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TITLE: The Role of Lifestyle Factors in Ovarian Cancer Prognosis

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The Role of Lifestyle Factors in Ovarian Cancer Prognosis

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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, we actively recruited participants in the three hospital sites indicated in the proposal. We have found that, overall, recruitment rates are lower than expected based on the information at hand when the study was designed. This is being resolved with no impact on the budget through an increased duration of recruitment.

Lifestyle, post-diagnosis, recruitment rate, high grade ovarian cancer, recurrence

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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 behaviours 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?

   *Please note that the tasks outlined below refer to the updated SOW dated May 9, 2017 that granted us a 12-month extension without funds.

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**	**% 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	Oct 2015	100%	Nov 2015 to Mar 2016
Major Task 1.2: Recruitment and interviews	**Target date**	**% completion**	**Actual completion date**
Recruitment of target population #1; telephone interview and self-administered CDHQII	Months 4-18	100%	April 2017
Recruitment of target population #2; telephone interview and self-administered CDHQII	Months 4-30	75%	Ongoing
Ongoing checks of telephone interview data; scanning of CDHQII	Months 1-30	75 %	Ongoing
189 CDHQIIs will be processed at Alberta Health Services	Month 31	Year 3 activity	
Milestone(s) achieved: Baseline interview of 105 women		*79%*	*We have recruited 83 women up to now, with 5 months left of recruitment*

Major Task 1.3: Review of Patient Pathology Reports/Charts for Remission Status	**Target date**	**% completion**	**Actual completion date**
Chart reviews; ongoing task with 3 months at end of recruitment to finalize and verify reviews	Months 1-33	75%	Ongoing
Milestone(s) Achieved: Determining eligibility to remain in statistical analysis		*75%*	*Eligibility status has been confirmed for all 83 participants.*
Major Task 1.4: Follow-up	**Target date**	**% completion**	**Actual completion date**
2nd telephone interview and 2nd self-administered CDHQII	Months 8-34	56%	Ongoing
Ongoing follow-up of patient charts for outcome assessment (i.e. recurrence)	Months 12-36	56%	Ongoing; each chart without the outcome is re-assessed periodically
Milestone(s) Achieved: Second interview completed and outcome assessed for all women that will have confirmed remission			*59 participants have had their 2nd interview; Outcome assessment is ongoing and will be completed in year 3.*
Major Task 1.5: Statistical Analyses, Manuscript preparation	**Target date**	**% completion**	**Actual completion date**
Analyses; preliminary analyses for programming to be completed by the end of recruitment; analyses updated with updated outcome assessment data	Months 25-36	Year 3 activity	
Manuscript preparation; first drafts based on preliminary analyses with everything finalized after final analyses	Months 30-36	Year 3 activity	
Milestone(s) Achieved: One manuscript is planned for submission to Cancer Epidemiology, Biomarkers and Prevention or International Journal of Cancer			*This will occur during this 3rd year.*
Aim 2. To estimate the prevalence of participation in healthy post-diagnosis lifestyle behaviours in ovarian cancer patients.			
Major Task 2.1: Statistical Analyses, Manuscript preparation	**Target date**	**% completion**	**Actual completion date**
Major task 1.1 to 1.4 described above apply here	1-33	1.1 completed 1.2 -1.4 Ongoing	
Analyses; preliminary analyses will commence after 24 months of recruitment, which will be finalized at the end of recruitment	25-33	Year 3 activity	
Manuscript preparation; first drafts based on preliminary analyses with everything finalized after final analyses	30-36	Year 3 activity	
Milestone(s) Achieved: One manuscript is planned for submission to JNCI or Clinical Epidemiology			*This will occur during this 3rd year*

What was accomplished under these goals?

The major activities carried out during year 2 from October 1, 2016 to September 30, 2017 was the continuation of recruitment with first interviews as well as the second interviews. During this second year, we identified 79 candidate participants (4 had been identified at the end of year 1, but participated in year 2). Of the 79 candidate participants identified in year 2, 9 were not eligible (5 did not go into remission, 1

had cognitive problems precluding participation, 1 had a mental health issue, and 2 had a language barrier), and 5 were unreachable. 3 were recently identified but have not yet been contacted (they are thus potential cases for year 3). Of the remaining 62 eligible women, 52 agreed to participate, for a participation rate of 84%. First interviews have been completed among 47 of these women, with 5 other interviews already scheduled but that will occur in year 3.

The second and final interview has been completed for 35 women during this reporting period. Combined with second interviews in year 1, this brings the total to 59, with several more scheduled over the following months, in year 3. Overall and thus far, 9 women who were eligible to conduct the second interview refused.

Follow up of participants for recurrence is through chart review, which is an ongoing activity. In the last year, we have consulted 56 charts at least once. For participants who do not experience the outcome (i.e. recurrence), their chart is continually re-checked. Among the 56 participants that have had their chart reviewed for the outcome, we have identified 8 recurrent cases.

In addition to the interview, participants also complete a diet questionnaire within one week of their telephone interviews. Inconsistencies and errors have been followed up with the women, when necessary. Last year we tested out the data processing and were able to fix errors so that the data is accurate. Processing of the diet questionnaires is a year 3 activity. The processing of the data from the completed telephone interviews is ongoing (83 total; 36 in year 1, 47 in year 2.)

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) Complete recruitment of all participants; specifically, we will:
- complete the baseline interviews at the end of February 2018
- complete the second interviews at the end of June 2018
- continue with checks of telephone interview data
- continue with checks, verifications and scanning of the CDHQIIs

(2) Continue chart reviews for our outcome of interest, i.e. recurrence
- this is a major activity that will be carried out in year 3

(3) Continue statistical analyses:
- this is also a major activity that will be carried out in year 3
- a MSc student in epidemiology is analyzing the baseline data in a project to estimate the prevalence of engagement in physical activity 6 months post-treatment, which is directly related to aim 2; she will also examine the cross-sectional relationship between physical activity and our measures of quality of life, as measured using the FACT-O and the HADS
- other data has also been extracted and analysis files have been set up

4. **IMPACT:**

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

As described in our letter requesting a 12-month extension to the performance period of this award and in our annual report of October 2016, we have experienced a considerably lower recruitment rate in the study than had originally been expected and thus proposed. Our original projections of the number of eligible women, defined as having completed treatment for a high-grade ovarian cancer, were based on 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). However, we do not observe that 80% are high grade, rather the distributions, as discerned from a review of the pathology reports of contemporaneous cases in the study base, showed that only 50% are high-grade ovarian cancers (25% are low-grade and 25% are borderline).

Given the much poorer prognosis of high-grade ovarian cancers compared to low-grade and borderline cancers, this is a very promising statistic for women affected by ovarian cancer, and we intend to pursue this line of inquiry to better understand the distribution of different ovarian cancer types. But in terms of this project, this means that there are fewer eligible cases for the originally proposed recruitment period. As there exists very few studies on the influence of lifestyle factors in this particular patient population, the data and results generated from this study are still of very high value despite a limited sample size, given that the knowledge gained will contribute to a current gap. However, the accuracy of the estimates generated from this study are improved if they are based on a larger sample size. Given the definition of our study base, and the rationale for the inclusion of and restriction to the three specialized hospital centres, as described in the original proposal, the only way to augment the sample size was to lengthen the period of recruitment.

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

We have not changed our approach during year 2, but we did increase our recruitment period, as described above.

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

Problems/delays encountered during the reporting period:

Other than the factors leading to the increase in recruitment period with a 12-month extension without funds, as described above, we have not encountered any problems or delays during year 2.

Actions or plans to resolve problem

Nothing to report.

Changes that had a significant impact on expenditures

The expenditures for recruitment are primarily based on the time of the Research Assistant and Study Coordinator. The majority of their work hours, particularly that of the Research Assistant, corresponds to the tasks of recruitment, so with a slower recruitment rate, our expenditures for their work have accordingly been lower. However, the remaining funds will be used for the completion of recruitment during the extension year.

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.

Journal publications

Nothing to report.

Books or other non-periodical, one-time publications

Nothing to report.

Other 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?

Anita Koushik, no change
Nancy Faraj, no change

Name:	*Julie Lacaille*
Project Role:	*Study Coordinator*
Researcher Identifier:	n/a
Nearest person month worked:	*4*
Contribution to Project:	*Ms. Lacaille monitors and reviews patient charts to identify candidate participants and to follow up for outcomes.*
Funding Support:	*This award*

Name:	*Samia Qureshi*
Project Role:	*Database Manager/Statistical Programmer*
Researcher Identifier:	*n/a*
Nearest person month worked:	*2*
Contribution to Project:	*Ms. Qureshi conducts data checks and will assist in statistical analyses.*
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