*27 September 2022*

RE: NPJDIGITALMED-03331

Dear Editor,

Thank you for your last communication of the 18th August, inviting us to revise and resubmit our manuscript, now entitled *Vaximap: route optimisation for housebound vaccination.* We are grateful for the thoughtful feedback provided by the reviewers and are pleased that they judged the work to have merit, notwithstanding the technical simplicity of our contribution.

I attach below a point-by-point response to the comments made by the reviewers.

I hope you will find this revised manuscript to your satisfaction and look forward to hearing from you in due course.

Kind regards,

Dr Thomas Kirk

*on behalf of the co-authors*

Institute of Biomedical Engineering,

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Text in black is a reviewer comment

Text in blue is our response

Text in green is a direct quote from the revised manuscript

**Please note all line numbers refer to the final manuscript, without markup.**

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Associate Editor (Remarks to Author):

In addition to the Reviewers' comments could the authors please also discuss how different refrigeration, reconstitution and dose presentations of various vaccines may also impact on optimal delivery strategy.

This is an important aspect of the problem, though not one we have addressed, and the discussion has been amended around line 243 and via the addition of table 1.

Reviewer #1 (Comments to the Author):

I found this to be a well-written and very easy-to-read document. As someone whose background is in operations research (O.R.) and not medicine/healthcare, I will say that there is nothing that is particularly profound or scientifically novel from the standpoint of the methodology used; however, it is refreshing to see a nice application of well-known O.R. techniques to a real-world problem. So I do believe that this sort of work should be well disseminated.

A couple of comments from an O.R. perspective: I think some clarification is warranted in terms of exactly what is being optimised once clusters of locations (“nodes” in network parlance) have been created by the clustering algorithm. There’s some confusion here in how the term “Traveling Salesman Problem” (TSP) is being used. The TSP refers to the case where you are given some network of nodes and arcs and the objective is to find a minimum-length “tour.” Here, a tour is defined as starting at a node (any node, actually), traveling along available arcs, and eventually returning to that node after visiting every other node exactly once. So in this application, that node would presumably be the GP’s office. However, this seems to be an “optional” formulation here and the default seems to be one where you don’t start and end at the same place. You have fixed starting and ending points A and B, and the objective seems to be to visit every other node in the cluster en route, such the total distance traversed is minimized (it appears that is the problem solved by the Bing app). It’s not clear to me if this process is then tried for every combination of A and B to minimize the total distance traveled or if the start and finish are fixed in advance. Either way, this is commonly referred to as a routing problem and not a TSP, and this routing problem is VASTLY simpler to solve than a TSP.

At the end of the day none of this really matters because the focus here is on the application and not the methodology; moreover, problems of the size considered here are trivial to solve optimally. However, in the interest of scientific accuracy, I suggest the authors not get too much into TSP. Perhaps simply say there are two options available – (1) start and end where you start after visiting every other point, or (2) start at some point and end at another point after touching every other point on the way (and please clarify if the start and finish can be selected or if they are fixed). The former is solved by formulating and solving a TSP, the latter by the “waypoints” method, and they are agnostic to the method and just use the Bing app to do this for them.

We thank the referee for this comment. Our explanation was designed to summarise the context and implementation in a way tractable to a general audience, and thus we limited detailed explanation. We do not intend this explanation to be inaccurate or ambiguous at the expense of detail and have therefore clarified as follows (line 36):

"When the route must start and end at the same location (a GP surgery, for example), this is the travelling salesman problem (TSP), or, when the start and end points are unrestricted, this is the vehicle routing problem (VRP); both problems have been extensively studied in the domains of computer science and operational research."

We have also removed mention of TSP in the abstract. Regarding the start and end points, when no fixed start/end is defined, we add the following (line 96):

“Optimise waypoints requires a start and end point for each cluster’s route to be specified in advance, after which it will optimise the order of points in between the two. In the case where the user has specified a fixed start and end point for all routes (i.e., their GP surgery), a conventional TSP is recovered. In the case where no fixed start and end point is given, a VRP is recovered and it is necessary to algorithmically specify start and end locations for each cluster’s route (the API does not select them).”

We have added a comment in line 102 in line with the reviewers suggestion:

"In either case, the Bing maps API handles the optimisation for the order of intermediate locations."

A couple of other clarifications/comments. I’m not sure why the authors have expended so much effort in computing the monetary savings (especially when the final estimate is relatively minor considering the overall time period in question). This appears to be a bit forced to me; really, a detailed qualitative discussion would be adequate.

This is an astute point. The objective of this work was to demonstrate the impact of Vaximap. In the ideal scenario it would have been possible to estimate this quantitatively in terms of clinical outcomes (hospital admissions avoided, lives saved) but this would be methodologically complex and requires access to data that we do not have. We estimate time and financial savings instead as these are feasible, and the manuscript now states this in line 199. Financial quantities are used throughout resource planning and allocation in the NHS (for example quality of life adjusted years, QALYs). Financial savings are also pertinent given the NHS is facing a severe resourcing crisis, though the reviewer is correct the magnitude is not substantial at the national scale. Nevertheless, our results suggest that further savings could be obtained if route optimisation were adopted for the day-to-day management of housebound care (which, we now know from this experience, cannot be assumed of all GPs).

The savings in “route planning” was computed empirically and I can certainly buy into the approach described. However, the computation of the savings in the “route following” is a bit shaky to me, given that the empirical plot from the paper by Dry is for the TSP and the problem the volunteers were asked to solve here was not the TSP (as far as I can tell). Perhaps they can just say that they are using this as an approximation to estimate the extra distance of a suboptimal trip? Either way, I think the more important thing here is the provision to healthcare workers of an automated method to quickly plan out an optimal vaccination strategy, thus saving them a lot of headaches with logistical planning for which they are not trained and having them be able to focus on what they do best - to me that is ample justification!

The reviewer is exactly correct that our approach is nothing more than an approximation; the text has been amended to reiterate this (line 164). It is also noted that the majority of routes generated with Vaximap contained less than 25 patients, for which Dry’s empirical model implies a distance penalty of less than 5%, hence the error associated with this approximation should not be substantial. Ultimately, the results we obtain show that the time savings accrue mainly in the *planning* of routes, not the *following*, so weight attached to this approximation is limited.

Finally, one thing I was curious about – can the authors comment on how or whether they recommend accounting for human error w.r.t vaccine wastage. For example, if a vial has 8 doses it seems highly **conservative** to have exactly 8 people in the cluster – if one dose were to be wasted it would mean a separate trip for just the one person in the cluster who could not be covered! Of course, this doesn’t change the solution methodology but it would seem like there should be some balance between the risk on the one hand of having to make a separate trip because the vial got mishandled and a dose was lost, and on the other hand, having an extra dose left over at the end. I suspect a recipient could always have been found for the latter situation; I recall that here in the US it was common back in 2020 for people to line up outside clinics late in the day in the hope of getting vaccine left over in an open vial at the end of the day!

The authors made no attempt to, nor do they recommend a strategy for, dealing with this, though it is an important aspect of the problem. At the time the tool was developed, time was of the essence and GPs did not request such functionality (which remains the case now, 18 months later). Further, dealing with this aspect would likely require some statistical modelling around error/wastage rates; at the time of development insufficient data on error/wastage was available to inform such modelling because the campaign had only just begun. Finally, as the reviewer notes, many alternative grass-roots initiatives to re-allocate spare doses emerged and it is reasonable to assume that spare doses from home vaccination would have found a willing arm by this route. These points are addressed around line 243.

The reviewer may be interested to learn that the original goal of the authors was to set up a service to re-allocate spare vaccine doses and a prototype was duly built. Unfortunately, the NHS and lead contractor for booking vaccine appointments (Accurx) were unwilling to engage with us; fortunately for housebound vaccination we could solve the problem without their engagement. The reviewer may be yet more interested to learn that the person who set up the equivalent service for vaccine re-allocation in France, *Vite Ma Dose*, was awarded the Order of Merit for this work (Guillaume Rozier).

Reviewer #2 (Comments to the Author):

Thank you for sharing your success story of Vaximap. It is good to see that there are large scale adoption of mathematical solutions in the healthcare industry. People are typically change resistant to new technology. Congratulations on this achievement!

Some remarks that may improve the paper from my perspective:

1. Mention is made in the introduction about the traveling salesman problem as been extensively studied in computers. It would be worth mentioning the contributions made in the domain of operations research, wherein the TSP and vehicle routing problems are extensively studied, perhaps one of the main focuses in operations research.

We thank the referee for highlighting this - it is not our intention to overlook areas of research which have significantly advanced understanding in this regard. As such, we have clarified the contributions within operations research, and have included references to reviews of existing and emerging approaches to both the TSP and VRP in the context of both operations research and computer science (Laporte 1992, Breakers 2016, Vidal 2020). Lines 39 and 256 now make direct reference to operations research.

2. The problem described seems to be more related to vehicle routing problems, than TSP. I find the lack of mention puzzling. Perhaps it is worth considering the vehicle routing problem (VRP) literature, which is similar to TSP, but considers multiple routes with vehicle capacities (i.e. only a certain number of patients can be visited). For example, VRP with multiple vehicles (for multiple healthcare practitioners visiting patients), or VRP with multiple depots (if starting locations are not all from the same location), or VRP with time windows (to incorporate the time limit in which vaccines can be outside of the cold chain), or the capacitated vehicle routing problem.

We thank the referee for this comment. We acknowledge that is important to mention both the VRP and TSP here and thus have clarified this as part of the amendment to line 36:

“When the route must start and end at the same location (e.g. the GP surgery), this maps exactly to the travelling salesman problem (TSP) or, when the start and end points are unrestricted, this is the vehicle routing problem (VRP); both problems have been extensively studied in the domains of computer science and operational research.”

Regarding the proposed extensions to include multiple depots or vehicles, this would indeed be a very useful addition should the software be adopted more widely by the NHS, e.g. to manage future Covid vaccination efforts at the trust level. However, in the context of the rapid roll out of Vaximap during the early phase of the vaccination programme, this was not something we had the time or resources to implement. Furthermore, in discussions with healthcare practitioners during this time, it was clear that vaccination centres/surgeries were operating independently and covering their own lists of vulnerable patients, hence the utility of supporting multiple depots/vehicles would have been limited at this time. Line 258 now explains that variants of the VRP with extra constraints would be suitable for future work incorporating the cold-chain requirements of vaccination.

3. After the paragraph ending in line 45, to focus the article on the success story of vaximap, it would be good to include a paragraph here to refer to the change management or any strategies used to get buy-in from healthcare practitioners to use the software to the extend it was used. There are many related open source software on vehicle routing available, with perhaps more advanced modelling implemented than what is described in this paper, which were not used by the healthcare practitioners. Why do the optimisation community struggle to get buy-in from end-users. It would be good to comment on this in the introduction, which would link well with the last paragraph of section 2 (line 56).

This is an excellent point and has been addressed both in the introduction (line 50) and discussion (line 220).

4. In the methods and materials section, it would be good to comment on the choice of methodology. It is a simple modelling approach that is followed, and a straightforward simple interface with not many features compared to other related software, and not necessarily of interest to researchers in vehicle routing problems. I understand the emphasis was on rapid deployment and keeping it simple enough for healthcare practitioners to remove the ``barrier to entry'. Perhaps it would be good to comment on it as part of the strategy and reason for success --- this is what is noteworthy to optimisation specialists in terms of behavioural operations research, perhaps solutions are sometimes just over complicated, and require too much initial training in an already strained environment.

The reviewer is generous to suggest this discussion point. Raising the need for training alongside the deployment is particularly astute - at no point could we provide training for this service, hence our focus on simplicity, whereas a lack of training may have hindered the use of more advanced solutions. This is addressed in the paragraph starting line 220.

5. As mentioned above, there are related free digital vehicle routing technology available, for example see this link [https://www.goodfirms.co/route-planning-software/blog/best-free-open-source-route-planning-softwar](https://www.goodfirms.co/route-planning-software/blog/best-free-open-source-route-planning-software)e and this link <https://github.com/VROOM-Project/vroom>. Mention should be made of other related technology, and the improvement that vaximap brought in comparison to these. I recommend putting the focus on `{\it why}' certain simplifying decisions were made regarding vaximap, and not just `{\it what is vaximap}' in the article.

Similarly to the point raised above, this is discussed in the paragraphs starting at lines 220 and 256. The VROOM project is now cited as an example of a more sophisticated open source solution.

It is later also mentioned that Microsoft Bing's mapping API is used - does this include clever routing, i.e. not just distance savings, but time savings in terms of road congestion). Was the Logistics and Fleet Management API of Bing Maps used?

Yes and no. It does account for road and traffic conditions, but at the time of route generation, which is not necessarily the time the route will be followed under our simple implementation. Logistics and fleet management facilities were not used. The manuscript has been amended on line 94.

6. The 20 volunteers chosen - please provide more information? Were the volunteers healthcare specialists, were they typically responsible for the route planning in the healthcare industry, i.e. how experienced are they with route planning?

The volunteers were chosen from a cross-section of professions, including some healthcare specialists. None had experience or training in route planning, within the healthcare industry or otherwise. In line with the initial demand from the healthcare industry (discussed on line 5) and in discussions with/testimonials received from end users, this sample was chosen to be representative of the typical healthcare workers who were charged with formulating delivery routes during the pressures of the Covid-19 pandemic, e.g. practise nurses, doctors, practice managers or volunteers, with no specific training in route planning. A detailed breakdown of the test subjects follows. Line 142 now gives more information within the manuscript.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Age** | **Sex** | **Occupation** |
| **0** | 28 | M | Finance |
| **1** | 27 | M | Research |
| **2** | 34 | F | Doctor |
| **3** | 68 | F | Business Owner |
| **4** | 71 | M | Company Director |
| **5** | 26 | M | Data Scientist |
| **6** | 26 | M | Corporate Data Analyst |
| **7** | 35 | M | Doctor |
| **8** | 59 | F | Psychologist |
| **9** | 35 | M | Finance |
| **10** | 53 | F | Prescriptions Clerk |
| **11** | 26 | F | Producer |
| **12** | 65 | M | Retired (Chartered Accountant) |
| **13** | 28 | M | Chartered Accountant |
| **14** | 76 | F | Retired Teacher |
| **15** | 78 | M | Retired |
| **16** | 30 | M | IT analyst |
| **17** | 55 | M | Company director |
| **18** | 55 | F | Data Engineer |
| **19** | 26 | F | Physiotherapist |

7. If more information is provided regarding the Microsoft Bing API, the comparison would be more clear. Is the solution provided by Bing Maps a clever solution in terms of travel time, road congestion?

We assume that the Bing maps API uses proprietary technology. The API documents do indicate that road conditions and traffic are factored into the optimisation, though these are captured at the time of route generation which is not necessarily the same time that the route will be followed. The manuscript has been amended on line 93.

8. It is not clear from the comparison, if the actual time to upload patients on vaximap, and selection of parameters, and runtime of vaximap for the same problem instances as those considered by the volunteers, was considered in the time savings calculation? I.e. are apples compared to apples here?

The reviewer is correct to point out that the comparison is unfair. We have added a 30 second penalty per user request: this approximates the time taken to choose parameters and generate the results. The manuscript has been amended on line 157.

9. Provide information on what can still be improved from a methodology and software development point of view (future work).

The discussion now addresses this, starting from line 256. The logical next steps would be to adopt the strategies used by existing (and more advanced) solutions, permitting the incorporation of further constraints (temperature storage requirements, human error/wastage). A wider goal would be to investigate whether aspects of this solution could be applied to the day-to-day provision of housebound care, which seems eminently likely.

Reviewer #3 (Comments to the Author):

The paper addressed a practical problem by developing a tool for route decision-making of dispatching vaccines to patients. The underlying problem is a classical TSP problem which is NP-hard. The authors leverage the existing algorithm to address the problem. The major contribution is tool development. This tool has been used for planning over 400,000 patients and the impact shows promising. Some comments are as follows.

1. The focused TSP problem seems to assume that there is a direct path between all patients (locations). In other words, the distance matrix is complete which may not be the case in practice. It is necessary to eliminate those non-existing paths when constructing the distance matrix.

The reviewer is correct to point out this flaw in the methodology. Implicit in the clustering step is a distance matrix that assumes direct paths between all patients. By contrast, the Bing maps API could be used to generate a true distance matrix that does not make this assumption, but the key difference is that this is more expensive (growing with the square of patients) than geocoding each individual patient and calculating the distance matrix offline, making the aforementioned assumption. At the time of creation, the API charges were billed to an author’s personal credit card and the sum reached £1,200 before external funding was secured. The clustering used here provided a simple means of minimising API charges at the expense of some optimality. It is worth pointing out that the subsequent route generation step does not assume direct paths. The manuscript has been amended at line 85.

Also, the length of the path directly affects the travel time. Another factor that can be considered is congestion. Some routes naturally encounter larger delays compared with others which play a role in the investigated routing problem. These aspects need some discussion and clarification.

The Bing maps API does account for road speed and traffic, but only at the time of route generation. Under our implementation, the time at which the route will be followed is not known, and the conditions may have changed by then. The manuscript has been amended at line 93.

2. It is also possible that there is more than one patient at each location. In this case, the nodes (locations in the route) have weights, which affects the number of locations the practitioner can cover (knowing that there is a limit D on the number of patients each practitioner can visit). The part of the model can be clarified further.

The co-location of patients is an extremely important edge case and there are numerous checks in the software to ensure they are handled appropriately. Both the clustering and route generation steps are robust to this. We highlight this in the amendment to line 87.

3. The problem itself is a classical routing problem. The formulation and methodology used are traditional. And it actually can be used for any other similar resource dispatch settings. The reviewer did not see the model captures well the unique features of COVID-19 vaccination distribution, e.g., the maximum time to complete constraint for each route for each practitioner due to vial considerations. It is also suggested to justify further the challenges of the problem solved in the manuscript.

We thank the reviewer for this opportunity to further clarify the impact of Vaximap, here and in the manuscript.

During the early days of the Covid-19 vaccination effort, there were no easily accessible route-planning resources geared towards healthcare practitioners, which is discussed in lines 5 and 29. Vaximap provided an immediate solution to this issue, using a minimal amount of data (i.e. postcodes) to greatly simplify an otherwise complicated task of route planning. The inputted data and our transparency on how that data would be stored ([https://vaximap.org/policy/](https://vaximap.herokuapp.com/policy/)) allayed any patient data concerns, from the healthcare practitioners' perspective, making the tool highly accessible; this is in contrast to other route-finding tools with a wider range of features and thus more complex/difficult to interpret data management policies.

As regards capturing the unique features of Covid-19 vaccination, we highlight that the service accommodates the vial size, and clusters the postcodes accordingly so as to minimise wastage. The vial size can be adjusted, so as to capture the various brands of vaccines, as can the method of travel. Routes can be returned via email, as a file which can be loaded into mobile mapping software. This reduced the problem of delivering an effective vaccine rollout to the housebound population to a critical mass of features.

We accept the reviewer's suggestion to further justify the challenges of the problem solved here. This is addressed on line 30, and the following new passage has been added at line 53:

“Of vital importance was a strict data-management policy: Vaximap requires only the bare minimum of non-identifying data (patient postcodes) in order to function. This was crucial to satisfy GP's justified caution in adopting a new technology”