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Abstract

Background: Cancer is common, with most cancer patients presenting initially to a general practitioner. The COVID-19 pandemic led to changes in the delivery of primary care, which could have affected cancer referrals. This observational study looked at two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown in 2020, at a GP practice in the Wirral, England. **Methods:** A search was conducted to find the cancer referrals made between 23rd March 2020 - 1st July 2020, during the first lockdown. Using the same methodology, cancer referral data was collected for the corresponding time periods in 2019 and 2021. The number of 2WRs and positive diagnostic yields were then compared. **Results:** The number of cancer referrals decreased by 40.4% in 2020, compared to 2019. In 2021, the number of referrals then increased by 225%, compared to 2020. Overall, the number of cancer referrals increased between 2019-2021. The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020. Overall, the positive diagnostic yield increased between 2019-2021. **Conclusion:** The numbers and outcomes of cancer referrals at this Wirral GP practice have changed considerably following the first UK COVID-19 lockdown in 2020, and the influence of the pandemic was still affecting cancer referrals in 2021. A greater focus on early cancer detection in primary care could help overcome the ways in which the pandemic has affected primary care delivery.

Introduction

Around one in three people in the UK will develop cancer in their lifetime.¹ The detection of people who have a possible cancer mainly happens in primary care, because most patients present initially to a primary care clinician.¹

UK cancer referral guidelines have been developed using a "risk threshold" – if there is a high enough risk that a symptom is being caused by a cancer, then a referral is justified.¹ For an urgent cancer referral in England, the patient should be investigated for cancer within two weeks of presenting to their GP with their symptom(s). Scotland, Wales and Northern Ireland have slightly different timeframe limits compared to England with regards to how soon cancer referral patients should be investigated for cancer. However, throughout the UK, patients referred down the urgent cancer referral pathway will be seen by a specialist as soon as possible.²

The beginning of the COVID-19 pandemic led to a decrease in the number of routine GP patient consultations.³ Following the announcement of a UK national lockdown on 23rd March 2020,⁴ the Royal College of General Practitioners published data showing that there had been a shift in primary care delivery - about 70% of patients were receiving remote GP care, rather than

face-to-face.³ This could have had substantial implications to many aspects of patient care, including cancer referrals.

The aim of this study is to look at the differences in two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown at a GP practice in Birkenhead, Wirral, England. Contrasting the number of 2WRs made, as well as the outcomes of patients' investigations following their referrals, should help demonstrate some of the consequences that this pandemic has had on patients' health outcomes.

Methods

Study Design and Data Collection

The design of this study was an observational study, looking at three separate data sets in 2019, 2020 and 2021, respectively. The data was collected by searching and reading through patient notes at a Wirral GP practice:

A search was carried out on 'EMIS' (Egton Medical Information Systems), which is a healthcare technology provider used in primary care in the UK.⁵ The search was to find all the 2WRs that were made at the Wirral GP practice in question, during the time period between 23rd March 2020 - 1st July 2020 (at the time that the UK was in its first COVID-19 lockdown⁶).

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Each patient from this collected data set was individually searched on 'EMIS' to look at their 2WR in more detail. 'Docman', which is a clinical correspondence software,⁷ was then used to read through the subsequent clinical letters sent regarding each patient, to follow the timeline of investigations resulting from their initial referral, to determine whether each 2WR patient ultimately was, or was not, diagnosed with cancer.

Inclusion / Exclusion Criteria

Every patient's two-week referral was reviewed and the following were excluded:

- Any 2WR patient whose records were not accessible (e.g. inactive patient record on 'EMIS'), as the outcome of their referral could not be determined.
- Any patient whose 2WR led to a positive cancer diagnosis, but who had already previously been diagnosed with this same cancer. The reason these 2WRs were excluded was because this paper is looking at new cancer diagnoses only. The effect of the pandemic cannot not be studied by looking at old cancer diagnoses, where the initial diagnosis was made before the first COVID-19 lockdown
- Any 2WR where the patient was lost to follow-up.
- Any 2WR that was rejected.
- Any 2WR where the patient was incorrectly referred i.e. if the patient being referred did not have a suspected cancer.

Data Analysis

After the application of this criteria, a positive diagnostic yield was calculated to determine the proportion of 2WRs that led to a positive cancer diagnosis. The positive diagnostic yield was calculated by dividing the number of positive cancer diagnoses by the total number of 2WRs. The result of this calculation was multiplied by 100, to give a percentage.

The same methods were then used to collect data for the 2WRs for the same time periods, but in 2019 and 2021, in order to make comparisons.

The 2WR data collected for this study was scrutinized in terms of its validity, before conclusions were made. During this process, it was considered whether bias could have had any effect on the results, or whether this had been avoided.

The aim of the specific exclusion criteria was to avoid any ambiguity with regards to which cancer referrals should be included in this data set. In this way, sampling bias should not have affected which referrals were used in this study. As well as this, the intention of the systematic approach in the methods of this study was to prevent observer bias affecting the data being collected. This study's methods involved specifying the quantitative data that needed to be collected for each patient (number of 2WRs; positive/negative cancer diagnosis). In this way, the data collection process did not involve interpreting any subjective information, avoiding observer bias from influencing the data collection process. Furthermore, the fact that this paper

received no financial support can categorically rule out the possibility that funding bias could have skewed the results of this study.

Results

The diagnostic outcomes and reasons for excluding certain referrals in each data set are summarized in Tables 1 and 2, respectively.

Table 1 displays the total number of 2WRs, the number included after applying exclusion criteria, the number of positive cancer diagnoses, and the positive diagnostic yield for each year studied. For the 2019 data set, there were a total of 117 2WRs during the time period between 23^{rd} March – 1^{st} July. Once the exclusion criteria had been applied, 114 2WRs were included in the 2019 data set. Out of these 114 referrals, 8 of the patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 7%.

For the 2020 data set, there were a total of 75 2WRs during the time period between 23^{rd} March – 1^{st} July. Once the exclusion criteria had been applied, a total of 68 2WRs were included in the 2020 data set. Of these 68 referrals, 12 patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 17.6%.

For the 2021 data set, there were a total of 172 2WRs during the time period between 23^{rd} March – 1^{st} July. Once the exclusion criteria had been applied, a total of 153 2WRs were included in the 2021 data set. Of these 153 referrals, 24 patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 15.7%.

Table 1. Diagnostic Outcomes for the 2WRs Made in the Time Period Between 23^{rd} March 2019 – 1^{st} July for the 2019, 2020 and 2021 Data Sets.

	2019	2020	2021
Total referrals	117	75	172
Included referrals	114	68	153
Positive cancer diagnoses	8	12	24
Positive diagnostic yield (%)	7	17.6	15.7

Table 2 outlines the reasons for excluding certain 2WRs from each year's data set. The exclusions were due to inaccessible patient records, prior diagnosis of the same cancer, patients lost to follow-up, rejected referrals, or incorrect referrals where the patient was not suspected of having cancer. Notably, the number of patients lost to follow-up increased in 2021 compared to previous years.

Figure 1 illustrates the changes in the number of 2WRs over the three years studied. The number of 2WRs decreased by 40.4% in 2020, compared to 2019. In 2021, the number of 2WRs then increased by 225%, compared to 2020. Overall, the number of 2WRs increased by 34.2% between 2019-2021. Put simply, the



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number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019.

Figure 2 depicts the positive diagnostic yields calculated for each year. The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020. Overall, the positive diagnostic yield increased by 224.3% between 2019-2021. The positive diagnostic yield was higher after the lockdown, compared to before.

Table 2. Justification for Each 2WR that was Excluded in the 2019, 2020 and 2021 Data Sets.

	2019	2020	2021
Patient records were not accessible	0	3	2
Patient had already previously been diagnosed with the same cancer	0	3	4
Patient was lost to follow-up	2	1	12
2WR was rejected	1	0	0
Incorrect 2WR – patient was not referred for a suspected cancer	0	0	1

Figure 1. The Difference Between the Number of 2WRs Made in the 2019, 2020 and 2021 Data Sets.



Figure 2. The Difference Between the Positive Diagnostic Yields Calculated for the 2019, 2020 and 2021 Data Sets.



Discussion

The results of this study have demonstrated two key findings. Firstly, the number of 2WRs decreased from 2019 to 2020, before more than doubling from 2020 to 2021. As well as this, the positive diagnostic yield increased from 2019 to 2020, and then slightly reduced in 2021.

With regards to the decrease in the number of 2WRs made in the 2020 data set, compared to that of 2019 - there could be several reasons for this change.

The COVID-19 pandemic led to a "decline in routine patient consultations" in primary care.³ Aside from the main purpose of their appointment, routine consultations provide patients with an opportunity to speak to their doctor about any other health concerns they may have. The decrease in these routine appointments during lockdown³ could have reduced the number of opportunities for doctors to pick up on their patients' red flag symptoms (symptoms suggesting more serious pathology⁸), which could have decreased the number of 2WRs being made.

2020 also saw a shift to remote GP care with data from the Royal College of General Practitioners published in April 2020 showed that, at that time, the majority of consultations were being delivered remotely. This same publication showed how, in March/April 2019, the majority of GP care was face-to-face.³ This transition to remote GP care could have changed the rapport between patients and their GPs - doctors weren't seeing their patients in person, so could have missed some patients' signs or symptoms that would warrant a 2WR.

For example, unexplained weight loss is considered a red flag for malignancies.⁹ If a doctor is speaking to a patient over the phone, rather than face-to-face, they won't notice that the patient has lost weight, and may therefore be less inclined to ask the patient about any weight changes. In this way, over-the-phone consultations could have meant that opportunities were missed for patients' red flag symptoms to be noticed. It follows that this may have also contributed to the reduction in the number of 2WRs that were made in 2020, compared to 2019.

As well as changes in GP care delivery, there could also be patient factors that may have led to fewer 2WRs. For example, some patients may have feared leaving the house during the pandemic,¹⁰ or may have falsely believed that GP surgeries were closed.¹¹ The reduction in the number of 2WRs seen in the 2020 data set could therefore be a result of a combination of doctor and patient factors associated with the lockdown.

This Wirral GP practice's data follows a national trend of a decrease in 2WRs during the first COVID-19 lockdown: a paper by Watt et al. demonstrated that, in England, "primary care consultations per person fell from an average of 4.1 before mid-March in 2020 to 3 consultations per person per year (around a 30% reduction) the week after the introduction of lockdown at the end of March." The same paper also found that, "from the middle of March to the end of June there were 43% fewer 2-week wait referrals than in the same weeks in 2019."¹² This Wirral study

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therefore adds to a body of evidence that the COVID-19 lockdown affected cancer referrals.

A more recent study by Watt et al. looked at how deprivation influenced the reduction in the detection of new cancers since the beginning of this pandemic. The results showed that the poorest areas had the greatest reduction in the number of 2WRs.¹³

The relevance of Watt et al.'s findings to this Wirral observational study is that this study was done in a GP practice in Birkenhead, where there is a high index of multiple deprivation.¹⁴ The GP practice is in an area which is in the second most deprived decile in the country.¹⁵ Perhaps an area of further research to contextualise this study's findings would be to repeat the same study but in a more affluent area in the Wirral. There is considerable disparity in affluence across the different areas in the Wirral,¹⁶ so this would be a good location to compare how deprivation affects health outcomes such as cancer referrals. Such research would give a better idea as to how the inverse care law¹⁷ affected cancer detection during the pandemic.

Perhaps, during this pandemic, there have been particular factors in more deprived areas that are affecting cancer detection rates more so than in other areas. One suggestion could be to focus resources in such areas to hopefully tackle the barriers that these communities are facing where cancer detection is concerned.

With regards to the results from the 2021 data, there was a substantial increase in the number of 2WRs, compared to both the 2019 and 2020 data. The number of 2WRs more than doubled in the 2021 data compared to 2020 - there may have been influencing factors, following the easing of lockdown restrictions,⁶ that contributed to this change.

The pandemic has led to a "growth in remote consultations" which "has allowed for a substantial increase in the number of overall consultations."¹⁸ It therefore follows that, if GPs are having more patient consultations overall, the number of cancer referrals would proportionately increase, too. Perhaps this was a contributing factor to the increase in cancer referrals seen in this study in 2021 (following the easing of lockdown restrictions⁶), compared to 2020.

Another suggestion is that patients who feared leaving the house during the pandemic¹⁰ felt more comfortable visiting their GP in 2021, compared to 2020. The cohort study by Williams et al. done during the pandemic suggested that there could be a "rebound in future workload" following the lifting of COVID restrictions.¹⁹ Perhaps the increase in 2WRs in 2021 was as a result of this anticipated 'rebound,' therefore.

With regards to the positive diagnostic yields - various inferences could be made about the difference in percentages calculated. The National Institute for Health and Care Excellence (NICE)'s two-week referral guidelines use parameters that have a \geq 3% positive predictive value,¹ which would mean that at least 3% of all patients referred (based on a particular parameter) would receive a confirmed cancer diagnosis. The positive diagnostic

yield for both the 2019, 2020 and 2021 data sets from the above results are considerably higher than this 3% set out in the NICE guidelines. It could be argued that this demonstrates a successful implementation of the two-week referral pathway, where doctors were referring the right kind of patients down each two-week pathway accordingly. Alternatively, it could be the case that doctors were not referring enough patients who have red flag symptoms of a lower predictive value, whose 2WR would be less likely to lead to a cancer diagnosis.

However, the fact that the positive diagnostic yield in the 2020 data increased by more than two-fold compared to the same time period in 2019, suggests that there was a change in the type of patients that were being referred down the two-week referral pathways during the first COVID-19 lockdown.

A poll by NHS England revealed in April 2020 that "four in ten people" were "too concerned about being a burden on the NHS to seek help from their GP."²⁰ One hypothesis is that, during the COVID-19 lockdown, patients were more reluctant to go to their GP unless they had symptoms that they were very worried about, because patients were not wanting to bother the perceived busy NHS. Hence, perhaps the proportion of 2WR patients who received a negative cancer diagnosis in 2020, during lockdown, decreased because patients with more benign symptoms simply weren't going to their GP about it.

This increase in the positive diagnostic yield in the 2020 data set adds to the current evidence base, 12, 13, 19 by showing in more detail how the COVID pandemic has potentially affected cancer diagnoses, compared to another similar study in this field. A retrospective cohort study of general practices in Salford by Williams et al. showed that the gap between observed and expected cancer diagnoses between March 1 and May 31, 2020 was not statistically significant.¹⁹ This study at the Wirral GP practice showed a considerable increase in the proportion of 2WRs that led to a positive cancer diagnosis in the 2020 referrals, compared to 2019. Furthermore, this study collected data over a three-year period, whereas Williams et al. collected data over a three-month period. This paper has therefore helped by allowing us to get a better idea of how the pandemic has affected cancer diagnoses, over a larger period of time, in a field where there is no clear relationship between COVID-19 and cancer referrals.

With regards to the positive diagnostic yield calculated in 2021, the results showed that it was 10.8% lower than that of 2020. However, the 2021 diagnostic yield was still more than double that of the 2019 positive diagnostic yield.

Perhaps it was the case that, those who were "too concerned about being a burden on the NHS to seek help from their GP"²⁰ in 2020, felt more comfortable booking a GP appointment in 2021, following the easing of lockdown restrictions.⁶ It could be that, in 2021, patients were going to their GP about less worrying symptoms, whereas in 2020 patients were less likely to go to see their GP unless they had very worrying symptoms. This could be why the positive diagnostic yield decreased in 2021, compared to 2020, because the proportion 2WR patients having sinister pathology decreased.

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The positive diagnostic yield in 2021 only decreased by 10.8%, however, compared to 2020, representing only a small change. The 2021 positive diagnostic yield still remained considerably higher than the pre-pandemic diagnostic yield for the 2019 data. This demonstrates how the proportion of 2WR patients in 2021 that resulted in cancer diagnoses was still much higher than that of 2019, and indeed the national average of 3%.¹

This finding shows how fewer patients with benign pathology are being referred along the two-week referral pathways than before the pandemic, even after lockdown restrictions eased in 2021.⁶ This could be associated with the "growth in remote consultations" since the pandemic.¹⁸ The fact that a greater proportion of patients were being seen face-to-face in 2019, compared to 2021,¹⁸ could be why there are still differences in the types of patients being referred down cancer pathways.

This increase in remote consultations seems to be a more permanent change following the pandemic, as the number of remote consultations has not decreased back to pre-pandemic levels following the lifting of lockdown restrictions.^{6, 18} The ways in which red flag symptoms are identified during virtual consultations should be considered, therefore, moving forwards.

Future Applications

A future application of this study's finding could be to increase public awareness of red flag symptoms. Some vulnerable patients still feared COVID-19 in 2021, despite the shift to a 'new normal'²¹ - hopefully, those that are still reluctant to visit their GP because of the current pandemic will be more likely to contact their doctor about potential cancer symptoms, if their awareness of red flag symptoms increased. It could be suggested, therefore, that GPs could increase their cancer detection rates during this pandemic by increasing their cancer health promotion.

It was mentioned earlier that the poorest areas had the greatest reduction in the number of 2WRs during lockdown.¹³ Perhaps it was the case that, in more deprived communities, the awareness of red flag symptoms was lower. According to Public Health England, "people with limited financial and social resources are more likely to have limited health literacy."²² It could be suggested that, having population-specific approaches to raising awareness of red flag symptoms in deprived communities could help bridge this gap. Such approaches could include "ensuring that health materials are clear and concise"²³⁻²⁷ as well as "using trained community workers or health champions to relay health messages."²²

It would be useful to carry out further studies following such future applications, to determine how effective these measures have been. For example, it would be interesting to see whether the positive diagnostic yield would decrease at all after increasing public awareness of red flag symptoms.

Strengths and Limitations

This paper's findings have enabled the aim of this study to be well-achieved, with regards to looking at numbers of 2WRs made, as well as investigation outcomes of the referrals (cancer diagnosis/no cancer diagnosis). By comparing the time period of the first COVID-19 lockdown to the exact same dates but different years, this study allowed the effect of the lockdown to be looked at more closely. If the 2WRs for different months were to be studied, for example, it might have been harder to determine whether the differences between the data sets were just due to variations during different times of the year, or whether it was the effect of lockdown.

However, the aim could have been better achieved if the investigation results of the cancer referrals had been looked at in closer detail. Perhaps further studies into e.g. what stage each cancer was at diagnosis in the different data sets, would allow us to look at the effect of the lockdown on cancer referrals in even closer detail, by comparing the prognosis of the patients that were diagnosed with cancer in the different data sets.

Another way of looking at the cancer referrals in more detail would be to look at whether certain referral pathways were affected more than others by the lockdown. It would be valuable to find out whether there were particular factors that led to the lockdown affecting some cancer referral pathways more so than others. This would help to give a better idea of what sort of future applications would be most effective, with regards to improving the detection of cancer in primary care. It would help to indicate which cancer referral pathways should perhaps be focused on, helping to determine which particular areas of the healthcare system to allocate extra resources to.

Since the positive diagnostic yields have been calculated as percentages, the potential inaccuracies of these calculated proportions should be considered. The data was collected by reading through the patients' notes - this study was therefore reliant on the patients' documents being correct and detailed enough, as well as being uploaded in a timely manner. The use of such qualitative data, rather than quantitative, in this study could be considered a weakness by some, however there was no alternative way of determining which patients' referrals led to a cancer diagnosis.

It is also important to consider the effect that excluding some of the referrals may have had on the results. The proportion of 2WRs that were excluded from each of the three data sets, respectively, was different. It could be argued that this may have skewed the results slightly.

The relatively large sample sizes used in this observational study should mean, however, that such factors would have less of an impact on the overall findings, compared to if smaller sample sizes had been used. This gives further confidence that the established differences found between the data sets are valid.

It therefore seems plausible to suggest that the considerable increase in the positive diagnostic yield of 2WRs in 2020, compared to 2019, was more likely to be related to the influence of the lockdown, rather than any limitations in the data.

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Conclusion

Overall, this study's findings have shown a striking change in the numbers and outcomes of cancer referrals at this Wirral GP practice following the implementation of the first UK COVID-19 lockdown.⁴ The 2021 data has demonstrated that the influence of the pandemic is still affecting cancer referrals, despite the easing of lockdown restrictions.⁶ Although more such audits at other GP practices would validate this paper's findings further, it can be concluded from this study that it would be beneficial to put even more of a focus on early cancer detection in primary care, whilst GPs are still seeing a lower proportion of their patients face-to-face compared to before the pandemic.¹⁸

Summary – Accelerating Translation

Title: The Impact of the COVID-19 Lockdown on Cancer Referrals in Primary Care in the UK: Two Years On

Main Problem to Solve:

The COVID-19 pandemic led to a change in the delivery of primary care. This shift in primary care delivery could have had significant implications to many aspects of patient care, including cancer referrals. Understanding how cancer referrals have been affected could help us improve cancer detection moving forwards, as we adapt to a 'new normal.'

Aims of the Study:

To look at the differences in two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown at a GP practice in Birkenhead, Wirral, England. Contrasting the number of 2WRs made, as well as the outcomes of patients' investigations following their referrals, should help demonstrate some of the consequences that this pandemic has had on patients' health outcomes.

Methodology:

- A search was carried out to find all the 2WR's that were made between 23rd March 2020 1st July 2020.
- The subsequent clinical letters sent regarding each patient's 2WR were then read. This method was used to determine the outcome of

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every 2WR made between 23^{rd} March $2020 - 1^{st}$ July 2020 at the Wirral GP practice, to determine whether each 2WR patient ultimately was, or wasn't, diagnosed with cancer.

- Once every patient's 2WR had been reviewed in this way, it was decided which referrals from the initial data set should not be included in this audit, using exclusion criteria.
- After the application of the exclusion criteria, the remaining 2WR patients were included in the data set for further analysis. A positive diagnostic yield could then be calculated, to represent the proportion of 2WR's that led to a positive cancer diagnosis in the time period between 23rd March 2020 1st July 2020.
- The same method was used to study 2WR's made during the same time period, but in 2019 and 2021.

Results:

- The number of 2WRs decreased by 40.4% in 2020, compared to 2019. In 2021, the number of 2WRs then increased by 225%, compared to 2020.
- Overall, the number of 2WRs increased by 34.2% between 2019-2021. The number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019. Put simply, the number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019.
- The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020.
- Overall, the positive diagnostic yield increased by 224.3% between 2019-2021: the positive diagnostic yield was higher after the lockdown, compared to before.

Conclusion:

This study's findings show a striking change in the numbers and outcomes of 2WRs in primary care following the implementation of the first COVID-19 lockdown. Even more of a focus on early cancer detection in primary care would be beneficial, following the shift from face-to-face to virtual GP consultations since the beginning of the pandemic.

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Conceptualization: OW, LB, RC. Data Curation: OW, LB. Formal Analysis: OW, LB, JG. Investigation: OW, LB. Methodology: OW, LB, RC. Project administration: OW, RC. Resources: RC. Supervision: RC. Validation: RC. Visualization: OW. Writing – original draft: OW. Writing – review & editing: OW, LB, RC, JG.

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