertheless, providing inaccurate data does not occur systematically, for example, according to Chan (Chan, 2009) it is unlikely that the respondents would lie about their demographics, such as gender and ethnicity. While it is true that respondents tend to falsify their responses in experimental studies, this problem is less likely to occur in the measures used in field studies and naturalistic settings.

In the questionnaire, check-all-that-apply (CATA) lists were proposed. Many authors discourage researchers from using this type of questionnaire and recommend using forced responses such as Yes / No, arguing that CATA can lead to inaccurate data collections (Lau and Kennedy, 2019). However, for the purposes of this thesis, check-all-that-apply was an appropriate choice. In fact, they are effective in measuring the overall ranking of the selected items. Furthermore, they effectively measure true favorites or best responses. They counteract the prejudices of acquiescence bias that lead respondents to say "yes" to everything (Hopper, 2019). An alternative way would have been to use a Likert scale of responses: typically "strongly disagree", "disagree", "neither", "agree" and "strongly agree". Such a design makes it easy to evaluate responses and standardize results. On the other hand, the answers are limited. Participants can experience that none of the answers match their opinions or situations. Using the Likert scale, some people

tend to respond to the extreme ends of the scale, others to the middle of the scale, and researchers need to take this into account when interpreting the results (Telnes Instanes, 2021).

The responses not suggested in the list, e.g. the lack of resources as an issue or the teamwork as a reason for satisfaction, were probably underrepresented. Therefore, those spontaneously given answers are very useful in designing a possible future main study.

The survey could potentially be answered an infinite number of times and no Google identification or login was asked to keep it completely anonymous. However, this is unlikely to have happened because it was only sent to biobanks and biobankers and was not posted on common social networks.

Finally, it was not possible to assess the ratio of females to males in the management area because the exact number of leadership members was not clear. Many biobanks were nested in a core organization such as a hospital or university, and some respondents answered accordingly. For example, some managers reported more team members than the total number of employees of the biobank. During the data cleaning phase, I realized that the sample was very heterogeneous and that the data on the team/manager could not be used to evaluate the proportion between the two sexes.

Limitations of the websites search

Using photos to assign gender to leadership members is a limitation because self-identification with a particular gender does not always match outward appearance. Moreover, from the simple list of names, it could not be defined (unless using professional software). Some names belong to different genders in different cultures such as Andrea or Gabriele, and in any case, the name may not be representative of the self-identification of the genus. In this context, photographic analysis was the best option, nevertheless, it must be considered that some errors may have occurred.

Limitations of the systematic review

Not evaluating the validity of the included studies by assigning a weight or a score was a limitation. The Newcastle-Ottawa Scale (NOS), a widely used tool for assessing the quality of the meta-analyses, was not applicable to this study. Nevertheless, the inclusion

criteria were a filter for good quality studies, therefore poor quality studies or that did not provide sufficient information on the sampling methods were excluded a priori from the systematic review. There are only a few examples in the literature of systematic review and meta-analysis of surveys, one of which is Fanelli's study of scientists fabricating and falsifying research (Fanelli, 2009). The author did not grade the included papers on a quality scale because, according to Jüni and colleagues, the validity and use of quality measures in meta-analysis are controversial (Jüni et al., 1999).

Willingness to participate is hypothetical and does not mean an effective donation. This concept was examined by Johnsson and colleagues, whose study aimed to verify whether hypothetical participants corresponded to actual participants (Johnsson et al., 2010). The authors compared 11 surveys on willingness to donate conducted in Sweden, Iceland, United Kingdom, Ireland, United States, and Singapore to factual participation rates in 12 biobank studies. The match was carried out by country and approximate period. Consequently, in about half of the comparisons the factual willingness to participate in biobank research was greater than the hypothetical, in a quarter the opposite, and in the rest the difference was not significant. The authors recognized some limitations that probably led to underestimation of the actual willingness, beside the topic is complex and an accurate estimate is difficult to achieve.

Conclusions

Despite the fact that biobanks turned out to be healthy workplaces where most respondents said they had no major problems, many employees found some organizational aspects of their biobanks unsatisfactory such as unclear roles or high workload. There are many opportunities offered to manage work-life balance; however, just over half of the biobankers in this cohort were satisfied with it overall, an aspect that should be taken into account in the decision-making process. No gender differences were identified in the number of hours contractually worked per week or in monthly overtime, nor in overall job satisfaction or dissatisfaction. The most dramatically significant difference was in the perception of discrimination. Women felt negatively discriminated against in hiring opportunities, career opportunities, in the behavior of superiors towards them, in the way ideas/proposals are considered and in the way needs/complaints were

considered compared to male colleagues. Therefore, a culture of gender equality is eagerly needed also in the biobanking field. Regarding willingness to participate in biobanks, half of the included studies found a gender association, particularly men were more willing to donate than women. This could introduce biases affecting the data and should be taken into consideration. Overall, these results support the hypothesis that there are gender biases in biobanks; however, this thesis should be considered a pilot study, which might help design a possible future main study.

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Annex

Gender in biobanking

The present survey is designed to assess the working conditions of employees working in biobanks with special attention to gender equality.

#	Variable name	Question	Answers
Demographic assessment			
1	gender	To which gender identity do you most identify?	○ Female ○ Male ○ Transgender ○ Gender Variant/Non-Conforming ○ Prefer not to answer ○ Other [please specify]
2	age	What is your age?	○ Below 24 ○ 25-34 ○ 35-44 ○ 45-54 ○ 55-64 ○ Above 64 ○ Prefer not to answer
3	area	What is your area of employment?	○ Management ○ Administration ○ Quality/Risk management ○ Project/Data management ○ Study nurse ○ Information Technology (IT) ○ Laboratory technician ○ Biologist ○ Training and education personnel ○ Other [please specify]
Biobank characteristics Please refer to the biobank you are working for			
4	biobank_type	What type of biobank do you work for?	○ Public (Hospital and/or University-based) ○ Private company/stand-alone ○ Other [please specify]
5	biobank_age	How long has your biobank been in existence?	○ Below 1 year ○ 1-5 years ○ 6-10 years ○ 11-15 years ○ 16-20 years ○ More than 20 years ○ I am not sure
6	country	Where is your biobank located?	Drop-down list [195 Countries]
Job organization			

7	team_size	How many employees work with you on the team, if it is the case, including you?	[number]
8	team_females	How many women work with you on the team, if it is the case, including you?	[number]
9	hours_week	How many hours do you work per week per contract?	○ Less than 10 ○ 11-20 ○ 21-30 ○ 31-40 ○ More than 40
10	overtime_month	How many overtime hours do you usually work per month?	○ Less than 5 ○ 6-10 ○ 11-20 ○ 21-40 ○ More than 40
11	issues team_coll_consider sup_consider sup_career equip_strength issue_resources issue_org_aware	Which of the following issues do you think makes your job difficult? Check all that apply	▪ No particular issues ▪ I am often ignored by my team ▪ My colleagues do not support me ▪ I am often ignored by my superiors ▪ My superiors are less trained/qualified than me ▪ My superiors do not allow me to professionally grow ▪ Insufficient physical strength (e.g. to lift racks with samples) ▪ Incorrect size/proportion of the equipment (e.g. personal protective equipment) ▪ Other [please specify]
Personal satisfaction Please refer to your everyday job			
12	satis_job	Are you satisfied with your job?	○ Never or almost never ○ Rarely ○ Sometimes ○ Often ○ Always or almost always
13	research salary prestige publications teamwork self_development	What makes you satisfied with your job? Check all that apply	○ Contribution to research ○ Salary ○ Social prestige ○ Publications and scientific awards ○ Other [please specify]
14	inadequate_training bureaucracy low_salary career_opportunities life_work_imbalance overqualification demotion high_workload	What makes you dissatisfied with your job? Check all that apply	○ Inadequate training ○ Too much bureaucracy ○ Salary too low ○ Few opportunities for career advancement/further education ○ Life-work imbalance ○ Overqualification for the job ○ Demotion ○ High workload

	resources_awareness dissatisfaction		○ Other [please specify]
15	satis_tasks	Are you satisfied with the tasks assigned to you?	○ Very unsatisfied ○ Unsatisfied ○ Neutral ○ Satisfied ○ Very satisfied
16	balance_satis	Are you satisfied with your work-life balance?	○ Very unsatisfied ○ Unsatisfied ○ Neutral ○ Satisfied ○ Very satisfied
Work-life balance and gender balance			
17	lw_maternity_leave lw_paternity_leave lw_smart_working lw_flexible_h lw_part_time lw_kindergarten lw_home_office lw_no_not_sure	What options does your biobank offer to achieve a sustainable work-life balance? Check all that apply	▪ Maternity leave ▪ Paternity leave ▪ Smart working ▪ Flexible working hours ▪ Part-time job ▪ Kindergarten on-site ▪ Home office ▪ No opportunities ▪ I am not sure ▪ Other [please specify]
18	bal_no_not_sure balance_report balance_plan balance_training balance	How is gender balance taken into consideration in your biobank? Check all that apply	▪ It is not taken into consideration ▪ A gender balance report is periodically made ▪ There is an “Equal Opportunity” plan ▪ There is a gender equality training for employees ▪ I am not sure ▪ Other [please specify]
Discrimination Please refer to current workplace			
19	discr_hire	Do you feel that your gender affects your hiring opportunities?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]
20	discr_career	Do you feel that your gender affects your career opportunities?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]
21	discr_colleagues	Do you feel that your gender affects your colleagues’ behaviour towards you?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]
22	discr_superiors	Do you feel that your gender affects your superiors’ behaviour towards you?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]

23	discr_ideas	Do you feel that your gender affects how your ideas/proposals are taken into consideration by your superiors?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]
24	discr_needs	Do you feel that your gender affects how your needs/complaints are taken into consideration by your superiors?	○ No ○ Yes, negatively ○ Yes, positively ○ Other [please specify]
Comments			
25	Comments	If you have any comments or suggestions, please write here	[please specify]
Gender balance of the biobank [Questionnaire for management only]			
26	biobank_size	How many employees work for the biobank?	[number]
27	employees_females	How many women are employed in the biobank?	[number]
28	female_ manager	How many women employed in the biobank occupy a leadership position at any level?	[number]