Research Article

iMedPub Journals
http://www.imedpub.com/

Journal of Cancer Epidemiology and Prevention

2017
Vol.2 No.1:1

Representation of Minorities and Elderly in Cancer Clinical Trials at a Single Institution-The William Beaumont Hospital Experience

Mohammed Ibrahim, Foluso Ogunleye, Jennifer Roye, Siddhartha Yadav, DiAne Townsel, Zhou Yu, the Beaumont Health Hematology and Oncology Consortium* and Ishmael Jaiyesimi

Beaumont Health System, Royal Oak, Michigan

Corresponding author: Mohammed Ibrahim MD, Beaumont Health System, 3577 W. 13 Mile Rd, Suite 202a, Royal Oak, MI 48073, Tel: 248-551-4975; Fax: 248-551-3154; Email: Mohammed.Ibrahim@beaumont.edu

Received date: February 21, 2017; **Accepted date:** March 10, 2017; **Published date:** April 01, 2017

Citation: Ibrahim M, Ogunleye F, Roye J, et al. Representation of Minorities and Elderly in Cancer Clinical Trials at a Single Institution-The William Beaumont Hospital Experience. J Cancer Epidemiol Prev. 2017, 2:1.

***Members of the Beaumont Health Hematology and Oncology Consortium:**

John Robertson, MD, Adil Akhtar, MD, Robin Duris, RN, Paul Rigo, BS, Dana Zakalik, MD, Jeffrey Margolis, MD, Matthew Cotant, MD, Laura Nadeau, MD, Joseph Anderson, MD, Michael Stender, MD, Susanna Gaikazian, MD, Marianne Huben, DO, George Howard, MD, Harry Wasvary, MD, Eric Brown, MD, Daniel Krauss, MD, Jannifer Stromberg, MD and Thomas Lanni, MBA.

Running head: Minorities and elderly in cancer trials

Funding: None Conflict of interest: None

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Acknowledgements: The authors would like to acknowledge the help provided by Ms Rose Callahan, MS in editing this manuscript.

Abstract

Background: Disparities in the enrollment of minorities and elderly in cancer clinical trials have been reported in large national studies. We studied patient enrollment in clinical trials at William Beaumont Hospital for the years 2002 to 2013.

Methods: We obtained data on patient enrollment in cancer clinical trials for the time period of 2002 to 2013 from William Beaumont Hospital Community Clinical Oncology Program and Cancer Clinical Trials Office. We acquired data on cancer incidence at William Beaumont Hospital for the years 2002 to 2013 from the Beaumont Cancer Registry. Enrollment rate was calculated as the ratio of trial enrollment to the cancer incidence for different races and ethnicities, age groups and genders.

Results: The overall enrollment rate for the years 2002 to 2013 for all patients was 3.5%. The enrollment rate for men was significantly lower at 1.2% compared to 5.4% for women ($p<0.001$). The enrollment rates were similar for white and minority patients at 3.8% and 3.6% respectively. The enrollment rate was highest for the age group 31-49 years (6.9%) and lowest for the age group of over 75 years (0.8%).

Conclusions: The overall enrollment rate remains low. Enrollment rates were low, but similar for both white and minority patients. Increasing availability and access to clinical trials should increase enrollment rates for all patients. More efforts are needed to address the significantly low enrollment rates in all groups of patients, especially those over the age of 65 years.

Keywords: Minorities; Disparities; Cancer Clinical Trials

Introduction

Cancer is one of the leading causes of death worldwide. In 2017, it is estimated that 1,688,780 new cases of cancer will be diagnosed in the US and 600,920 people will succumb to the disease [1]. Cancer is the second most common cause of death in the United States, behind only coronary artery disease, and accounts for nearly 1 in 4 deaths [1].

In the US, cancer related deaths have declined overall from 2003 to 2012 by 1.8% per year among men and 1.4% per year among women [2]. However, certain ethnic and racial groups continue to suffer from a disproportionately higher incidence of cancer and have significantly worse outcomes. African American men, for instance, have a higher incidence of prostate cancer as well as higher risk of dying from their disease [3]. African American women have a higher incidence of triple negative breast cancer compared to other racial and ethnic groups [3]. A higher incidence of liver cancer has been found in Asian and Pacific Islander populations [2]. It is critical to have adequate representation of minorities in clinical trials in order to better understand disease biology and optimize treatment options. Unfortunately, several studies have shown that minorities are under-represented in cancer clinical trials [4-6].

The objectives of our study were to evaluate the enrollment of minorities and the elderly in our clinical trials and use this information to formulate an action plan to address any disparities.

Methods

We obtained Institutional Review Board (IRB) approval for this study. We acquired data on patient enrollment in cancer treatment clinical trials from the Community Clinical Oncology Program (CCOP) and the Cancer Clinical Trials Office (CCTO) at William Beaumont Hospital for the years 2002 to 2013. We collected data on patient demographics including race/ethnicity, age, gender, type of clinical trial and disease site. Patients under 18 years of age were excluded. Data on cancer incidence was obtained from the Beaumont Cancer Registry for the years 2002 to 2013. Enrollment in cancer trials was examined for 4 major cancer types: colorectal, lung, breast and prostate. We assigned patients into 1 of 6 mutually exclusive racial/ethnicity categories: White, Black, Hispanic, Asian, Native Hawaiian and American Indian.

Statistics

Enrollment rate was calculated as the ratio of trial enrollment to cancer incidence for different racial/ethnicity, age and gender groups, as recently described by Zullig et al. [6]. Odds ratio was calculated for each group with 95% confidence intervals. P values were calculated using Fisher's exact test. All tests were 2 sided. Data analysis was performed using SPSS version 21 statistical software.

Results

A total of 55,408 patients over 18 years of age were diagnosed with cancer at William Beaumont Hospital from 2002 to 2013. Of these 55,408 patients, 1,924 patients were enrolled in cancer clinical trials, yielding an enrollment rate of 3.5%.

Race was not reported in 5,209 of the 55,408 patients who were diagnosed with cancer. Race was also not reported in 9 of the 1,924 patients enrolled in clinical trials. The enrollment rate for minority patients (3.6%) was similar to that for the white population (3.8%) [OR 0.94, 95% CI 0.81-1.10]. Enrollment rate for Blacks, Hispanics, Asians and Native Hawaiian patients was 3.5%, 7.6%, 3.4% and 5.6% respectively. Table 1 shows the cancer incidence and enrollment rates, odds ratios with 95% confidence intervals and p values for different racial and ethnic groups.

Table 1: Cancer incidence and accrual data in cancer clinical trials at Beaumont Health System (2002-2013) based on race, age and gender.

	Cancer incidence	Patients enrolled	Enrollment Rate %	OR (95% CI)	P value
All Patients	55408	1924	3.5		
Male	25473	316	1.2	Referent	
Female	29931	1607	5.4	4.51 (3.99-5.10)	<0.001
Not documented	4	1			
White, non-Hispanic	44707	1715	3.8	Referent	
All minorities	5492	200	3.6	0.94 (0.81-1.10)	0.5
Black	4354	152	3.5	0.90 (0.76-1.07)	0.256
Hispanic	275	21	7.6	2.07 (1.32-3.24)	0.001
Asian	772	26	3.4	0.87 (0.58-1.29)	0.501
American Indian	73	0	0		
Native Hawaiian	18	1	5.6	1.47 (0.19-11.08)	0.506
Not documented	5209	9			

The mean age of diagnosis with cancer was 64 years, whereas the mean age at enrollment in clinical trials was 45.9 years. Patients over the age of 65 years were significantly less likely to be enrolled in cancer treatment trials compared to patients under the age of 65 years. The enrollment rate was 1.8 % for patients over 65 years compared to 5.2% for patients under the age of 65 years [OR 0.34, 95% CI 0.31-0.37]. Table 2

shows the enrollment rates with odds ratios for the different age groups.

Table 2: Cancer incidence and accrual data in cancer clinical trials at Beaumont Health System (2002-2013), based on race, age and gender.

	Cancer incidence	Patients enrolled	Enrollment rate %	OR (95% CI)	p-value
Age (Elderly vs Younger patients)					
< 65 years	26781	1395	5.2	referent	
> 65 years	28609	529	1.8	0.34 (0.31-0.37)	<0.001
Age stratified					
31-49 years	7494	516	6.9	referent	
18-30 years	872	41	4.7	0.66 (0.48-0.92)	0.014
50-64 years	18415	838	4.6	0.64 (0.57-0.72)	<0.001
65 -74 years	13951	405	2.9	0.40 (0.35-0.46)	<0.001
> 75 years	14658	124	0.8	0.11 (0.09-0.14)	<0.001
Race and Gender					
White male	20618	265	1.3	referent	
White female	24085	1450	6	4.92 (4.31 - 5.61)	<0.001
Black male	1883	42	2.2	1.75(1.26-2.43)	<0.001
Black female	2471	110	4.5	3.75 (2.85-4.48)	<0.001
Race and Age					
White < 65 years	21125	1231	5.8	referent	
White >65 years	23570	484	2.1	0.33 (0.30-0.37)	<0.001
Black > 65 years	2113	33	1.6	0.25 (0.18-0.36)	<0.001
Black < 65 years	2239	119	5.3	0.90(0.74-1.10)	0.34
Age and gender					
Male < 65 years	11379	178	1.6	referent	
Male > 65 years	14089	138	1	0.62(0.49-0.77)	<0.001
Female > 65years	14516	391	2.7	1.74(1.45-2.08)	<0.001
Female < 65years	15402	1216	7.9	5.39(4.60-6.32)	<0.001

On further stratification of age groups, patients in the age group of 31-49 years had the highest enrollment rate (6.9%), while patients over the age of 75 years had the lowest enrollment rate (0.8%). Patients in the age group of 65-74 years had an enrollment rate of only 2.9% compared to an enrollment rate of 6.9% for patients in the age group of 31-49 years [OR 0.40, 95% CI 0.35-0.46].

The enrollment rate for women (5.4%) was substantially higher than that of men (1.2 %) [OR 4.51, 95% CI 3.99-5.10]. White women had significantly higher enrollment rate of 6% compared to white men (1.3%), [OR 4.92, 95% CI 4.31-5.61]. Black women (4.5%) and black men (2.2%) also had higher enrollment rates than white men ([OR 3.57, 95% CI 2.85-4.48] for black women and [OR 1.75, 95% CI 1.26-2.43] for black men respectively).

We compared enrollment rates for men and women over and under the age of 65 years. Men under the age of 65 years had an enrollment rate of only 1.6%. Women under 65 had a significantly higher enrollment rate of 7.9% when compared to men under the age of 65 [OR 5.39, 95% CI 4.60-6.32]. Women over the age of 65 also had higher enrollment rate (2.7%) than men under the age of 65 years [OR 1.74, 95% CI 1.45-2.08]. Men over the age of 65 years had an even lower enrollment rate of 1% [OR 0.62, 95% CI 0.49-0.77] when compared to men under the age of 65 years. Table 2 provides more information regarding combined race and sex, race and age and age and gender subgroup analyses.

We analyzed cancer incidence and enrollment data for 4 major cancer types: breast, colorectal, prostate and lung cancer. On average, we have 12-15 breast cancer trials, 2-3

colon cancer trials, 3-4 lung cancer trials and 3-4 prostate cancer trials that are open annually. The overwhelming majority of these trials are NCI supported and funded cooperative group studies. 11,923 patients were diagnosed with breast cancer during the years 2002 to 2013, of which 1,333 patients were enrolled in clinical trials, yielding an enrollment rate of 11.2%. The enrollment rates were similar for both black (13.1%) and white (12.8%) patients in breast cancer trials. The enrollment rates were much lower in trials for lung cancer (1.2%), colorectal cancer (2.7%) and prostate cancer (1.8%) as shown in table 3. Black patients had higher enrollment rates compared to white patients in colorectal and prostate cancer trials. Table 3 provides information on overall and race-based enrollment in breast, colorectal, prostate and lung cancer trials.

Table 3: Cancer incidence and accrual data for white and minority patients in breast, colon, prostate and lung cancer clinical trials at Beaumont Health System (2002-2013).

	Cancer incidence	Patients enrolled	Enrollment rate %	OR (95% CI)	p-value
Cancer Type					
Breast	11923	1333	11.2	referent	
Colorectal	4557	122	2.7	0.21(0.18-0.26)	<0.001
Lung	6459	80	1.2	0.10(0.07-0.12)	<0.001
Prostate	7373	131	1.8	0.14(0.12-0.17)	<0.001
Cancer Type and Race					
Colorectal-white	3749	102	2.7	referent	
Colorectal-black	402	20	5	1.87(1.14-3.05)	0.018
Lung-white	5361	75	1.4	referent	
Lung-black	544	5	0.9	0.65(0.26-1.62)	0.44
Breast-white	9412	1208	12.8	referent	
Breast-black	883	116	13.1	1.02(0.83-1.26)	0.797
Prostate-white	5622	107	1.9	referent	
Prostate-black	692	24	3.5	1.85(1.18-2.90)	0.01

Discussion

In our study, we found that the overall enrollment rate in cancer treatment clinical trials was only 3.5 %. This is similar to the low enrollment rates of less than 5% noted in other large studies [4-7].

The enrollment rate for women (5.4%) was significantly higher than that of men (1.2 %) Though women represented 54% of patients diagnosed with cancer, they accounted for over 80% of the enrollees in our cancer treatment trials. There is a preponderance of breast cancer trials at our institution and this accounted for the significantly higher proportion of women enrolled in cancer clinical trials in our institution, compared to men. In our study, 11% of patients diagnosed with cancer and 10% of enrollees in cancer clinical trials belonged to a minority subgroup.

Our catchment area includes the densely-populated Oakland, Macomb and Wayne counties, that center around the city of Detroit in south-eastern Michigan and account for 40% of Michigan's population. In addition, we also serve Lenawee, Monroe, Washtenaw, Livingston, Genessee, Lapeer and St Clair counties. Although Detroit's suburbs are predominantly white, nearby urban and suburban communities exist that have diverse racial and ethnic populations in proximity (within a 30-minute drive or less) to our hospitals. Our overall catchment area includes a minority population of 19%. 12.8% of the population in our overall catchment area is African American, 2.3% is Hispanic, 2.4% is Asian, 0.2 % is American Indian and 1.2% is multiracial.

Though the overall enrollment rates were low, we did not find a statistically significant difference in the enrollment of minority patients compared to white patients. Several initiatives have been started at our institution to address the low enrollment rates in the minorities. One of the first initiatives was the development of a minority outreach program. A previous study by Vicini et al (8) from our institution looked at minority participant accrual by the Beaumont CCTO from 1988 to 2010. This study found that the development of the CCOP lead to a ten-fold increase in clinical trial accrual (p=.001). The minority outreach program, initiated in 2003, targeted metropolitan Detroit areas and provided bilingual cancer education including information on screening and prevention, which helped improve accrual of minorities in our clinical trials to 11% by 2010 (8) The minority outreach program and the CCTO at Beaumont have engaged in fruitful collaborations with various community leaders and faith-based

organizations in the Metro Detroit area, especially those that serve minorities. Educational materials and resources including clinical trials information, American Cancer Society pamphlets and NCI resource pamphlets are provided to the communities. Many of the educational materials are also provided in Spanish and Arabic to serve the needs of the non-English speaking population. The "Cancer Clinical Trials Awareness Week- Fruit Tray Sunday" program was initiated in 2014. This program involved community awareness programs in various churches in metro Detroit area, targeting African American, Hispanic and Arab American populations. In addition to advice on healthy diet and exercise, these programs have helped introduce and explain the concept and importance of clinical trials.

Second, a diverse, multilingual staff at our CCTO assists patients navigate through the clinical trial process, scheduling appointments, insurance authorizations and transportation, and provides social support. After discussion of the clinical trial process with their physicians, patients meet with the staff at the CCTO where the clinical trial protocol is reviewed again in more detail. Patients are educated on the rationale of the study, the type and duration of treatment, need for additional testing or procedures, the randomization process, the major and minor risks including need for more doctor and clinic visits and time off from work as well as possible benefits. Patients are informed about their right to decline participation in a clinical trial without any consequences to their medical care. They are also informed that they can decide to stop participation in the clinical trial at any time. They are provided with contact information for the CCTO office so they have an ongoing resource to answer any additional questions. Once patients understand and agree to the clinical trial, their written consent is obtained.

We suspect that other factors may also influence clinical trial participation and may play a bigger role than race and ethnicity alone, such as educational level, insurance status, access to health care, transportation issues, social support and income level.

It is critical to recognize the disparities in age with regards to clinical trial enrollment. Patients over the age of 65 account for over 60% of all cancer cases in the US, but are only 25% of the participants in clinical trials [9]. Similarly, in our study cohort patients over the age of 65 accounted for 52% of all cancer diagnoses, but were only 27% of patients in clinical trials. Patients over the age of 65 and especially those over the age of 75 are under-represented in our clinical trials. The enrollment rates for patients in the age group of 65-74 (2.9%) and over 75 (0.8%) are significantly lower compared to their younger counterparts. Several studies have examined the incidence of cancer in the elderly and the causes of poor enrollment in cancer clinical trials [10-14]. Elderly patients are likely to have significant comorbid illnesses, which may preclude their participation in clinical trials [12-14]. Physicians attitudes regarding the elderly population can also be a barrier to trial enrollment. Physicians may consider patients' medical co-morbidities, cognitive factors, toxicity concerns, costs, transportation and compliance to be prohibitive [12-14]. Also, physicians may have concerns about insurance coverage for clinical trials, although Medicare does cover routine clinical trial costs [15].

We not only studied enrollment of patients over the age of 65, but also looked at gender and race-based enrollment in that age group. We found that overall enrollment of elderly patients is uniformly low, regardless of race or gender. In our study, the enrollment rates were significantly lower for both white and black patients over the age of 65 (2.1% and 1.6% respectively), compared to the population of white patients under the age of 65 (5.8%) as shown in Table 2. Similarly, both men and women over the age of 65 had lower enrollment rates of 1% and 2.7% compared to women under the age of 65 (7.9%).

Strategies to increase the enrollment of elderly patients should include relaxing eligibility criteria. In one study, for instance, it was found that if the exclusion criteria related to organ system abnormalities and performance status were relaxed, the participation of elderly patients would approach 60%, in line with the cancer incidence in this population [9]. Another strategy would be to increase the number of clinical trials targeting the elderly population, with careful selection of patients. In addition, physician education is necessary to help overcome the attitudinal beliefs regarding elderly patients. In some trials, the incidence and severity of toxicity from chemotherapy was not significantly higher in the elderly than that observed in the younger population, as long as patients were carefully selected [16,17]. Thus, physicians' concerns about tolerability of treatment may be unfounded for many patients.

Breast cancer trials had heavy accrual in our institution compared to colorectal, prostate and lung cancer trials. Breast cancer patients accounted for 21% of all new cancers diagnosed during 2002 to 2013, but represented 69% of enrollees in cancer clinical trials. This underscores the fact that the single main factor that affects clinical trial enrollment is actually the availability of clinical trials. Strategies that increase the number of cancer clinical trials in our institution will lead to increased enrollment of all patients.

In a recent review by Unger et al., barriers to clinical trial participation were discussed [18]. These included structural (clinic access and availability of clinical trials), clinical (eligibility requirements), attitudinal (both physician and patient's attitudes regarding the clinical trial process), demographic and socioeconomic factors [18]. Several studies have shown that even if patients have access to cancer care, the lack of an available clinical trial precludes participation for 50% of patients [19-23]. Even if a clinical trial was available, stringent eligibility criteria, mostly related to co-morbid illnesses, resulted in exclusion of approximately 20% of patients [19-23].

Physician attitudes also play a very important role in clinical trial participation. In addition to those specific to elderly patients discussed above, such attitudes may include concerns about interference with physician-patient relationship [24,25]. uncertainty regarding the randomization process, lack of incentives [27] and concerns about extra workload [25,27].

Patient attitudes include concerns about experimentation and randomization [26,28] toxicity of treatments [29] mistrust of medical science due to past abuses [30] transportation issues [19,31] and cost [31,32].

Socioeconomic status also plays a significant role in trial enrollment. In one study, patients earning less than $50,000 per year were 27% less likely to participate in clinical trials compared to those earning higher salaries [33].

Several actions have been taken at our institution to increase overall accrual to clinical trials. The most important activity has been the frequent educational sessions provided to Medical Oncology, Radiation Oncology and Surgical Oncology physicians. CCTO staff provides information on open clinical trials at various tumor board meetings. In addition, the physicians are provided with updated pocket handbooks every month, which serve as a reference for currently open clinical trials to which they may refer their patients. The CCTO staff helps physicians and patients navigate the path to the clinical trials in an expeditious manner. Other activities included the "Cancer Clinical Trials Awareness Day" that was organized at Michigan's Capitol, Lansing, in June 2014 to increase the awareness of clinical trial activity in the state. The "Royal Oak Coffee with CCTO" event helped create an open dialogue between the CCTO staff and patients, visitors, physicians, community leaders and other Beaumont staff regarding the mission, events and resources the CCTO has to offer. The "Lunch and Learn-Improving Health Professionals' Understanding of Clinical Trials" program at the Beaumont, Royal Oak campus also helped disseminate information about clinical trials to physicians, nurses and other health care staff. The "Eat Healthy, Be Active" workshops, organized by the CCTO's community health educator along with other organizations, included discussions on clinical trials in addition to healthy lifestyle resources and tips on cancer prevention. One of these workshops was targeted to residents of a Senior Living apartment facility, which aimed to help increase the enrollment of the elderly in clinical trials.

Our study is unique in many ways. We looked at clinical trial enrollment only from our institution. Our intention was to study our current accrual patterns so that we could plan and implement strategies to address any disparities and improve overall enrollment. We plan on using this data to guide decisions regarding the allocation of available resources of the Beaumont-NCORP (National Cancer Institute Community Oncology Research program) and CCTO in the future. We believe that the combination of a dedicated minority outreach program and a well-trained CCTO staff that provides both education and support to patients and physicians helps improve accrual for both minorities and the overall population. Other institutions can utilize a similar approach to address the disparities in their accrual. Our data also underscore the idea that the biggest hurdle to clinical trial enrollment is the lack of availability of a clinical trial. The heavy accrual in our breast cancer trials compared to other trials is one example.

Our study had some limitations. We only studied enrollment in clinical trials for adults over the age of 18 years and did not study data for the pediatric population. The pediatric population in general has much higher rates of enrollment in cancer clinical trials than the adult population, especially for those under the age of 15 years, where enrollment rates are typically reported as being greater than 50% [34,35]. Also, race was not reported in 5,209 of the 55,408 patients who were diagnosed with cancer. Race was also not reported in 9 patients in clinical trials. The reasons for this could be several. In our databases, patients self-identified their race. Either race was not asked for or documented for these patients, patients declined to disclose their race or they belonged to a race that is not one of the Federal government-recognized categories. The city of Dearborn, located in Wayne county, Michigan is home to the largest concentration of Arab Americans in the U.S, including Lebanese, Yemenis, Iraqis and Palestinians, but the Middle Eastern ancestry is not a federally recognized race or ethnicity. In most cases, Middle Eastern patients have been considered as Caucasian. It is also unclear how multi-racial patients were reported in the database. Information on factors such as socioeconomic status, insurance status, or educational level was not collected and may influence the results as well. Also, there is a preponderance of breast cancer trials in our institution. This leads to heavy accrual of both white and minority women compared to their male counterparts. Lastly, we only included cancer treatment-related trials in our analysis and excluded other trials on cancer screening, prevention, genetic and biobank studies, etc. It is unclear if the enrollment patterns would differ if these patients were also studied.

The future of Oncology depends on well designed, properly matched clinical trials that have rapid accrual of patients of all age, social and demographic groups. More efforts are needed to increase enrollment of all cancer patients to clinical trials in general and the elderly in particular.

References

1. Cancer Facts and Figures 2017, American Cancer Society, pp:4.
2. Ryerson A, Blythe CR, Eheman SF, et al. (2016) Annual Report to the Nation on the Status of Cancer, Featuring the Increasing Incidence of Liver Cancer. Cancer 122: 1312-1337.
3. National Cancer Institute: The Biology of Cancer Health Disparities.
4. Murthy VH, Krumholz HM, Gross CP (2004) Participation in Cancer Clinical Trials: Race-, Sex-, and Age-Based Disparities. JAMA 291: 2720-2726.
5. Stewart JH, Bertoni AG, Staten JL (2007) Participation in Surgical Oncology Clinical Trials: Gender- Race/Ethnicity and Age-Based Disparities. Annals of Surg Oncol 14: 3328-3334.
6. Zullig LL, Fortune-Britt AG, Rao S (2016) Enrollment and Racial Disparities in Cancer Treatment Clinical Trials in North Carolina. NC Med J 77: 52-58.
7. Tejeda HA, Green SB, Trimble EL (1996) Representation of African-Americans, Hispanics and whites in National Cancer Institute cancer treatment trials. J Natl Cancer Inst 88: 812-816.
8. Vicini F, Nancarrow-Tull J, Shah C (2011) Increasing Accrual in Cancer Clinical Trials with a Focus on Minority Enrollment. Cancer 117: 4764-4771.

9. Lewis JH, Kilgore ML, Goldman DP (2003) Participation of Patients 65 Years of Age or Older in Cancer Clinical Trials. J Clin Oncol 21: 1383-1389.

10. Havlik RJ, Yancik R, Long S (1994) The National Institute on Aging and the National Cancer Institute SEER collaborative study on comorbidity and early diagnosis of cancer in the elderly. Cancer 74: 2101-2106.

11. Yancik R (1997) Cancer burden in the aged: an epidemiologic and demographic overview. Cancer 80: 1273-1283.

12. Kemeny MM, Peterson BL, Kornblith AB (2003) Barriers to clinical trial participation by older women with breast cancer. J Clin Oncol 21: 2268-2275.

13. Kornblith AB, Kemeny M, Peterson BL (2002) Cancer and Leukemia Group B. Survey of oncologist's perceptions of barriers to accrual of older patients with breast carcinoma to clinical trials. Cancer 95: 989-996.

14. Townsley CA, Selby R, Siu LL (2005) Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials. J Clin Oncol 23: 3112-3124.

15. Centres for Medicare & Medicaid Services- Medicare Coverage Clinical Trials- Final National Coverage Decision.

16. Chen H, Cantor A, Meyer J (2003) Can older cancer patients tolerate chemotherapy? A prospective pilot study. Cancer 97:1107-1114.

17. Mariano C, Francl M, Pope J (2015) Comparison of toxicity experienced by older versus younger patients enrolled in breast cancer clinical trials. Clin Breast Cancer 15:73-79.

18. Unger JM, Cook E, Tai E (2016) The Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence and Strategies. ASCO pp: 185-198.

19. Lara PN Jr, Higdon R, Lim N (2001) Prospective evaluation of cancer clinical trial accrual patterns: identifying potential barriers to enrollment. J Clin Oncol 19: 1728-1733.

20. Klabunde CN, Springer BC, Butler B, White MS, Atkins J (1999) Factors influencing enrollment in clinical trials for cancer treatment. South Med J 92: 1189-1193.

21. Javid SH, Unger JM, Gralow JR, Moinpour CM, Wozniak AJ et al. (2012) A prospective analysis of the influence of older age on physician and patient decision-making when considering enrollment in breast cancer clinical trials (SWOG S0316). Oncologist 17:1180-1190.

22. Begg CB, Zelen M, Carbone PP, Mc Fadden, Brodovsky H, et al. (1983) Cooperative groups and community hospitals, Measurement of impact in the community hospitals. Cancer 52: 17601767.

23. Hunter CP, Frelick RW, Feldman AR (1987): Selection factors in clinical trials: results from the Community Clinical Oncology Program Physician's Patient Log. Cancer Treat Rep 71: 559-565.

24. Taylor KM, Margolese RG, Soskolne CL (1984) Physicians reasons for not entering eligible patients in a randomized clinical trial of surgery for breast cancer. N Engl J Med 310: 1363-1367.

25. Benson AB, Pregler JP, Bean JA, Rademaker AW, Eshler B et al. (1991) Oncologists reluctance to accrue patients onto clinical trials: an Illinois Cancer Centre study. J Clin Oncol 9: 2067-2075.

26. Institute of Medicine (2010)-Transforming Clinical Research in the United States: Challenges and Opportunities, Workshop Summary. Washington DC, The National Academies Press.

27. Somkin CP, Altschuler A, Ackerson L (2005) Organizational barriers to physician participation in cancer clinical trials. AmJ Manag Care 11: 413-421.

28. Klabunde CN, Springer BC, Butler B (1999) Factors influencing enrollment in clinical trials for cancer treatment. South Med J 92: 1189-1193.

29. Ellis PM, Butow PN, Tattersall MH (2001) Randomized clinical trials in oncology: understanding and attitudes predict willingness to participate. J Clin Oncol 19: 3554-3561.

30. Jones JH (1993) Bad Blood- The Tuskegee Syphilis Experiment, New York, pp-7.

31. Unger JM, Hershman DL, Albain KS, Moinpour M, Judith A, et al. (2013) Patient income level and cancer clinical trial participation. J Clin Oncol 31: 536-542.

32. Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S et al. (2008) Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer 112: 228-242.

33. Unger JM, Gralow JR, Albain KS (2016) Patient income level and cancer clinical trial participation: a prospective survey study. JAMA Oncol 2:137-139.

34. Bond MC, Pritchard S (2006) Understanding clinical trials in childhood cancer. Paediatr Child Health 11: 148-150.

35. Hunger SP, Lu X, Devidas M (2012) Improved survival for children and adolescents with acute lymphoblastic Leukemia between 1990 and 2005: a report from the Children's Oncology Group. J Clin Oncol 30:1663-1669.