DataLab - Demonstrating Value For Rapid Evaluation of Evidence for NICE Guidance

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Executive Summary

In August 2018 Health Innovation Manchester agreed to fund an initial "proof-of-value" project to deliver insight and understanding as to how Data Lab could support NICE objectives defined as: *"To support the adoption of well-evidenced, innovative technologies into the NHS and social care systems for the benefit of patients and citizens."* Two "Minimum Viable Product" (MVP) projects were selected, one looking at statin prescribing and another on anti-microbial resistance, to create outputs that demonstrate the value to NICE of the DataLab, to increase the understanding of the place of real world evidence (RWE) analysis in NICE and to understand the challenges of working in partnership across the three organisations, NICE, University of Manchester and HInM.

This combinatorial approach allowed for the development of a new pathway for evidence generation. Bringing together a team of different backgrounds and approaches across health economics modelling, policy, data and analytics and patient and public involvement and engagement (PPIE) created new ways of working and new insights and is entirely consistent with the 'sprint' approach used in agile methodology. In particular, the presence of NICE staff helped to ensure that the projects were connected directly to NICE's need and best practice, for example by providing researchers with access to the latest NICE health economic models.

The value to NICE has been captured as:

- The value of new knowledge. The knowledge generated has value, although difficult to quantify in monetary terms. Knowledge generated specifically to inform areas of uncertainty in NICE's guidance and to inform future decisions regarding the need for updated guidance
- A new environment – breaking boundaries with the creation of an environment outside of NICE's core business and provides opportunity for cross-fertilisation, joint formulation of NICE research problem statements and interactions with experts, the NHS and datasets.
- Agility and speed using a digital transformation methodology. There are cost savings by not having to commission studies and time savings when speed means quicker paths to improving patients' lives.
- Ability for NICE to work in a Greater Manchester 'learning healthcare' system with newly established NICE Data and Analytics team
- Trusted partnership where sharing of information and data is possible (e.g. expedited access to health economic models)
- Generation of further research ideas and defining NICE problem statements by working synergistically with data analytics and health economics.
- The opportunity to inform research questions by patients' views.

These projects have shown that the ability of NICE to derive benefits from technology is far more dependent on the people, processes and culture than it is on the technology. For this approach to continue the following recommendations are made to:

- to run Innovation Labs (NICE/UoM/HInM) to co-develop clear problem statements for current health and guidance challenges.
- Establish clear processes and governance for DataLab, including a formal leadership group and establish pipeline of projects as a learning health platform.
- Identify and confirm pathways for future funding, both locally and nationally.
- to establish HInM processes for rapid access and integration with GM data sources.
- Continue to develop the Innovate UK programme for delivery.
- Develop a proposal for a Health Data Research UK (HDRUK) Digital Innovation Hub.

Introduction

Since late 2017, the National Institute for Health and Care Excellence (NICE) has been in discussions with the University of Manchester (UoM) and Health Innovation Manchester (HInM) regarding the opportunities to collaborate on the use of real-world evidence in the development of new guidance NICE. This has been undertaken within the remit of the existing Memorandum of Understanding between the three parties, with the project known as the Big Data Evidence Lab, or "DataLab." Initial in-kind resource worked to develop the initial business case, supported by the NICE board in March 2018, as well as an industry workshop with the University of Manchester Connected Health Cities (CHC) project. In August 2018 Health Innovation Manchester agreed to fund an initial "proof-of-value" project to deliver insight and understanding as to how Data Lab could support NICE objectives defined as:

"To support the adoption of well-evidenced, innovative technologies into the NHS and social care systems for the benefit of patients and citizens."

In discussion at the meeting two initial "Minimum Viable Product" (MVP) projects were selected, along with a commitment for a research working group and a project board agreeing to meet every two weeks. These groups were made of representatives from each of the three MoU partners. The role of the MVPs was to create outputs that demonstrate the value of the DataLab approach to NICE, to increase the understanding of the place of real world evidence (RWE) analysis in NICE, to understand the practical challenges of working in partnership across the three organisations, and to deliver two projects with practical results that would be of value to NICE: a project looking at statin prescribing and another on anti-microbial resistance. These projects concluded their work on 8th February 2019 and the outcomes from each are included in this report.

Proof of Value

General Learnings

Focusing on delivery of the two MVP projects allowed for a short, intensive commitment from partner organisations demonstrate new ways of working. This type of approach has been widely adopted across multiple industries to derive value from digital approaches through lean or agile methodologies. Focus on specific problems with short times to resolve can provide a clarity of purpose with a faster time to value, but can be challenging within highly regulated, formal environments and requires different behaviours and ways of working from traditional approaches.

The team was made up of members from all three organisations to create a multi-disciplinary approach, as shown in Figure 1. By meeting every two weeks the research team was able to quickly and continuously review progress, identify and resolve issues, and work to understand the challenge from different viewpoints. This also promoted a level of enthusiasm that was shown through the commitment made by the team to participate in the project.

The project team included:

- NICE: Representation from NICE Guidelines and Science Policy and Research. Project management.
- UoM (Connected Health Cities): Data scientists, health economics, access to data sources, facilitation and oversight.
- HInM: Public and patient involvement workshops, funding.

A full list of members and clinical experts is included in Appendix 1. A timeline of the project activities is shown in Appendix 2.

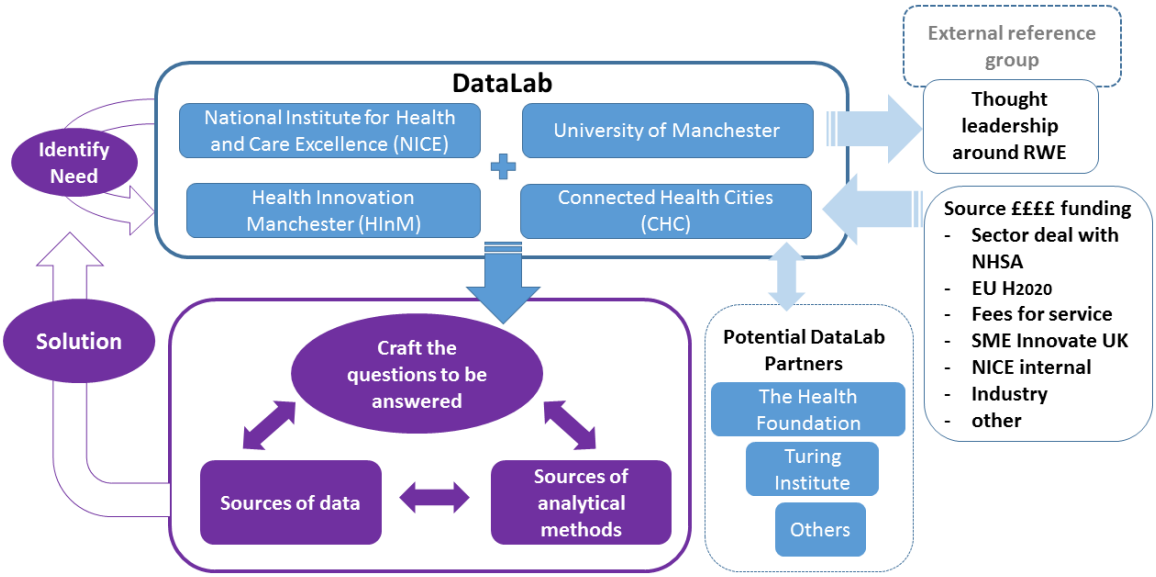

Figure 1 DataLab process

Route to Value

This combinatorial approach allowed for the development of a new pathway for evidence. Bringing together a team of different backgrounds and approaches across PPIE, health economics modelling, health policy, data and analytics, is a necessary step in creating new ways of working and new insights and is entirely consistent with the 'sprint' approach used in agile methodology. For example, the formulation of questions and answers was possible because of the mixture of people in the room that would not have otherwise happened. In particular, the presence of NICE staff helped to ensure that the projects were connected directly to NICE's need and best practice, for example by providing researchers with access to the latest NICE economic models. As well as demonstrating the viability of the approach, technical meetings between the team and NICE are now planned to discuss the specific evidence generated by the MVPs and the MVP approach to further embed the learning from the projects within NICE.

MVP1. Statins

These findings are of interest to NICE because they add to the evidence base that:

- Adherence is poor and improving adherence will have large benefit. Adherence gets worse/more inconsistent beyond the initial discontinuation.
- Delaying statin initiation to account for poor adherence has little clinical benefit.
- The optimal time to prescribe to prevent most CVD events is more dependent on age than it is on risk score.
- There is little change in risk score or age of patients being prescribed statins after NICE guidelines were changed.

MVP2. AMR

These findings are of interest to NICE because they suggest that we need more risk-based prescribing for antibiotics (as we do for other diseases) because:

- There was a significant variability in the number needed to treat (NNT) for infection-related hospital admissions across patients consulting their GP for different common infections.
- The likelihood of getting an antibiotic was not related to a patient's risk of being hospitalised, with possibly high-risk patients being undertreated and low risk patients overtreated.
- These data suggest that NNT should not used in NICE guidance, but it would be useful to further investigate whether NNT could be an effective additional tool or not.

Innovate UK

One other major benefit of the DataLab programme has been to identify the unique expertise that is available from Connected Health Cities, UoM, HInM and NICE. Following discussions with the Office for Life Sciences, an agreement with Innovate UK (IUK) has been made to support a funded consultancy offering that will be available to companies who are successful in the next round of Digital Health Catalyst applications. The contract between NICE and IUK has now been signed, with the sub-contract of Connected Health Cities in development.

Learnings and **Challenges**

The short timescale to establish and run the MVP projects inevitably created some challenges and learnings that should be understood and addressed for future project work. We have learned:

1. How to successfully work together at speed. We are from different institutes and different cultures, but we have established a team with a common goal.
2. How to formulate research questions/problem statements for NICE that can be answered with data analytics. We needed a new environment with new partners to ask the 'right' data questions which supports generation of relevant problem statements which are essential for agile approaches.
3. Future project selection should be validated using a "ground truth" approach (the process of gathering the proper objective data used in machine learning) through consultation with NICE staff, clinical experts and external patient public involvement at all levels. One approach for this that has been successful in other areas is an Innovation Lab style of event. This is discussed in Next Steps.
4. How to accommodate different language and terminology between the three partners. Projects need to ensure that appropriate consideration and time for learning to translate between organisations is necessary for success.

The challenges have been:

1. These projects have been concluded "at risk" as the process for funding has taken longer than anticipated. It is a credit to all organisations that their commitment has remained high, but it must be recognised that if other, external partners, such as companies, were included in future project work this could be a major block to delivery.
2. The process for the selection of research questions for the MVPs was undertaken in a high-level workshop in August 2019. As such it reflected a limited view of both NICE and Manchester system need, including questions such as access to data or a fully informed view of existing research and guidance.
3. Due to the time to access and current limited availability of local data, MVP project data was limited to national datasets that are already licensed within the University. There is a clear need to ensure that GM can provide a platform for data access as the LHCRE develops, or through projects such as the HDRUK Digital Innovation Sprint.

Next Steps

The DataLab MVP approach, funded by HInM is complete. Currently, a new DataLab partnership with IUK is underway and other project proposals are supported in an ad-hoc form between the University of Manchester and NICE. It has been recognised that MVP is a good model for quick assessment of guidance and for rapid, novel research that will be presented at an upcoming NICE Technical Forum meeting to ensure that the specific learning from these projects can be appropriately incorporated within NICE.

Future sustainability of the DataLab partnership requires agreed governance and pathways to funding. As the GM system continues to develop under the Health and Social Care Partnership it will be essential to incorporate this process into wider system opportunities. One significant opportunity will be to develop the next phase of DataLab as a Digital Innovation Hub, able to respond to HDRUK's funding call later in the year.

In order to identify future projects, it is recommended that one or more Innovation Lab events are run. These events would allow input from a range of stakeholders, including clinicians and NICE experts, to rapidly pitch, design and prototype ideas to test for viability and suitability. Multi-disciplinary teams can develop ideas around a problem of interest which can then be pitched to an expert panel for a decision on future funding. The approach is a relatively inexpensive and effective way to identify and "ground truth" ideas and identify those of value for further investment and investigation through a learning health system model, supported through the collaborative network of NICE, UoM and HInM. These events would provide a good opportunity to link NHS colleagues, researchers and NICE in developing ideas that would be of practical benefit to the health system and highlight areas for improvement. Our work has shown that the ability of NICE to derive benefits from technology is far more dependent on the people, processes and culture than it is on the technology.

For this approach to continue the following recommendations are made:

* Identify and confirm pathways for future funding, both locally and nationally. Including developing a proposal for a HDRUK Digital Innovation Hub.
* NICE/UoM/HInM to run Innovation Labs to co-develop clear problem statements for current health and guidance challenges.
* Establish clear processes and governance for DataLab, including a formal leadership group and establish pipeline of projects as a learning health platform.
* HInM to establish processes for rapid access and integration with GM data sources.
* Continue to develop the Innovate UK programme for delivery to businesses.
* Adopt a digital transformation methodology with the NICE Data Analytics group.

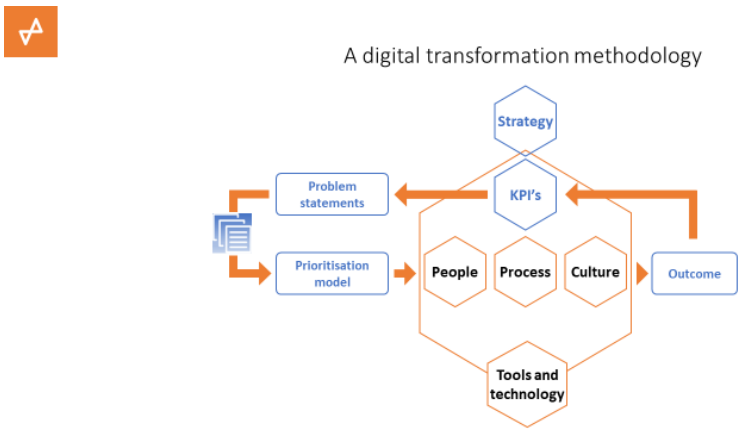

Figure 2 Digital transformation methodology.

Key to Figure 2: A problem statement would be "We have noticed that 'a' is causing 'b' with the consequences of 'c' with the implications of 'd'". Good problem statements are devoid of embedded solutions and include quantified metrics where possible.

MVP1. Statins

Key learning:

These findings are of interest to NICE because they add to the evidence base:

- Adherence is poor and improving adherence will have large benefit. Adherence gets worse/more inconsistent beyond the initial discontinuation
- Delaying statin initiation to account for poor adherence has little clinical benefit.
- The optimal time to prescribe to prevent most CVD events is more dependent on age than it is on risk score.
- There is little change in risk score or age of patients being prescribed statins after NICE guidelines were changed.
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Background and rationale

In England, lipid modification via statin prescription is recommended in individuals for primary prevention of cardiovascular disease (CVD) where there is a 10% or higher risk (called a 'risk threshold') of a cardiovascular event occurring the next 10 years. (1) Cardiovascular (CV) events can include: fatal or non-fatal angina, myocardial infarction (MI), transient ischaemic attack (TIA) or stroke. To measure cardiovascular risk, NICE currently recommends the use of QRISK2, a validated cardiovascular risk prediction algorithm. Updated guidance will likely consider the use of QRISK3 with evidence suggesting better performance for people with type 1 diabetes and chronic kidney disease.(2) Cardiovascular risk thresholds for statin initiation differ widely internationally: 7.5% in the USA,(3) the European Society of Cardiology recommends initiation at 10 year risk of a fatal CVD of 5%, which equates to ~ 15% risk of any CV event.(4) In Scotland, recent guidance has recommended a risk threshold of 20% over 10-years for individuals who are asymptomatic.(5) Variation in benefits by age and sex, and statin prescribed,(6) costs incurred,(7) and concerns about side effects leading to suboptimal adherence by patients have led to questions about the appropriateness of the thresholds.

Two factors that will affect whether the NICE guidelines are providing optimal benefit is whether practitioners are prescribing statins according to risk scores, and whether patients are taking the medicines as prescribed.

The NICE clinical guideline on lipid modification assessed the cost-effectiveness of the 10% risk threshold for initiating a statin prescription.(8) In an economic model it was assumed that people's adherence to statins is 100% and that a person will continue to take the statin for the rest of their life. In sensitivity analysis, statin discontinuation and switching rates were altered at levels (2-5%) linked to reported adverse events reported from clinical trials.(8) Altering statin discontinuation and switching rates at low levels did not change the conclusion that 10% was a cost-effective risk threshold. However, subsequent analysis of real-world prospective cohort data suggests discontinuation rates may be higher than examined in the model (47%), and some people do not even start taking the statin.(9, 10) However, the picture is complicated by the finding that >70% of people who stop taking the statin then restart.(9)

Poor adherence to statins has been associated with increased risk of CV events and deaths.(11, 12) If this discontinuation rate is high across the target population, more benefit may be generated if statins are started later, when people have a higher risk of a CV event, rather than at the current threshold recommendation of 10%, particularly if discontinuation is higher with lower baseline risk.

Aims of this project

Primary aims:

- To describe discontinuation and recontinuation rates in statins in primary prevention.
- To determine the optimal point on the risk trajectory to start statins in this patient group, given real-world statin consumption, by examining the impact of delaying statin initiation from initial risk assessment.
- To examine the impact of improving adherence on patient outcomes.

Secondary aim:

- To determine the impact of NICE guideline introduction in 2014 on risk scores of patients being initiated on statins for primary prevention in England.

Methods

We used routinely collected primary and secondary care data: the Clinical Practice Research Datalink (CPRD), Hospital Episode Statistics (HES) and the Office for National Statistics (ONS). These datasets were linked to identify two nationally representative cohorts of people who were a)statin users or b)eligible for risk assessment for primary prevention of CVD as per the inclusion/exclusion criteria in QRISK3.(13) Data in CPRD were used to determine CVD risk and statin adherence. HES was used to identify CVD events requiring hospitalisation, and deaths were identified from ONS. Linking the three datasets restricted the dataset to England.

Describing patient adherence (discontinuation and recontinuation) rates in statins

We determined the discontinuation and recontinuation rates of those who were prescribed statins using prescribing data in CPRD, over 10 years from first prescribing event. Statin prescribing data in CPRD were used as a proxy measure for patient adherence (discontinuation and recontinuation), as it is not currently possible to link routine prescribing and prescription-filling data in UK primary care. As people discontinued and recontinued more than once, we investigated up to, and including, the third recontinuation period.

Impact of delaying statin initiation from initial risk assessment on CVD event rates

We modelled the CVD risk over the lifetime of patients who were eligible for statins for primary prevention of CVD. This allowed us to calculate the potential number of CVD events prevented by initiating prescribing at risk thresholds given the discontinuation and recontinuation rates we see in practice. The risk threshold was varied between the minimum and maximum risks of patients in 40, 50 and 60-year old cohorts. The number of CVD events prevented per 100 people if statin initiation was delayed from initial risk assessment by increasing numbers of years was estimated.

Impact of statin adherence on CVD event rates

These estimates were recalculated assuming the discontinuation rates were reduced to 5/6, 2/3, 1/2 of the rates we found in practice, and a scenario was presented assuming no discontinuation. A common risk score for a patient of each age was chosen for each of these scenarios.

Impact of NICE guidelines on initiation of statin prescribing in primary care

Using patient data in CPRD (age, sex, cardiovascular risk factors), we calculated the 10-year cardiovascular risk score of those being prescribed statins for the first time, to assess trends in statin prescribing and to assess the impact of NICE guidelines on risk scores of patients being initiated on statins for primary prevention. The model used to derive these risk scores was developed using the same criteria and variables as QRISK3 and developed using the primary prevention cohort.(13)

Results

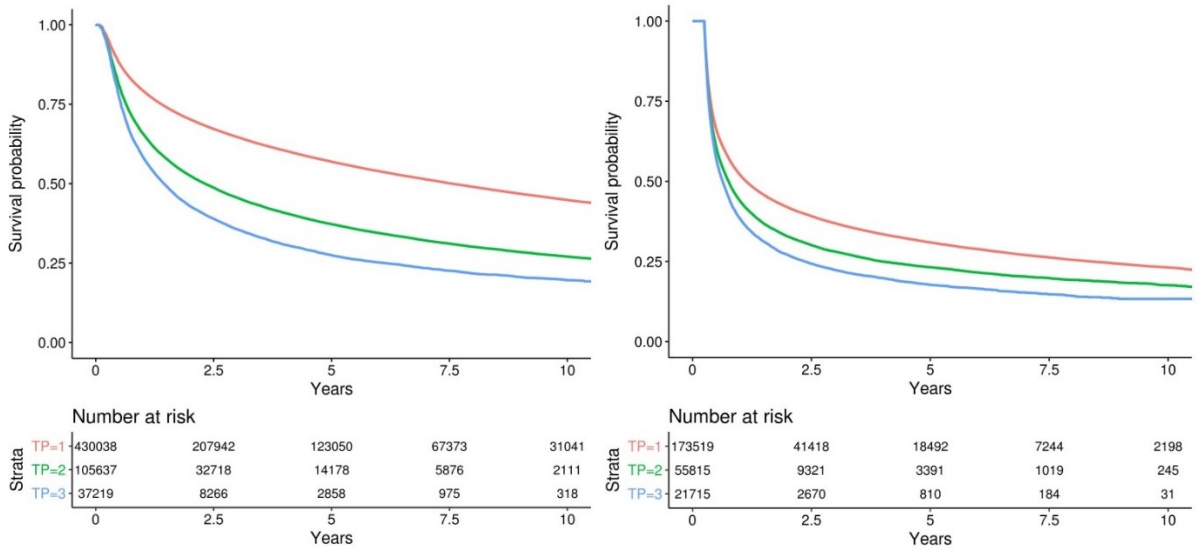
The primary prevention cohort comprised 3,855,660 patients (1,965,078 female). The statin users cohort comprised 430,038 patients (204,701 female).

Describing patient adherence (discontinuation and recontinuation) rates in statins

Figure 1 presents the discontinuation and recontinuation rates over the first 10 years from entry to the station users cohort. Figure 1A indicates the probability of still being on treatment at different time periods, for the first, second and third treatment period. Figure 1B shows the probability of staying off the treatment, after having discontinued for the first, second and third time. This demonstrates that 21% patients have stopped taking statins by the end of the first year of follow-up during the first treatment period, 30% have stopped after 2 years, and by 10 years 55% have stopped. Of all the patients that discontinue, around 48% have restarted a year after the initial discontinuation, 58% after 2 years, and 77% after 10 years. The second discontinuation and restarting rates suggest patients who restart are much more likely to discontinue/restart than during the initial discontinuation and restarting periods. This trend continues with an even higher discontinuation and restarting rate amongst those on their third treatment period.

Figure 1: Kaplan Meier plots of the time until discontinuation or restarting for the first three treatment periods

A Discontinuation *B Restarting*



Impact of delaying statin initiation from initial risk assessment on CVD event rates

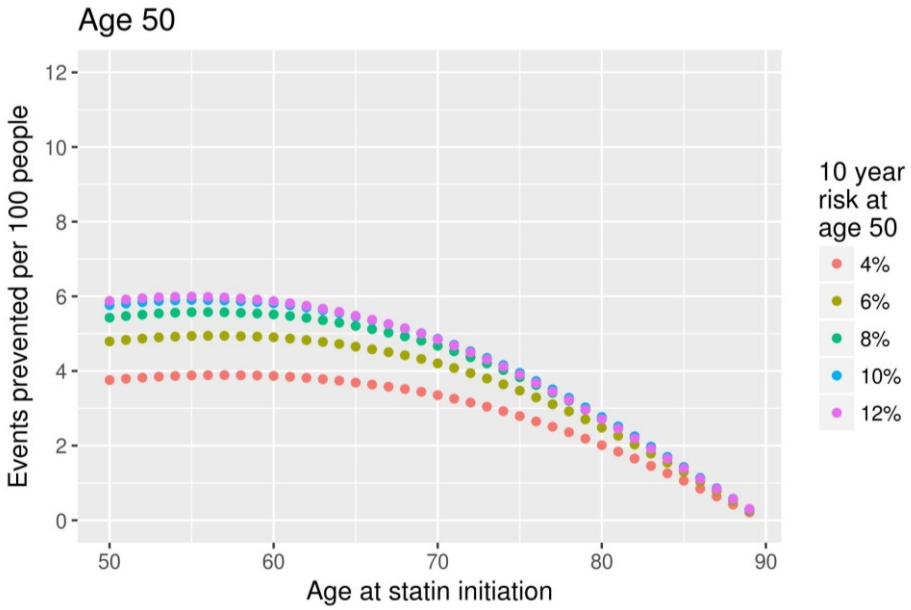
We present results here on the male cohort as this is the higher risk group and males are more likely to receive statin treatment. The results from the female cohort give similar conclusions and can be found in the Appendix. Figure 2 shows the number of CVD events prevented compared to no statin treatment when delaying statin initiation from initial risk assessment. We present the results considering 50-year old men, with a risk of either 4, 6, 8, 10 or 12% at risk assessment (all results available in Appendix). Each point on a trajectory represents the same cohort of individuals, all that is changed is the year in which statins are initiated (and therefore the risk level of the individuals at statin initiation also). We are interested of the maxima of each trajectory, as this represents the optimal time to initiate statins for this group. These results show that the gains that can be made from delaying statin initiation are marginal, and this is the case irrelevant of the risk score at assessment. The number of events prevented begin to

drop off more steeply if statins are initiated beyond the age of 70 as the total time spent on statins by the population reduces significantly due to the competing risk of death.

Illustrative example: If we prescribe a statin to a cohort of 50-year old men with a 10% 10-year CVD risk, we prevent 5.76 events per 100 individuals over the course of 40 years. If we took this same cohort of men, but instead waited 10 years before initiating statins, at which point there 10-year risk of CVD would be around 20%, then we would prevent 5.84 events per 100 individuals over the 40 years period of follow up.

The small gains are likely due to the trade-off between prescribing to everybody at a higher risk, to losing out on total amount of time on statins, as some patients would have adhered to their treatment for the entire duration of the study. The patients who don't adhere to their treatment for very long would therefore benefit from the raising of the threshold (delaying statin initiation), whereas the patients who adhere to their treatment would lose out.

Figure 2: Simulation results presented as CVD events prevented depending on when statins are initiated using discontinuation rates derived from data (male cohort)

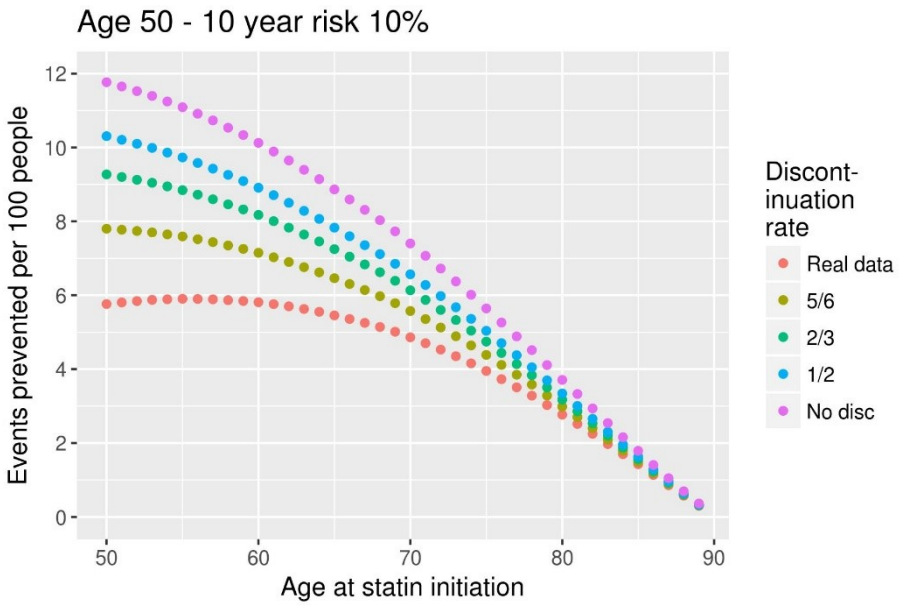


Impact of statin adherence on CVD event rates

Figure 3 shows the effect of reducing the discontinuation rate to 5/6, 2/3, 1/2 of the rate we found in practice, and the effect of no discontinuation. We again use a cohort of 50-year old men, this time every trajectory considers the same group with a 7% risk at assessment, which is the median for this age. It can be seen from this graph that the more adherent to statins people are, the more benefit they receive, and this benefit is increased the earlier prescribing is initiated. This is in contrast to the trajectory derived from real-life discontinuation rates, which suggests little difference between initiating statins at age 50 or 60. The results suggest that improved adherence to statins may have a significant benefit in reducing CVD events. The benefit of improving adherence is increased the earlier statins are initiated.

Illustrative example: Suppose that the rate of discontinuation in each treatment period is halved through some intervention, restarting rates remain the same. If we prescribe a statin to a cohort of 50-year old men with a 10% 10-year CVD risk, we prevent 10.31 events per 100 individuals over the course of 40 years. If we took this same cohort of men, but instead waited 10 years before initiating statins, at which point their 10-year risk of CVD would be around 20%, then we would prevent 8.91 events per 100 individuals over the 40 years period of follow up.

Figure 3: Simulation results presented as CVD events prevented depending on what discontinuation profile is used (male cohort)



Impact of NICE guidelines on initiation of statin prescribing in primary care

Table 1 shows the average 10-year risk of patients that were initiated on statins in two-year periods from June 1998 to June 2016. There is a downward trend between 2004 and 2012 as the average risk drops from 19.44 to 16.36. The drop in average age from 62.54 to 60.66 explains some of this trend, but some must also be explained by changes in other key variables. Importantly, there is no discernible change in the risks or ages of patients being initiated on statins after the guidelines were changed in 2014. The average risk in the two years before was 16.56 and the average risk if the two years after was 16.62. If clinicians changed prescribing practices when the threshold was changed we would expect to see a drop in the average risk here.

Table 1: Mean and median 10-year risk score and age of patients being initiated on statins for the first time

Year*	Mean risk	Median risk	Mean age	Median age	N
1998 - 2000	16.00	13.15	60.45	61.51	18266
2000 - 2002	18.42	15.70	61.64	62.68	28109
2002 - 2004	19.44	16.84	62.54	63.36	53995
2004 - 2006	18.21	15.62	62.44	63.01	75296
2006 - 2008	17.26	14.82	61.89	62.43	72519
2008 - 2010	16.53	14.10	61.20	61.94	66297
2010 - 2012	16.36	13.99	60.66	61.61	51770
2012 - 2014	16.56	14.46	61.19	62.22	44136
2014 - 2016	16.62	14.58	61.71	62.79	19650

* Time periods run from June to June, so that the cutoff matches the date the prescription threshold was changed, June 2014

Implications of the results

Key results of this study are that, delaying statin initiation until patients are at a higher risk will not have a clinically relevant effect on the number of CVD events prevented. Rather than adjusting the risk at which we initiate statins in patients, it may be better to focus on improving adherence amongst those patients. Furthermore, the data presented suggest that the optimal time to prescribe in order to prevent the most CVD events is far more dependent on age than it is on the risk score.

The adherence rates are much lower than those reported in trials, or used in the NICE guideline economic model to estimate cost-effectiveness of the threshold. Increasing patients' adherence to statins, especially early on, is likely to have a much bigger impact on reducing CVD events than delaying statin initiation until patients are at a higher risk.

Our data also suggest that statin prescribing in primary care has not been hugely influenced by the NICE guidelines and that risk score at initiation varies quite widely.

How adherent are people to statins?

The data presented here support other studies that suggest that statin adherence is much lower in practice than reported in clinical trials.(9, 14) One review comparing statin adherence in observational studies and RCTS, summarised that 49% of patients were adherent to statin medications at 1 year of follow-up in observational studies compared with 90% in RCTs.(15) A recent review of 84 studies reporting adherence in statins illustrated the methodological complexity associated with measuring adherence, with adherence ranging from 28-100%. (16). However, those studies using administrative datasets tend to suggest that adherence is around 40-68% at one year after initiation (17-21). Adherence to statins tends to drop off in the first year, with studies reporting high discontinuation rates of 15-28% even after the first prescription refill. (18, 21). A recent UK study using CPRD data reported 47% discontinuation in the first year, with discontinuation rates four time higher in the first year of use (32 per 100 person years) than after the first year of use (7.4 per 100 person years).(9) This study reported that 72% of those discontinuing going on to restart. The data reported here suggest a more complex picture where people repeatedly stop and start their statin. This needs to be taken into account when estimating the beneficial effects of the statin.

Why don't people take their statins?

Factors affecting patient adherence can be classified into three categories: patient-related (e.g. age, income), physician-related (e.g. speciality, communication skills), and health care system-related (e.g. co-payments). Three reviews of studies examining factors affecting adherence to statins report consistent relationships between non-adherence and female gender, ethnic minority status, reduced income, lower number of concurrent cardiovascular medications, new statin users, use of statins for primary prevention, smoking, depression, reduced follow-up and increased co-payments.(22-25) A U-shaped relationship between non-adherence to statins and age was reported.

There has been a wide debate regarding the role of side effects (actual and anticipated) in statin non-adherence.(26) Work suggests that the side effects associated with statin treatment are not as common as reported.(27) Anticipation of side effects can have as much impact on adherence as experience of actual side effects.

In summary, this suggests that non-adherence to statins is multifactorial, but is likely to be more of a problem in new statin users being prescribed the statin for primary prevention, where they have few other cardiovascular comorbidities. Adults under 60 are more likely to be paying a prescription charge, which may also adversely affect adherence.

How can we improve adherence to statins?

There are many complex interventions for improving adherence that show little effectiveness(28) because they are based on clinicians' and researchers' perceptions of why people are non-adherent (such as needing more information), rather than the actual reasons. The most recent Cochrane review of 35 studies of statin adherence improving interventions suggested that only intensified patient care interventions (telephone reminders, calendar reminders, integrated multidisciplinary educational activities and pharmacist-led interventions) improved statin adherence when compared with usual care. (29) The interventions of this type appeared to provide improvements in short term (6 months) and long term (over 6 months) periods.

The reduction in adherence to a new medicine for a chronic condition in the first few months has been described in many diseases. When patients receive a new (to them) medicine for a long-term condition, they often experience problems which lead to a proportion becoming non-adherent.(30) Targeting a patient-centred, theory-based low-cost intervention which focuses on patients' concerns during this key initial period has been shown to improve adherence by 11% in a range of chronic illnesses,(31-33) and forms the basis of an NHS-commissioned service delivered by community pharmacists in England (New Medicines Service, NMS).(34) This service is not currently provided to people starting statins. Interestingly, an RCT of delivery of the same intervention in people who have been taking statins for longer also demonstrated improved adherence.(35) This suggests that extension of NMS into statin users could demonstrate effectiveness.

Next steps

The original aim of the economics workstream was to design a model to understand the economic impact of delaying starting treatment in people with specific risk scores, using quality-adjusted life year (QALYS), and associated cost to the National Health Service. However, given the results from the analysis and simulations above, it is clear that the priority rather, is to make recommendations about ways to support better adherence by patients. This requires some further analytical work and engagement with key stakeholders. The analytical work is already planned to take place from April to October 2019. RAE and GG, supported by a health economics trainee, will examine the clinical and economic impact of introducing interventions to improve adherence. Working with AP and TvS, this will involve incorporating the data presented in this report into the NICE statin guidelines economic model, (permission to use the executable model for this process has been obtained from NICE) along with effectiveness estimates of selected interventions. The analytical work will require the collaboration developed between UoM and NICE to continue. The selection of appropriate interventions to investigate will require continued collaboration with the NICE PPIE team and HInM to provide access to key stakeholders.

References – see Appendix 4

Key learnings

These findings are of interest to NICE because they suggest that more risk-based prescribing for antibiotics (as we do for other diseases) is needed because:

- There was a significant variability in the number needed to treat (NNT) for infection-related hospital admissions across patients consulting their GP for different common infections
- The likelihood of getting an antibiotic was not related to a patient's risk of being hospitalised, with possibly high-risk patients being undertreated and low risk patients overtreated.
- These data suggest that NNT should not be used in NICE guidance, but it would be useful to further investigate whether NNT could be an effective additional tool or not.

Authors:

Birgitta van Bodegraven, Dr Victoria Palin and Professor Tjeerd van Staa

Background and rationale

Current clinical guidelines, created by The National Institute for Health and Care Excellence (NICE), state that antibiotics should be withheld from the majority of patients except those at high risk of serious complications (1). Respiratory tract infections (RTIs) and urinary tract infections (UTI) are commonly occurring bacterial infections and are often self-limiting. Patients with self-limiting common infections often get better without antibiotic treatment however, antibiotics are regularly prescribed in primary care (2). The risks of complication after common infections are recognized to be low but when they happen, they can be debilitating and, in some cases, fatal.

The number needed to treat (NNT) is a clinical tool to determine how many patients would need to be treated to prevent one event, in this case, an infection-related hospital admission (3). This information can be clinically relevant, informing GPs when it is appropriate to prescribe an antibiotic or not to the individual patient.

The objective of this study was to evaluate NNT variability for patients at risk of hospitalisation after common infection by accounting for individual patient characteristics using real world data.

Aims of this project are:

- To determine risk factors that need consideration in the modelling of NNT in primary care.
- To model individualised NNT for multiple common infections with these factors.
- To examine the antibiotic prescribing behaviour by general practitioners (GPs) comparing patients at high and low risk of hospital admission.

Methods

Data

The Clinical Practice Research Datalink (CPRD), an anonymous primary care database with routinely collected health records representing 8% of the UK general population, was used in this study (4). The dataset contained patient-level electronic health records (EHRs) from 346 English general practices (GP) linked with hospital admission data (Hospital Episode Statistics (HES)). Data from 48.8 million incidental GP visits were available for analysis. An incidental GP visit was defined as the first infection-related consultation at the GP and the first antibiotic prescription issued in a patient's EHR in 3 months.

Statistical analyses

The follow-up period for diagnosis of infection-related hospital admission was 30 days. Three common infections were evaluated including upper respiratory tract infection (URTI), lower respiratory tract

infection (LRTI), and urinary tract infection (UTI). URTI comprised of unspecified URTI, tracheitis, laryngitis, common cold, cough, sore throat and tonsillitis. LRTI comprised of unspecified LRTI, unspecified chest infections and bronchitis, excluding chronic obstructive pulmonary disease and pneumonia. Numbers needed to treat (NNT) were calculated using individual patient level survival probabilities from Cox models and practice level relative rate (RR) from negative binomial models.

Multivariable cox models were fitted and a Cox Proportional Hazard (PH) model was used to calculate 30-day survival probabilities based on patients that did not receive antibiotic. Survival probabilities of antibiotic users were predicted based on the model beta parameters of the non-antibiotic users. The following variables accounting for patient variability were included in the model: age, sex, Charlson comorbidity score, body mass index (BMI), smoking, ethnicity, socioeconomic status, influenza vaccination, prescription in previous year, hospital admission in previous year, referral outpatient in previous year, year of consult, and season.

Negative binomial models were fitted at practice level using antibiotic prescribing propensity and the number of events for each outcome. Variables to be included in negative binomial models were transformed with the interquartile range (IQR) to make regression coefficients more clinically relevant and meaningful (5). This transformation created a natural comparison between high and low prescribing GPs. Negative binomial models were adjusted for age, sex, Charlson comorbidities index, ethnicity, body mass index (BMI), smoking status, socioeconomic status, influenza vaccination, and hospital admission in previous year.

The NNT formula is shown here:

$$NNT = 1 / (Rate \times RR)$$

where Rate = 1 – patient level survival probability at 30 days.

Results

Patients who visited the GP for LRTIs had the highest incidence of infection-related hospital admission by number of GP visits (0.27%). This was followed by GP visits for URTIs (0.10%) and UTIs (0.06%). The antibiotic prescribing propensity for patients with hospital admission and all patients followed a similar pattern with most antibiotics prescribed for LRTIs (72.7%) and UTIs (75.2%).

Table 1. Antibiotic prescribing propensity in cases of hospital admission for three common infections

Primary reason for GP visit	Infection-related hospital admission (no. cases (%))	ABX prescribed in patients with hospital admission (%)	ABX prescribed in all patients (%)
All infections (n= 48 827 968)	46047 (0.09%)	62.1%	55.4%
URTI (n= 8 983 606)	8669 (0.10%)	57.2 %	48.1%
LRTI (n= 2 258 010)	6045 (0.27%)	72.7 %	87.7%
UTI (n= 1 553 004)	1006 (0.06%)	75.2 %	87.6%

*ABX: Antibiotics

The NNT was calculated for all infections combined and for URTI, LRTI, and UTI infections independently (Table 2). Significant NNT variability was observed, ranging from 200 (5th percentile) to 14877 (95th percentile) across all infections. This variability was maintained during individual infection analysis (Table 2), with a mean NNT of 5164 and 6621 for URTI and LRTI, respectively. The mean NNT for LRTI was lower at 579.

Table 2. Variability in number needed to treat (NNT) for all infections, URTI, LRTI, and UTI

	NUMBER NEEDED TO TREAT (by percentile, mean, range)							
	5th	25th	50th	75th	95th	mean	min	max
All infections	200	648	4392	7903	14877	5208	5	51119
URTI	219	602	4700	7796	14191	5164	8	44631
LRTI	35	93	488	917	1550	579	4	5053
UTI	142	860	3079	10014	23486	6621	6	93277

Further NNT analyses were conducted for specific patient characteristics. Modelling of the NNT was performed in relation to patient age after categorising age into quintiles (Table 3).
For the oldest patients (age-groups 60-74, 75+), the NNT could not be calculated because the RR was greater than 1. For these groups, antibiotics are not effective in reducing the incidence of infection-related hospital admission. Significant variability observed for combined and individual infections was maintained after age categorisation, with no clear age-related pattern (Table 3).

Table 3. Variability in number needed to treat (NNT) for all infections, by age groups

Age (years)	NUMBER NEEDED TO TREAT (by percentile, mean, range)							
	5th	25th	50th	75th	95th	mean	min	max
<18 (n= 14 332 802)	217	652	5488	8778	16497	17299	3	7.95×10^8
18-39 (n= 11 423 164)	373	920	8912	13905	21305	343513	10	4.66×10^9
40-59 (n= 11 102 490)	336	803	6158	10132	16233	6406	10	40912
60-74 (n= 7 270 813)	Not Available							
75+ (n= 4 698 699)	Not Available							

The antibiotic prescribing propensity by NNT quintile was evaluated to determine GP ability to identify patients at higher and lower risk of hospital admission. NNTs were sorted into quintiles (20th, 40th, 60th, 80th, and 100th) to show antibiotic prescribing propensity by increasing NNT.

For all three infections (URTI, LRTI, UTI), the antibiotic prescribing propensity remains stable across NNT quintiles as GPs prescribe antibiotics equally for patients at higher risk of hospital admission (NNT quintile 1) and those at lower risk (NNT quintile 5). For URTI, GPs prescribed antibiotics in 48.7% of cases in quintile 1 (NNT: 8 - 472), 45.9% in quintile 3 (NNT: 3278 – 5802), and 50.4% in quintile 5 (NNT: 8727 – 44631) (Figure 1). For LRTI the antibiotic prescribing propensity in quintile 1 (NNT: 4 - 77) was 85.3% and in quintile 5 (NNT: 1017 – 5053) it was 89.8% (Figure 2). For UTI the antibiotic prescribing propensity in quintile 1 (NNT: 6 – 629) was 85.8% and in quintile 5 (NNT: 12098 – 93277), 88.4% ((Figure 3).

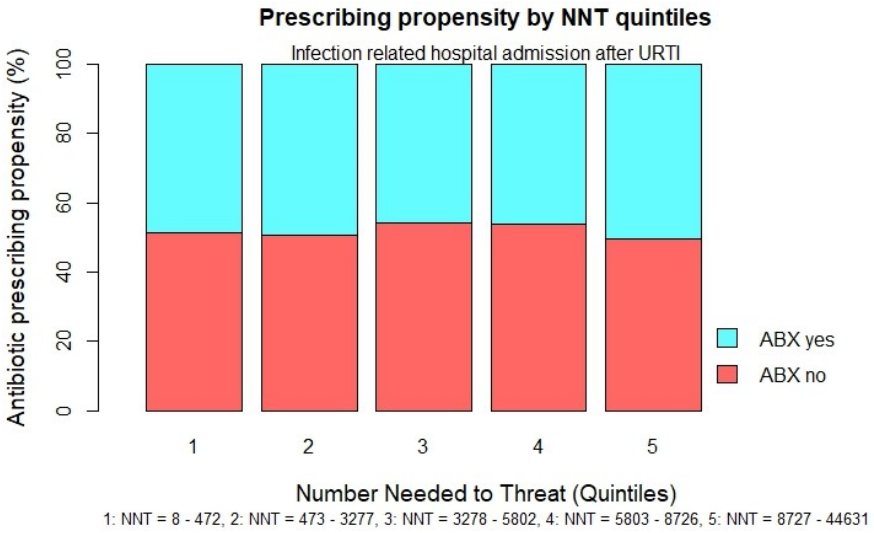


Figure 2: Antibiotic prescribing (ABX) for URTIs is 45-50% across all NNT quintiles.

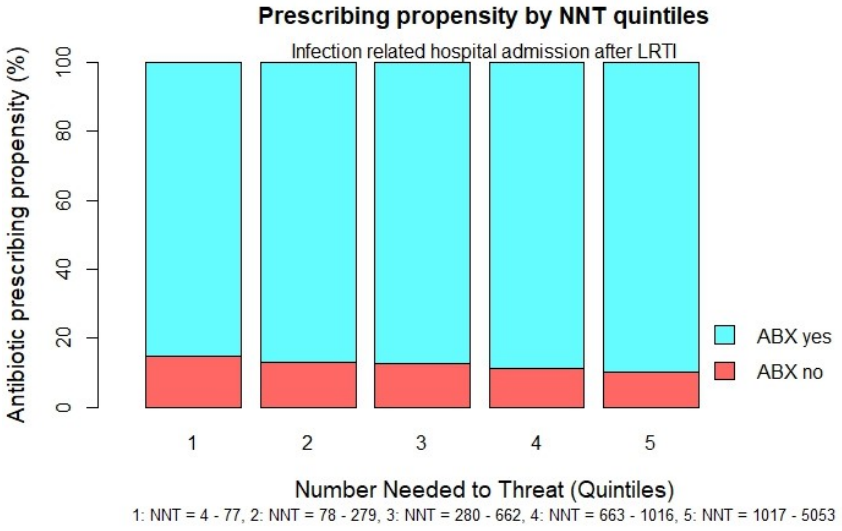


Figure 3: Antibiotic prescribing (ABX) for LRTI is 85-90% across all NNT quintiles.

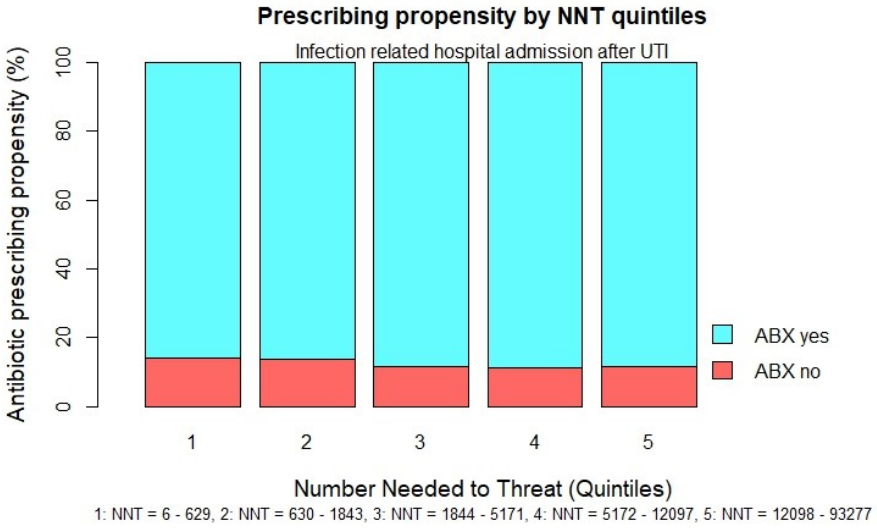


Figure 4: Antibiotic prescribing (ABX) for UTI is 85% across all NNT quintiles

Findings and Implications of the results

The rate of antibiotic resistance is exceeding the rate of new antibiotic development. As a result, antibiotics should be prioritised for those at high risk of serious complication and withheld from patients who are likely to improve without antibiotics. Therefore, it is necessary to investigate the current practice of antibiotic prescribing in primary care. To address this, DataLab set out to choose a set of indicators to be used in modelling of the NNT and then developed a model that estimates NNT for common infections in general practice using real world data. The results of that model are presented here.

This project has revealed significant NNT variability for common infections and substantial differences between current antibiotic prescribing behaviour by GPs. However, antibiotic prescribing propensity is independent of NNT variability which suggests that high risk patients are not being identified and treated in clinical practice. These data demonstrate that routinely collected real world data can provide new insights into antibiotic prescribing behaviour in the UK population. Moreover, these data could be used to inform clinical practice and target patients who are at risk of serious complications.

The number needed to treat is an understandable concept that is not currently used by NICE in their guideline development. DataLab would recommend using NNT for guideline development as a supportive tool for GPs because detailed knowledge on who are high and low risk patients is valuable although more work on the best way to present NNT to GPs and patients will be needed. Additionally, DataLab recommends using NNT for furthering research on targeted antibiotic prescribing. How this information is presented to GPs and patients' needs further work, as it is known that the concept of NNT is not always readily understood. Reducing unnecessary antibiotic prescribing through targeted prescribing to individuals at risk of complications should be a priority for healthcare providers. A central role exists for NICE to provide strategic support to GPs for a change in overall antibiotic prescribing behaviour.

Next steps

Further analytical work using data from other locations the UK will broaden the understanding of GPs targeted antibiotic prescribing behaviours. An example for other data is the SAIL databank which contains approximately 75% of Welsh GP practices. Identifying and selecting tools that GPs require to move towards targeted antibiotic prescribing is necessary for a fundamental change in prescribing behaviour to occur. This will require continued collaboration with NICE, PPIE, HInM and other key stakeholders. This work can then be disseminated together with recommendations for GPs to create better risk based antibiotic prescribing habits.

References – see Appendix 5

Public and Patient Involvement

Key Findings

- Involvement of the public served to break down barriers between patient partners and researchers enabling the project team to gauge public opinion and examine whether research was on track.
- DataLab would have benefited from embedding PPIE so that the involvement of public contributors *occurred at a much earlier stage*, e.g. in co-designing the project.

Authors

Nicky Timmis

Introduction to PPIE

DataLab aims to demonstrate the value of bringing together knowledge and expertise from across the health research system, and this includes the insight, opinion and lived experience of the citizens of Greater Manchester. The project included a specific Public and Patient Involvement and Engagement (PPIE) work stream (WS7), an associated PPIE budget and a PPIE Lead to support the development and implementation of a dynamic PPIE Plan. An initial task for the DataLab team was to clearly define the purpose of public participation and the potential to influence the development of the Project. Researchers focusing on statins and antimicrobial resistance (AMR) were encouraged to review their respective projects to consider where PPIE would add the most value. Feedback from the researchers indicated the need for dialogue with patients and the public on the following topics: -

- The prescribing of both statins and antibiotics.
- Public opinion around the mass prescribing of statins.
- The public's perception of DataLab as a concept.

The discussions in DataLab meetings led to the development of some additional questions exploring wider issues; how health care professionals can effectively explain AMR to patients in a short consultation and communicate risks to the public. (See Appendix 6)

Engagement Strategy

Various PPIE approaches were considered in relation to DataLab; 1:1 interviews, questionnaires and a Citizens Jury approach. The team agreed discussion groups were the most effective way of balancing the needs of public contributors with those of a complex project. A group setting also provided participants with the opportunity to clarify discussion points, ask questions and create an environment conducive to constructive discussion.

The PPIE Lead developed a 'Discussion Group Request' and a 'Frequently Asked Questions' information sheet and these documents were circulated to existing PPIE groups and networks across greater Manchester via contacts held by Health Innovation Manchester (HInM) and the University of Manchester. This resulted in 32 expressions of interest from public partners; ten were then selected at random and of these: five public contributors attended and engaged in Discussion Group 1 hosted at HInM on Friday 11th January 2019 and two participants, living with a diagnosis of dementia and a carer, participated in Discussion Group 2 on Tuesday 22nd January 2019.

Statins Background

The current NICE guidelines advise health care professionals to consider prescribing Statins where the risk of a cardio-vascular event is assessed as 10% or more. In the discussion group, patient partners were presented with DataLab findings which indicated considerable variance and non-adherence amongst patients prescribed statins. Group 1 also reviewed the Discontinuation Chart and the DataLab findings relating to 'Average Risk.'

The groups were asked to consider whether the guidelines should be adjusted to delay prescribing until the risk had increased from 10% to 20% so patients receive the greatest benefit. Participants were also asked how health care professionals could effectively communicate risk to patients.

Statins Feedback

There was a consensus in both discussion groups that the DataLab findings were inconclusive and did not enable participants to make an informed decision around the prescribing guidelines. Public contributors noted that more information and understanding of the risk was needed because:

- The sample size was small (n200) and variation in adherence to statins could exist, even within the UK. A larger study which examined different populations in various countries, could ensure the data were robust.
- The 'Discontinuation Chart 'was considered misleading; the x axis was ambiguous because it inferred the 'time period' rather than the 'time duration.'
- Greater clarity was required on the statins cohort; the gender, age distribution of the sample and 'when' the treatment episodes took place.

It is important to understand the patient behaviour behind the statistics; the impact of mental health, memory or practical issues, of co-morbidities where patients may be taking multiple drugs with different treatment regimens that are challenging to manage and statins regarded as a low priority. Public contributors did recognise the absolute value of DataLab in defining further research. An exploration of why the mean value of risk was constant for the period 2010-2012 and 2012-2014, despite changes to the prescribing guidelines during this period, was identified as an example of this.

In terms of communicating risk, there was the perception that patients may indeed need support to make informed decisions about their health but currently there is a lack of access to clear, balanced information regarding both the value or side effects of statins.

The use of jargon, the promotion of conflicting messages within the NHS and sensationalist headlines in the media was also fuelling mistrust and confusion amongst patients and that this could be particularly damaging for high risk groups. Participants made the following points:

- *"The 10% versus 20% guidelines are arbitrary."*
- *"The public are not great at assessing risk for example crossing road versus travelling by plane but the NHS asks parents to bring a baby that only has a cough, underlining a culture of fear, complaints and legalities."*
- *"It requires a PHD to understand accompanying literature or accessible professional guidance even online, with some patients without online access."*
- *"More information is needed about cholesterol. I have high cholesterol but my partner who eats a high fat diet, has low cholesterol. It could be genetic. At one time, the public were encouraged to smoke for their health"*
- *"Statins may be really important in preventing or delaying the onset of dementia. This is particularly the case regarding vascular dementia but because of the negative press, people are very suspicious of them."*
- *"Media coverage means patients are far more sceptical and less trusting."*

- *"Patients need to be able to trust the NHS and that that guidelines are based on accurate and robust data."*

Public Opinion: Mass Prescribing

Participants overall were resistant to mass prescribing noting that the evidence available did not adequately support such a drastic intervention. There was also a determination amongst group members to preserve the right to make informed decisions about their own health based on their individual circumstances, with the role of the NHS being one of empowerment. Comments included:

- *"GPs should inform public of concerns."*

- *"I am not happy about mass medicating - the idea of prescribing everyone statins is abhorrent to me, and I believe it is a civil liberty issue. Mass medication by stealth - fortifying foods with vitamins, fluoridation of water - has, of course been done, but I believe this is a different issue. Statins have a significant impact on some individuals and the evidence is equivocal for their efficacy in some groups - women being one, the over 70s are another."*

- *"The Government regard individuals on mass, whilst individuals considered what is good for them as individuals and the two perspectives, are just not compatible."*

AMR and Communicating Risk

There was the perception that GPs are under pressure to prescribe antibiotics, but Group 2 also highlighted the economic pressure on patients and families to present to the work place.
Public contributors shared researchers' concerns that 20% of the population have been prescribed 9 episodes of antibiotics over a 3-year period and there was a consensus that this cohort warranted further investigation. There was also a concern that the public still regarded antibiotics as a 'magic bullet' and that there is a lack of awareness that the immune system can effectively fight infection. From a patient perspective, however the responsibility for addressing this seemed to sit firmly with health care professionals:

- *"As a child there was understanding to eat well and if there was an illness, people recognised they would recover in a matter of days."*

- *"The public no longer have awareness that it is normal for the 'animal' to get ill and immune systems naturally help us get better."*

- *"Much is dependent on GP communication with patients."*

- *"It is the GPs that are writing the prescriptions, so the problem must be with GPs."*

Public contributors made some suggestions regarding how the NHS could address AMR which included peer support for GPs focusing on the effective management of patient relationships in consultations. It was suggested that this should be supported by communication that is blunt, to the point and included reference to the impact of over-prescribing on the wider community:

- *"If we were to go out into Manchester, there would be a variety of abilities. We are not professionals and our understanding is limited so give us a chance and make it easier for us to understand."*

- *"The public needed to understand it is not only about the individual but there are dangers for children or your best friend."*

Public Opinion: Utilisation of DataLab

There was a consensus in both groups that Minimal Viable Products are assets that should be subject to further analysis and whilst the results may not empower the public to draw definitive conclusions, the questions they highlight are nevertheless adding value.

- *"We already have the data. It's there. Why did we collect it if not to use it?"*

From a patient perspective, DataLab creates a forum where the public can engage and interact with current health research and have a voice that influences the direction and scope.
Positive feedback was received from researchers regarding the value of PPIE as an integral part of DataLab. Researchers reported the involvement of patient partners enabled the researchers to triangulate perceptions and interpret findings from a patient perspective and also understand the value of clarity in terms of communication and messaging around prescribing decisions.

Feedback also indicated that the involvement of the public served to break down barriers between patient partners and researchers enabling the project team to gauge public opinion and confirm that research was on track. The DataLab team commented:

- *"What I found really encouraging/ interesting was how in line with patient and public views are with our own. With regard to Statins for example, they mentioned the role of the media, the idea of targeting individuals and getting that balanced view with respect to mass prescribing. "*

- *"Knowing that the public is thinking about the problem in the same way makes me think that we are asking the right questions, which is really valuable."*

Limitations of Datalab PPIE

DataLab would have benefited from embedding PPIE so that the involvement of public contributors *occurred at a much earlier stage* and continued for the duration of the study. Patient partners could be involved in co-designing the project; identifying priorities to inform work programmes, developing and delivering an effective PPIE strategy and the consultation questions, active participation in project meetings.

Due to limited time and resources, this discussion group activity was also limited to a small and relatively homogeneous group of local people aged 40+, with no BME groups included. Future work should involve reaching out to enable wider participation including to those individuals and communities at high risk of a cardiovascular event such as people with a South Asian or African Caribbean background and other disengaged groups, whose voices are seldom heard.

Acknowledgements

The DataLab team wishes to acknowledge all those who have participated in this project, as listed in Appendices 1 and 2. The team have come together from multiple backgrounds with a sense of learning and openness without which this project could not have succeeded. We would also like to thank Jane Garnett for her commitment over almost the entire lifespan of the project so far as she will be leaving the project at the end of March. Without Jane's enthusiasm for DataLab over the last eighteen months the project would not have developed to its current position.

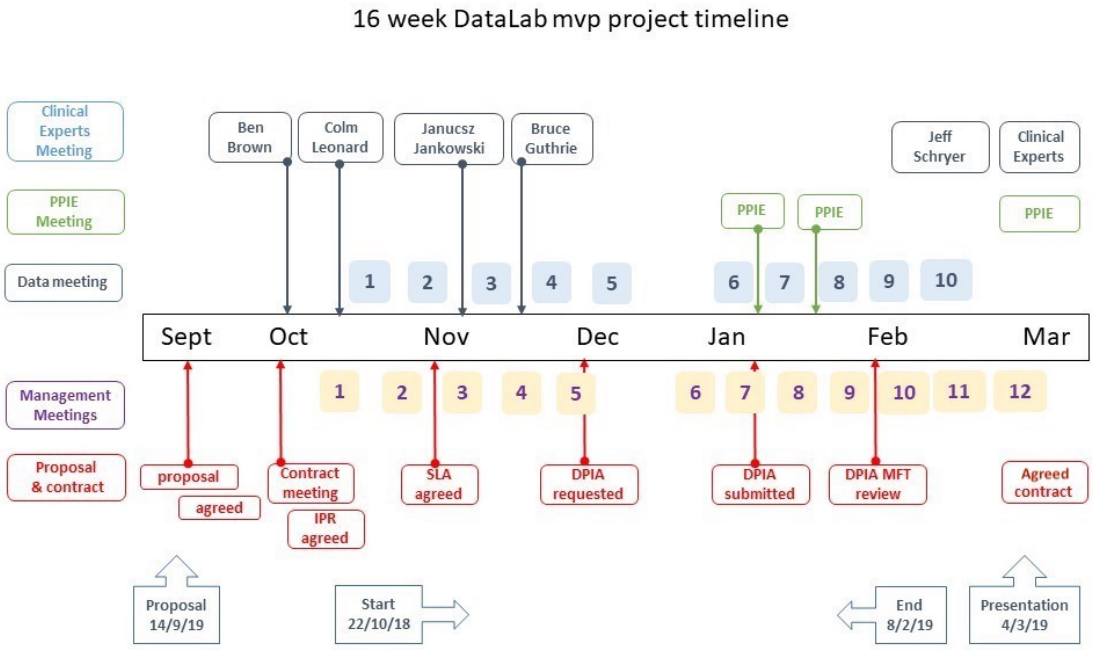
Appendix 1 - List of DataLab Team Members & Clinical Experts

Linda Magee OBE	Life Sciences Industry Adviser to the Dean, FBMH University of Manchester
Gary Leeming	Chief Technology Officer, Connected Health Cities & University of Manchester
Tjeerd van Staa	Professor in Health e-Research, Connected Health Cities & University of Manchester
Victoria Palin	Post-doctoral RA, Connected Health Cities AMR project
Birgitta van Bodegraven	Graduate RA, Connected Health Cities – AMR project
Alexander Pate	Graduate RA, Connected Health Cities – Statin project
Rachel Elliott	Professor of Health Economics at the Manchester Centre for Health Economics, University of Manchester
Alexander Thompson	Post-doctoral Fellow, Health economist, at the Manchester Centre for Health Economics, University of Manchester
Georgios Gkountouras	Post-doctoral RA, Health economist, at the Manchester Centre for Health Economics, University of Manchester
Nicky Timmis	Public & Patient Involvement and Engagement Manager, Health Innovation Manchester
Steve Mosby	Project Manager, Health Innovation Manchester
Eamon McAndrew	Public & Patient Involvement, Health Innovation Manchester
Linda Walley	Strategy Advisor, Health Innovation Manchester
Pall Jonsson	Associate Director, Research and Development, NICE Science Policy and Research
Gabriel Rogers	Technical Advisor, NICE Centre for Guidelines
Jane Garnett	DataLab Project Manager, NICE Science Policy and Research

List of DataLab Clinical Experts

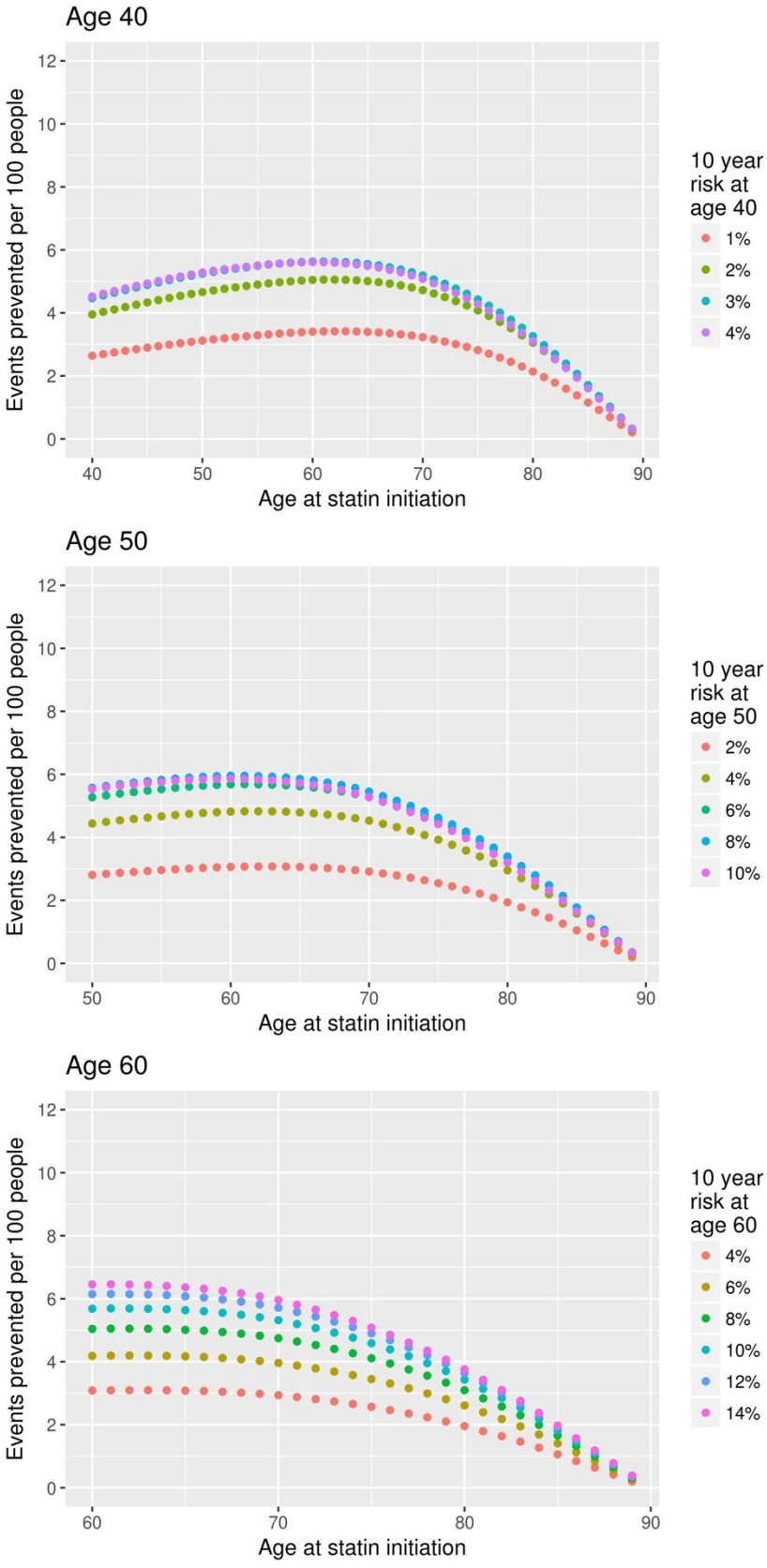
Dr Benjamin Brown, MRCGP, MSc, MPH, PhD	UoM Health Services Research & Primary Care GP & NIHR Academic Clinical Lecturer
Professor Bruce Guthrie, MB BChir MSc PhD	Professor of Primary Care Medicine Consultant Clinical Adviser to NICE NICE Multimorbidity Clinical Guideline
Professor Janusz Jankowski MSc, MD, PhD, FRCP, FACG	Consultant Clinical Adviser to NICE Acute and Chronic Diseases Panel of NICE
Dr Colm Leonard, MB, BCh	Consultant Clinical Adviser to NICE NICE Topic Selection Centre for Health Technology Evaluation
Dr Jeffry Schryer	Chair of NHS Bury CCG GP Dementia Lead, GM Strategic Clinical Network

Appendix 2 Project Timeline

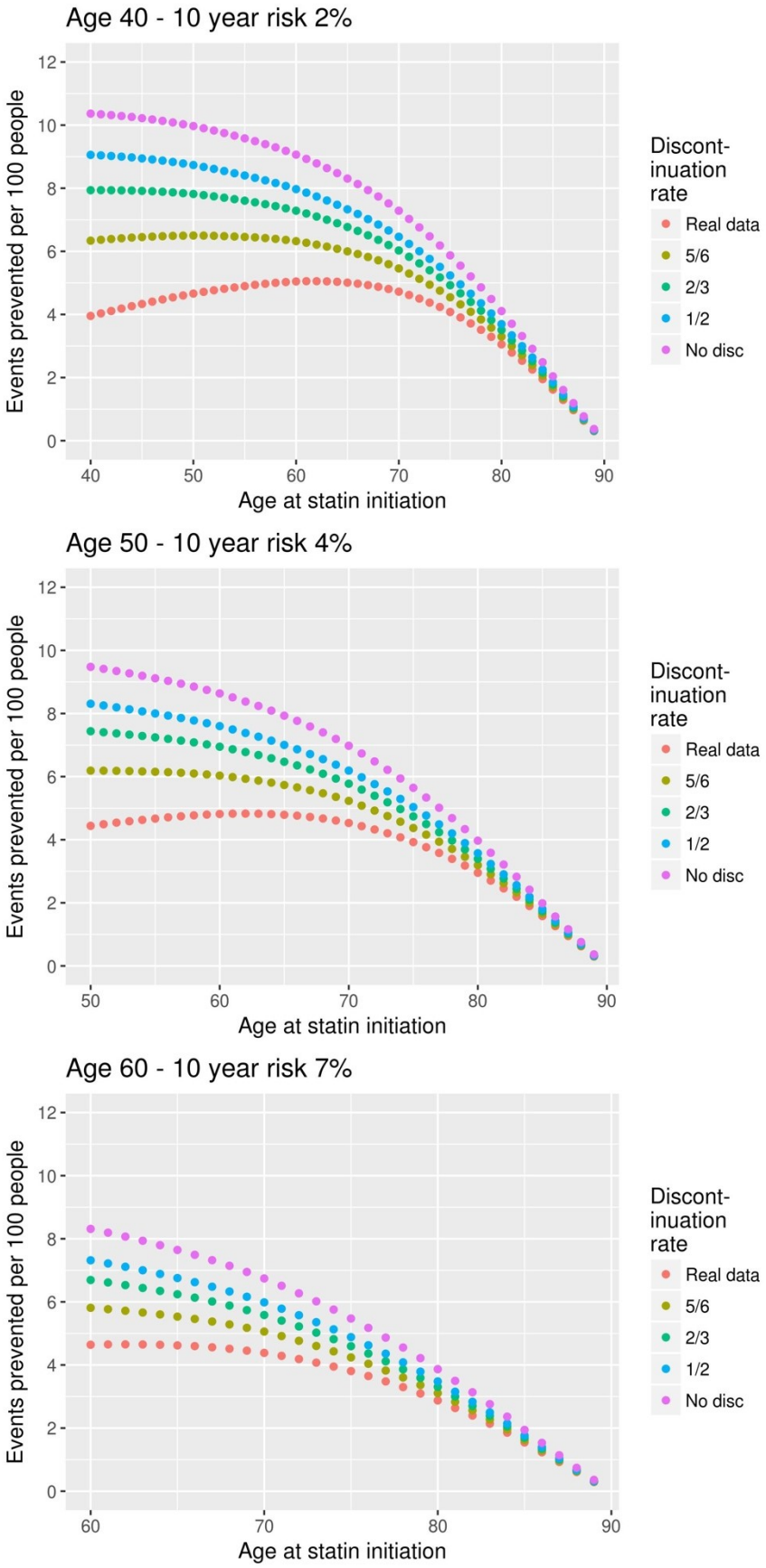


Appendix 3 MVP1. Events prevented in simulation for female cohort

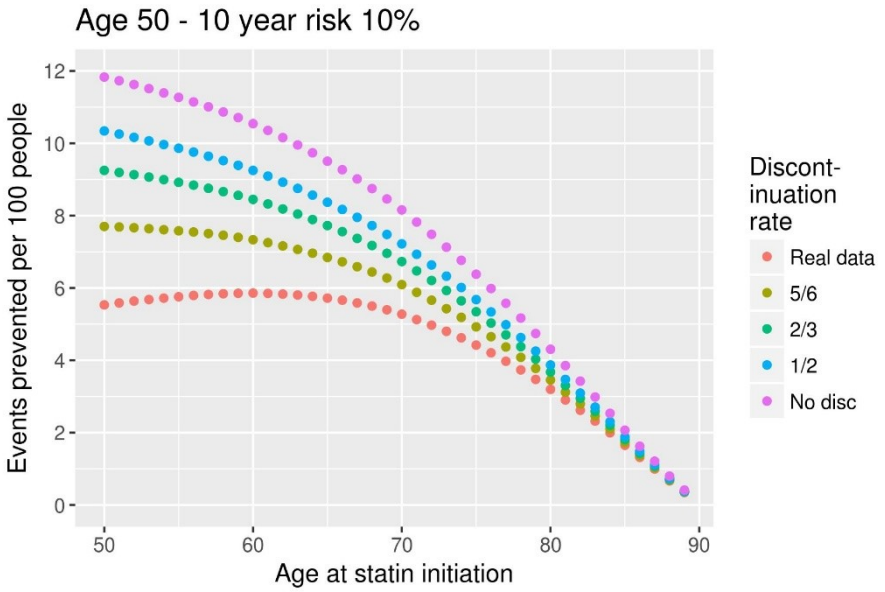
Supplementary Figure 1: Full simulation results presented as CVD events prevented depending on when statins are initiated using discontinuation rates derived from data (female)



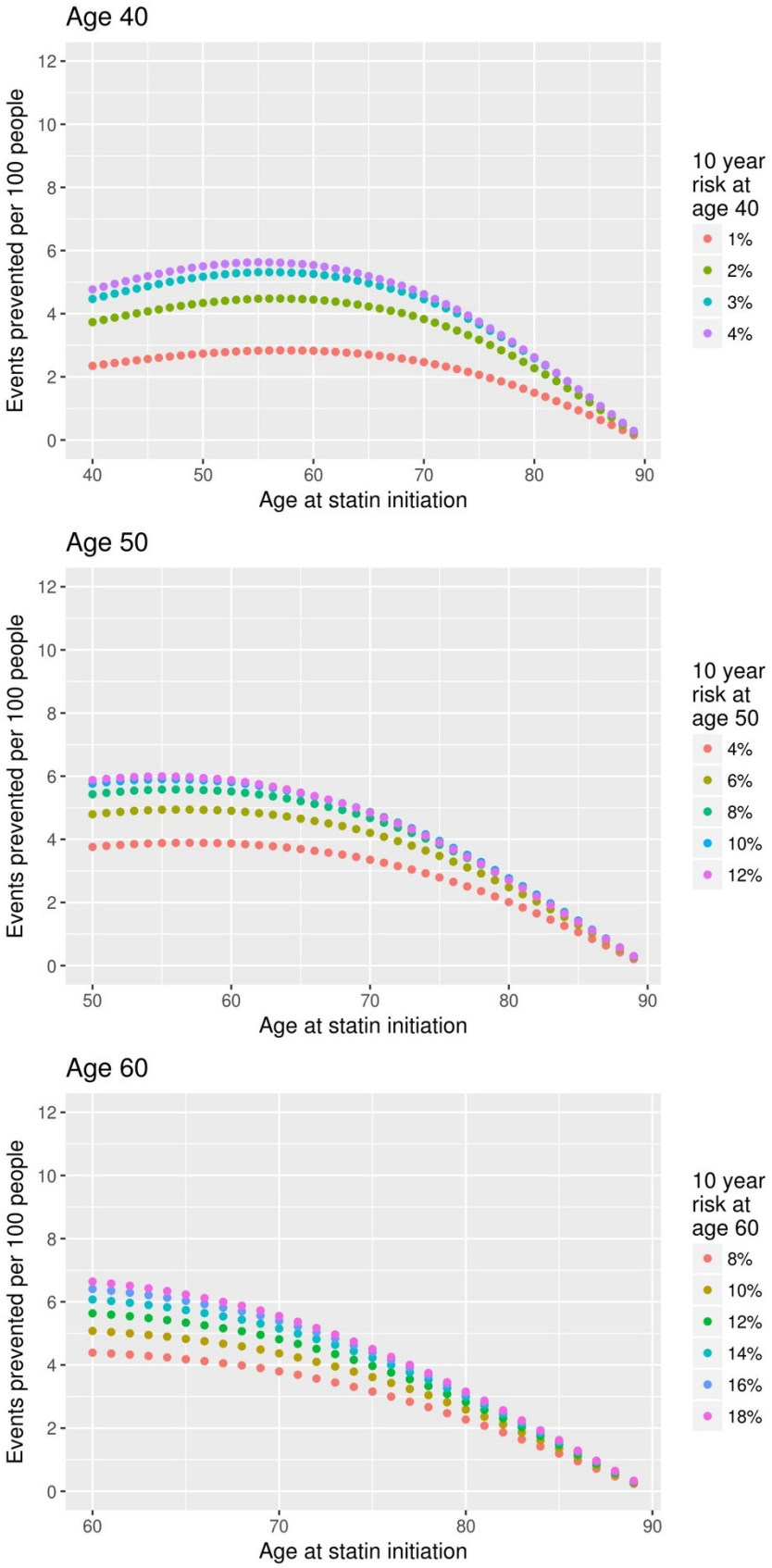
Supplementary Figure 2: Full simulation results presented as CVD events prevented depending on what discontinuation profile is used (female cohort)



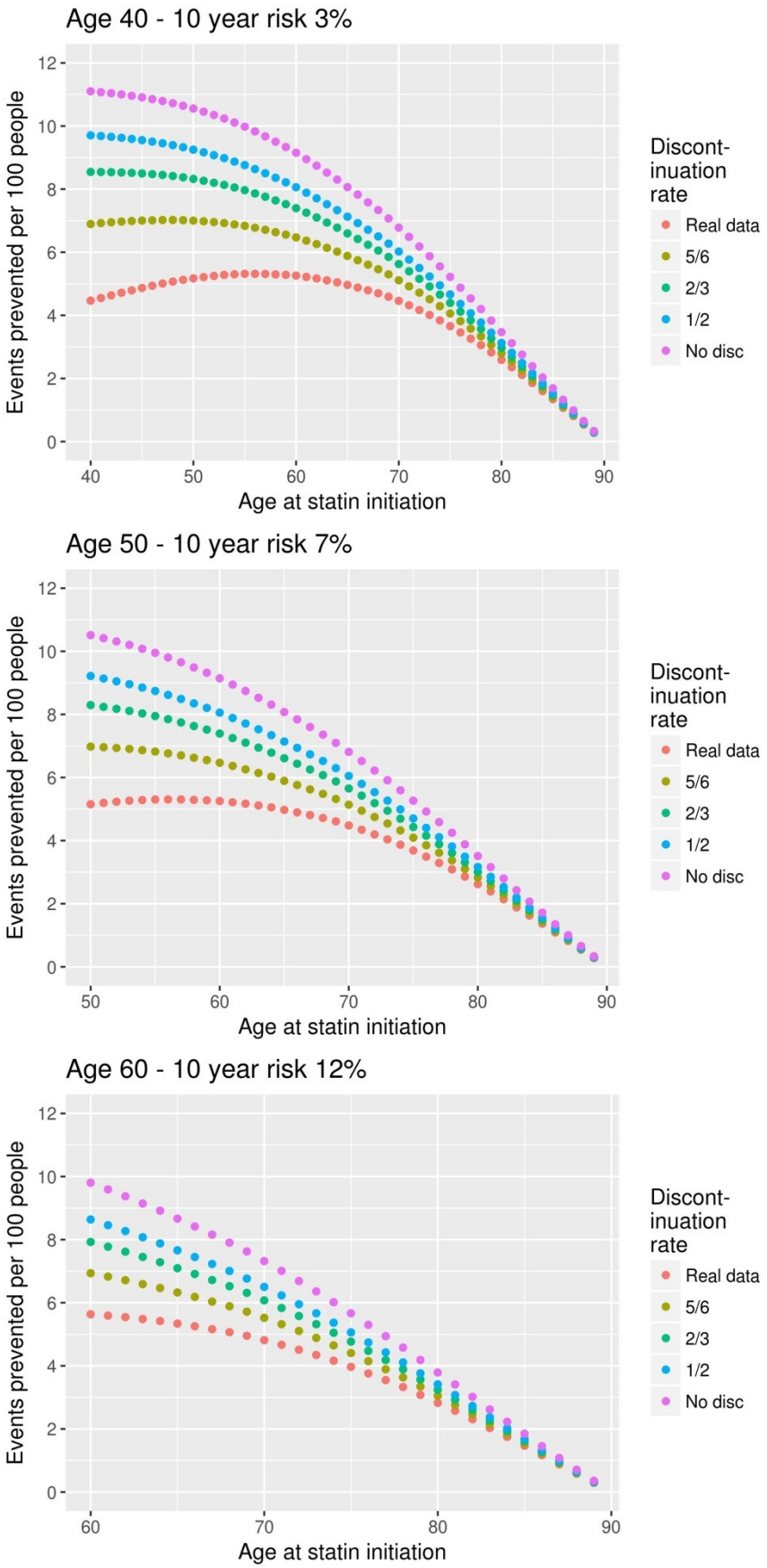
Supplementary Figure 3: Simulation results presented as CVD events prevented depending on what discontinuation profile is used, aged 50, 10-year risk of 10% (female)


Age 50 - 10 year risk 10%
Events prevented per 100 people
0
2
4
6
8
10
12
50
60
70
80
90
Age at statin initiation
Discont-
inuation
rate
Real data
5/6
2/3
1/2
No disc

Supplementary Figure 4: Simulation results presented as CVD events prevented depending on what discontinuation profile is used, all ages (male)



Supplementary Figure 5: Simulation results presented as CVD events prevented depending on what discontinuation profile is used, all ages (male cohort)



Appendix 4 References for Statins

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Appendix 6 – PPIE Group Questions and Discussion Points

Statins
• Do you think that health care professionals such as GPs and nurses, should consider waiting until the risk of a heart attack or stroke is a greater than 10%. For example, should the prescribing of statins be delayed until the risk has increased from 10% to 20%? • It could be cheaper to prescribe statins to the entire population than to educate the public regarding the benefits of taking these. This could mean that alongside a full health check, all 65-year olds could in principle, also receive a prescription for statins. What are your views on a mass prescribing approach? • Should we be paying greater attention to educating the public about the value of taking statins long term and how can we encourage this? • How should health professionals, GPs or prescribing nurses explain statins to patients. In other words, how should the NHS and health professionals communicate risk to patients?
AMR
• How can we explain the concerns around the over prescribing of antibiotics to patients in a short GP consultation that will lead to a change in patient expectations? • How best should a GP communicate information to patients about risk to patients?
DataLab
• What are your thoughts on DataLab as an idea or concept?

Discussion Points: The DataLab Findings
Statins
• The project explored the data available in relation to a random sample of 200 patients that were prescribed statins over a ten-year period. This found that patient behaviour was extremely varied with many of the sample initially starting to take statins and then never taking them again. Others starting and stopping statins at different times. • The guidelines around the prescribing of statins have changed during the period 2010 to 2014 but DataLab has found that the average risk of patients in the sample experiencing a cardiovascular event remained the same. This suggests that GPs may not be following the current guidelines in the prescribing of statins, but further research is needed.
Antibiotics
• DataLab has found that 20% of the population have been prescribed 9 or more courses of antibiotics over a 3-year period and there is an absence of research into the issues this raises. • DataLab also showed that people that fall into this category, tend not to recover to the same extent as other groups. This means that their risk of further infections remains high. This reinforces the view that people are building a resistance and tolerance to antibiotics and that this is affecting a significant number of population that currently, we know very little about.