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A systematic review and meta-analysis of surgery delays and survival in breast, lung and colon cancers: Implication for surgical triage during the COVID-19 pandemic

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Abstract

Background: Thousands of cancer surgeries were delayed during the peak of the COVID-19 pandemic. This study examines if surgical delays impact survival for breast, lung and colon cancers.

Methods: PubMed/MEDLINE, EMBASE, Cochrane Library and Web of Science were searched. Articles evaluating the relationship between delays in surgery and overall survival (OS), disease-free survival (DFS) or cancer-specific survival (CSS) were included.

Results: Of the 14,422 articles screened, 25 were included in the review and 18 (totaling 2,533,355 patients) were pooled for meta-analyses. Delaying surgery for 12 weeks may decrease OS in breast (HR 1.46, 95%CI 1.28–1.65), lung (HR 1.04, 95%CI 1.02–1.06) and colon (HR 1.24, 95%CI 1.12–1.38) cancers. When breast cancers were analyzed by stage, OS was decreased in stages I (HR 1.27, 95%CI 1.16–1.40) and II (HR 1.13, 95%CI 1.02–1.24) but not in stage III (HR 1.20, 95%CI 0.94–1.53).

Conclusion: Delaying breast, lung and colon cancer surgeries during the COVID-19 pandemic may decrease survival.

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Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has indirectly threatened the health of thousands of cancer patients by disrupting their treatment schedules.1 To conserve resources and limit the spread of the virus, many hospitals were forced to delay elective surgeries.2 Nearly 38% of cancer surgeries are estimated to have been canceled worldwide during the 12-week peak of the pandemic.3 During this time numerous professional associations4–7 published guidelines for triaging cancer cases. The speed at which these were created provided rapidly needed guidance to individual healthcare institutions, given that triaging of cancer surgeries in the United States (U.S.) is not a common practice.8 However, the need for immediate guidance also limited the amount of anticipatory research that could occur before issuance of these recommendations. The majority of guidelines were based on the opinions of a small panel of experts, which resulted in discordance between recommendations.9 Therefore, it is imperative to adduce sufficient medical evidence to update and strengthen guidelines in preparation for future waves of COVID-19.

Few reviews and meta-analyses have examined the relationship between delays in surgery and survival for breast, lung and colon cancers. A meta-analysis10 published in 1999 reported a 3 month delay in treatment for breast cancer was associated with a 12% lower rate of survival. That review did not examine delays in surgery alone but instead included all initial treatment modalities. A 2007 meta-analysis11 found delays in surgery for colorectal cancers...
did not worsen survival, however, the interpretation of these results is limited since colon and rectal cancers were not evaluated separately. A systematic review from 2018 examined the relationship between time-to-surgery (TTS) for colon cancer and outcomes, however no meta-analysis was performed. Two reviews evaluated treatment delays in lung cancer, but neither examined surgery-specific delays.

Although numerous studies have examined the impact that increasing TTS has on survival in cancer patients, there is no evidence-based standard that can serve as an empirical benchmark for when a cancer surgery should be considered delayed. This leads to inconsistent results between studies and potential confusion in efforts to determine the true impact of delaying surgery. We addressed this gap in the literature by conducting a systematic review and meta-analysis, whose primary objective was to evaluate if delaying surgery by 12 weeks impacts survival for breast, lung, and colon cancers.

### Materials and methods

#### Protocol and search strategy

This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. Structured searches of the PubMed/MEDLINE, EMBASE, Cochrane Library and Web of Science databases were conducted (April 2020) to identify relevant articles. The defined search strategy, available in Appendix A, yielded a preliminary collection of articles. Filters were used to limit results to English language and full-text papers published prior to April 1, 2020. Abstracts and full-texts of articles with relevant titles were reviewed. Additionally, references of included publications were examined to identify studies not captured in the preliminary search.

#### Eligibility criteria and study selection

Assessment of eligibility was conducted independently by the first author (B.A.J.) and studies in question were further evaluated by a second reviewer (A.C.W). Eligible studies fulfilled the following inclusion criteria: (1) the majority of the population diagnosed with invasive ductal or lobular breast cancer, non-small cell lung cancer or adenocarcinoma of the colon; (2) surgery was the initial treatment; (3) surgical delays analyzed separate from all other treatment delays; (4) TTS interval clearly defined as diagnosis to surgery; and (5) appropriate reporting of outcomes (discussed below). To minimize the effect of confounding variables between comparison groups, only studies which fulfilled the following additional criteria were included in the meta-analyses: (1) relevant prognostic factors identified; and (2) published findings incorporated multivariate risk adjustment for relevant prognostic factors or balanced such covariates between comparison groups.

Studies were excluded for any of the following: (1) abstracts only and review articles; (2) sample sizes <100; (3) non-invasive tumors included in analysis; (4) the majority of the patient population analyzed had metastatic (stage IV) disease; (5) multiple cancer types included in analysis; or (6) duplicate study populations.

#### Study quality

Included studies were evaluated using the Newcastle-Ottawa Scale (NOS) which identifies the quality of nonrandomized studies. The scale ranges from 0 to 9 with a score of ≥7 indicating a high quality study. Descriptions of the categories used to evaluate each study are in Appendix A.

#### Summary measures and data collection

The primary endpoint was overall survival (OS). Secondary endpoints included cancer-specific survival (CSS) and disease-free survival (DFS). For inclusion into this paper, outcomes must be reported as hazard ratios (HRs), odds ratios (ORs), risk ratios (RRs) or as p-values. Studies that reported HRs with 95% CIs for OS were considered for inclusion in the meta-analyses. Additional variables extracted from individual studies included: years of diagnosis of sample population; country study took place; source of data; inclusion criteria; sample sizes; mean/median TTS; mean/median follow-up; ages of sample population; any adjuvant therapy received; and prognostic factors controlled for.

#### Statistical analysis and bias assessment

HRs were converted to represent a 12-week delay in surgery and then pooled using the method described in prior meta-analyses. A random-effects model was fitted given the prospect of moderate to high heterogeneity. Heterogeneity was quantified by calculating P and a sensitivity analysis further evaluated the impact each study had on the overall heterogeneity. Publication bias was assessed via visual inspection of funnel plots and the Egger’s regression test for analyses with 10 or more studies. Statistical significance was defined as a p-value <0.05 and all tests were 2-sided. Statistical analyses were performed using SAS® software version 9.4 (SAS, Inc., Cary, NC) and R® software version 3.6.0 (R Development Core Team, Vienna, Austria).

#### Results

After 14,422 publications were screened, a total of 186 abstracts/ full texts were evaluated. Ultimately, 25 observational studies met inclusion criteria for the review, of which 18 studies, consisting of 2,533,355 patients, met inclusion criteria for meta-analysis. Of the seven studies excluded from the meta-analyses, six did not report HRs and/or 95% CIs for OS and one contributed an overall weight of <0.0%. The inclusion process is illustrated by the flow diagram in Appendix A.

Years of publication of included studies ranged from 2002 to 2020 and sample sizes ranged from 398 to 683,604 patients. A total of 23 studies examined OS, 5 examined DFS and 5 examined CSS. A summary of findings from each study is listed in Table 1 and further study characteristics are available in Appendix A.

The mean score on the Newcastle-Ottawa Scale was 7.8 for all included studies and 7.9 for only the studies included in the meta-analyses. Among the studies included in the meta-analyses, 10 did not have an average follow-up of at least 5 years, 3 did not control for tumor stage and 3 had sample populations not representative of the total population at risk. Little to no asymmetry was observed in the funnel plots for lung and colon cancers, indicating a low risk of publication bias. Although minor asymmetry existed on the breast cancer funnel plot, the value for Egger’s test was 0.11, indicating non-significant asymmetry. Detailed results of the Newcastle-Ottawa Scale and the funnel plots are available in Appendix A.

#### Breast Cancer

OS was reported in twelve breast cancer studies; including eleven analyses of non-stage specific (multiple stage) disease, four of stage I only disease, four of stage II only disease, and three of stage III only disease.

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Table 1
Summary of findings from 25 studies included in the systematic review.

| Source          | Site     | Outcomes measured | Patient No. | Stage(s)       | TTS Comparison Groups (Days) | Raw^1 HR | 95% CI   | p-value |
|-----------------|----------|-------------------|-------------|----------------|-----------------------------|----------|----------|---------|
| Khorana et al, 2019 | Breast   | OS                | 683,604     | I              | 1-42 vs 43-180              | 1.017    | 1.014–1.020 |
|                 |          |                   | 387,198     | II             | 1.006                       | 1.003–1.009 |
|                 |          |                   | 193,058     | I              | 1.024                       | 1.022–1.026 |
|                 |          |                   | 49,386      | II             | 1.017                       | 1.014–1.021 |
| Shin et al, 2013 | Breast   | OS                | 1946        | I-III          | 1-28 vs 29-56               | 1.33     | 0.77–2.31  |
|                 |          |                   | 398         | I-II           | 0.77                        | 0.39–1.97 |
|                 |          |                   | 1-28 vs 57-84 | 1.91           | 0.42–1.48                   |
|                 |          |                   | 1-28 vs 85-365 | 1.05           | 0.67–1.65                   |
|                 |          |                   | 1-28 vs 57-84 | 0.65           | 0.28–1.48                   |
|                 |          |                   | 1-28 vs 85-365 | 0.79           | 0.42–1.48                   |
| Yung et al, 2012 | Breast   | OS                | 29,047      | I-IV           | 1-31 vs ≥ 32                | 1.59     | 1.37–1.84  |
|                 |          |                   | 9094        | I              | 1.13                       | 1.02–1.25 |
|                 |          |                   | 21,379      | I              | 1.10                       | 1.00–1.21 |
| Mateo et al, 2020 | Breast   | OS                | 351,087     | I-III          | Each 30-day delay           | 1.104    | 1.08–1.13  |
|                 |          |                   | 7939        | I-III          | Each 30 vs 31-60            | 1.23     | 1.08–1.40  |
| Ho et al, 2020   | Breast   | OS                | 5389        | I              | 1-30 vs 61-90               | 1.38     | 1.04–1.83  |
|                 |          |                   | 1-30 vs 91-180 | 1.68           | 1.15–2.46                   |
|                 |          |                   | 1-30 vs 31-60 | 1.12           | 0.95–1.32                   |
|                 |          |                   | 1-30 vs 61-90 | 1.06           | 0.72–1.56                   |
|                 |          |                   | 1-30 vs 91-180 | 1.55           | 0.98–2.45                   |
| Eaglehouse et al, 2019 | Breast | OS                | 9699        | I-III          | 1-21 vs 22-35               | 0.97     | 0.78–1.21  |
|                 |          |                   | 5033        | I              | 1.14                       | 0.73–1.77 |
|                 |          |                   | 3735        | II             | 0.92                       | 0.68–1.25 |
|                 |          |                   | 901         | III            | 1.21                       | 0.75–1.95 |
| Erickson et al, 2018 | Breast | OS                | 7017        | I-III          | Each 1-day delay            | 1.011    | 1.006–1.016 |
| Mansfield et al., 2017 | Breast | DFS               | 1131        | I              | Each 30-day delay           | 0.576    | 0.320–1.014 |
|                 |          |                   | 835         | II             | 1.202                      | 0.723–1.997 |
| Bleicher et al, 2016 | Breast | OS                | 94,544      | I-III          | Each 30-day delay           | 1.09     | 1.06–1.13  |
|                 |          |                   | NR          | I              | Each 60-day delay           | 1.26     | 1.02–1.54  |
|                 |          |                   | OS†         | NR             | Each 30-day delay           | 1.13     | 1.08–1.18  |
|                 |          |                   | OS †        | II             | Each 30-day delay           | 1.84     | 1.10–3.07  |
|                 |          |                   | OS †        | SR             | Each 30-day delay           | 1.06     | 1.01–1.11  |
|                 |          |                   | OS †        | NR III          | Each 30-day delay           | 1.04     | 0.82–1.33  |
|                 |          |                   | 115,790     | I-III          | Each 30-day delay           | 1.10     | 1.07–1.13  |
| Pulverini et al, 2016 | Breast | OS                | 420,792     | I-III          | 1-27 vs 28-55               | 0.98     | 0.96–1.00  |
|                 |          |                   | 1-27 vs 56-83 | 1.03           | 0.99–1.06                   |
|                 |          |                   | 1-27 vs 84-182 | 1.14           | 1.09–1.20                   |
|                 |          |                   | NR          | I              | 1.07                       | 1.02–1.13 |
|                 |          |                   | 1-27 vs 56-83 | 1.19           | 1.11–1.28                   |
|                 |          |                   | NR          | II             | 1.16                       | 1.08–1.25 |
| Yoo et al, 2016  | Breast   | OS                | 1702        | I-III          | 1-29 vs ≥ 30                | 0.95     | 0.782–1.572 |
|                 |          |                   | DFS         | I-IV           | 1.109                      | 0.65–1.42 |
|                 |          |                   | 4143        | I               | 1.11                        | 0.69–1.78 |
| Smith et al, 2013 | Breast   | OS                | 5389        | I-III          | 1-25 vs 39-62               | 1.09     | 0.93–1.29  |
|                 |          |                   | 397         | I-III          | NR                         | 0.93–1.29 |
|                 |          |                   | 27,022      | I-III          | NR                         | 1.05–1.07 |
| Redaniel et al, 2013 | Breast | OS                | 182        | I-III          | NR                         | 1.29–1.49 |
| Vujovic et al, 2009 | Breast | DFS               | 201         | I-III          | NR                         | 1.06–1.09 |
|                 |          |                   | 561         | I              | NR                         | 0.8–1.3  |
| Huang et al, 2020d | Lung    | OS                | 4984        | I              | NR                         | 0.7–1.4  |
| Yang et al, 2017  | Lung     | OS                | 1082        | I-II           | Each 14-day delay          | 1.06     | 1.05–1.07  |
| Samson et al, 2015 | Lung    | OS                | 118,504     | I-III          | Each 14-day delay          | 1.02     | 0.92–1.14  |
| Aragonese et al, 2002 | Lung    | OS                | 4685        | I-III          | Each 14-day delay          | 1.03     | 0.90–1.17  |
| Grass et al, 2020  | Colon    | OS                | 1-7 vs 8-14  | 1.05           | 0.89–1.23                   |
| Bagaria et al, 2018 | Colon   | OS                | 1-7 vs 15-21 | 1.12           | 0.92–1.36                   |
|                 |          |                   | 1-7 vs 22-28 | 1.14           | 0.89–1.46                   |
|                 |          |                   | 1-7 vs 39-35 | 1.11           | 0.79–1.56                   |
|                 |          |                   | 1-7 vs 43-49 | 1.17           | 0.86–1.60                   |

(continued on next page)
Sample sizes ranged from 1702 to 420,792 with a mean of 176,657 patients. Increasing TTS was associated with a decreased OS in 9/11 non-stage specific studies, 4/4 stage I only studies, 3/4 stage II only studies, and 0/3 stage III only studies.

Results of the meta-analysis for non-stage specific breast cancers are illustrated as a forest plot in Fig. 1. The results suggest a delay in surgery of 12 weeks is associated with decreased OS (HR 1.46, 95%CI 1.28–1.65, I² 86%). Results of the stage-specific breast cancer meta-analyses are illustrated as forest plots in Fig. 2. The results suggest a delay in surgery of 12 weeks is associated with decreased OS for stages I (HR 1.27, 95%CI 1.16–1.40, I² 97%) and II (HR 1.13, 95%CI 1.02–1.24, I² 89%) diseases but not for stage III (HR 1.20, 95%CI 0.94–1.53, I² 63%) disease.

The sensitivity analysis for studies of non-stage specific breast cancers indicates excluding Polverini et al. decreases overall heterogeneity from I² = 86% to 77% and increases the overall HR [95% CI] from 1.46 [1.28–1.65] to 1.52 [1.35–1.71]. For stage I only all studies were found to contribute equally to overall heterogeneity. For stage II only studies excluding Khorana et al decreases overall heterogeneity from I² = 89% to 44% and increases the overall HR [95% CI] from 1.13 [1.02–1.24] to 1.17 [1.08–1.27]. For stage III only studies excluding Eaglehouse et al decreases overall heterogeneity from I² = 63% to 0% and the overall HR remains insignificant.

Lung Cancer

OS was reported in seven lung cancer studies; including three analyses of non-stage specific (multiple stages) disease, four of stage I only disease, and one of stage II only disease. Sample sizes ranged from 398 to 242,444 with a mean of 40,798 patients. Increasing TTS was associated with decreased OS in 1/3 non-stage specific studies, 4/4 stage I only studies, and 1/1 stage II only studies.

Results of the meta-analysis for lung cancer are illustrated as a forest plot in Fig. 1. The results suggest a delay in surgery of 12 weeks is associated with decreased OS (HR 1.46, 95%CI 1.28–1.65, I² 86%).

Table 1 (continued)

| Source                  | Site | Outcomes measured | Patient No. | Stage(s) | TTS Comparison Groups (Days) | Raw* HR | 95% CI | p-value |
|-------------------------|------|-------------------|-------------|----------|------------------------------|---------|--------|---------|
| Flemming et al, 2017    | Colon | OS                | 4326        | I-IV     | 1-7 vs 85+                   | 1.47    | 1.02–2.11 | 0.04    |
|                         |      | CSS               |             |          | 1-55 vs ≥ 56                 | 1.07    | 0.91–1.24 | 0.42    |
|                         |      |                   |             |          | 0.82                         | 0.66–1.03 | 0.83 |
| Wani et al, 2017       | Colon | OS                | 908         | I-II     | 1-30 vs ≥ 31                 | 0.823   | 0.627–1.081 | 0.17 |
| Amri et al., 2014      | Colon | OS                | 741         | I-IV     | Each quartile delay 1         | 0.886   | 0.611–1.283 | 0.52 |
| Simunovic et al, 2009  | Colon | OS                | 7989        | I-IV     | 1-14 vs 15-28                | 1.0     | 0.9–1.1    | 0.74    |
|                         |      |                   |             |          | 1-14 vs 29-42                 | 1.0     | 0.9–1.1    | 0.76    |
|                         |      |                   |             |          | 1-14 vs 43-120                | 1.12    | 1.1–1.3    | 0.003   |
|                         |      |                   |             |          | 1-14 vs 15-28                 | 0.9     | 0.8–1.0    | 0.21    |
|                         |      | CSS               |             |          | 1-14 vs 29-42                 | 0.9     | 0.7–1.0    | 0.08    |
|                         |      |                   |             |          | 1-14 vs 43-120                | 1.0     | 0.8–1.1    | 0.63    |
| Iversen et al, 2009    | Colon | OS                | 458         | I-IV     | 1-29 vs ≥ 30                 | 0.84    | 0.62–1.13 | NR      |

TTS, time-to-surgery; HR, hazard ratio; CI, confidence interval; NR, not report; NS, non-significant; OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival. Studies expressed in bold indicate inclusion in the meta-analysis. HRs; 95% CIs; p-values expressed in bold indicate statistical significance. Empty cells indicate the text above applies for the row.

a Hazard ratios as reported in each individual study.

b Analysis of SEER-Medicare dataset.

c Analysis of NCDB dataset.

d Excluded from meta-analysis because study contributed an overall weight of <0.0% to final pooled analysis.

e Expressed in terms of relative risk.

f Quartile ranges include days 1–13; 14–23; 24–37; 38–798.

Fig. 1. Meta-analysis of the estimated hazard ratio for overall survival for a delay in surgery of 12 Weeks among patients with breast cancer.
The results suggest a delay in surgery of 12 weeks is associated with decreased OS (HR 1.04, 95%CI 1.02–1.06, $I^2$ 84%). Too few HRs were reported to perform meaningful stage-specific analyses. In the sensitivity analysis for lung cancer all studies were found to contribute equally to overall heterogeneity.

**Colon Cancer**

OS was reported in 8 colon cancer studies\(^{33,36,47–52}\) and all analyses were of non-stage specific (multiple stages) disease. Sample sizes ranged from 458 to 118,504 with a mean of 19,874 patients. Increasing TTS was associated with decreased OS in 3/8 studies.

Results of the meta-analysis for colon cancer are illustrated as a forest plot in Fig. 4. The results suggest a delay in surgery of 12 weeks is associated with decreased OS (HR 1.24, 95%CI 1.12–1.38, $I^2$ 71%).

The sensitivity analysis for studies of colon cancer indicates excluding Grass et al.\(^{27}\) decreases overall heterogeneity from...
\[ I^2 = 71\% \text{ to } 40\% \] and decreases the overall HR [95% CI] from 1.24 [1.12–1.38] to 1.18 [1.06–1.33].

**Discussion**

The lack of evidence-based standards for what is considered a delay in cancer surgery has led to inconsistent study designs and few attempts at synthesizing data between studies. By converting HRs to a common 12-week delay in surgery, for the first time we were able to pool findings from studies evaluating surgical delays and survival in breast, lung and colon cancers. The results of the meta-analyses indicate a surgical delay of 12 weeks is associated with decreased overall survival in these three cancer types. Results from the stage-specific analyses for breast cancer suggest delaying surgery by 12 weeks decreases overall survival for stage I and II diseases but not stage III disease. Findings from this study should be utilized to empirically strengthen and modify existing triage guidelines in preparation for future waves of COVID-19.

The pooled HR for breast cancer was the largest among the three cancer types examined, which may indicate survival in these patients is especially sensitive to surgical delays. The stage-specific analyses performed for breast cancer are of particular interest since COVID-19 triage guidelines differ by tumor stage. Most guidelines recommend delaying early-stage breast cancers and to instead consider neoadjuvant treatment with chemotherapy or endocrine therapy. However, our results suggest these cancers are most impacted by delays in surgery. Although alternative treatments exist, it is important to consider that under normal circumstances chemotherapy is not given for many early-stage (especially stage I) breast cancers. While the current literature does suggest endocrine therapy can safely be utilized in the neoadjuvant setting, the appropriate patient population and the exact treatment regimen are not yet well defined. For stage III, the impact of surgical delays trended toward worse survival, however, significance was not reached. Compared to stages I/II, it is possible delaying surgery for stage III disease has a negligible impact on survival since these patients already experience significantly poorer outcomes from their ‘delay’ in diagnosis. Therefore, our results suggest surgeries for stage III breast cancers should be delayed prior to stages I/II during future waves of COVID-19. If delays for stages I/II become necessary, surgeries should first be delayed for patients who likely would receive adjuvant chemotherapy under normal circumstances, given the well-established efficacy of neoadjuvant chemotherapy.

The pooled HR for lung cancer suggests a delay in surgery of 12 weeks is associated with a slight decrease in overall survival. It is noteworthy that 4/5 of the studies in our analysis included only stage I and/or II diseases. While this limits the comparability of the

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### Fig. 3

Meta-analysis of the estimated hazard ratio for overall survival for a delay in surgery of 12 Weeks among patients with lung cancer.

### Fig. 4

Meta-analysis of the estimated hazard ratio for overall survival for a delay in surgery of 12 Weeks among patients with colon cancer.

**Legend** (Figs. 1, 2, 3, 4) The size of the boxes represents the weight the study has in the overall analysis; the black lines coming off of each box represent the 95% confidence intervals of the study; confidence interval lines that cross the line of no effect indicate results are not significant; the center of the diamond(s) represents the overall HR and the edges represent the 95% confidence interval; Abbreviations: OS, overall survival; HR, hazard ration; CI, confidence interval.
results to the triage recommendations for stage III disease, our analysis suggest early-stage lung cancers are sensitive to delays in surgery. Many of the guidelines recommend delaying small and early stage lung cancers and to consider alternative non-surgical treatments such as stereotactic ablative radiotherapy, cryotherapy or radiofrequency ablation. However, curative surgery is often the single treatment for early-stage lung cancer and the efficacy of alternative treatments has been shown to be inconsistent. Our results suggest if delaying surgery for stages I/II lung cancers becomes necessary during future waves of COVID-19 it should be done with caution and rescheduled for the earliest possible date.

The pooled HR for colon cancer suggests a delay in surgery of 12 weeks is associated with decreased overall survival. Most triage guidelines discourage delaying curative-intent surgery for colon cancer, which our findings support. If it becomes necessary to delay surgery for colon cancer during future waves of COVID-19 our results suggest that it should be done with extreme caution and rescheduled for the earliest possible date.

**Limitations**

The most substantial limitation to this paper is the heterogeneity found between pooled studies, most notably for breast and lung cancers. However, results of the meta-analyses remained similar following the sensitivity analyses. Second, since individual studies did not compare consistent TTS lengths, it was necessary to standardize each time interval in order to compare findings. To accomplish this, we relied on the assumption a log-linear relationship exists between the effect of TTS and OS. Third, even though the overall assessment of quality indicates the inclusion of high-quality studies, there were numerous studies which did not control for stage and/or did not have an appropriate length of follow-up. Fourth, only full-text articles in English were included which may cause publication bias, although the funnel plots/Egger's test indicate the risk for bias was low. The decision to only include full-text articles was made after a cursory reading of seemingly relevant abstracts revealed that upon their full-text reviews, studies often indicate the risk for bias was low. The decision to only include full-text articles was made after a cursory reading of seemingly relevant abstracts revealed that upon their full-text reviews, studies often indicate the risk for bias was low.

**Conclusion**

The results of the meta-analyses suggest a delay in surgery of 12 weeks is associated with decreased overall survival in breast (especially for stage I and II), lung and colon cancers. Triage guidelines for cancer surgeries during the COVID-19 pandemic should take into consideration the emerging medical evidence adduced by this and other similar studies. Future research would benefit from the synchronization of study designs, implementation of a constant TTS interval and use of similar TTS comparison groups in order to improve comparability of findings. To help better guide surgical triage recommendations during future waves of COVID-19, studies should further evaluate which stages and subtypes are most impacted by delays in surgery in these and other cancer types.

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**Appendix A. Supplementary data**

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amjsurg.2020.12.015.
