RESEARCH LETTER

The Inclusion of Women in Global Oncology Drug Trials Over the Past 20 Years

Thirty years have passed since the enactment of the National Institutes of Health (NIH) Revitalization Act, which encouraged NIH-funded investigators to include adequate numbers of women in clinical studies.[1] Since then, there have been important steps taken to ensure better representation of women and racial and ethnic minority groups in biomedical trials.[2] However, lack of representation remains problematic in oncology. Previous research suggests that women represent approximately 30% to 40% of participants in trials leading to drug approvals in the US.[3,4]

Supplemental content

In 2010, the NIH Office of Research on Women's Health[5] set forth a vision to advance the understanding of sex-specific disease differences by 2020. As clinical trials become international in scope, we sought to evaluate the global movement toward this vision in oncology. In this cohort study, we reviewed enrollment patterns of completed cancer drug trials over the past 20 years to compare sex-specific trial participation to current cancer incidence rates. Using data from the International Agency for Research on Cancer (IARC),[6] we identified 6 common solid tumor types for women (lung, colon, thyroid, melanoma, kidney, and pancreas).

Methods | We conducted a systematic search of cancer drug trials registered on ClinicalTrials.gov between 2000 and 2020 for 6 common cancers for women (excluding breast and uterus). The investigation of publicly available trial protocols was exempt from institutional review board approval. We included completed drug trials with results for adults (≥18 years). Behavioral, device, procedure, and radiotherapy trials were excluded (eFigure in the Supplement). Pearson χ^2 test of independence was used to evaluate the association between female and male enrollment and phase (1, 2, 3), tumor type, and funding source. *P* values used 2-tailed tests, with $P < .05$ being significant. We explored changes in sex-specific enrollment patterns over 2 decades by stratifying trials as 2000 to 2010 and 2011 to 2020. Cancer incidence rates were calculated by dividing the number of new male and female cases by the total number of new cases per tumor type (2020).[6] Data analysis was performed using R statistical software, version 1.1.463 (R Foundation).

Results | We identified 505 oncology clinical trials that met the eligibility criteria between 2000 and 2020. Of the total 182 416 participants, 73 103 (40%) were women, while 109 313 (60%)

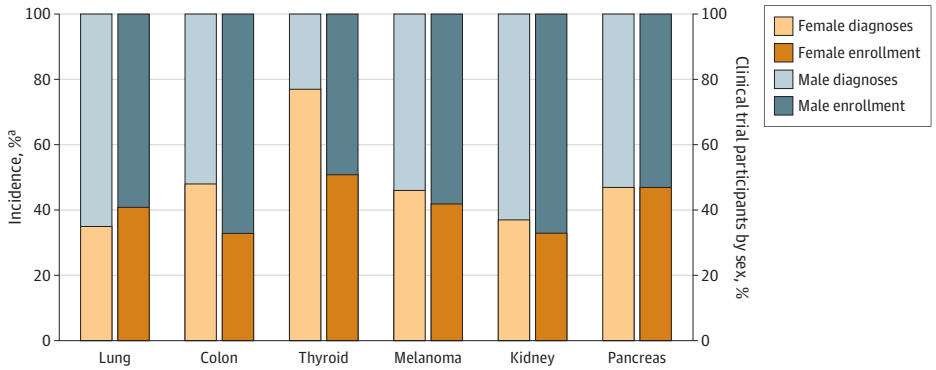
Table. Comparison Between Sex-Specific Enrollment and Clinical Trial Characteristics

Characteristic	Sex, No. (%)		*P* value[a]
	Female	Male	
Total enrolled	73 103 (40)	109 313 (60)	<.001
Trial phase			
1	3034 (48)	3322 (52)	.001
2	18 838 (43)	24 508 (57)	<.001
3	40 139 (38)	66 611 (62)	<.001
Year			
2000-2010	23 350 (40)	34 745 (60)	<.001
2011-2020	49 753 (42)	68 022 (58)	
Tumor type			
Lung	40 829 (41)	57 979 (59)	<.001
Colon	7600 (33)	15 266 (67)	<.001
Thyroid	904 (51)	875 (49)	.50
Melanoma	11 317 (42)	15 529 (58)	<.001
Kidney	6586 (33)	13 127 (67)	<.001
Pancreas	5867 (47)	6537 (53)	<.001
Sites			
US	49 911 (40)	75 755(60)	<.001
Canada	29 603 (39)	45 372 (61)	<.001
China	23 456 (41)	33 645 (56)	<.001
United Kingdom	28 472 (39)	44 478 (61)	<.001
Australia	28 505 (39)	44 332 (61)	<.001
Funding (US)			
Industry	41 391 (41)	60 473 (59)	<.001
NIH	6828 (48)	7285 (52)	

Abbreviation: NIH, National Institutes of Health.

[a] *P* values from Pearson χ^2 test of independence.

Figure. Composition of Trial Enrollment and Incidence by Sex per Tumor Type



[a] New cases by sex per International Agency for Research on Cancer 2020 data.[6]

were men. We observed significant differences between the enrollment of sexes across all trial phases and tumor types except thyroid (**Table**). Drug trials for colon and kidney cancer enrolled the least number of women, with 33% participation rates (**Figure**).

Comparing 2000 to 2010 with 2011 to 2020, we observed a marginal increase in female participation, from 40% to 42%, respectively ($P < .001$). We evaluated the association between industry and NIH-sponsored studies in the US (n = 358) and found that NIH-funded trials enrolled a higher proportion of women (48%) compared with industry trials (41%) ($P < .001$).

Discussion | It is essential that women be enrolled in clinical trials in numbers that, at least, mirror the distribution of the disease in the population so that potential biological differences can be understood. Our analysis, although limited to 6 tumor types, suggests that sex differences persist in clinical trials. In 2020, women represented 77% of newly diagnosed thyroid cancer cases worldwide[6] yet comprised only 51% of participants in trials investigating thyroid drugs (Figure). Similarly, women represented 48% of global colon cancer cases[6] yet accounted for only 33% of trial participants for colon cancer therapeutics (Figure).

Higher enrollment of women in NIH-funded studies (48%) compared with industry studies (41%) warrants further exploration, but the stagnant rates of women in trials suggest that regulatory initiatives[2] over the past 2 decades may be insufficient. Our analysis, although limited to sponsor- and manufacturer-disclosed information, demonstrates that persistent inequities remain in the recruitment of female participants in trials investigating new therapeutics for certain tumor types in oncology.

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Use of an Analytics and Electronic Health Record–Based Approach for Targeted COVID-19 Vaccine Outreach to Marginalized Populations

Equity in vaccine outreach and delivery has been prioritized given the disproportionate harms of the COVID-19 pandemic on communities of color and those with lower socioeco-