Supporting local implementation of NICE Technology Appraisal 325 on reducing alcohol consumption in adults with alcohol dependence

a NIC-designated project

The NICE Implementation Collaborative (NIC) was established in 2012 as a partnership between the NHS, the life sciences industry, healthcare professional bodies, and key health organisations, including NICE and the Association of the British Pharmaceutical Industry, which have committed to work together to understand, analyse, and overcome the challenges and tensions to implementation and widespread adoption of NICE recommendations. NHS England is one of the founding partners of the NIC and provides some of its core funding. The NIC underpins NHS England's commitment to work in collaboration with industry to address challenges and tensions to adoption and variations in uptake.

This report has been developed by Oxford Academic Health Science Network (AHSN), Innovation Agency North West Coast AHSN, and MGP and initiated on behalf of NIC, which is a collaborative including the membership, among others, of NICE, NHS England, AHSNs, and the Association of the British Pharmaceutical Industry. Innovation Agency North West Coast AHSN and Oxford AHSN have provided strategic project leadership, and Lundbeck Ltd has contributed funding support for this project. Lundbeck Ltd has had no editorial input into the content of the report but was able to review it for technical accuracy.

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Foreword

Alcohol dependence is now one of the biggest health problems facing the NHS today. In the past 40 years alcohol-related deaths have risen over three-fold and alcohol is now the leading cause of death in men aged under 50 years, and it is likely that this trend will be replicated in women in the next decade. Since the formation of the NHS there have been only three pharmacological treatments with marketing authorisations for use in people with drinking problems—acamprosate, disulfiram, and very recently, naltrexone. These drugs are indicated to help maintain abstinence and have limited efficacy, in part because the almost universal consumption of alcohol by adults in the UK makes abstinence socially very stigmatising.

One might therefore expect that an innovative treatment, such as nalmefene, which supports people to reduce their drinking would be acclaimed as a great advance. Sadly, despite the best efforts of NICE, the uptake of nalmefene has been disappointing and is one of the reasons that the manufacturer is no longer promotiong it. This report collates data on the reasons for poor uptake, which has not been mirrored in other countries (e.g. France).

At all levels the NHS and other staff involved in the implementation of NICE Technology Appraisal 325 were found wanting. There were issues of cynicism over the value of reducing drinking because the mindset of abstinence-only outcomes pervades many alcohol services. Also, the profound value of investment in alcohol treatment is poorly understood by many in healthcare provision, probably because so many people drink above the recommended limits. Finally, the complexity of service provision when so many different stakeholder groups are involved is intimidating; without committed treatment champions it is unlikely any new interventions will be introduced with dedicated funding.

The lessons of nalmefene need to be learned even though it is probably too late to prevent the pharmaceutical industry from completely withdrawing from research into addiction treatment. We must try to ensure that other new interventions in psychiatry do not fall foul of the same problems. This review will help us do this if its recommendations are heeded.

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Executive summary

Nalmefene is a treatment option for adults with alcohol dependence who have high drinking risk levels, without physical withdrawal symptoms, and who do not require immediate detoxification. NICE Technology Appraisal 325 (TA325) was published in November 2014 and recommends nalmefene within its marketing authorisation, as an option for reducing alcohol consumption, for people with alcohol dependence when offered with ongoing psychosocial support (PSS). Since publication of TA325, adoption of nalmefene and PSS as a treatment option has been very low in England, and is used in only a fraction of the patients that NICE predicted would be eligible for the drug.

The objectives of this project were to:

- understand the key issues surrounding implementation of NICE TA325 and the steps required to overcome them
- take stock of barriers to commissioning, service design, and implementation and prescribing
- assess clinician awareness of nalmefene, TA325, and the supporting policies and pathways
- highlight best practice where possible through case studies.

Primary and secondary research, involving clinicians and clinical commissioning group (CCG) medicines management leads, were conducted in selected localities across England. In the sample regions involved in this work, significant variation was observed in terms of prescribing levels of the drug, the status of nalmefene in local formularies, and whether or not regions had developed and implemented suitable pathways for eligible individuals to access the drug.

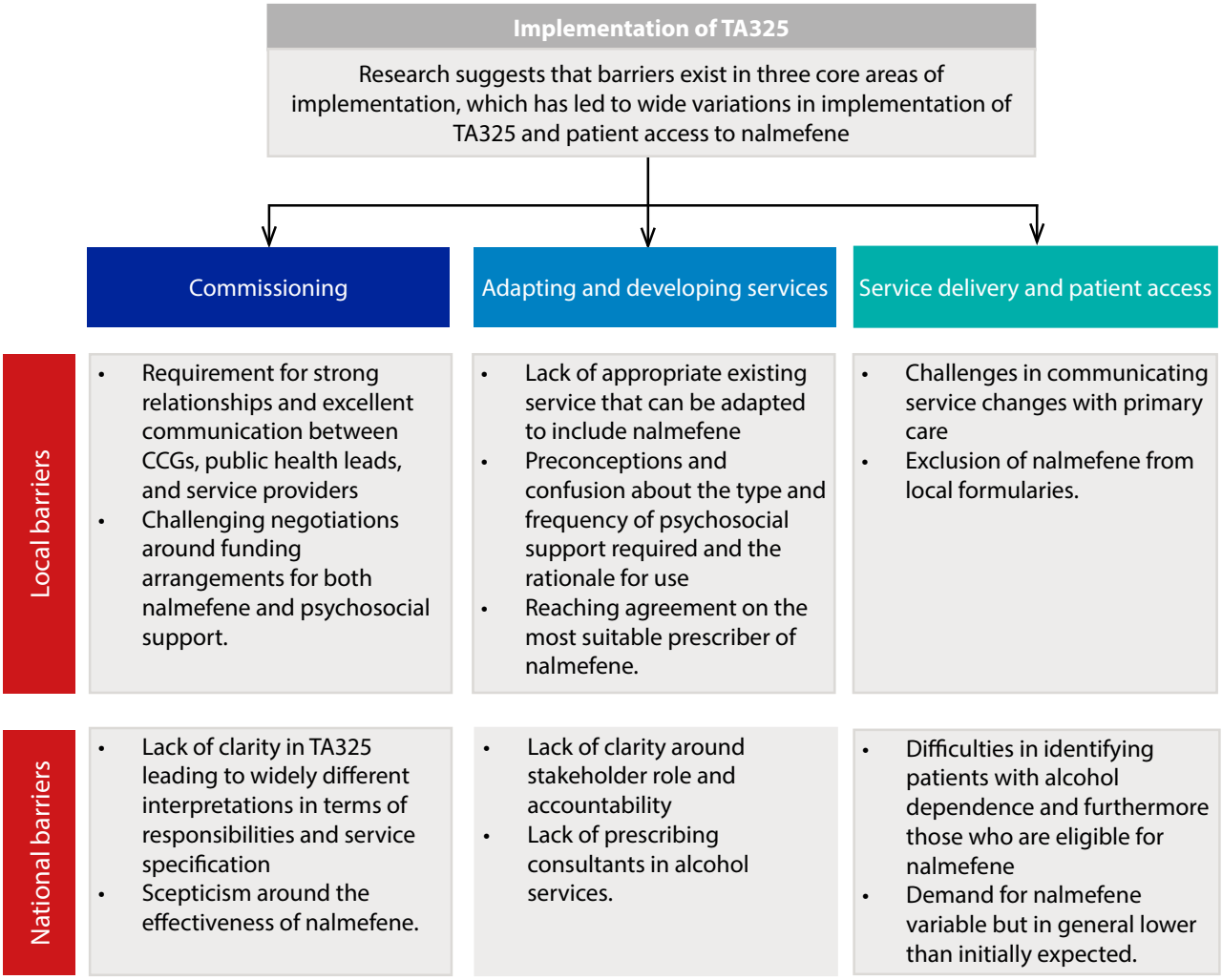
This work identified and explored three key barriers to implementation of NICE TA325 and the issues contributing to these barriers (see Figure 1, p.4):

- commissioning:
  - forming effective local working groups with a shared commitment to make the change happen
  - scepticism about the effectiveness of nalmefene and the lack of local arrangements to monitor its effectiveness
  - lack of clarity around how services should be delivered
- adapting and developing services:
  - the need for robust pathways in line with TA guidance
  - financial issues in terms of funding and acquisition cost versus cost effectiveness
  - limited agreement on the type, format, and frequency of PSS
- delivery and patient access:
  - awareness of the drug, TA325, and local pathways
  - identification of individuals with harmful drinking
  - inclusion of nalmefene in local formularies.

Recommendations

1. Local project leads should look to assemble local working groups with all relevant stakeholders to scope, plan, and manage the integration of suitable nalmefene pathways into existing alcohol misuse services
2. A national patient outcomes framework should be developed with alcohol service providers to monitor the effectiveness of nalmefene and psychosocial support in reducing alcohol consumption while minimising any additional clinical burden
3. During the development of TAs that may be difficult to implement because they affect a wide range of stakeholders, NICE should work with Academic Health Science Networks and Public Health England (where appropriate) to facilitate knowledge exchange and to reduce the likelihood of local groups 'reinventing the wheel'
4. Local working groups should facilitate early negotiations to reach agreement of suitable service models and the division of responsibilities for each facet of care (e.g. prescribing, psychosocial support, monitoring, review, and management)
5. NICE should look to provide definitive guidance on what is and is not appropriate in terms of the type, format, and frequency of the psychosocial support associated with TA325 to help local working groups understand the potential options
6. There is a need to develop systematic methods of engaging and communicating with healthcare professionals in primary care regarding new TAs, their implementation and local pathways or guidelines
7. Local working groups may wish to consider developing strategies to improve opportunistic screening and early identification of drinkers at any level of risk in primary care, secondary care, and third party organisations. This may fit with developing an integrated alcohol care pathway in partnership with relevant organisations across the locality
8. In implementation of pathways for nalmefene, CCG members of local working groups should ensure that nalmefene is listed in an appropriate way by area prescribing committees in the local formulary. This should ensure its traffic light status is not a barrier or a deterrent to prescribing.

Figure 1: Overview of local and national barriers to the successful implementation of NICE Technology Appraisal 325



Role and remit of the NICE Implementation Collaborative

The NICE Implementation Collaborative (NIC) is a collaboration between NICE and a cross-section of partners involved with healthcare in the UK, including the NHS, pharmaceutical industry, and a variety of professional and public bodies. The primary role of the NIC is to focus on areas of clinical care where accepted NICE guidelines are in place, but which have not been fully implemented. Partial implementation may be due to a delay in uptake of new practices and treatments or because of logistical and practical issues. The NIC seeks to encourage innovation across the NHS, empowering a culture shift that achieves rapid integration of NICE guidance and specific technology appraisals, where appropriate. NIC groups are convened in specific clinical areas to highlight the challenges faced within the NHS.

Introduction

Importance of nalmefene in treating alcohol dependence

Alcohol consumption is reported to be one of the highest lifestyle risk factors for both disease and death in the UK, after only poor nutrition, smoking, and obesity.[1] There is a strong correlation between the level of alcohol consumption and the risk of developing hypertension, stroke, coronary heart disease, pancreatitis, and liver disease.[2–4]

The Chief Medical Officers' guideline recommends that it is safest for men and women to not regularly drink more than 14 units per week to keep health risks to a low level.[5] It is estimated that over 10 million adults exceed this lower risk threshold and approximately 1.6 million adults have some degree of alcohol dependence.[6]

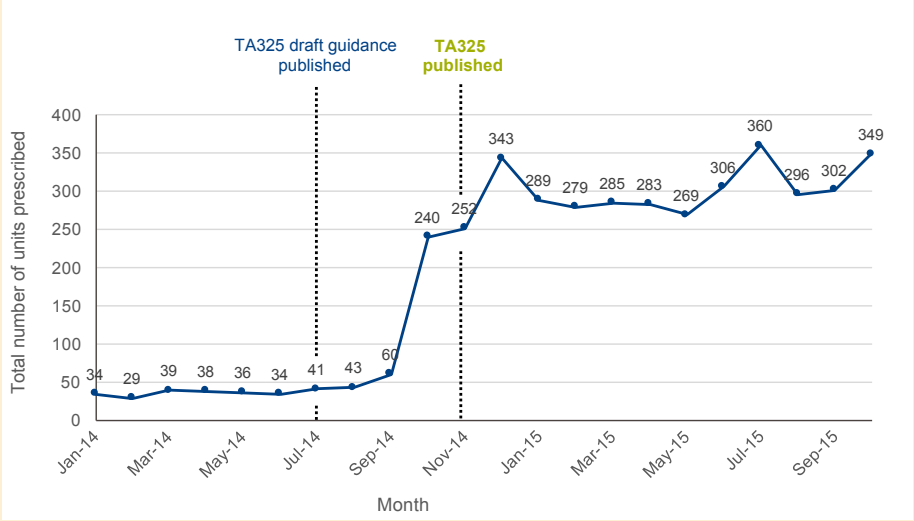
Box 1: Impact of NICE Technology Appraisal 325

Section 7(6) of the NICE (Constitution and Functions) and the HSCIC (Functions) Regulations 2013 requires CCGs, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in NICE Technology Appraisal (TA325) within 3 months of its publication date. This would mean that nalmefene should be accessible if a clinician believes that it is an appropriate treatment option for their patient.[11]

Prescribing data for nalmefene (see Figure 2, below) either side of publication of TA325 (May 2013–October 2014 and January–December 2015) suggests that:

- the average number of items prescribed increased 6-fold between periods of May 2013–October 2014 and January 2015–December 2015
- nalmefene was not prescribed at all in 27 CCGs (13%) in England between May 2013 and December 2015[12]
- very few individuals were prescribed nalmefene outside of CCG-funded services (including local authority commissioned alcohol services).[12]

Figure 2: Prescribing of nalmefene in England between January 2014 and October 2015[13]



Alcohol dependence remains both under-diagnosed and under-treated in the UK. It is estimated that alcohol dependence affects 4% of people aged 16–64 years; of whom only 6% receive treatment each year.[7,8]

Nalmefene is the first pharmacological drug licensed for the reduction of alcohol consumption in people with alcohol dependence. Current management of harmful drinkers with mild alcohol dependence is primarily based on a non-pharmacological approach using psychological approaches, such as alcohol brief interventions. Although other medicines (acamprosate, disulfiram, and naltrexone) are licensed for maintaining abstinence following alcohol withdrawal, they are not licensed for use in helping people to reduce their alcohol consumption.[9]

NICE TA325 on *Nalmefene for reducing alcohol consumption in people with alcohol dependence*, was published in November 2014.[9] It recommends nalmefene as a treatment option for reducing alcohol consumption in people with alcohol dependence who have a high drinking risk level (defined as >60 g per day for men and >40 g per day for women) without physical withdrawal symptoms who do not require immediate detoxification. This recommendation is aligned with the requirements of the marketing authorisation, which states that nalmefene should only be prescribed in conjunction with *continuous psychosocial support* focused on treatment adherence and that nalmefene should only be initiated in patients who continue to have a high drinking risk level *2 weeks after initial assessment*.[10]

Figure 3: Breakdown of key barriers to implementation of Technology Appraisal 325

NICE TA325 was the first of its kind in that the recommendations covered both health and social care since the formalisation of the NICE and the Health and Social Care Information Centre (HSCIC) Regulations 2013.[11] Clinical commissioning groups (CCGs) hold responsibility for primary care services and prescribing of medication and public health typically commissions services around substance misuse, and in particular, psychosocial elements of care. This departmental divide was suspected to be at the core of the challenges in the implementation of TA325 and the wide variation in adoption of nalmefene across England.[10]

Objectives

The objectives of this project were to:

- understand the key issues surrounding implementation of NICE TA325 and the steps required to overcome them
- take stock of barriers to commissioning, service design, and implementation and prescribing
- assess clinician awareness of nalmefene, TA325, and the supporting policies and pathways
- highlight best practice where possible through case studies.

Approach

Two qualitative surveys were developed to gain insight and to provide both qualitative and quantitative data on the key issues around TA325:

- A qualitative survey that was sent to GPs, hospital doctors, pharmacists, and practice nurses in England to gauge information on their awareness of TA325 and understand the barriers to prescribing of nalmefene
- CCG medicines management leads and local authority public health leads at selected sites were invited to complete a pro forma focused on implementation of TA325 in their locality. As part of this, stakeholders were asked if they were interested in being included as case studies. Those that agreed were followed up with a 45-minute semi-structured interview.

Site selection for completion of the pro forma was based on an expression of interest in supporting the project. Based on the reach of the partnering Academic Health Science Networks (AHSNs), stakeholders were engaged in both the North West Coast and Thames Valley regions as well as other sites.

Results

Responses

The clinician survey was sent out in January 2016 to over 16,000 clinicians (including GPs, hospital doctors, community and practice pharmacists, and practice nurses across England). In the 1 month in which the survey was open, only 62 responses were received. This low response demonstrated one of the challenges in connecting and communicating with clinicians on topics such as alcohol dependence.

Information on commissioning of nalmefene and associated services was collected through a separate pro forma. The partnering AHSNs employed their network of public health and medicines management leads to invite all organisations within the region to input into the pro forma. Organisations that completed the pro forma (n=32) are listed in Table 1 (see p.6).

Barriers to implementation of NICE TA325

Data collected from the two qualitative research tools were aggregated and analysed. Both tools looked to identify key barriers and critical success factors in local implementation of TA325. Barriers were broken down into three core areas (see Figure 3, above).

Table 1: Organisations that supported the completion of the commissioning proforma

Academic Health Science Network	Clinical commissioning group or local authority	Academic Health Science Network	Clinical commissioning group or local authority
Oxford	Aylesbury Vale CCG Bedford Borough Council Bedfordshire CCG Bracknell and Ascot CCG Buckinghamshire County Council Central Bedfordshire Council Chiltern CCG Newbury and District CCG North and West Reading CCG Oxfordshire County Council Reading Borough Council Slough CCG South Reading CCG West Berkshire Council Wokingham CCG Wokingham Borough Council Windsor, Ascot and Maidenhead CCG	Innovation Agency North West Coast	Blackburn with Darwen CCG Liverpool CCG Wirral CCG St Helens CCG St Helens Council Wirral CCG Wirral Metropolitan Borough Council
		Additional localities	Dudley Metropolitan Borough Council Gloucestershire CCG Gloucester City Council North Staffordshire CCG Portsmouth CCG Portsmouth City Council Staffordshire County Council Wiltshire CCG Wiltshire Council

1. Commissioning

Forming effective local working groups

Key critical success factors to implementation included: the working relationships, trust, and communication between key organisations involved. Localities that were able to introduce a pathway for nalmefene rapidly, reported strong collaboration and good lines of communication between key partners involved in implementation. Local working groups (LWGs) appeared to be a key part of this process and were usually bought together through CCG or local authority (LA) project management. The makeup of local working groups (LWG) varied, as did their roles and responsibilities in the group. Figure 4 (see p.9) shows the key stakeholders involved in LWGs and how they contributed to both nalmefene pathway design and implementation. It was noted by four respondents that a shared commitment to 'make the change happen' was core to the successful implementation.

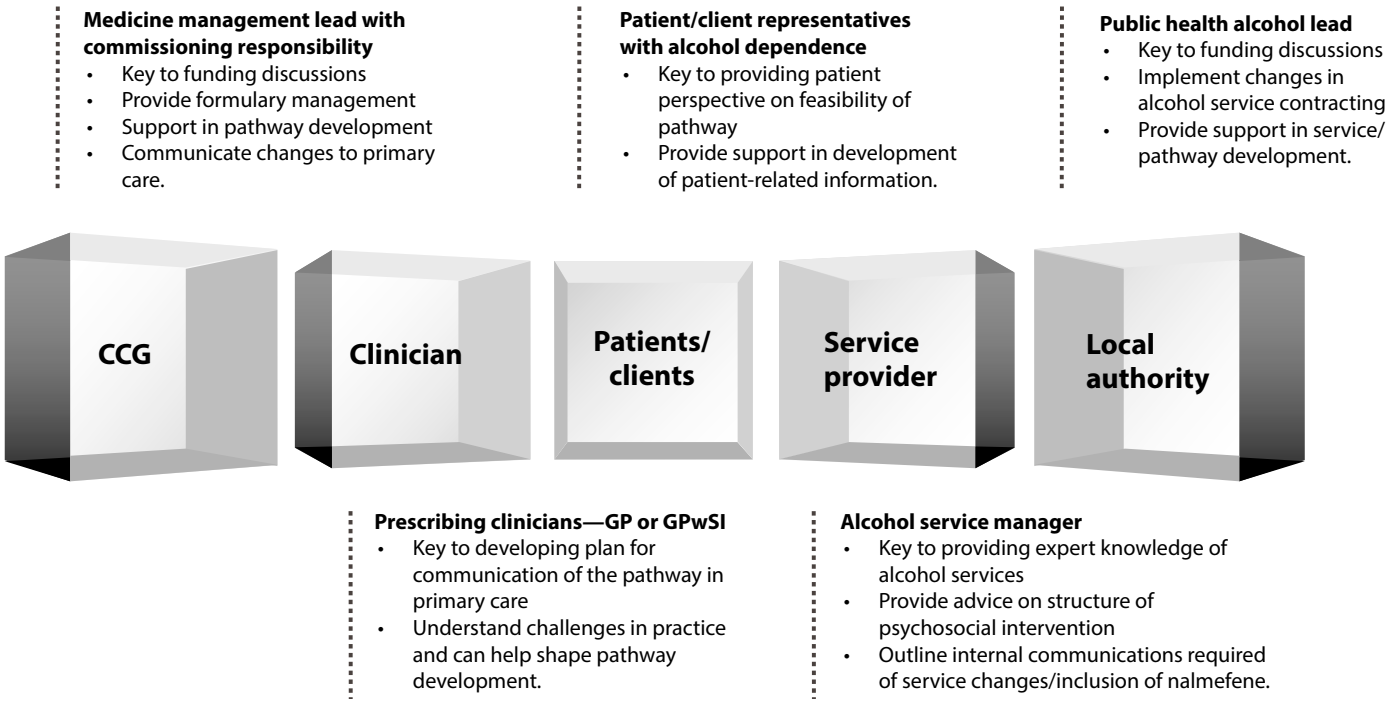
Locality representatives who reported that nalmefene pathways had not been put in place, drew reference to the fact that such working groups had not been successfully formed, or that communication had broken down in early negotiations.

Recommendation 1: Local project leads should look to assemble local working groups with all relevant stakeholders to scope, plan, and manage the integration of suitable nalmefene pathways into existing alcohol misuse services

Tackling scepticism about the effectiveness of nalmefene

The appraisal committee for TA325 concluded that nalmefene is both clinically and cost effective and should be considered as a treatment option for

Figure 4: Types of stakeholders involved in local working groups and their role in implementation of Technology Appraisal 325



reducing alcohol consumption for people with alcohol dependence[9] and should be accessible to prescribers. Patients receiving nalmefene should be monitored to ensure that they continue to meet the criteria for treatment, and outcomes should be recorded.

The evidence for clinical effectiveness was based on three randomised controlled trials (ESENSE1, ESENSE2, and SENSE) in adults with alcohol dependence, comparing 18 mg nalmefene (on an as-needed basis) plus psychosocial support (BRENDA) with placebo plus psychosocial support.[10]

A significant number of the commissioners surveyed in this work described doubts around the supporting evidence for the effectiveness of nalmefene, outlining that in view of the resource limitations, clinicians, in many cases would find it simpler to employ alternative pharmacological therapies or to use psychosocial interventions alone to treat patients with alcohol dependence. Additionally, some prescribers may lack experience and therefore lack confidence in prescribing nalmefene. This might be mitigated if the NICE TA process facilitated discussion of the evidence, recommendations, and shared experiences between healthcare professionals. Respondents believed that further evidence in either clinical- or practice-based research would be helpful in reassuring stakeholders of the benefits.

Across the 14 localities that engaged in this work, only six reported that arrangements were in place to monitor the effectiveness of nalmefene in practice. In localities where arrangements were in place, monitoring, data collection, and reporting were seen as the responsibility of the alcohol service provider. In almost all cases, data collection was not deemed rigorous, and wide variation was noted in terms of the outcomes that were being monitored. It is possible that the lack of monitoring results from confusion on where responsibilities lie. It was noted by two respondents that the low numbers of patients prescribed nalmefene would mean that any local evaluation would have limited statistical power.

One respondent suggested development of a national framework for collecting data on the effectiveness of nalmefene. This would increase patient numbers and over time would reassure prescribers and commissioners of the effectiveness of nalmefene. However, this process would need to be carefully designed to minimise clinical burden.

Recommendation 2: A national patient outcomes framework should be developed with alcohol service providers to monitor the effectiveness of nalmefene and psychosocial support in reducing alcohol consumption while minimising any additional clinical burden

Reducing variation and accelerating implementation

One universal challenge faced by individuals participating in this study was that the guidance in TA325 around implementation is ambiguous, leaving it open to interpretation, which in turn has led to wide variation in implementation. NICE may have looked to provide flexibility to local commissioning teams by deliberately keeping the guidance at a high-level without providing detail on how they expected it to be implemented. However, respondents felt that the lack of clarity around how nalmefene services should be most efficiently delivered was a stumbling block, requiring many sites to '*reinvent the wheel*'.

Points on where more clarity was required, included:

- which commissioning organisation is responsible for funding provision of nalmefene and/or the psychosocial (PSS) programme?
- which clinicians in which care setting would prescribe nalmefene and monitor patient eligibility?
- what is the specification for an acceptable PSS programme to support nalmefene prescribing?

Commissioning of alcohol services was handled very differently across the localities surveyed. These differences appear to be due to existing variations in local service agreements and contracting, historic local arrangements around funding, and whether or not localities had or were developing an *integrated* alcohol care pathway. Responses from those surveyed suggested that few participants had a good understanding of how TA325 was implemented in neighbouring localities. Although some had published local nalmefene pathways online, more effective sharing of information and data around implementation was recognised as a measure that would be of real value to commissioners. It has been suggested that alongside the technology appraisal adoption support, it would be helpful to also have a guide to service provision along with commentary from key opinion leaders and insights into the finances from both a provider and commissioner perspective.

Academic Health Science Networks have been commissioned across England to support knowledge exchange, to build alliances across existing networks and to actively share best practice, in order to provide rapid evaluation and early adoption of new innovations. Whilst assessing the awareness of AHSNs and the value of their support in TA implementation was out of the scope of this work, it was recognised by two case study respondents that the AHSN may have a role to play in sharing best practice and models of implementation with regional partners. See case study 1 (p.11) on collaborative working.

Recommendation 3: During the development of TAs that may be difficult to implement because they affect a wide range of stakeholders, NICE should work with Academic Health Science Networks and Public Health England (where appropriate) to facilitate knowledge exchange and to reduce the likelihood of local groups 'reinventing the wheel'

2. Adapting and developing local services

Designing robust pathways in line with TA guidance

All respondents agreed that given the requirements for prescribing nalmefene, a robust, well communicated patient pathway was an absolute requirement for ensuring patient access to the drug. Nalmefene was incorporated into existing or new local pathways in less than 50% of localities surveyed in this work.

Models of nalmefene provision

In localities where pathways were in place, respondents shared pathways and supporting documentation. From the pathways provided, there appear to be two commonly used models of nalmefene provision (Figure 5, see p.12). The models represented are not necessarily the only ways in which nalmefene can be incorporated into local pathways.

The models in Figure 5 differ in the division of labour and responsibilities between primary care and alcohol services as part of public health. In Model 1 the GP plays a more central role in care, is often responsible for identifying patients, and might assess the patient's level of dependence and eligibility if competent to do so, or prescribes the drug after confirmation of eligibility from the alcohol service team. Although patients may still self-refer to alcohol services, the

Case study 1: Collaborative working in Bedfordshire

Appropriate modifications to the alcohol service in Bedfordshire were made very soon after publication of TA325 to ensure that nalmefene was available and accessible to individuals who would benefit from the drug.

Bedford Borough Council (BBC), Central Bedfordshire Council (CBC), and Bedford Clinical Commissioning Group assembled a local working group (LWG) with the local alcohol service provider and a GP lead, to develop plans for nalmefene commissioning, service redesign, and implementation. The LWG recognised that existing services were effective at reducing the risk of further alcohol dependence and saw implementation of TA325 as an opportunity to reach further high-risk drinkers.

In Bedfordshire, a Tier 2 alcohol misuse service was already in place prior to publication of TA325. This was central to the provision of nalmefene and was responsible for assessment of patient eligibility for nalmefene, providing psychosocial support as well as monitoring patients (see Model 1 in Figure 5, p.11). In Bedfordshire the LWG agreed early on that nalmefene would be an adjunct to existing alcohol services and should be funded by public health. Primary care was considered the most appropriate setting for prescribing nalmefene. Arrangements were put in place for the CCG to invoice public health and to provide evidence that the patient adhered fully to the stringent eligibility criteria outlined in the pathway.

Pathway development and implementation were a truly collaborative effort with the service provider bringing the technical knowledge of the service and guiding discussions on the most effective use of resources, the CCG partners understanding the feasibility of GP engagement and how best to drive change in primary care, and public health professionals leading on finance and contracting. One of the biggest challenges for the LWG was the communication of the nalmefene pathway to prescribers in local general practice.

Between April and August 2015, a total of 16 people were prescribed nalmefene across eight general practices. This figure was significantly lower than that expected from original estimates based on the TA325 costing template of over 150 patients a year.

Case study learning points

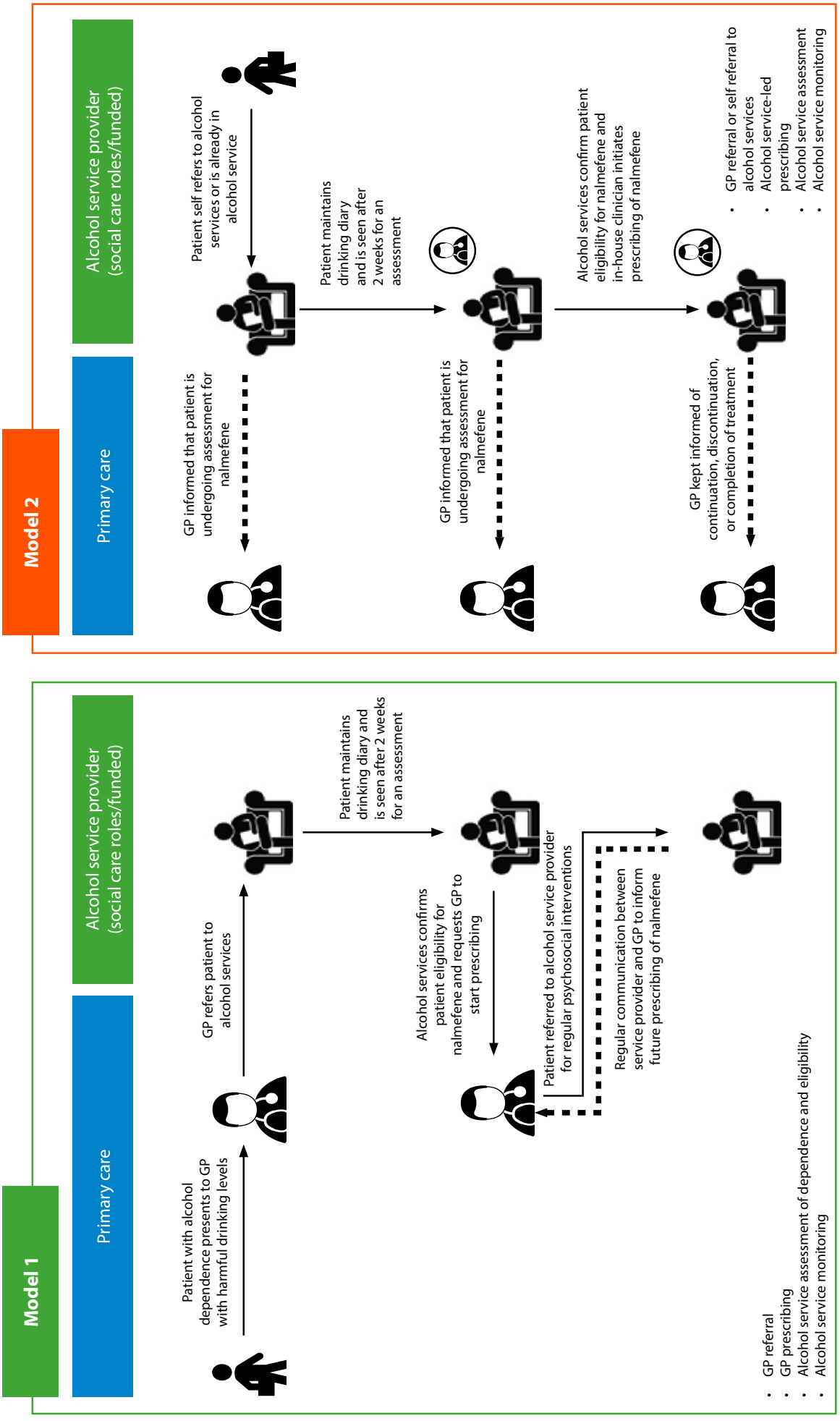
- It is important to manage expectations regarding the effectiveness of nalmefene and view TA325 as an opportunity to reach more individuals with harmful drinking behaviours
- Partnership and collaboration are essential. It is critical that key stakeholders are present from the start, are engaged throughout, and remain committed to making the change happen
- GP leads within the team should be a key part of pathway design and implementation to maximise the effectiveness of GP-engagement activities and communication of the pathway.

GP still plays a key part in the decision to prescribe nalmefene. In Model 2, all core activities around assessment, prescribing and monitoring are handled by the alcohol service provider who regularly informs the patient's GP of the treatment status

Some commissioners took issue with Model 1, highlighting that the GP involvement was not a great use of primary care resources and that prescribing would be better delivered in secondary care. This point was also raised by a number of GPs who believe that nalmefene provision sits with specialist services. GPs are also familiar with the idea that prescribing for naltrexone, acamprosate, and disulfiram requires psychosocial interventions that are provided initially in secondary care, so it was unclear to them as to why nalmefene should be any different. The distinction that treatment for moderate or severe dependence requires extensive psychosocial interventions, but that mild dependence requires a lower level of psychosocial support was not familiar to many GPs.

On the other hand, a large proportion of the respondents saw nalmefene as a primary care intervention in view of the mild dependence on alcohol. Furthermore, sites without a prescriber in their open access low threshold alcohol misuse services, preferred the shared-care model described by Model 1. Resourcing a prescriber in specialist alcohol services to support provision of nalmefene was not considered to be cost effective, given the relatively low demand for the drug experienced to date. Additionally, some drug and alcohol service providers were concerned about the conflict between supporting people on abstinence programmes, and supporting patients on nalmefene to reduce alcohol consumption.

Figure 5: Schematics of two commonly adopted models of nalmefene provision



Nalmefene has a UK marketing authorisation for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level without physical withdrawal symptoms and who do not require immediate detoxification.

Allocation of funding for nalmefene was variable and was perceived as a 'sticking point' in negotiations. Nalmefene was funded by CCGs in over 50% of the localities surveyed: other sources of funding included the public health alcohol budget, the alcohol service provider, and the standard prescribing budget.
It should be acknowledged that the analysis for NICE TA325 did not take into account the costs of service reconfiguration or development of new services. Recognition of *affordability* in addition to *cost-effectiveness* was considered to be an important consideration in the implementation of TAs that are more complex that prescription of a drug

Clinicians in some areas appear to be putting acquisition cost before cost effectiveness, which goes against the mandate for implementation of NICE TAs. Moreover, beneficial longer-term efficiencies and, most importantly, patient outcomes that may result from this medicine are potentially not being realised by primary care and public health.

One of the key features of localities able to make nalmefene accessible early and to a greater extent was the presence of existing open access, low threshold service provision for mildly dependent drinkers that could be augmented to include nalmefene. For those localities implementing Model 2, it was also considered simpler if the service contract with the alcohol service provider was nearing expiry, allowing nalmefene provision and management to be included as a component of the contract renewal.

Recommendation 4: Local working groups should facilitate early negotiations to reach agreement of suitable service models and the division of responsibilities for each facet of care (e.g. prescribing, psychosocial support, monitoring, review, and management)

Addressing preconceptions about psychosocial support

One area in which there was little agreement from commissioners was around the type, format, and frequency of the PSS that is provided alongside nalmefene. Respondents outlined a number of PSS strategies currently in place, the most common of which included:

- brief psychosocial interventions:
  - the online programme provided by the manufacturer or other organisations (e.g. Breaking Free Online)
- motivational enhancement training and interviewing
- promotion of treatment adherence for both nalmefene and the psychosocial intervention.

Some localities already had a PSS service in place to support patients with a high drinking risk level and alcohol dependence. Provision of PSS was considered to be possible through the following channels:

1. GPs, nurses, or pharmacists during routine appointments.
2. Specialists in libraries, leisure centres, and GP surgeries.
3. Alcohol services provided by the practice nurse in primary care (akin to stop smoking services).
4. Community drug and alcohol services.
5. Third-sector organisations.

Once again, commissioners and specialist alcohol workers were reported to be frustrated with the lack of specific guidance around the requirements for the service. Although some information is available in the additional resources for TA325, respondents felt that this was largely left for local decision making. See case study 2 (p.14) on interpretations of guidance.

Responses to the commissioner pro forma suggested that the majority of commissioners believed that the most appropriate PSS would be through 1 :1 or group sessions with existing alcohol services. Around 40% of commissioners believed that PSS could be provided through online or telephone channels. Ambiguity in the guidance has resulted in confusion around the most appropriate PSS for patients. In some cases, the PSS provided by current services may be different from those used in the clinical trials for nalmefene, as described in TA325.

Recommendation 5: NICE should look to provide definitive guidance on what is and is not appropriate in terms of the type, format, and frequency of the psychosocial support associated with TA325 to help local working groups understand the potential options

Case study 2: Interpretations of guidance in Buckinghamshire

Commissioners in Buckinghamshire faced a number of challenges, many of which were outside the control of the local project team. These barriers have over the last year slowed the pace of implementation of TA325. A rapidly changing stakeholder/project team meant that effective planning and negotiation around the service and TA implementation changed direction multiple times. In addition, local stakeholders interpreted the TA guidance around prescribing of nalmefene differently and in ways that were not perceived to fit well with the existing service delivery model.

Prescribing of nalmefene was considered as a secondary care responsibility, and it was felt that GP prescribing of the drug would complicate the pathway and require too much 'back and forth' between GPs and specialist alcohol services. However, the alcohol service provider offering psychosocial support, had no prescribing capabilities that could be leveraged for the provision of nalmefene. Recruitment of a consultant or non-medical prescriber into the service could not be justified given the relatively low demand for nalmefene. Getting agreement from all stakeholders on the most suitable service model for the provision of nalmefene has been a significant challenge. Clearer guidance in the TA around prescribing responsibilities might have allowed stakeholders to commit to an agreement faster.

The project team has also been challenged by the scepticism of local clinicians around the evidence of the effectiveness of nalmefene and psychosocial support versus psychosocial support alone. The local project team are meeting regularly to address these issues in order to reach an agreement on how best to make nalmefene accessible across the region.

Case study learning points

- Clearer guidance in TA325 on service redesign would have been of real benefit to local project teams, helping teams to come to earlier agreement on the most appropriate service model
- Sharing the lessons learned from localities that have successfully implemented pathways for nalmefene would offer further assurances to teams initiating discussions around implementation of TA325.

3. Service delivery and patient access to nalmefene

Raising awareness of the drug, the TA, and local pathways

GPs or GPs with special interests made up 70% of the respondents to the clinician survey with the remainder comprising hospital clinicians, practice nurses, pharmacists, and substance misuse specialists. Although 86% of clinicians surveyed felt that their level of knowledge and awareness of alcohol misuse/dependence was excellent, good, or average, more than 55% of clinician respondents were not aware of nalmefene, its traffic light classification, or if local guidelines had been developed on its use (see Figure 6, p.15).

All commissioners in both CCGs and public health were all aware of both TA325 and nalmefene.

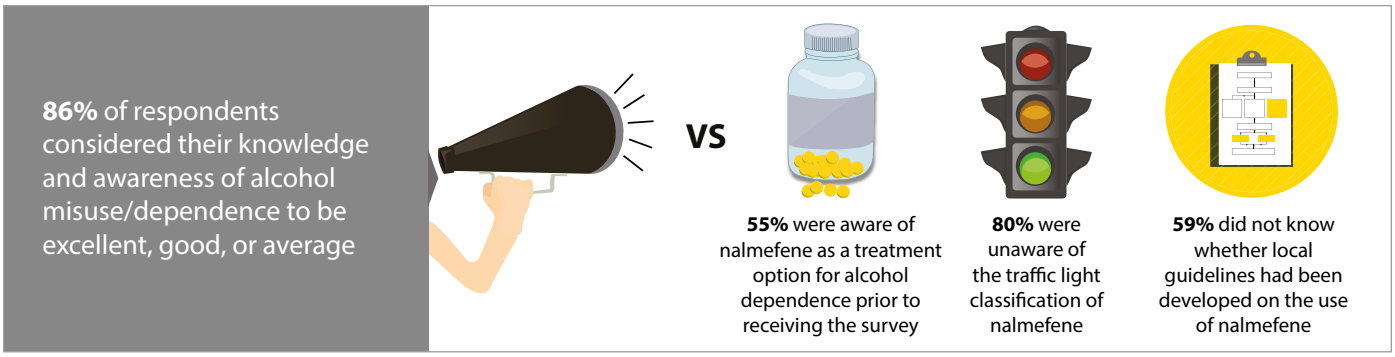
The lack of a vocal patient organisation may contribute to the lack of awareness and accessibility of nalmefene.

The differences in understanding of where nalmefene is most likely to be prescribed were of particular interest. The majority of clinicians surveyed (of whom 70% were based in primary care) believed that nalmefene was being prescribed either by community or by hospital-based specialist alcohol teams. On the other hand, most commissioners gave an account that prescribing of nalmefene occurred in primary care by GPs or GPs with special interests (see Figure 7, p.16). Although these two sets of responses were not matched by locality, these data do reinforce the message from commissioners around the difficulty in communicating service changes to GPs.

The respondents participating in this small study suggested a number of possible strategies to improve GP awareness of pathways, processes, and policies around alcohol misuse. These strategies included:

- holding regional/sub-regional workshops and learning events
- communications of posters, flyers, and information by post
- using CCG IT infrastructure
- formal training on tackling alcohol misuse.

Figure 6: Breakdown of key barriers to implementation of Technology Appraisal 325—respondent knowledge and awareness



For localities in which the GP is the prescriber, few felt that clinicians had received and fully understood the message and pathway around nalmefene.

Recommendation 6: There is a need to develop systematic methods of engaging and communicating with healthcare professionals in primary care regarding new TAs, their implementation and local pathways or guidelines

Improving identification of individuals with harmful drinking

One significant challenge picked up in this work was that of identifying patients with alcohol dependence and those who might be appropriate for treatment with nalmefene and PSS. The licence and TA325 explicitly state the eligibility criteria for considering nalmefene as an option to reduce drinking levels: nalmefene is licensed for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level without physical withdrawal symptoms and who do not require immediate detoxification.

This represents an important group of patients who:

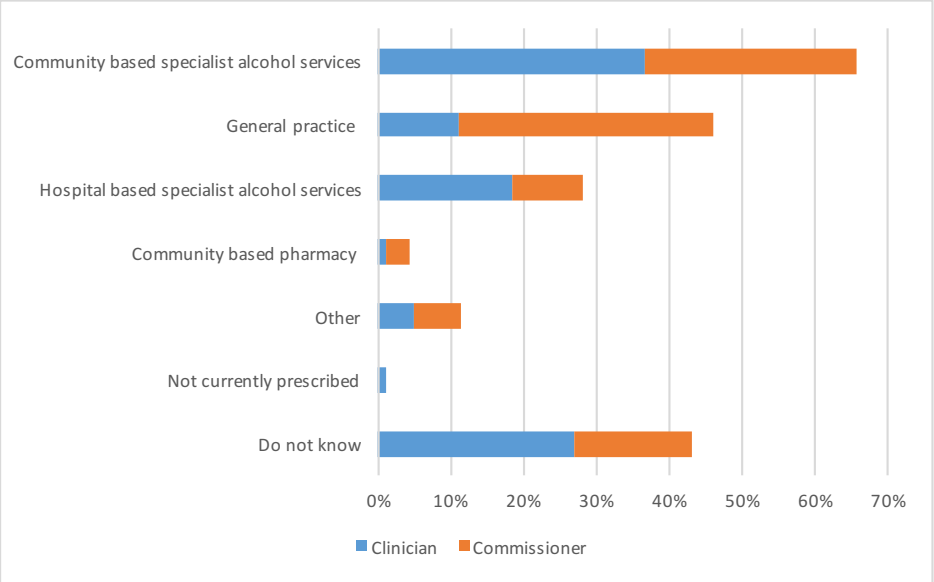
- are not routinely screened for in primary care (some individuals may be captured when registering with a practice, undergoing the NHS Health Check, or because of management of other co-existing conditions)
- will not be known to, or engaged with, alcohol services or alcohol specialist teams
- may not acknowledge a need for an alcohol-reduction intervention or may not wish to draw attention to this need, given the stigma attached.

Five public health respondents recognised that significant improvements were required in terms of screening individuals to identify drinking risk levels. Currently, patients with alcohol dependence are identified via self-presentation, screening programmes, or referred in from other services. In primary care, systematic identification of drinking levels in newly registered patients, universal patient screening, and targeting common triggers are advised in the adoption support for TA325. However, it remains unclear as to whether these approaches have been adopted systemically.[9] See case study 3 (p.16) on raising awareness in primary care.

Although many of the respondents' comments related the problem back to an increased need for GP training and education, this issue is likely to span beyond just primary care and is likely to require a collaborative approach from primary care, and public health, as well as third-party organisations. The Thanet and South Kent Coast Alcohol Integrated Care Pathway Project has taken a holistic approach to tackling the problem systemically and has successfully brought together a wide range of services, support and information for people in Kent. A key component of this pathway is in screening and early identification of harmful drinking behaviours.

Recommendation 7: Local working groups may wish to consider developing strategies to improve opportunistic screening and early identification of drinkers at any level of risk in primary care, secondary care, and third party organisations. This may fit with developing an integrated alcohol care pathway in partnership with relevant organisations across the locality

Figure 7: Respondents perceptions of how nalmefene prescribing occurs in their locality (more than one clinician archetype could be selected)



Responses presented as a percentage of the total number of responses for all clinicians in either the clinician survey (blue – n=62) or the commissioner pro-forma (orange – n=22)

Case study 3: Raising awareness in primary care in Portsmouth

Commissioners in Portsmouth had good knowledge of nalmefene prior to the publication of TA325 as Portsmouth was a pilot site for the introduction of nalmefene.

Prior to publication of TA325, a local working group assembled at the start of project, which included public health leads; the Alcohol Strategy Lead; CCG medicines management, a GP lead, and the CCG Director of Professional and Clinical Development. The pathway developed in Portsmouth saw clinicians in primary care responsible for prescribing of nalmefene (see Model 1 in Figure 5, p.10). Public health was responsible for funding the psychosocial support, but the CCG was responsible for the funding of nalmefene.

GP prescribing was considered the best fit for both the team's interpretation of the guidance and also in providing an environment that patients would feel comfortable in. The nalmefene pathway took advantage of an existing open access low threshold provision that was led by two alcohol specialist workers. On finalising the pathway for nalmefene, the service model was communicated through a number of channels that helped to reinforce the message that nalmefene was available and accessible. These channels included:

- posting information on the CCG intranet
- public health distributed information regarding the drug, the guidance, the pathway, and how primary care can improve identification of patients with a high drinking risk level
- the manufacturer of nalmefene partnered with the Royal College of General Practitioners to provide local training on the identification of alcohol dependence—at this meeting a copy of the pathway and guidance was again shared

The Portsmouth public health team engaged with the service delivery team to ensure both the pathway and requirements were clear.

GPs, alcohol specialist workers, and public health leads had reservations about the evidence for the effectiveness of nalmefene. It was reported that many felt that nalmefene with psychosocial support (PSS) was no more effective than PSS alone. Only 10 patients have been prescribed nalmefene through the official pathway in Portsmouth, but only one of these was treated for any significant length of time. Although initially specialist alcohol workers were excited to have an additional tool to work with, to date there has been little use of it.

Case study learning points

- The close working relationship and strong lines of communication between CCG and public health was key to the rapid and successful design and implementation of the nalmefene pathway
- Both CCGs and public health focused on raising awareness of the drug and the pathway in primary care, through a number of channels.

Case study 4: Nalmefene prescribing in Wiltshire

In the period January–October 2015, Wiltshire had the highest prescribing of nalmefene out of the sites investigated in this study (see Table 2). This was attributed in part to the involvement of Wiltshire as a pilot site for nalmefene prior to publication of Technology Appraisal 325, and to the commissioner funding alcohol training events for GPs that included distribution of the local nalmefene pathway.

In Wiltshire, prescribing of nalmefene is the responsibility of GPs. All individuals considered appropriate for nalmefene by the alcohol service provider see a prescribing doctor and are reviewed at a minimum of every 3 months, or sooner, if risk dictates, by a doctor or a non-medical prescriber. However, a number of factors have recently led to a drop in GP prescribing of nalmefene:

- nalmefene is considered a 'recovery based medication' and in Wiltshire there is rarely an end-date associated with prescribing. Individuals often complete their structured treatment with the alcohol service provider but specialist workers are unable to exit them from the service because of prescribing needs. As a service, public health has looked to limit prescribing of this medication to 3 months
- GPs in certain areas of Wiltshire have been unable to prescribe nalmefene due to cost, which demonstrates variation and fragmentation across the locality. Nalmefene was viewed as being no more effective than naltrexone and was four times more expensive. As a consequence, naltrexone is often used as a first treatment option within the specialist service (naltrexone is not licensed for reducing alcohol consumption).

Case study learning points

- The budget requirements for provision of nalmefene appears to be a critical factor for sustainable adoption of nalmefene and may limit use of nalmefene across Wiltshire in the future unless the budget is ring fenced
- Ensuring that the pathway has controls in place for initiation and discontinuation of treatment with nalmefene is important in assuring GPs and funding organisations that the intervention is not open-ended.

Ensuring nalmefene is included in local formularies

The inclusion of nalmefene in the local formulary appeared to bear little relation to the level of prescribing that was taking place in the area. The traffic-light classification of nalmefene was variable with a few areas deeming the medicine as a red medicine meaning it can only be prescribed in secondary care, while others have classified it as an amber medicine meaning it has to be initiated in secondary care, and others as a green medicine, which permits prescribing in primary care or secondary care; some areas have not classified the medication but permit treatment according to local criteria (see Table 2, p.17).

Looking at the key attributes of the three areas that have seen the largest levels of prescribing per population—Gloucestershire, St Helens, and Wiltshire—all have incorporated nalmefene into local pathways and the respective local Area Prescribing Groups have reviewed the inclusion of the drug into the local formulary.

Although prescribing figures are useful in understanding the total volume prescribed, they do not indicate the numbers of patients who receive nalmefene in each region. Anecdotal evidence from the case study sites suggested that most sites had fewer than 20 patients receiving nalmefene. An important point to note is that prescribing over the period January 2015–October 2015 in all regions investigated was considered low in relation to the original usage estimates provided in the NICE TA325 costing template, which suggested that commissioners should budget for ~85 individuals accessing nalmefene per 100,000 population.[15] See case study 4 (above) on nalmefene prescribing.

Recommendation 8: In implementation of pathways for nalmefene, CCG members of local working groups should ensure that nalmefene is listed in an appropriate way by area prescribing committees in the local formulary. This should ensure its traffic light status is not a barrier or a deterrent to prescribing

Table 2: Status of Technology Appraisal 325 implementation at sites taking part in survey

Area	Nalmefene incorporated into local pathway	Nalmefene formulary position reviewed	Formulary status	Nalmefene scripts Jan – Oct 2015[1]	Population estimate[2]	Scripts per 100,000 people (Jan-Oct 2015)[3]
Aylesbury Vale	No	03/08/2015	Red: restricted prescribing on the advice of the Drug and Alcohol Advisory Team in line with NICE TA325	6	156,886	4
Chiltern	No	03/08/2015		10	248,277	4
Bedfordshire	Yes	01/02/2015	No traffic light: Bedford Borough and Central Bedfordshire Public Health nalmefene pathway launched	42	337,005	12
Blackburn with Darwen	Yes	Yes; no date available	Nalmefene to be supplied via a locally commissioned specialist service in conjunction with continuous PSS Red: primary care prescribers should not be asked to prescribe	0	108,506	0
Dudley	No	Unknown	No traffic light: should be made available to patients, where appropriate, and therefore be included in the formulary and adopted by the local healthcare providers and commissioners	21	247,916	9
Gloucestershire	Yes	Yes; no date available	No traffic light: only to be prescribed in conjunction with continuous PSS focused on treatment adherence and reducing alcohol consumption	89	214,497	42
Liverpool	No	28/01/2015	Amber: medicines recommended or initiated by specialists in primary or secondary care. Non-specialist prescribing in primary care may follow according to specified criteria.	37	383,171	10
Bracknell and Ascot	Yes	16/06/2015	Green but non-formulary (only to be commissioned by locally agreed pathways)	20	103,594	19
Slough	Yes	16/06/2015		1	104,708	1
Windsor, Ascot and Maidenhead	Yes	16/06/2015		4	110,751	4
St Helens	Yes	28/01/2015	Amber: Medicines recommended or initiated by specialists in primary or secondary care. Non-specialist prescribing in primary care may follow according to the RAG criteria	76	140,774	54
Oxfordshire	Yes	Under review	Non-formulary: should not be used unless approval has been obtained from Medicines Management and Therapeutics Committee	72	520,521	14
Newbury and District	Yes	17/06/2015	Amber: prescribe in primary care under shared care with local Drug and Alcohol Advisory teams	8	81,687	10
North and West Reading	No	17/06/2015		20	77,078	26
South Reading	No	17/06/2015		2	86,311	2
Wokingham	Yes	17/06/2015		4	122,233	3
North Staffordshire	Yes	Unknown	Grey: Not to be included in the joint formulary	8	174,970	5
Portsmouth	Yes	Unknown	No traffic light—primary care only	25	165,725	15
Wirral	Yes	No	Not listed—drug is initiated by specialists only	12	253,315	5
Wiltshire	Yes	Yes, 28/04/2015	Green in the north of the county (Included in the formulary) Amber: the south of the county	190	379,183	50

*Number of items prescribed (listed as nalmefene or Selincro®) between Jan 2015 and Oct 2015 as reported by health and social care information centre GP prescribing data.[14]
†Does not include scripts from acute hospitals.
‡Population estimates from Office for National Statistics 2014. Figures reported relate to adults aged 18 years and above.[16]
§Items prescribed [listed as nalmefene or Selincro®]/estimated population of age 18 or above.

Limitations of this work

This study looked to draw out and understand the important factors that have been involved in implementing TA325. However, the analysis, which this report is based on, had a number of limitations such as small sample sizes and selective site participation in completion of the pro forma. This means that the views expressed in the analysis may not provide an accurate representation of implementation across England.

Importantly, this study may have been subject to selection bias, given that the sample was one of convenience, relying on engagement from site leads in Oxford and the North West Coast.

Secondary care and acute hospitals manage a significant proportion of the patient group under discussion and are under represented in this analysis.

Conclusions

The objectives of this project were to assess the barriers and critical success factors involved in implementing NICE TA325. This work highlighted three key areas for future efforts to focus on: commissioning; adapting and developing services; and service delivery and patient access. The issues raised will be key considerations in implementation of other TAs that are known to cut across departments.

Importantly, the scope of this work focused on the implementation of TA325 and the barriers that exist to making nalmefene available to patients who might benefit from the drug. An interesting observation from this work was that low levels of prescribing of nalmefene were noted across England, irrespective of whether:

- measures had been taken to implement TA325
- pathways had been put in place for provision of nalmefene and PSS
- the drug had been made available in the formulary.

This suggests that the low use is less a factor of slow or poor implementation of the guidance but due to broader factors that have led to low demand for the pharmacological element of the treatment:

- low volumes of eligible patients identified as suitable for treatment
- poor communication processes outside working groups and knowledgeable professionals
- poor patient and prescriber awareness of the drug
- prescribers' lack of confidence in the drug and the guidance:
  - limited clinical experience with the drug
  - scepticism about the evidence.

Many commissioners agreed that improvements in screening and identification were required in order to reach a higher proportion of individual patients with harmful drinking behaviours. Those that had implemented pathways for nalmefene and made nalmefene available to the prescriber in their locality considered that it was sufficient to fulfil their responsibility in complying with the TA implementation mandate. Despite wanting to reach more people with effective alcohol services, none of the commissioners asked, had intentions of further promoting the adoption of nalmefene.

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Nalmefene will no doubt remain an important clinical option to reduce drinking levels in individuals with alcohol dependence. However, until screening and identification of at-risk drinkers is improved, prescriber awareness of the drug is increased, and the effectiveness of the drug in practice is demonstrated it is difficult to see that adoption will significantly increase. A study published in June 2016 has added to the uncertainty on the supporting efficacy data for nalmefene,[17] and may negatively impact on future implementation of TA325.

The association of improvements in outcomes for patients with alcohol dependence with national indicators and targets may help to drive change. For example, the CCG Outcomes Indicator Set includes indicators on alcohol admissions and readmissions and mortality from liver disease. Public Health England has published a guide to social return on investment for alcohol and drug treatment commissioners.[18]

Next steps

Representatives from the CCG, public health, and the alcohol service provider should review local implementation of TA325 and the use of nalmefene, and consider what changes or actions could be implemented to reduce variation and improve patient care, for example:

- reviewing strategies on the identification of people with alcohol dependence (e.g. developing common standards and review tools [e.g. AUDIT C] and links to hospital admissions and attendance for alcohol-related conditions)
- improving knowledge and awareness of alcohol treatment pathways, especially with GPs through training and communication from alcohol services
- agreeing on funding and service between CCG, public health, and the alcohol service provider, which ensures an effective local pathway
- developing robust local pathways for pharmaceutical adjuncts to psychosocial treatments
- reviewing whether current prescribing of nalmefene occurs in the most appropriate setting
- reviewing provision and content of psychological support to ensure minimum standards are understood and delivered
- collecting data and monitoring patient outcomes that can feed into a local data set
- establishing nalmefene as a treatment that is recognised in local strategic plans for reduction of alcohol-related harm.

Appendices can be found on p.21–23.

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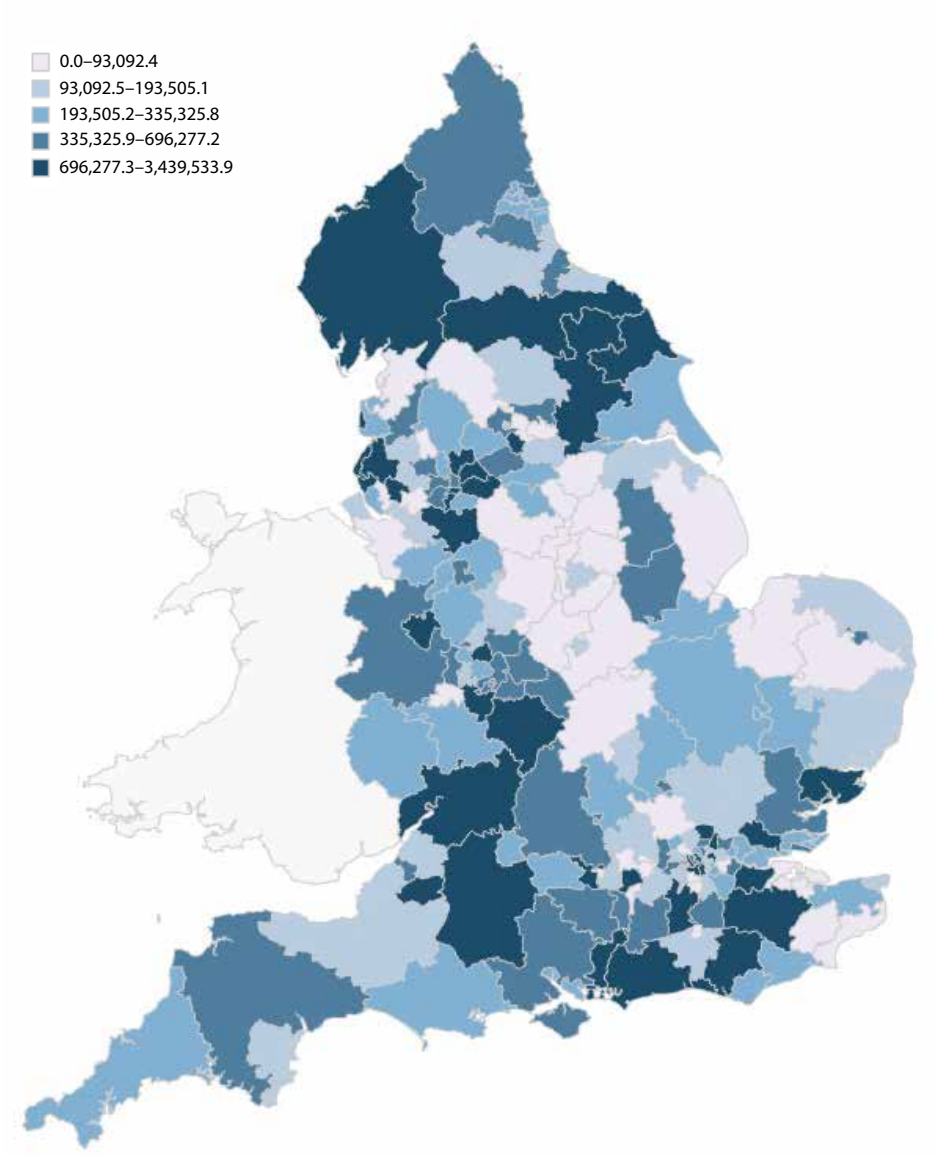
Appendix 1: Nalmefene daily defined dose per 100,000 resident populations for the period July 2014–June 2015

Defined daily doses are a World Health Organization statistical measure of medicine consumption. They are used to standardise the comparative usage of various medicines between themselves.



Source: Innovation Scorecard January 2016, Prescribing and Medicines Team, HSCIC

Appendix 2: Table of barriers to implementation of Technology Appraisal 325

Local barriers	National barriers
Commissioning ■ Limited commissioning capacity and 'patchy' commissioning of alcohol services ■ Challenging negotiations between CCG and local authorities ■ Quality of relationships between CCG and public health teams	**NICE Technology Appraisal 325 scope** ■ Lack of guidance around 'responsible' organisations funding and prescribing ■ Knowledge and awareness of drug and TA325
Pathway design ■ Variations in access to prescribers in drug and alcohol services ■ Difficulty agreeing adequate psychosocial support for users	**Targeted patients** ■ Patients with alcohol dependence may not present to services—stigma attached to label of dependent drinker ■ Licensed indication for medicine is narrow so it can be difficult to identify patients who might be appropriate for treatment
Access and delivery ■ Difficulty agreeing adequate psychosocial support for users ■ Prescribing of nalmefene not permitted in locality ■ Lack of drug and alcohol team staff in some areas	**Evidence** ■ Difficulty agreeing adequate psychosocial support for users ■ Evidence base is not considered robust and faces repeat challenges from clinicians and commissioners in both CCGs and public health

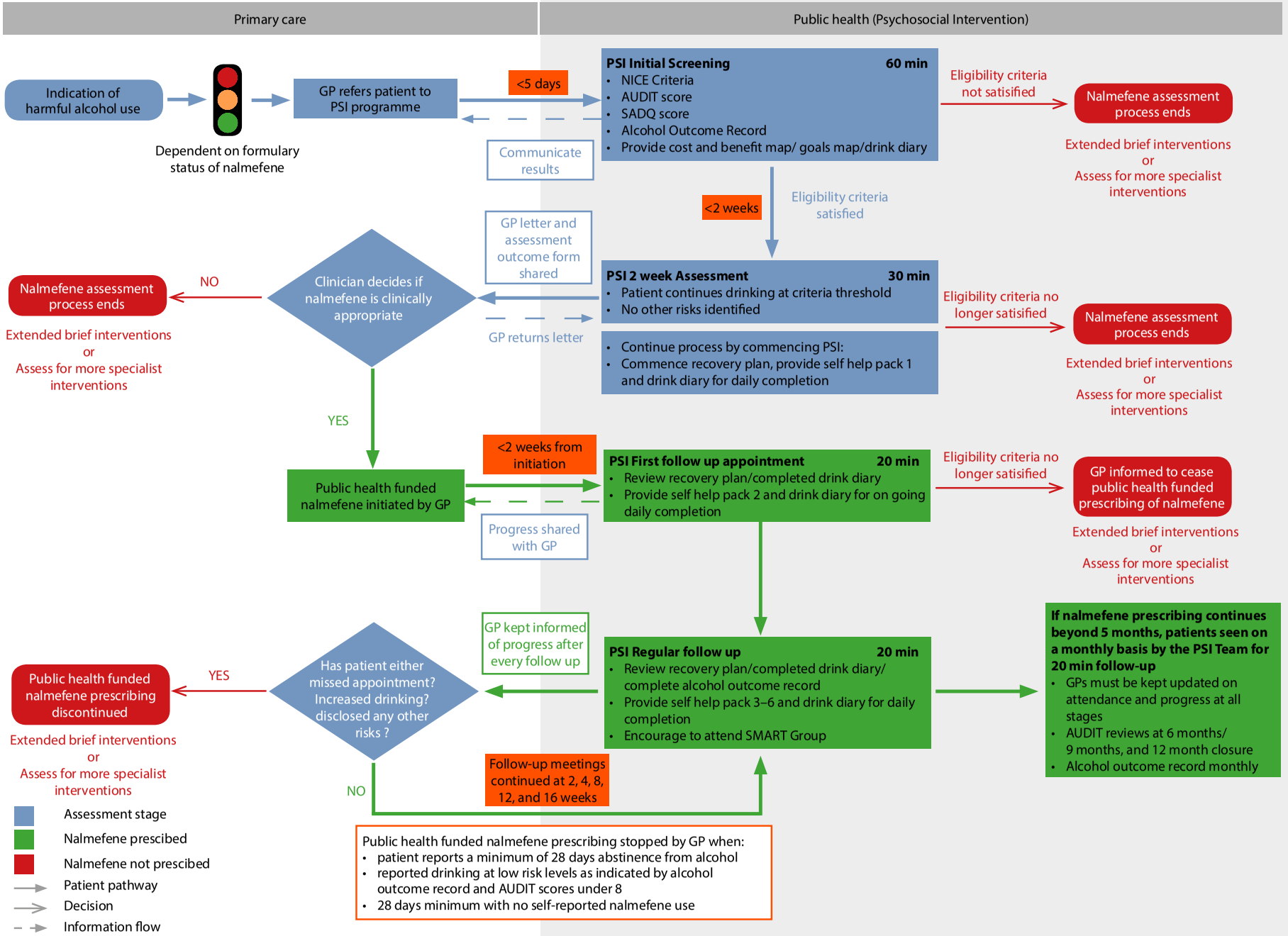
Appendix 3: Table of barriers to further adoption of nalmefene

Patients	Clinicians	Commissioners
■ Poor awareness of drug ■ Uptake of drug not as high as anticipated ■ Discontinuation of pharmacological treatment due to unsuitable drinking levels and/or side-effect profile	■ Limited awareness of the TA, the drug and local pathways for provision of nalmefene ■ Experience of clinical and cost effectiveness ■ Scepticism around the evidence base ■ Confusion between psychosocial support and psychosocial intervention	■ Content with having made nalmefene available ■ No capacity or appetite to drive a campaign for further use of the drug ■ Scepticism around the evidence base

Appendix 4: Table of barriers to further adoption of nalmefene

Local actions	National actions
■ Improve knowledge and awareness of pathways, especially in GPs ■ Review strategies on the identification of people with alcohol dependence ■ Agreement on funding arrangements ■ Review of use and effectiveness of nalmefene ■ Robust data collection to track use and outcomes ■ Reconfiguration of drug and alcohol action team services to enable prescribing ■ Development and use of local pathways ■ Agreement on local arrangements between CCG, public health, and alcohol service provider	■ Raise profile of alcohol dependence and its impact among healthcare professionals and the public ■ National framework for data collection to provide evidence for use of nalmefene

Appendix 5: Example pathway from Bedfordshire for patients receiving nalmefene



AUDIT=Alcohol Use Disorders Identification Test; SADQ=Severity of Alcohol Dependence Questionnaire; PSI=psychological interventions