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Telehealth Utilization in Gynecologic Oncology Clinical Trials

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Abstract

Objective: Prior to the COVID-19 pandemic, telehealth visits and remote clinical trial operations (such as local collection of laboratory tests or imaging studies) were underutilized in gynecologic oncology clinical trials. Current literature on these operational changes provides anecdotal experience and expert opinion with few studies describing patient-level safety data. We aimed to evaluate the safety and feasibility of telehealth and remote clinical trial operations during the COVID-19 Pandemic.

Methods: Gynecologic oncology patients enrolled and actively receiving treatment on a clinical trial at a single, academic institution during the designated pre-Telehealth and Telehealth periods were identified. Patients with at least 1 provider or research coordinator telehealth visit were

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included. Patient demographics, health system encounters, adverse events, and protocol deviations were collected. Pairwise comparisons were performed between the pre-Telehealth and Telehealth period with each patient serving as their own control.

Results: Thirty-one patients met inclusion criteria. Virtual provider visits and off-site laboratory testing increased during the Telehealth period. Delays in provider visits, imaging, and laboratory testing did not differ between time periods. Total and minor protocol deviations increased in incidence during the Telehealth period and were due to documentation of telehealth and deferment of non-therapeutic testing. Major protocol deviations, emergency department visits, admissions, and severe adverse events were of low incidence and did not differ between time periods.

Conclusions: Telehealth and remote clinical trial operations appeared safe and did not compromise clinical trial protocols in a small, single institutional study. Larger scale evaluations of such trial adaptations should be performed to determine continued utility following the Pandemic.

Introduction

Clinical trials are essential for testing new cancer directed therapies. They must employ standardized protocols that specify the delivery of treatment, ensure patient safety, and reliably collect outcomes data. Historically clinical trial protocols required nearly all in-person clinic visits to the study center in order to ensure validity, accuracy, safety.

Prior to the COVID-19 pandemic, telehealth (such as video or audio-only provider and research staff monitoring visits) and remote clinical trial operations (such as local collection of laboratory tests or imaging studies) were underutilized in oncologic clinical trials in the United States.[1] As the COVID-19 pandemic posed quarantines, travel restrictions, and safety concerns to clinical trial participants, health care providers, and research staff alike, pandemic mitigation plans were needed in order to keep clinical trials open. In April 2020, the Society of Gynecologic Oncology published a clinical practice statement encouraging the use of remote clinical trial operations, such as telehealth and local collection of laboratory testing and imaging when appropriate.[2] Aspects of clinical trials deemed non-essential, such as surveys and non-critical biopsies, were temporarily paused. These recommendations were supported by the National Cancer Institute and Food and Drug Administration.[2,3] In response, study sites rapidly adjusted operations to carry out these recommendations.

Telehealth has been successfully implemented in clinical trials in various specialties of medicine, however, the feasibility and safety of utilization of telehealth in the oncologic patient population bears further investigation. Since the start of the pandemic, organizations have advocated for the continuation of protocol amendments made during the Pandemic, such as telehealth and local collection of laboratory testing and imaging; however, many of these recommendations are based off expert opinion without patient-level safety analyses.[4] To investigate the safety and feasibility of pandemic mitigation plans, we conducted a retrospective cohort study of gynecologic oncology patients enrolled on clinical trials during the COVID-19 pandemic and hypothesized that telehealth is safe and feasible in this patient population. We assessed safety, defined by measures of adverse clinical outcomes, such as

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documented adverse events, emergency department visits, hospital admissions. We assessed feasibility, defined by the rate of clinical trial protocol deviations and number of patient touchpoints as a surrogate marker for research team workload.

Methods

We conducted a retrospective cohort study evaluating patients enrolled in gynecologic oncology therapeutic clinical trials who were undergoing active treatment (9/2019 through 8/2020), comparing receipt of care prior to— versus during—the Telehealth period, whereby each patient served as their own control. This study was approved by the University of Pennsylvania Institutional Review Board (IRB-844075). All data was collected retrospectively.

Inclusion Criteria

Patients enrolled in clinical trials through the Gynecologic Oncology Research Unit at the Perelman Center for Advanced Medicine within the University of Pennsylvania Health System (UPHS) from 9/2019 through 8/2020 were identified. Inclusion criteria required that each patient was enrolled and actively receiving treatment during both the pre-Telehealth period (9/30/2019 – 3/15/2020) and the Telehealth period (3/16/2020 – 8/30/2020). Patients on surgical only trials or CAR T Cell trials were excluded. Patients must have had at least one visit conducted virtually (video or audio-only) with either a clinical trial provider (MD or NP) or clinical research coordinator during the Telehealth period to be included.

Demographics, Exposure and Outcome Variables

Patient demographics (including zip code and race), cancer specific information, and clinical trials' protocol operations information (including type, timing, and location of provider visits) were abstracted from clinical trial records and electronic health records. Encounters for laboratory testing were collected, both for on-site (study site) and off-site (within and outside of health system) testing. Similarly, imaging encounters both on-site and off-site were collected. Data regarding research-only related laboratory testing (such as pharmacokinetics), research-only related biopsies, and patient reported outcome questionnaires were not collected as these evaluation methods were considered non-essential during the pandemic and, in many instances, were paused.[2]

Delays in provider visits, laboratory testing, and imaging studies as defined by each clinical trial protocol were collated. Clinical trial deviation events were collected from the Gynecologic Oncology Research Unit deviation log.

Clinical outcomes, such as readmissions and documented adverse events, were collected through manual review of electronic health records. Adverse events were defined using the Common Terminology Criteria for Adverse Events v5.0 (CTCAE). Visits and admissions that were for routine, non-oncologic care not related to the trial were excluded.

Patient touchpoints, defined by portal email messages and telephone calls, were collected in aggregate. For patient portal messages or phone calls where more than one exchange may have occurred between the patient and research team, each thread was considered as a single

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encounter. Touchpoints not related to the clinical trial, such as need for disability paperwork, were not included.

Outcome metrics were reported as the proportion of defined events divided by total expected number of completed events. For example, regarding delayed visits or imaging, we reported the number of delayed visits divided by total completed visits or required imaging sessions. Unexpected events, such as number of patient touchpoints, were standardized as the number of defined events divided by the time enrolled in the respective time period.

Statistical Analysis

We compared events occurring during the pre-Telehealth period to that of the Telehealth period, and each patient served as her own control. Data points were collected, analysed, and presented as 1) absolute counts for the entire cohort, 2) per patient's time period (proportion, patient encounters divided by required encounter type), and 3) as rate of encounters per month (number of patient encounters divided by number of required encounters per month on trial). Pairwise comparisons were performed and included paired *t*-test and Wilcoxon signed rank test. Unpaired analyses were performed where appropriate, including *t*-test, logistic regression, and ANOVA. A 2-sided p-value of less than 0.05 was utilized and considered statistically significant. All analyses were conducted in Stata (Version 17, StataCorp LLC, College Station, TX).

Results

Demographics

Thirty-one patients met criteria for inclusion in this study. Demographic information for the cohort is summarized in Table 1. The median age was 63 years (Interquartile range (IQR): 60-72). A majority of patients identified as White, non-Hispanic (83.9%). Median distance from home zip code to study site was 25.2 miles with a range from 1.9 to 170 miles. A large majority of the population had high grade serous ovarian carcinoma (83.9%) and advanced stage disease (Stage III: 48.4%, Stage IV: 38.7%). Median duration of enrollment was similar between the pre-Telehealth (5.2 months, IQR 3.2-5.6) and Telehealth periods (5.6 months, IQR 3.8-5.6), (p = 0.682).

Patients were enrolled on eleven different clinical trials, with eight of the thirty-one patients being the largest cohort on a single protocol. Fifteen patients (48.4%) were on combined oral (PO) and intravenous (IV) chemotherapy trials, nine (29%) on PO-only chemotherapy trials, and seven (22.6%) were on IV-only chemotherapy trials. Over half (61.3%) of the patients remained active on trial at the conclusion of the data collection period. Nine patients experienced disease progression and were taken off their clinical trial regimen. Two patients completed their trial regimens and continued onto active follow up, and one patient withdrew due to concern regarding clinical trial participation during the pandemic.

Clinical Trial Operations

Clinical trial operations are summarized in Table 2, comparing pre-Telehealth vs. Telehealth encounters. Results were consistent using parametric and non-parametric tests, with the

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exception of total trial deviations, thus parametric results are reported below. Data comparing Pre-Telehealth to Telehelath period is reported in total counts (Count), events per patient (Per Patient), and events per patient divided by enrollment duration in each timeframe (Rate).

Telehealth provider visits, including video and audio-only, increased (Count: 0 vs. 66; Per patient: 0 (0-0) vs. 2.13 (0-7), p = <0.001; Rate: 0 (0-0) vs. 0.41(0-1) p<0.001). Of note, 9 patients did not use telehealth for provider visits and utilized telehealth for research coordinator visits only. Delays in provider visits were of low incidence and did not differ between time periods (Count: 8 vs. 6; Per patient: 0.26 (0-4) vs. 0.19 (0-3) p = 0.73; Rate 0.06 (0-0.8) vs. 0.04 (0-0.43), p=0.688) (Table 2). Missed provider visits were of low incidence and did not differ between timeframes (Count: 2 vs. 2; Per patient: 0.06 (0-1) vs 0.06 (0-1), p = 1.00).

Telehealth utilization for provider visits differed by type of trial (PO, IV, or PO/IV combination). Use of virtual visits was associated with trial type (PO = 37, IV =15, PO/IV combination = 14; p=<0.001). On pairwise comparison, patients receiving PO-only therapy utilized a greater proportion of virtual visits (Median: 83%, Range 0.25-1) than those on combination PO/IV combination therapy (12.5%, Range 0-0.75) (p=<0.001). There was no difference in median telehealth visits when comparing PO-only to IV-only therapy (33%, Range 0-1) (p=0.064) or patients on combination PO/IV combination therapy to IV only (p=0.212). Use of virtual visits was not associated with distance of patients' zip code to the study site (Pearsons co-efficient = 0.20, p = 0.274).

Telehealth utilization for coordinator visits increased in the Telehealth period (Count: 4 vs 167; Per patient: 0.13 (0-1) vs. 5.39 (1-12), p=<0.001). Incidence of delayed (Count: 7 vs. 6; Per patient: 0.23 (0-3) vs. 0.19 (0-3), p=0.813) and missed (Count: 7 vs. 8; Per patient: 0.23 (0-1) vs. 0.26 (0-2) p=0.801; Rate: 0.04 (0-0.25) vs. 0.07 (0-0.5) p = 0.334) coordinator visits were not different between time periods (Table 1).

Off-site laboratory testing increased during the Telehealth period (Count: 20 vs. 66; Per patient: 0.65 (0-4) vs. 2.13 (0-12) p=0.013; Rate: 0.12 (0-0.8) vs. 0.31 (0-1) p=0.025) while use of off-site imaging studies did not (Count: 14 vs. 22; Per patient: 0.45 (0-3) vs. 0.71 (0-2) p=0.118; Rate: 0.35 (0-1) vs. 0.41 (0-1), p=0.316) (Table 2). Use of off-site laboratory testing was not associated with distance of patients' zip code to the study site (Pearsons co-efficient: 0.04, p = 0.230), while use of off-site imaging was associated with distance from the study site (Pearsons co-efficient 0.44, p= 0.013). An increase in off-site imaging was associated with telehealth use (Pearsons coefficient 0.59, p = 0.002). Delayed laboratory testing (Count: 6 vs. 11; Per patient: 0.19 (0-2) vs. 0.35 (0-6) p=0.531; Rate: 0.05 (0-0.67) vs. 0.05 (0-0.86) p=0.930) and imaging studies (Count: 4 vs. 9; Per patient: 0.13 (0-1) vs. 0.29 (0-2), p=0.134; Rate: 0.10 (0-1) vs. 0.17 (0-1) p=0.999) were of low incidence and did not differ between the time periods (Table 2).

Deviations, including total, minor, and major deviations, were tabulated and compared between pre-Telehealth and Telehealth periods (Table 2). Total deviations increased during the Telehealth period (Count: 52 vs. 125; Per patient: 1.68 (0-11) vs. 4.03 (0-18) p=0.005).

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The rate of deviations was not different between time periods on parametric testing (Rate: 0.73 (0-10) vs. 0.99 (0-4.56) p=0.366); however, it was different on non-parametric testing (p=0.010). Total deviations were then assessed and there was no difference in incidence of total deviations between time periods (Count: 52 vs. 49; Per patient: 1.68 (0-11) vs. 1.58 (0-8), p=0.819; Rate: 0.73 (0-10) vs. 0.40 (0-3.04) p = 0.314). Minor deviations were increased during the Telehealth period (Count: 47 vs. 122; Per patient: 1.52 (0-11) vs. 3.94 (0-17) p = 0.005); Rate: 0.37 (0-1.98) vs. 0.97 (0-4.56) p0.002); however, when the exclusions (deviations for telehealth utilization, lack of protocol- required physical exams due to telehealth, incomplete vital signs reported by patients during telehealth visits, and deferment of research-only related laboratory testing) were applied, there was no difference in number of minor deviations (Count: 47 vs. 46, Per patient: 1.52 (0-11) vs. 1.48 (0-8) p= 0.938; Rate: 0.37 (0-1.98) vs. 0.38 (0-3.04) p=0.903). There was no difference in major deviations between timeframes (Count: 4 vs. 3; Per patient: 0.13 (0-2) vs. 0.10 (0-2) p=0.745; Rate: 0.35 (0-10) vs. 0.02 (0-0.36) p = 0.313).

Patient Outcomes

The rate of additional, unscheduled (termed “Extra”) provider visits and laboratory testing for monitoring of treatment-related toxicity or additional work up was similar between time periods (Table 3). There was no difference in number of patient touchpoints between timeframes (Count: 149 vs. 202; Per patient: 4.81 (0-22) vs. 6.52 (0-22) p=0.126). Extra imaging studies were increased in the Telehealth period (Count: 6 vs. 22; Per patient: 0.19 (0-1) vs. 0.71 (0-3) p= 0.003); Rate: 0.05 (0-0.64) vs. 0.17 (0-0.71) p=0.010. However, this increase was not associated with progression of disease (p = 0.540) during the Telehealth period. Emergency department visits, non-required transfusion/infusion visits, and hospital admissions were infrequent and similar in both timeframes (Table 3).

Treatment dose reductions and delays were of low incidence and rates were similar between time periods (Table 3). Incidence of total and severe adverse events (Grade 3 or higher) was similar between time points, but the rate of adverse events was lower in the Telehealth period (3.32 (0.18-15) vs. 2.12 (0-9) p= 0.046) (Table 3).

Discussion

This single institution retrospective cohort study investigated the feasibility and safety of telehealth and remote clinical trial operations during the COVID-19 pandemic in the gynecologic oncology clinical trials population. Findings revealed that remote clinical trial operations, including virtual provider visits and off-site laboratory testing, increased during the first six months of the COVID-19 pandemic without compromising patient safety (defined by adverse patient outcomes such as emergency department visits) or feasibility (defined by patient touchpoints and deviations once adjusted for pandemic mitigation protocol adaptations). While total and minor deviations were increased, when adjusted for protocol adaptations, such as lack of physical exam, there was no difference in protocol deviations between time periods. While limited to a small cohort at a single institution, this study highlights the pragmatic-- and contemporaneously-- necessary implementation of telehealth and remote clinical trial operations into eleven therapeutic clinical trials

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in gynecologic oncology without demonstrating increased adverse events, significant deviations, delays, utilization, or apparent clinical burden.

The COVID-19 pandemic spurred mitigation plans to ensure that clinical trials remained open and safe during a global pandemic while accelerating a paradigm shift in the conduct of clinical trials, a practice that had remained stagnant and unchanged for decades.[5-7] Initial COVID-19 pandemic mitigation plans were made based on pragmatic decisions in this data-free period. Over the past three years, many trial investigators and clinicians, based on expert opinion, have pushed for continued utility of mitigation plans as they streamlined trial processes; however, short- and long-term effects of these adjustments need to be assessed.[7] Additionally, early studies have shown that telehealth and remote clinical trial operations are acceptable and satisfactory to clinical trial patients of other solid tumor disease sites, such as lung and gaatrointestinal cancers.[8] Although there is significant commentary in the literature describing institution-level mitigation plans and enrollment rates during the pandemic, there has been limited published data regarding feasibility and safety of telehealth utilization in gynecologic oncology clinical trials.[9,10] Here we assessed incorporation of telehealth from multiple angles—including operational requirements per protocol, patient utilization of health system resources, as well as therapy related outcomes such as adverse events.

Our findings align with other published reports of early pandemic clinical trial operations for non-gynecologic solid tumor disease sites. Tolaney et al. (2021) performed a prospective cohort at a single institution of nearly 2400 medical and pediatric oncology patients and found that severe adverse events and major protocol deviations were of low incidence before the pandemic and during the early pandemic.[4] Bouleftour et al. (2021) performed a single institution study of medical oncology, radiation, and supportive care clinical trials utilizing telehealth in 2020 and found an 80% rate of deviations for descriptive or evaluation primary endpoints (such as lack of physical exam or vital signs); however, primary efficacy endpoints had a low deviation rate (20%).[11] We similarly found high rates of minor deviations during the early pandemic, but did not see any difference in total adverse events, severe adverse events, emergency department visits, admissions, or patient touchpoints. Follow up analyses of the long-term impact of such deviations are needed. Lastly, our findings of low withdrawal rates during the pandemic were similar to a retrospective study by Marcum et al. (2020) in which no patients came off trial for reasons other than progression of disease.[12] Our study specifically contributes gynecologic oncology data regarding telehealth incorporation into clinical trial operations. According to the American Society of Clinical Oncologists Standards and Practice Recommendations (2020) Telehealth in clinical trials operations should be applied beyond the timeframe of the period of restrictions of the COVID-19 pandemic.[1]

Telehealth and remote clinical trial operations may also decrease the burden of participating in clinical trials related to patient expenses and time. We assessed our geographic distribution of our clinical trial population and noted that our catchment area ranged up to 170 miles, with a majority of patients residing within 50 miles of our study site. Telehealth may ultimately spare some of the patient expense, time, and stress that otherwise would have occurred in the setting requiring all in-person visits. Given that 9-15% of women in the United States reside in areas with limited access to high quality gynecologic care including

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clinical trials, incorporation of telehealth into clinical trial protocols may improve access to care and improve disparities of under-enrollment of racial minorities and underserved populations, as well as increase access to patients affected by geographic disparities due to limitations of gynecologic oncology providers or clinical care sites.[8,13-15] According to the ASCO 2020 Standards and Practice Recommendations, telehealth utilization in oncology clinical trials are recommended as a method of increasing recruitment and reducing the burden of trial participation in participants.[1]

Our study has several potential limitations. First, this study is limited by its retrospective nature. Notably, this study is also limited by its small sample size and larger studies are needed to confirm our findings. Additionally, this study was conducted at a single academic institution and thus may not be generalizable to other clinical trial sites. Furthermore, there was heterogeneity within our cohort as eleven different clinical trial protocols were represented with eight patients on a single protocol being the largest single trial cohort. Our dataset may be incomplete as care received outside of our healthcare network may have been missed if not imported into our electronic health record or acknowledged in documentation; however, it is anticipated that rates of undocumented out-of-network events, such as emergency department visits, are low given comprehensive history intake performed by our providers and clinical research coordinators throughout trial participation. Additionally, use of patient touchpoints and deviations may be incomplete surrogates of clinical workload. With regards to feasibility, this study presented clinical trial operations during the first six months of the COVID-19 pandemic and may not reflect current clinical trial operations now that clinical research teams are more adept in remote operations. While continued analyses in larger, multi-institutional cohorts are needed, we are reassured that our results regarding lack of increase in clinically significant protocol deviations and adverse events were reflected in other published studies.[4, 11,12]

In summary, our study, which is limited by sample size, revealed that use of telehealth and remote clinical trial operations was not associated with adverse patient outcomes or increased researcher and provider workload at a single academic institution. Further investigation of the effect of telehealth and remote clinical trial operations is needed. Specifically outcomes such as trial efficiency, safety, and cost should be evaluated, in addition to clinical trials access, enrollment and cancer related outcomes. Use of multidisciplinary quantitative and qualitative analyses will be essential to establish new, effective, and evidence-based regulatory frameworks for creating a new paradigm for design of clinical trial protocols that permanently incorporate telehealth within gynecologic cancer care.

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Highlights

- Utilization of Telehealth and remote laboratory and imaging within clinical trials increased during the Covid pandemic
- No difference in adverse patient outcomes, such as emergency department visits, were observed with telehealth use
- Telehealth and remote testing in clinical trials appear safe and feasible
- Incorporation of telehealth and remote testing should be considered in future gynecologic oncology clinical trial protocols

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Table 1

Demographics and disease characteristics of gynecologic oncology patients enrolled in therapeutic clinical trials with utilization of telehealth

IQR = Interquartile Range

Age (Median (IQR))		63 years (60-72)	
Race	White, Non-Hispanic	26 (83.9%)	
	White, Hispanic	1 (3.2%)	
	Black, Non-Hispanic	2 (6.5%)	
	Asian	1 (3.2%)	
	Missing	1 (3.2%)	
Distance (Median (IQR))		25.2 miles (16-46)	
Gynecologic Malignancy	High grade serous ovarian	26 (83.9%)	
	Low grade serous ovarian	1 (3.2%)	
	Other epithelial ovarian	1 (3.2%)	
	Endometrioid endometrial	1 (3.2%)	
	Serous endometrial	1 (3.2%)	
	Concurrent high grade serous ovarian and endometrioid endometrial	1 (3.2%)	
Stage	I	2 (6.5%)	
	II	1 (3.2%)	
	III	16 (48.4%)	
	IV	12 (38.7%)	
	Not documented	1 (3.2%)	
Recurrent	Yes	12 (38.7%)	
	No	19 (61.3%)	
Duration of Enrollment (Median (IQR))	Pre-Telehealth	5.2 months (3.2-5.6)	P=0.682
	Telehealth	5.6 months (3.8-5.6)	
Clinical Trial Type	IV only	7 (22.6%)	
	IV and PO	15 (48.4%)	
	PO only	9 (29.0%)	
Status	Actively on trial	19 (61.3%	
	Progression	9 (29%)	
	Completed regimen	2 (6.5%)	
	Withdrew	1 (3.2%)	

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Table 2

Patient utilization of telehealth and remote clinical trial options, treatment details, and deviations prior to and during telehealth incorporation into gynecologic oncology therapeutic clinical trials. Total counts of events (Count), events per patient (Per Patient), and events per patient adjusted for enrollment time (Rate) are listed. Means and ranges are listed in Per Patient and Rate Columns.

Lab = Laboratory

* Denotes removal of deviations for documentation of telehealth utilization or research-related laboratory testing

P-values are listed for t-test, with non-parametric Wilcoxon signed-rank listed when differed in significance.

	Pre-Telehealth			Telehealth			Patient ttest p-value	Rate ttest p-value
	Count	Per Patient	Rate	Count	Per Patient	Rate		
Provider Visits								
Virtual Visits	0	0 (0-0)	0 (0-0)	66	2.13 (0-7)	0.41 (0-1.0)	<0.001	<0.001
Total Visit Delays	8	0.26 (0-4)	0.06 (0-0.8)	6	0.19 (0-3)	0.04 (0-0.43)	0.73	0.688
Missed Visits (Any Type)	2	0.06 (0-1)	0.01 (0-0.25)	2	0.06 (0-1)	0.01 (0-0.25)	1.00	0.697
Coordinator Visits								
Virtual Visits	4	0.13 (0-1)	0.02 (0-0.2)	167	5.39 (1-12)	0.87 (0.25-1)	<0.001	<0.001
Total Visit Delays	7	0.23 (0-3)	0.05 (0-0.67)	6	0.19 (0-3)	0.04 (0-0.43)	0.813	0.616
Missed Visits (Any Type)	7	0.23 (0-1)	0.04 (0-0.25)	8	0.26 (0-2)	0.07 (0-0.5)	0.801	0.334
Laboratory Testing								
Remote Lab Testing	20	0.65 (0-4)	0.12 (0-0.8)	66	2.13 (0-12)	0.31 (0-1.0)	0.013	0.025
Lab Testing Delays	6	0.19 (0-2)	0.05 (0-0.67)	11	0.35 (0-6)	0.05 (0-0.86)	0.531	0.930
Imaging								
Remote Imaging	14	0.45 (0-3)	0.35 (0-1.0)	22	0.71 (0-2)	0.41 (0-1.0)	0.118	0.316
Imaging Delays	4	0.13 (0-1)	0.10 (0-1.0)	9	0.29 (0-2)	0.17 (0-1.0)	0.134	0.999
Deviations								
Total	52	1.68 (0-11)	0.73 (0-10)	125	4.03 (0-18)	0.99 (0-4.56)	0.005	0.366
Adjusted Total	52	1.68 (0-11)	0.73 (0-10)	49	1.58 (0-8)	0.40 (0-3.04)	0.819	0.314
Minor	47	1.52 (0-11)	0.37 (0-1.98)	122	3.94 (0-17)	0.97 (0-4.56)	0.005	0.002
Adjusted Minor*	47	1.52 (0-11)	0.37 (0-1.98)	46	1.48 (0-8)	0.38 (0-3.04)	0.938	0.903
Major	4	0.13 (0-2)	0.35 (0-10)	3	0.10 (0-2)	0.02 (0-0.36)	0.745	0.313

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Table 3

Patient outcomes prior to telehealth and during telehealth incorporation into gynecologic oncology therapeutic clinical trials.

Lab = Laboratory, ED = Emergency Department, AE = adverse event SAE = severe adverse event

* Utilizing Common Terminology Criteria for Adverse Events

P-values are listed for t-test, with non-parametric Wilcoxon signed-rank listed when differed in significance.

	Pre-Telehealth			Telehealth			Patient ttest p-value	Rate ttest p-value
	Count	Per Patient	Rate	Count	Per Patient	Rate		
Extra Provider Visit	31	1.0 (0-10)	0.31 (0-3.10)	29	0.94 (0-5)	0.25 (0-1.90)	0.837	0.475
Patient Touchpoints	149	4.81 (0-22)	1.31 (0-7.67)	202	6.52 (0-22)	1.50 (0-6.08)	0.126	0.477
Extra Lab Testing	13	0.42 (0-4)	0.09 (0-0.77)	31	1.0 (0-8)	0.22 (0-1.56)	0.161	0.139
Extra Imaging	6	0.19 (0-1)	0.05 (0-0.64)	22	0.71 (0-3)	0.17 (0-0.71)	0.003	0.010
Treatment Reduction	4	0.13 (0-1)	0.03 (0-0.27)	9	0.29 (0-2)	0.09 (0-1.0)	0.169	0.089
Treatment Delay	10	0.32 (0-2)	0.07 (0-0.64)	13	0.42 (0-2)	0.11 (0-1.0)	0.476	0.407
Total AE*	321	10.35 (1-24)	3.32 (0.18-15)	285	9.19 (0-35)	2.12 (0-9)	0.302	0.046
Total SAE (Grade 3 or higher)*	19	0.61 (0-4)	0.33 (0-5)	19	0.61 (0-3)	0.12 (0-0.54)	0.999	0.187
ED Visits	4	0.13 (0-2)	0.03 (0-0.70)	6	0.19 (0-2)	0.04 (0-0.44)	0.625	0.915
Hospital Admissions	2	0.06 (0-2)	0.01 (0-0.36)	5	0.16 (0-2)	0.03 (0-0.36)	0.374	0.349
Transfusion/Infusion Visits	13	0.42 (0-8)	0.08 (0-1.44)	16	0.52 (0-8)	0.10 (0-1.44)	0.557	0.572