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TITLE: The Role of Lifestyle Factors in Ovarian Cancer Prognosis

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14. ABSTRACT
The primary aims of this study are to evaluate associations between ovarian cancer recurrence and of each of the following: (1) physical activity, (2) healthy diet, (3) vitamin D exposure, (4) smoking, and (5) alcohol intake, as well as to estimate the post-diagnosis prevalence of participation in these lifestyle behaviours among ovarian cancer patients. Over the last year, our efforts were concentrated on commencing recruitment at the three hospital sites originally indicated in the proposal. We had a later than anticipated start at two hospital sites, but recruitment at each of these sites is currently underway. We have found that, overall, recruitment rates are lower than expected based on the information at hand when the study was designed. This can be resolved with no impact on the budget through an increased duration of recruitment.

15. SUBJECT TERMS
None listed

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1. **INTRODUCTION:** This study addresses the research question of how we can improve the prognosis of ovarian cancer, but rather than focus on clinical features and tumor biology, which constitutes the bulk of research on ovarian cancer prognosis, we are examining lifestyle factors that the patients themselves can take action on. In particular, exposures are assessed for the period following ovarian cancer treatment, when patients are in remission and may engage in new lifestyle behaviors that could improve their outcomes. There are currently no published studies that have attempted to address this research question among patients who have traversed the course of diagnosis and treatment, to a state of remission. There are two aims to this study:
   Aim 1: To evaluate associations between ovarian cancer recurrence and of each of the following: (1) physical activity, (2) healthy diet, (3) vitamin D exposure, (4) smoking, and (5) alcohol intake.
   Aim 2: To estimate the prevalence of participation in healthy post-diagnosis lifestyle behaviours in ovarian cancer patients.
   In this study we include women diagnosed with ovarian cancer at three Montreal hospital centers with specialized units in gynecologic oncology.

2. **KEYWORDS:**
   Cohort, epidemiology, survivorship, lifestyle, diet, exercise, physical activity, vitamin D, smoking, alcohol, sun exposure, post-diagnosis exposure, recurrence

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

Aim 1. To evaluate associations between ovarian cancer recurrence and of each of the following: (1) physical activity, (2) healthy diet, (3) vitamin D exposure, (4) smoking, and (5) alcohol intake.			
Major Task 1.1: Study Preparations	**Target date in year 1**	**% completion**	**Actual completion date**
Prepare telephone interview documents, consent form	Oct 2015	100	Oct 2015
Pre-test questions for flow/readability Finalize consent form	Oct 2015	100	Oct 2015
Contract work to prepare computer assisted telephone interview data entry system commences	Oct 2015	100	Mar 2016
Submit grant, questionnaire, consent form, etc. to local IRB	Oct 2015	100	Aug 2015
Submit grant, questionnaire, consent form, etc. and local IRB approval to DoD HRPO	Oct 2015	100	Nov 2015
Local hospital chart access approval CHUM JGH MUHC	 Oct 2015 Oct 2015 Oct 2015	100	 Nov 2015 Feb 2016 Mar 2016
Major Task 1.2: Recruitment and interviews			
Recruitment of target population #1; telephone interview and self-administered CDHQII	Months 1-12 Oct 2015 to Sept 2016	Ongoing but delayed start	n/a
Recruitment of target population #2; telephone interview and self-administered CDHQII	Months 1-12 Oct 2015 to Sept 2016	Ongoing but delayed start	n/a
Ongoing checks of telephone interview data; scanning of CDHQII	Months 1-12 Oct 2015 to Sept 2016	Ongoing	n/a

Major Task 1.3: Review of Patient Pathology Reports/Charts for Remission Status			
Chart reviews; ongoing task with 3 months at end of recruitment to finalize and verify reviews	Months 1-12	Ongoing	n/a
Major Task 1.4: Follow-up			
2nd telephone interview and 2nd self-administered CDHQII	Months 5-12	Ongoing	n/a
Ongoing follow-up of patient charts for outcome assessment (i.e. recurrence)	Months 4-12	Ongoing	n/a

Major tasks 1.1 to 1.3 overlap with Aim 2. The tasks that are in the SOW but not included in this chart above refer to activities targeted for year 2.

What was accomplished under these goals?

The major activities carried out involved setting up and starting the study (i.e. recruitment, interviews). All of the activities, as listed for Major Task 1.1, were completed allowing us to begin recruitment. While complete ethics approval (i.e. local and the DoD HRPO) was obtained by November 2015, access to charts for the purposes of recruitment was a separate process and occurred later and at different moments at each of the hospital sites. This, therefore, led to a delay in the commencement of recruitment.

In our original grant application, we proposed interviewing the women first at 2 months after treatment. However, we found right from the beginning that this was still too soon following the completion of treatment. We have found that targeting 5-7 months after treatment leads to good participation. This later baseline means that some people will never be contacted because we will know in advance that they did not go into remission. However, these women would have been excluded from the analyses later, thus, this new procedure will minimize the number of 'over-recruitments'. The second interview is still conducted 4 months following baseline.

In total, we have identified 59 candidate participants between November 2015 and September 2016, of which 5 were not eligible (1 did not go into remission, 1 was >75 years old, 2 had a language barrier, and 1 left Montreal), and 3 were unreachable. 6 were recently identified but have not yet been contacted (they are thus potential cases for year 2). Of the 45 remaining eligible women, 80% (n=36) have agreed to participate and the baseline interview has been completed among all. The second and final interview has been completed during this reporting period among 24 women, with several scheduled over the following months.

Patient charts were consulted before and during contact with candidates. Follow up of participants for recurrence is through chart review, an ongoing activity, which we have started. So far, we have identified 5 recurrent cases. Participants also completed a diet questionnaire within one week of their telephone interviews. Inconsistencies and errors have been followed up with the women, when necessary. To pilot the processing of this data, 20 have been sent to Alberta Health Services, and we are currently examining this data to ensure that errors are minimized in the data processing.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

In the next reporting period, we plan to

(1) Continue recruitment and interviews, which will include:
-ongoing checks of telephone interview data;
-continue cleaning and scanning the CDHQIIs;
-continue and finish 2nd telephone interviews and 2nd self-administered CDHQIIs

(2) Continue chart reviews for our outcome of interest, i.e. recurrence

(3) Commence statistical analyses:
-we have conducted a preliminary data extraction of the first interview of those recruited during the first reporting period; once the CDHQII data is checked, we will also have the nutrition data
-these data will be used to set up analysis files and programming of statistical programs will commence over the next year

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?

We learned that women were not ready to be interviewed 2 months after their treatment ended. These women were still recovering and not yet back to their regular lifestyles. After 6 months, however, the majority were happy to participate in our study to give back to the professionals for the care they received and to help others. In particular, women are contacted at approximately 4 months post treatment, for a baseline interview at 5-7 months post treatment.

The delay in readiness to participate in the study may have pertinence to their readiness for the uptake of (new) healthy lifestyle behaviors, and this information on timing may be useful for other researchers conducting research similar to ours, or research on interventions among a similar study population.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. **CHANGES/PROBLEMS:**

Changes in approach and reasons for change

As described above, we have changed the baseline interview from 2 months after completion of treatment to 5-7 months because we found that 2 months was too soon as women were still recovering and not yet back to their regular lifestyles.

Actual or anticipated problems or delays and actions or plans to resolve them

Problems/delays encountered during the reporting period:

Local IRB approval was obtained in August 2015 and DoD HRPO approval was obtained in November 2015. Authorization to recruit was granted immediately after at the Centre Hospitalier de l'Universite de Montreal (CHUM). However, we experienced a slight delay in commencing recruitment at the Jewish General Hospital (JGH) and the McGill University Health Centre (MUHC). At the JGH, we were granted authorization to recruit in November also, however, we experienced a slight delay on determining the logistics of access to charts. Setting up a meeting with Dr. Susie Lau (who is a Co-Investigator on this study) took some time given that she has a very busy clinic and surgery schedule. With her, we investigated all their chart systems to determine the best way to identify candidate participants for this study. We were able to identify our first participants from the JGH in February 2016. At the MUHC, several factors led to the delay in recruitment. Many people were involved in the authorization processes and the MUHC had just moved to a new location. They had started a new web-based ethics review platform, which had some technical problems; also the cancer registry was short staffed. In March 2016, we were able to start patient recruitment at the MUHC.

A major issue that has had a significant impact on the study is the rate of recruitment, as explained in the table below. The first table in the column indicates the number of participants we expected to recruit as originally proposed in the grant application. Because of the delay in the commencement of recruitment, as described in the last paragraph, we didn't actually have 12 months of recruitment in the year 1 reporting period, but rather approximately 7.5 months, taking into consideration the start date at each of the 3 hospital sites (column 2). Thus, column 3 indicates the number of participants expected to have been recruited based on what we expected in the original proposal, and column 4 indicates the actual recruitment. Target population #1, as described in the original grant application, are those women that had participated in a case-control study carried out by our team. Using this population as a pool to recruit for this study greatly increased feasibility since we already had a relationship with these women and they had already indicated to us their willingness to participate in future research. Target population #2 are women who were not eligible for the case-control study due to geographical restrictions that were not relevant for this study. These women had not been contacted before for the case-control study.

Table. Expected and actual recruitment in the study

	# of participants expected in 12 months	Actual months of recruitment	# of participants expected given actual months of recruitment	Actual # of participants recruited
Target population #1[a]	80	7.5[c]	50	25
Target population #2[b]	28	7.5[c]	18	11

a Participants of the case-control study conducted by our team who meet the eligibility criteria of the proposed study
b Women who were not eligible for the case-control study due to geographical restrictions
c Average of the three hospital sites; actual months of recruitment ranged from 6 to 10 months

Thus, we have recruited 50% of what we expected from target population #1, and 61% of what we expected for target population #2. For target population #2, we have learned that a sizeable number of women who are treated and have early care for ovarian cancer at one of our hospital sites change their hospitals to a location closer to their homes once their treatment is completed. As our identification of candidate participants and follow-up of participants for the outcome of interest is based on chart reviews, women who are no longer patients at our three participating hospitals cannot be recruited into this study.

For target population #1, we have learned that the much lower than expected recruitment is related to the information we had when we developed the protocol for the study. In particular, we used the recruitment numbers from the case-control study being conducted by our team. At that time, we had not yet conducted the review of pathology reports, thus, to estimate for this study the number of women that would be eligible, defined as having completed treatment for a high-grade ovarian cancer, we used estimates from the published literature which indicated that approximately 80% of a case series would be a high-grade

ovarian cancer (while the rest would be low grade or borderline). We have now reviewed the pathology reports of all the participants in the case-control study and, in fact, ~50% are high-grade ovarian cancers (25% are low-grade and 25% are borderline), which is much lower than expected based on the literature.

Actions or plans to resolve problem

In the case-control study, the refusal rate among women with ovarian cancer was 22%. Because these women did not consent, we are unable to access and review their pathology reports. In general, many high-grade ovarian cancers are also late stage cancers, which is associated with a higher level of feeling ill. It is possible that women who refused for the case-control study, who are contacted earlier in the course of their disease compared to this study, may have been less inclined to participate in research because of their level of feeling ill. Though the case-control study and this cohort study are completely separate, the two studies have overlapped in time (until now as the case-control study has just ended). The ethics approval of the case-control study did not permit us to re-contact women who refused, and although this is a separate study, we are the same research team and thus abided by that request.

Now that the case-control study has ended, the identification of all candidate participants will be similar to the method used for target population #2, and does not involve having participated in another study by our team. Given that women are contacted approximately 4 months after treatment, when remission will have been achieved for the majority and women are feeling better, this moment of contact may prove to be associated with higher participation. If that is the case, this will ultimately increase our rate of recruitment of eligible participants during year 2 of this study.

An extension of the recruitment period will also result in an increased sample size, allowing us to better achieve our original study aims. We have successfully recruited 36 participants over ~7.5 months, which amounts to ~5 participants per month. Assuming that we will also have at least 1 additional participant per month amongst the women who may have refused the case-control study due their level of feeling ill, if we extend the recruitment period to the end of year 2, which when considering the delayed start means an extension from 18 months to 22 months, we will have approximately 108 participants. Ideally, we would continue recruitment during an extension year (an additional 6 months) to achieve the initially proposed sample size. Because we have had slower recruitment, our expenditures have been lower than budgeted (since the Study Coordinator and Research Assistant work according to the tasks that are needed). Thus, an extension will have virtually no impact on total expenditures.

Changes that had a significant impact on expenditures

The major change that has had a significant impact on expenditures is the delayed start and lower rate of recruitment, as explained above, and thus the salary expenditure on the Study Coordinator and Research Assistant with respect to the time it takes to carry out interviews.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals.

Nothing to report.

Significant changes in use of biohazards and/or select agent

Nothing to report.

6. **PRODUCTS:**

Publications, conference papers, and presentations

Nothing to report.

Website(s) or other Internet site(s)

Nothing to report.

Technologies or techniques

Nothing to report.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Nothing to report.

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

What individuals have worked on the project?

Name:	*Anita Koushik*
Project Role:	*Principal Investigator*
Researcher Identifier:	ORCID ID: 0000-0001-5304-7660
Nearest person month worked:	*2*
Contribution to Project:	*Dr. Koushik is the Principal Investigator of this study and oversees all aspects (approximately 1 full day per week).*
Funding Support:	*Dr. Koushik's salary as an Associate Professor at the Université de Montréal was supported through a New Investigator Award from the Canadian Institutes of Health Research (until June 30, 2016).*

Name:	*Nancy Faraj*
Project Role:	*Research Assistant/Interviewer*
Researcher Identifier:	n/a
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Faraj conducts all the interviews and assists in study coordination.*
Funding Support:	*This award*

Name:	*Julie Lacaille*
Project Role:	*Study Coordinator*
Researcher Identifier:	n/a
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Lacaille monitors and reviews patient charts to identify candidate participants and to follow up for outcomes.*
Funding Support:	*This award*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Organization Name: McGill University Hospital Centre
Location of Organization: Montreal, Quebec
Partner's contribution to the project
Financial support: None
In-kind support: Partner makes computers available to project staff
Facilities: Project staff use the partner's facilities to review partner's patient charts
Collaboration: Partner's staff work with project staff on obtaining patient charts
Personnel exchanges: No
Other: None

Organization Name: Jewish General Hospital
Location of Organization: Montreal, Quebec
Partner's contribution to the project
Financial support: None
In-kind support: Partner makes computers available to project staff
Facilities: Project staff use the partner's facilities to review partner's patient charts
Collaboration: Partner's staff work with project staff on obtaining patient charts
Personnel exchanges: Project staff keep partner's staff up to date on patients recruited
Other: None

8. **SPECIAL REPORTING REQUIREMENTS**

COLLABORATIVE AWARDS

Not applicable

QUAD CHARTS

Not applicable

9. **APPENDICES:**

Nothing to report