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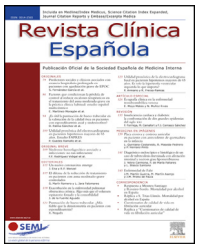

ORIGINAL ARTICLE

Women's leadership in clinical research: A retrospective observational study over two decades in Spain

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KEYWORDS
Clinical research;
Gender inequality;
Principal investigator

Abstract
Background and objective: Available data support differences by gender in the leadership of clinical investigations (CI). This study analyzes to what extent women lead these investigations.
Materials and methods: Observational-retrospective study in a tertiary university hospital associated with one of the most important health research institutes in Spain. We analyzed the principal investigators (PI) by gender from 2001 to 2020. *Main outcome*: proportion of CI led by female doctors (FD) during the study period. *Secondary outcomes*: differences in PI by gender according to the type of study: clinical trials (CT) or non-interventional-researches (NIR) and according to type of funding. Data sources: Research Ethics Committee (REC) and Human Resources Department registries.
Results: During the study, the REC approved 8466 protocols, 52% (4408/8466) were EC, the rest were NIR. Women led 39.7% (3360/8466) of the total. The gender gap was observed mainly in EC: FD were IP of 31.5% of them (1391/4408) and 48.5% (1969/4058) of NIR. This despite the increasing trend in the number of FD staff. By type of funding, when the studies were supported by private sector there was a wider gap markedly unfavorable for women.

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Conclusions: Our results show that there is underrepresentation of women in research leadership, mainly those with private financing. This study reinforces the idea that there is still a long way to go in this field. More studies are necessary to identify the existing differences that allow the implementation of actions at the institutional and cultural level that promote gender equality in the field of clinical research.

PALABRAS CLAVE
Investigación clínica;
Desigualdad de género;
Investigador principal

Liderazgo de la mujer en la investigación clínica: estudio observacional retrospectivo durante dos décadas en España

Resumen
Antecedentes y objetivo: Los datos disponibles avalan las diferencias por género en el liderazgo de las investigaciones clínicas (IC). Este estudio analiza en qué medida las mujeres lideran estas investigaciones.
Materiales y métodos: Estudio observacional retrospectivo en un hospital universitario terciario asociado a uno de los institutos de investigación sanitaria más importantes de España. Analizamos los investigadores principales (IP) por género (2001–2020). *Variable principal*: proporción de IC lideradas por mujeres durante el período de estudio. *Variables secundarias*: diferencias de IP por género según el tipo de estudio: ensayos clínicos (EC) o estudios de no-intervención (ENI) y según la financiación. Fuentes de datos: registros del Comité de Ética en Investigación con medicamentos (CEIm) y del Departamento de Recursos Humanos.
Resultados: Durante el estudio, el CEIm aprobó 8.466 protocolos; el 52% (4.408/8.466) fueron EC y el resto, ENI. Las mujeres lideraron un 39,7% (3.360/8.466) del total. La brecha de género se observó principalmente en EC: las mujeres fueron IP de un 31,5% de ellos (1.391/4.408) y de un 48,5% (1.969/4.058) de los ENI. Ello a pesar de la tendencia creciente del número de facultativas. Los estudios de financiación privada fueron más comúnmente liderados por hombres.
Conclusiones: Nuestros resultados demuestran que existe una infrarrepresentación de las mujeres en puestos de liderazgo en la investigación, principalmente en aquellos con financiación privada. Este estudio refuerza la idea de que todavía queda un largo camino por recorrer en este campo. Se necesitan más estudios para la identificación de diferencias existentes que permitan implantar cambios a nivel institucional y cultural que promuevan la igualdad de género en el ámbito de la investigación clínica.

Introduction

Inequalities in science are a reality that have not only not improved in recent years but have in fact worsened.[1] Data on gender inequalities reveal disproportionate differences between men and women in terms of involvement and leadership positions in clinical research.[2–6]

This gender gap is even more striking given that a higher proportion of women obtain university and doctoral degrees in research fields. Published data reveal that women account for almost half of postdoctoral fellows in biomedical sciences but only 19% of senior investigators. Furthermore, women lead fewer research projects.[7,8]

Despite the growing number of women enrolled in health-related university degrees, there is also gender inequality in this area. Although the number of female graduates in healthcare fields is higher, more men than women earn doctoral degrees; this disproportion is even greater in regard to the number of female professors.[4,9]

The main obstacle when studying women in science is a lack of gender-disaggregated data and statistics that are systematically collected and released. On the other hand, not all figures collected are published and those that are published are not always reported in a direct manner that would facilitate their study.

In light of this lack of data, this work aims to assess inequalities between male and female doctors' involvement in clinical research in the hospital setting and to provide new gender-disaggregated data on this issue.

Objetives

This work aims to analyze the extent to which female doctors (FD) working in hospitals are involved in clinical

research leadership and changes in this trend over two decades.

This work also evaluates gender differences in leadership according to study type, classified as either clinical trials (CT) or non-interventional research studies (NIR), as well as differences in the type of financial support for research: either private, public, or unfunded.

Material and methods

This work is a retrospective observational study of the gender distribution in the leadership of clinical research studies conducted in a tertiary hospital (1300 beds) from 2001 to 2020. The hospital analyzed is associated with one of the leading clinical health research institutions in Spain.

Given that all clinical studies conducted at the hospital were approved by the same hospital research ethics committee (REC), its database was used to search for all principal investigators (PI) over the study period and classify them by gender.

Furthermore, the hospital's Human Resources Department's records were used as a reference in order to determine the proportion of FD and male doctors (MD) who work in the hospital and who led clinical research studies. This database also allowed for analyzing changes in the proportion of MD and FD working in the hospital over the 20 year study period and changes in the proportion of men and women occupying the highest positions in clinical departments. Residents were not included in the study.

To evaluate the effect of time on the aggregated data by gender, a linear regression model was calculated for each gender. Adjustments to the data were evaluated using the coefficient of determination (R^2) and were analyzed using Microsoft Office 2003.

As this study did not involve patients, REC approval was not required for its conduct.

Statistical analysis

For the data analysis, a database was designed that reflected the content of the data collection notebook such that the data entry table had intervals or possible values, as well as the different coherence rules between variables. Data were analyzed using descriptive statistical measures (absolute and relative frequencies) of the differences in the number of FD and MD.

Results

From 2001 to 2020, the REC approved 8466 clinical studies, of which 52% (4408/8466) were CT and the rest were NIR. FD were the PI in 3360 of the 8466 studies (39.7%).

Table 1 shows the distribution of FD and MD in terms of doctors who work at the hospital, doctors who are department heads, and doctors involved in clinical research as a PI during the study period.

There has been an increase in the total number of research studies conducted at the center over the study period. In addition, an upward trend in the number of projects led by women has also been observed. However, the number of FD working in the hospital has also increased significantly over the same time period, with the number of FD surpassing the number of MD in 2011. At the end of the study period, FD accounted for 59.5% (736 FD vs 500 MD) of all doctors on staff. Given the greater proportion of FD, the gender gap persists when analyzing female involvement in clinical research (Fig. 1).

In regard to the type of research study—either CT or NIR—women led 1391/4408 (31.5%) of CT and 1969/4058 (48.5%) of NIR. Important differences between FD and MD were found when analyzing the data by study type: the PIs of CT were mostly MD whereas no important gender differences were observed in the leadership of NIR (Fig. 2).

The differences between male and female involvement in clinical research were also analyzed in economic terms. This work found different trends according to funding sources. When grants came from private organizations (mostly pharmaceutical companies for CT or scientific societies), the gap between female and male PIs was greater and markedly unfavorable for FD. However, when the funding came from public institutions or the research did not receive financial support, the gap was narrower (Fig. 3).

Changes in the total number of FD and MD, the number of FD and MD who occupied the top positions in departments (Fig. 4), and the proportion who served as PIs were also analyzed. An upward trend in the proportion of FD leading research projects was found, although the percentage was still very low compared to MD.

Discussion

The results of our study provide new data on the underrepresentation of FD in leadership positions in clinical research.

Our results show an increase in the absolute number of FD who have served as PIs of clinical research in our center over the study period. However, this has occurred in parallel with an increase in the number of MD who have served as PIs, even though there are more MD than FD; thus, the gender gap that existed at the start of the study has been maintained over time.

Other authors have also found evidence of gender disparities in this field.[2,10] Caprile et al.[11] identified different factors that may contribute to this discrimination, including pre-established stereotypes or less competitive attitudes among women. Other previously published research on this topic has also pointed to the influence of sexist stereotypes and gender biases to explain discrimination in scientific and academic settings in the field of health.[12,13]

Despite the commitment of important institutions, such as the European Commission, to promote women's scientific careers, the reality is that inequality in clinical research exists and has remained constant over the years. Moreover, available data show a ''glass ceiling'' and a shortage of FD in leadership positions in clinical research.[2,4,8]

The results of this study are even more disappointing when considering the high proportion of women who graduate from universities with health sciences degrees. In Spain, the percentage of women in these programs has increased by an average of 2.5 points over the last five years and today, 70% of health sciences graduates are women.[14]

Table 1 Distribution of the staff by gender over the study period (2001–2020).

	Staff doctor			Department head			Principal investigator (PI)			% of PI to total PI by gender		% of PI to total staff by gender	
Year	MS	FS	TS	MH	FH	TH	MPI	FPI	TPI	MPI/TPI	FPI/TPI	MPI/MS	FPI/FS
2001	602	367	969	54	8	62	111	37	148	75.0	25.0	18.4	10.1
2002	591	377	968	53	8	61	173	63	236	73.3	26.7	29.3	16.7
2003	583	394	977	53	8	61	149	63	212	75.9	29.7	25.6	16.0
2004	571	438	1009	49	8	57	189	60	249	75.1	20.1	33.1	13.7
2005	590	474	1064	52	12	64	157	52	209	72.3	24.9	26.6	11.0
2006	608	513	1121	51	13	64	191	73	264	70.7	27.6	31.4	14.2
2007	607	556	1163	54	12	66	249	103	352	65.6	29.3	41.0	18.5
2008	584	536	1120	54	11	65	208	109	317	59.9	34.4	35.6	20.3
2009	586	551	1137	51	12	63	226	151	377	63.5	40.0	38.6	27.4
2010	571	558	1129	45	10	55	244	140	384	63.5	36.4	42.7	25.1
2011	569	580	1149	47	9	56	282	165	447	63.1	36.9	49.6	28.4
2012	530	581	1111	47	6	53	275	159	434	63.4	36.6	51.9	27.4
2013	457	540	997	41	6	47	263	188	451	58.3	41.7	57.5	34.8
2014	494	613	1107	45	9	54	338	230	568	59.5	40.5	68.4	37.5
2015	482	642	1124	42	9	51	320	224	544	58.8	41.2	66.4	34.9
2016	474	655	1129	40	10	50	299	221	520	57.5	42.5	63.1	33.7
2017	474	663	1137	40	12	52	306	300	606	50.5	49.5	64.6	45.2
2018	473	685	1158	39	14	53	317	326	643	49.3	50.7	67.0	47.6
2019	486	701	1187	39	14	53	357	309	666	53.6	46.4	73.5	44.1
2020	505	736	1241	33	15	48	452	387	839	53.9	46.1	89.5	52.6

MS: male staff, FS: female staff, TS: total staff, MH: male department heads, FH: female department heads, TH: total department heads, MPI: male principal investigators, FPI: female principal investigators, TPI: total principal investigators.

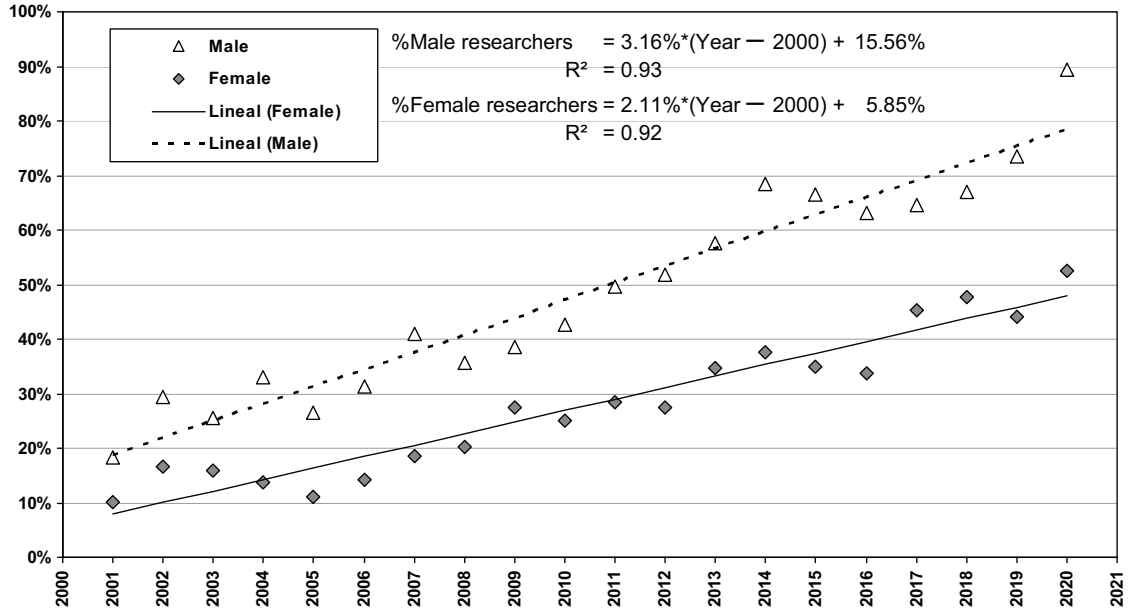


Figure 1 Changes in relative proportions by gender of principal investigators.
Y axis: ratio by gender (% of principal investigators/total number of staff doctors by gender, i.e. % of female principal investigators/female doctors and % male principal investigators/male doctors).
X axis: year.

Similarly, horizontal gender imbalances persist in positions of scientific renown and women are underrepresented in scientific institutions, both in decision-making positions and as contract researchers.[2] A possible cause of these imbalances is the so-called ''rush hour'' of a professional career, that is, the time of life when family demands are greater, which can lead to women to prioritize these family demands over career progression more

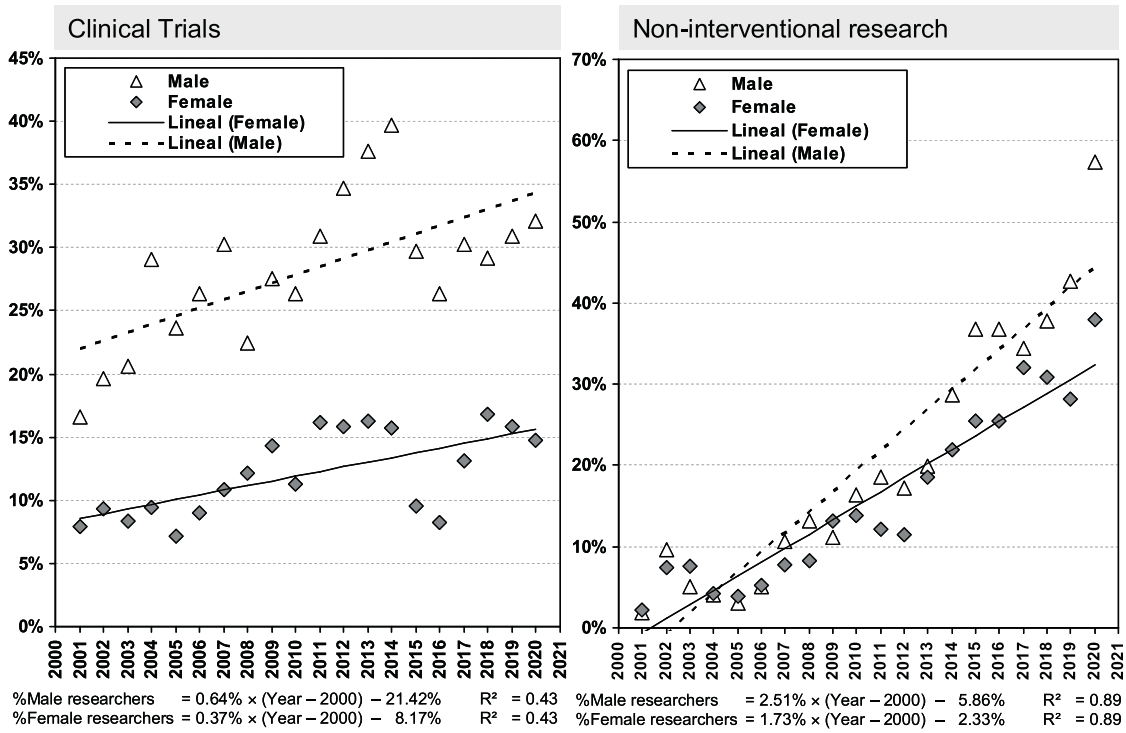


Figure 2 Evolution of gender in clinical research leadership by type of investigation.
Y axis: ratio by gender (% of principal investigators/total number of staff doctors by gender, i.e. % of female principal investigators/female doctors and % male principal investigators/male doctors).
X axis: year.

so than men; this situation can become perpetuated over time.[15–17]

This work also evaluated gender differences in clinical research in economic terms. It is known that women are vastly underrepresented in top income groups and a substantial pay gap remains between men and women. By disaggregating the data by type of funding, a substantial gender difference was found.

According to the data, the number of MD who serve as PIs of research studies that receive private financial support—projects for which the PI might receive additional remuneration for their leadership—increased over the study period. On the other hand, NIR, which usually receive no funding and are not sponsored by private entities, have been led equally by MD and FD. Once again, in view of these data, women are economically disadvantaged by this situation.

In line with these findings, previously published data have shown that women lead funded projects to a much lesser extent than men.[18–23] Denvy et al.[24] found that only one out of every ten published studies resulting from CT had a female investigator in the first or senior authorship position. The prestigious journal *Nature* has also analyzed this gender gap in science, finding that female scientists are paid less and that institutions grant fewer projects to women despite them holding equal qualifications.[15] The potential role of pharmaceutical companies in promoting gender equality in the leadership of CT merits mention, since they are responsible for selecting the PIs at each center.

Prior research works have suggested that gender parity in clinical research teams may produce higher quality research.[25] Moreover, greater visibility of FD in CT leadership positions could encourage the recruitment of female participants and attract more female investigators to these studies. Although this study did not assess causality, unconscious biases may lead to gender discrimination in the selecting CT leadership. The interplay of all these circumstances creates a vicious cycle, with the exclusion of women leading to further exclusion, a lack of recognition, and fewer promotions.[2,4,26]

In contrast to the trends observed with privately funded projects, this study noted less of a gender difference when the research was funded by public institutions. Indeed, over the last 20 years, the percentage of FD and MD in these studies has been similar.

This work also analyzed the gender ratios of the doctors working in the hospital year by year. From 2001 to 2010, the proportion of men was higher than that of women. Then, from 2010 to 2020, the trend reversed significantly. However, when analyzing gender trends in doctors who occupy highest positions in clinical departments, this shift in favor of FD was not found, but rather there was a gender gap.

An analysis of the data revealed a ''glass ceiling'' in the top positions: a significant difference according to sex was detected among department heads. This underrepresentation of women in positions of power in hospitals is also observed in institutions such as scientific societies and public research institutions.[2,27]

In relative terms, the data showed that despite the higher proportion of FD in our center, more MD lead clinical research. In our center, there is more clinical research

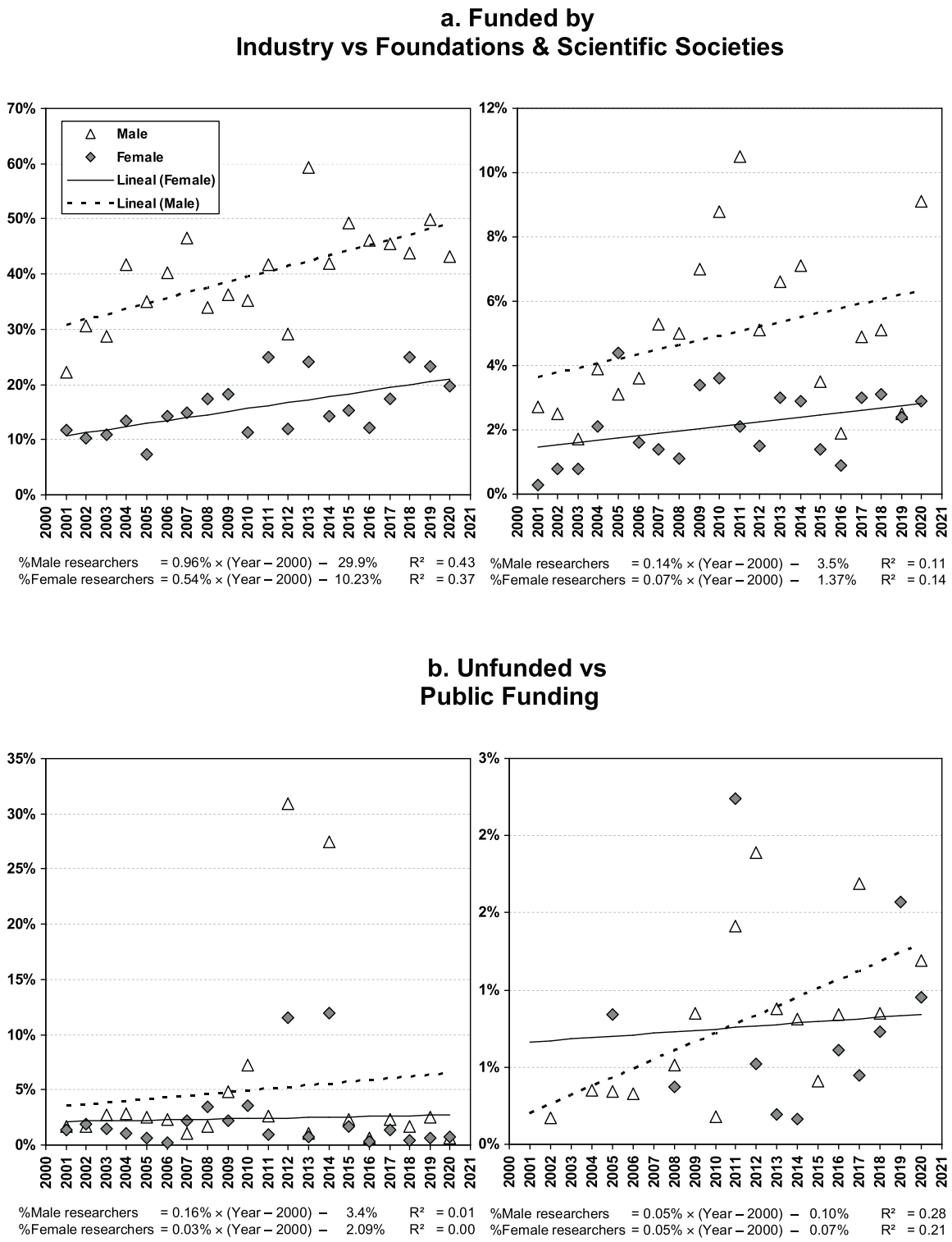
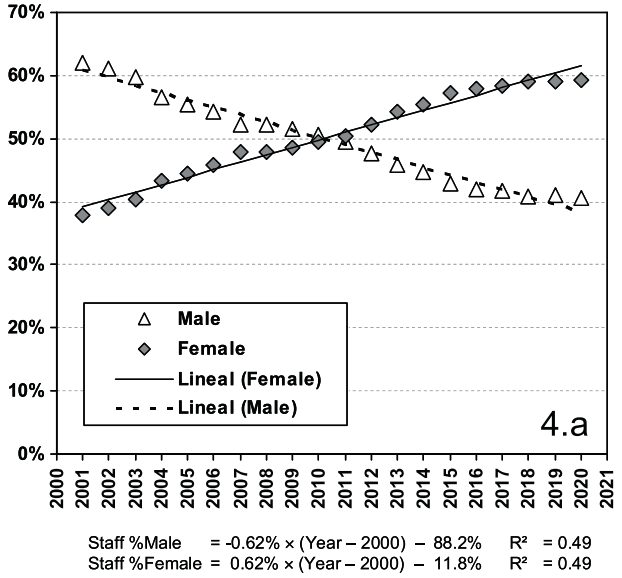


Figure 3 Differences in gender in research leadership according to funding source. (a) Funded by Industry vs Foundations & Scientific Societies. (b) Unfunded vs Public Funding.
Y axis: ratio by gender (% of principal investigators/total number of staff doctors by gender, i.e. % of female principal investigators/female doctors and % of male principal investigators/male doctors).
X axis: year.



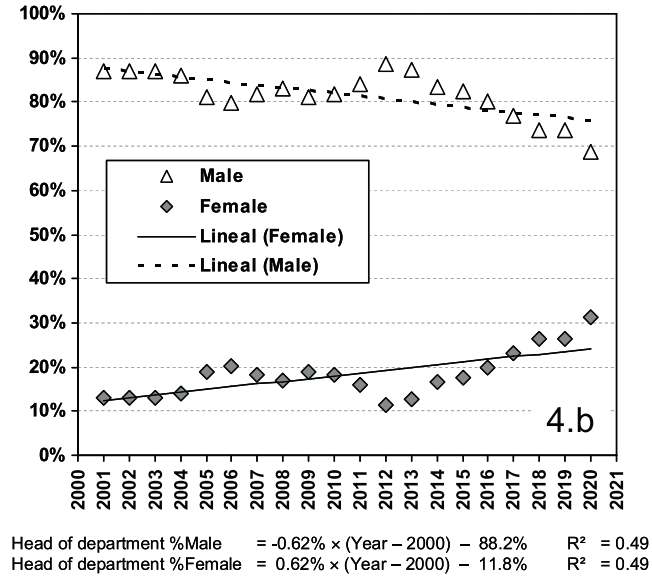


Figure 4 Evolution in the total number of female and male staff doctors and females and males in the highest professional positions.
Y axis: ratio by gender (4.a) % of staff doctors by gender, (4.b) % of department heads by gender.
X axis: year.

overall, as evidenced by the greater number of studies conducted over the last 20 years, yet despite this, the gender gap has remained constant.

This study has the potential limitations inherent to a descriptive analysis. The results may be biased due to unmeasured confounding factors that may influence the lesser involvement of women in research and funded projects. It must also be considered that the PI of CTs and funded projects is usually the department head and, as has been shown herein, most department heads over the 20 year study period have been men. This has likely influenced in the gender differences observed in the results. Indeed, it will likely take more than ten years for the gender distribution of hospital staff (with more FD in this case) to match the gender distribution in the assignment of PIs.

Conclusions

An upward trend has been observed in the number of FD leading clinical research over the last two decades: FD now lead around 50% of all research works conducted at our center. However, a gender gap persists because for the last ten years, more FD than MD have worked at our hospital. The gender gap is particularly large when specifically analyzing studies which received private financial support.

Further review will be needed in a few years to confirm whether the change in the gender balance among hospital staff has impacted the selection of FD as PI.

This study demonstrates that despite progress in reducing gender inequalities, there is still a long way to go in the field of clinical research. More data and more studies on this issue will allow for delving into the problem to detect possible causes and identify barriers.

On the other hand, it is hoped that this evidence of these differences will spur and strengthen actions and changes at the institutional and cultural level in order to promote gender equality in clinical research.

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Conflicts of interest

The authors declare no conflicts of interest.

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