LLWYNHENDY TUBERCULOSIS OUTBREAK EXTERNAL REVIEW REPORT 2nd DECEMBER 2022

Jointly commissioned by Public Health Wales and Hywel Dda University Health Board

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Contents

Executive Summary

An outbreak of tuberculosis (TB) related to a public house in Llwynhendy was identified in September 2010. Cases linked to this outbreak continue to occur more than a decade later. We estimate that there have been at least 31 cases of active pulmonary TB and perhaps more than 300 cases of latent TB infection associated with the outbreak. We have also observed that there is a higher-than-normal rate of latent TB infection in the local population that has not necessarily occurred because of this particular outbreak but may become the source of future outbreaks. The population at risk is UK-Born people who develop highly infectious pulmonary TB that may, due to their untypical demography go undiagnosed for longer than usual. This implies that, even in this area of low incidence for TB, there is a potential for further outbreaks which requires continuing vigilance.

The original source of the outbreak was traced to an individual worker at a public house in Llwynhendy who, due to a delay in the diagnosis of their pulmonary TB, was highly infectious for a prolonged period. The causative strain of TB was not unique to this outbreak having been identified before in England and in Wales. It is not known how this index case acquired the infection but subsequent genetic analysis points to an affected pub user in 2007. Following the diagnosis of the first case, the public health response included the initiation of an outbreak control team (OCT) and the deployment of contact tracing staff to identify onward transmission of infection. It appears that this initial response was inadequate mainly because it failed to recognise the highly infectious nature of the source and therefore did not extend the contact tracing sufficiently. As a result, infected people were unrecognised and developed active disease, passing the infection on to others. The outbreak control team was closed down prematurely and had to be re-opened on three further occasions as more cases presented including one fatal case which was highlighted in the media. The subsequent public health management improved considerably

and culminated in a large-scale community screening event that disclosed a high level of latent TB infection in the population.

The clinical management of individual patients with TB at the beginning of the outbreak, though satisfactory, was uncoordinated because of the lack of a dedicated TB service and a lead clinician. Also, at the outset, the local respiratory healthcare provision was inadequate due to service re-organisation and recruitment difficulties. This has largely been addressed with the appointment of a lead consultant and a dedicated TB nurse. However, changes are still needed to improve the TB service.

The relationship between the Health Board (HDUHB) and Public Health Wales (PHW) also attracted scrutiny. Although, the Health Board had the statutory responsibility for outbreak control, it should have been subject to greater oversight from PHW at the beginning. The initial response was deemed inadequate and the outbreak did not feature in the minutes of the boards of either organisation until 2019, though it is quite possible that discussions were occurring below this level. By this time there had been at least one death, widespread community screening and considerable public anxiety. The in-house review by PHW in 2019 recommended the introduction of a more structured approach to TB outbreaks but so far this has not materialised.

England has had a collaborative strategy for tuberculosis which has been in place since 2015 with a focus on disease control and migrant testing. TB rates in Wales are lower than England but the mortality rate is twice as high. Wales does not have a national strategy for tuberculosis although one has been proposed by the Welsh Respiratory Delivery Group. So far this has not been formally supported by the Welsh Government. There is an informal TB Cohort Review run by the Respiratory Delivery Group which should be also given a formal footing as part of a National TB Strategy.

1. Introduction

Tuberculosis (TB) is an infection which remains a problem in both the developed and the developing world. Despite the availability of effective treatment, it accounted for 1.5 million deaths globally in 2020 and remains a priority for the World Health Organisation (WHO). In the United Kingdom there are approximately 350 preventable deaths per year related to tuberculosis. The incidence of TB has gradually fallen in the United Kingdom primarily because of public health measures, improved affluence and effective treatment. However, TB has not been totally eradicated and, over the years, repeated relaxation of public health surveillance has led to a resurgence of cases. At this time in the UK, cases of tuberculosis are mostly, but not exclusively, in the urban population and 76% of these are born abroad (UK HSA 2021). Once diagnosed, TB remains largely treatable though drug resistance is a growing concern. This is the context in which the TB outbreak in Llwynhendy in 2010 will be reviewed.

2. Tuberculosis in the United Kingdom

In England, where the figures are available, the incidence of TB has fallen dramatically from the beginning of the 20th century and fell further with the introduction of anti-tuberculosis therapy. By the beginning of the 21st century the numbers had stabilised but then started to rise again and in 2011 there were 8280 cases (Fig 1). The Collaborative (Public Health England and NHSE) Tuberculosis Strategy for England was launched in 2015. This required focus on diagnostics, drug resistant TB, underserved populations, LTBI migrant screening, workforce and BCG. The incidence of TB almost halved in the subsequent decade, but this progress appears to have stalled and cases have risen slightly following the Covid pandemic. The UK is considered by the WHO to be a low-incidence country. However, in England in 2020 there were 1091 UK-born individuals with TB, the majority (68%) of whom had pulmonary disease. It follows that UK-born

people are likely to be more infectious because they have a higher incidence of pulmonary TB.

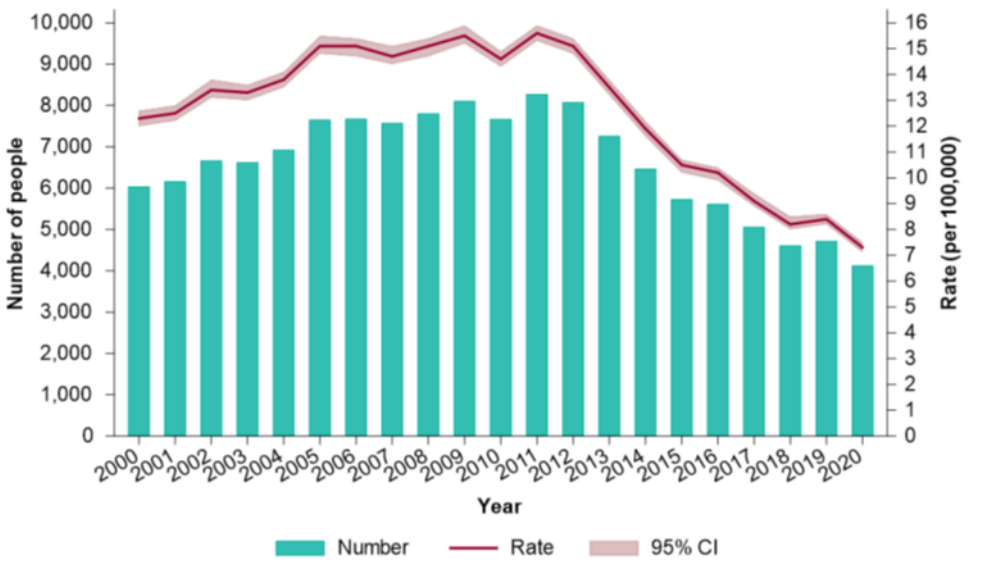


Figure 1. TB cases and rates in England (2000-2020)

Like the rest of the UK, the pattern of disease in Wales is predominantly seen in non-UK born people in conurbations and is a mixture of pulmonary and non-pulmonary disease. The latest report on tuberculosis in Wales published in 2019 documents a steady decline in incidence with case numbers for the whole of Wales now around 100 per annum (Fig 2). Like the rest of the UK, the pattern of disease in Wales is predominantly seen in non-UK born people in conurbations and is a mixture of pulmonary and non-pulmonary.

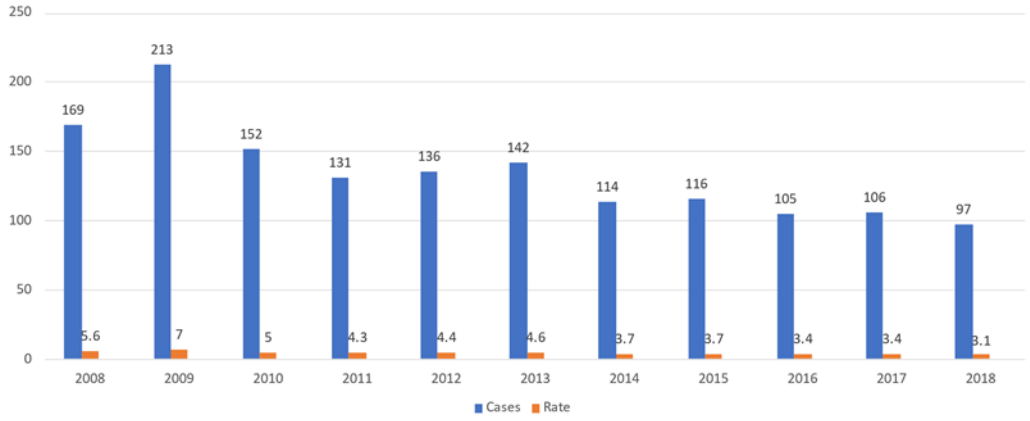


Figure 2. TB cases and rates in Wales 2008-2018

TB case rates are very low in Hywel Dda compared with other parts of England and Wales but they are not negligible (Fig 3). Peaks occurred in 2004, 2006, 2012 and 2014.

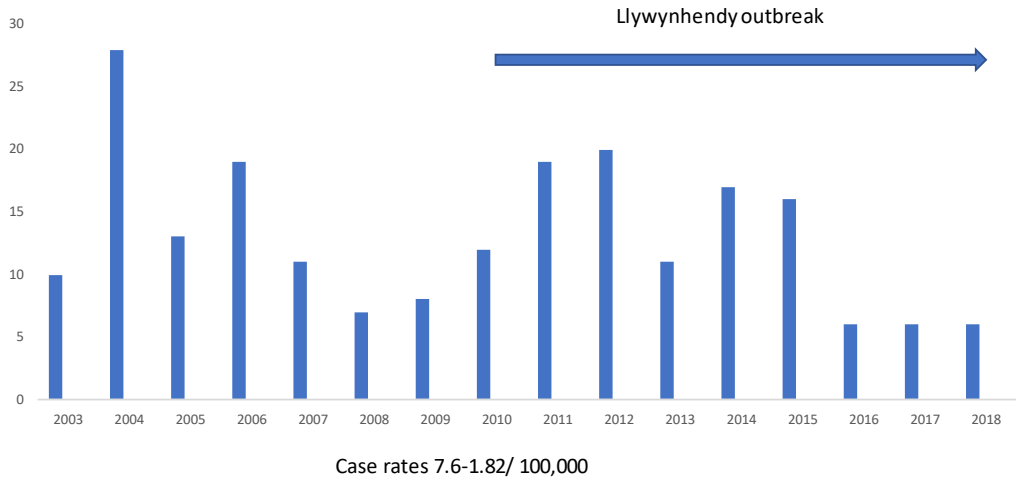


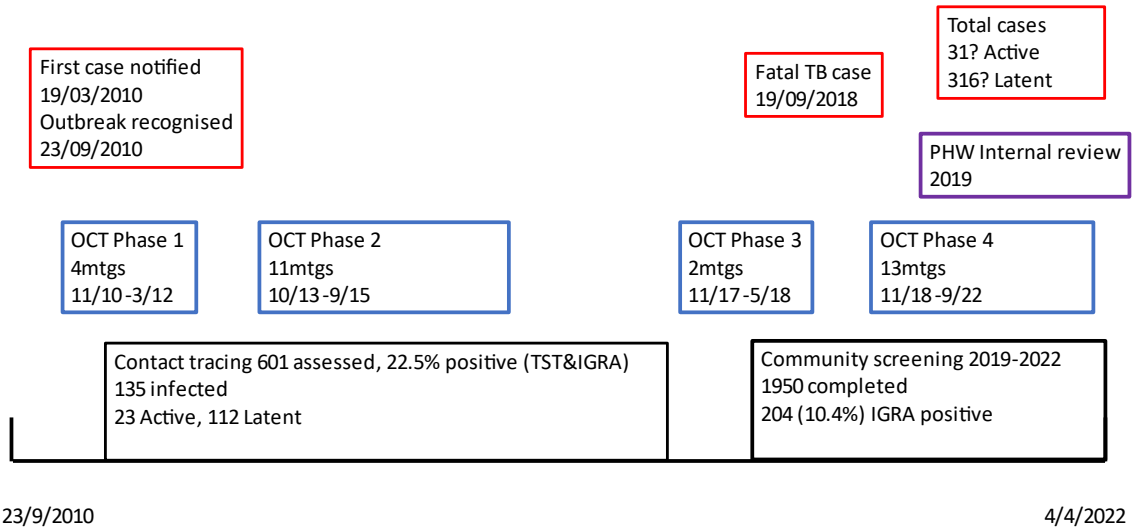
Fig 3. Hywel Dda (Pop 384,000. TB case nos 2003-2018)

3. The Llwynhendy Outbreak

The first case in the outbreak was notified in March 2010. Two further cases were subsequently identified and an outbreak was suspected in September 2010 and confirmed at an outbreak control team meeting on 11th October 2010. The source of the outbreak (the index case) was considered to be an individual worker of a public house in Llwynhendy though it remains uncertain how they acquired the infection. A case with a similar type of TB organism had occurred elsewhere in Carmarthenshire in 2005 but had no known links to the index case. A further case in 2007 later identified by whole genome sequencing (WGS) may have had links to the public house. The exact numbers affected by the Llwynhendy outbreak are not clear but could be at least 31 cases of active disease. Confusion about exact number has arisen because in some cases culture was not available to confirm the strain and because the case numbering throughout the outbreak was inconsistent, sometimes including the 2005 case that was later deemed to be unrelated to the Llwynhendy outbreak. Cases of TB with known connections to a local public house in Llwynhendy continued to be identified up until July 2020 for the active cases and April 2022 for the last latent case. The review has not considered any cases which may have come to light since March 2022 when the review was initiated. The geographical spread of cases related to the outbreak was predominantly local but some cases extended to Swansea Bay and beyond.

The response to the outbreak was overseen by an outbreak control team (OCT) containing clinical and public health personnel. The outbreak investigation was opened and closed three times resulting in four phases of team meetings between 2010 and 2022 (Fig 4 below).

Outbreak events



4. Case definitions and microbiological typing

There is no precise definition of an "outbreak" but it is taken to be more than two cases with epidemiological and microbiological links to a discrete source. In this case, the worker was considered to be the index case and their contacts would account for the subsequent spread of infection and further escalation of the outbreak. To trace the course of an outbreak the epidemiological evidence is linked to the microbiological strain of the infecting organism to ascertain that it is the same organism that is passed on. At the beginning of the outbreak the microbiological identification used was called MIRU-VNTR which is a PCR based technique for genotyping the organism. In this case the genotype is described by number as 32333 2432515324 which is a strain that had previously been isolated in the West Midlands in 2006 but not necessarily linked to the outbreak in Wales.

During the course of the Llwynhendy outbreak MIRU-VNTR typing has been superseded by whole genome sequencing (WGS) which is a higher resolution technique to confirm identity or near-identity between two strains of the causative organism, Mycobacterium tuberculosis (MTB). WGS would now be considered the gold standard for identification of the bacterial

strain related to an outbreak and is now routine in Wales. We now know that 18 of the outbreak cases with positive cultures have been further characterised by WGS though some of the earlier samples were not suitable for further analysis.

5. Rationale for an external review

The outbreak of TB in Llwynhendy has continued for over a decade and cases are still presenting. Furthermore, the necessity for population screening has resulted in local and national publicity. A fatal case of TB has also drawn attention to the outbreak. In 2019, a formal complaint about the conduct of the outbreak management was received by Hywel Dda UHB and PHW. This resulted in an internal inquiry and de-brief. Consequently, a decision was made to obtain an independent review of the outbreak management from its initial recognition to the present day. The purpose of the review is set out in the terms of reference (appendix 1). The review should identify lessons learned and make recommendations.

6. Conduct of the review

Members of the review panel are listed in the appendix and include clinical experts on tuberculosis, contact tracing, microbiology and public health. Virtual meetings took place over six months between March and September 2022. All relevant and available documents (see appendix) were reviewed over this period. In addition, a number of individuals, connected to the outbreak, were interviewed (see appendix) though we did not attempt to contact those involved at the beginning who had retired or left employment. A site visit to Prince Philip Hospital, Llanelli, took place on the 3rd August 2022 to examine the available clinical records of all cases diagnosed with active TB and their contacts. The panel was provided with administrative and organisational support by Hywel Dda University Health Board (HDUHB) and by Public Health Wales (PHW.) The review was jointly commissioned

by PHW and HDUHB but no members of either organisation were involved in the discussions of the panel.

7. Findings

The outbreak was first recognised in September 2010 when a cluster of similar cases of TB were identified with a connection to a public house in Llwynhendy. Formal designation as an outbreak followed with the formation of the first outbreak control team meeting on the 9th November 2010. Over the subsequent 12 years, the outbreak management was opened and closed on three occasions leading to four phases of the outbreak to be considered. To date there have been a total of 30 outbreak control meetings. For each phase, the aspects to be considered are:

- The case definition and microbiological context
- The public health response
- The organisational response
- Contact tracing
- Clinical management
- Resource constraints

The first case that appears to be genuinely related to the public house in Llwynhendy source was a 71 yr old female who presented in February 2010 with a three-month history characteristic of pulmonary TB. The diagnosis was confirmed on 19th March 2010. Two further cases with links to the public house in Llwynhendy were diagnosed later in July and in August 2010. These two cases reported symptoms dating from the beginning of the year. Over the years, the local incidence of TB in the area has fluctuated but cases with historical contact with the public house in Llwynhendy continued to appear. The total number of cases related to the outbreak is not clear because not all the cases had microbiological cultures that could

confirm linkage to the index strain of MTB. It is possible that as many as 35 active cases were related to the outbreak in addition to the many others, known and unknown, who are harbouring latent disease.

Phase 1 (November 2010-March 2012)

The first phase lasted from November 2010 to March 2012 and included four OCT meetings. It finished on 28th March 2012 when the outbreak was closed. There were four meetings during that period and attendees at OCTs were noted. Each OCT was chaired appropriately by the local consultant in communicable disease control (CCDC) who was a PHW employee and contained some additional representation from PHW and HDUHB.

Case definition

The initial case definition was agreed as a case of TB within the Llwynhendy area with links to the public house in Llwynhendy or any of the current cases. The cases were also characterised by the MIRU-VNTR typing (32333 2432515324). It is important to note that this strain of organism had, at the time, also been identified in 15 cases of TB in the previous 5 years in Wales. Four of these cases had been in Carmarthenshire. Although the MIRU-VNTR typings are known to suggest an outbreak they would now be considered to be less reliable than WGS and SNP distance. It is possible that some of the early cases where only MIRU typing was available may not in fact have been related. This strain, or a closely related strain therefore had been identified sporadically in England and Wales prior to the Llwynhendy outbreak and was not unique.

Contact tracing

A number of individuals considered to be at high risk of infection were invited for screening. This included family members, bar staff and members of the peripatetic darts team associated with pubs in the area.

A follow up OCT meeting took place three months later and described the results of 16 people who had attended screening, noting that 5 invitees had not attended. On this occasion, 3 of the screened subjects had positive

evidence of TB infection but no active cases were found at this stage. Meanwhile, a number of other cases of TB in the wider area were recorded but not felt to be related to the public house in Llwynhendy. It was agreed that GPs should be alerted and a statement was prepared for the media.

It was more than six months before the next OCT was held at which it was recorded that further family members of the index case had TB, some latent and some active TB. It was noted that at that stage the communication with GPs had not taken place and the statement to the media had not been taken up by the press. Further extended paediatric family screening was recommended but it was not thought necessary to screen adult contacts outside the family.

The final OCT meeting in this phase took place six months later in March 2012. In the absence of any new cases, the outbreak was considered closed at this point.

The Panel's view

The outbreak was identified promptly by microbiological surveillance once the initial patients were diagnosed. In this case, as in other outbreaks, individual patients had prolonged symptoms prior to diagnosis. This is a consequence of poor awareness of symptoms by the public and by health care professionals. We did not have access to primary care records to judge at what level this lack of awareness occurred.

The OCT was set up directly, was appropriately constituted and was chaired by a senior public health consultant. Three further OCT meetings were held but the frequency (six months between meetings) suggested that the team did not feel that the outbreak was likely to become as serious as it did. The later meetings had fewer attendees and the additional senior physical presence from PHW appears to have drifted away.

Outbreak Control Team record

The minutes of the four meetings of the first phase were available for review. There is also a draft outbreak report available, but the panel was

unable to identify a final report from the first phase. Compared to subsequent phase documentation, the minutes did not clearly identify proposed actions and when they were suggested, they were not followed through. The total number of active cases in the outbreak at this stage is also difficult to ascertain because patients infected with organisms of similar genetic typing or with lack of culture are sometimes included in the figures.

Contact tracing record

We were able to review the contact tracing paperwork for adult but not paediatric cases. In the initial phases documentation was considered poor and inconsistent. The contact tracing itself also lacked a systematic approach. Some contacts were screened either too early or after too much delay. The immune response to MTB may take up to 6 weeks to develop. The contacts who were screened early and had a negative test were not always recalled for repeat screening after 6-8 weeks. In addition, people who were identified as high-risk contacts who did not attend screening, including the darts team, were not physically pursued.

Overview of Phase 1

The Panel's view was that the initial public health management of the outbreak could have been better. The approach lacked a comprehensive strategic overview and was too casual but may in other circumstances have been adequate had the index case not been so infectious. It was obvious in retrospect that the index case was highly infectious as evident from the initial high rate of transmission (18.6% overall). The contact tracing focussed primarily on the family rather than the public house customers. There may also have been relevant environmental factors around the ventilation and extraction in the public house in Llwynhendy, but they were, apparently, unexplored. The extent of the contact screening was obviously too limited and there may have been a failure to appreciate the social interactions of pub customers who would regularly visit several other pubs. Lack of follow up of the darts team may also have reduced the effectiveness

of screening. The local services at the time were also under strain associated with the service reorganisation. The medical services were stretched because of staff shortages with locums in place and no defined TB service or lead clinician. The contact tracing will have been performed either by local respiratory nurses or by PHW nurses working in unfamiliar territory. It is possible that there was a lot more contact tracing activity going on in the background, but this is not recorded in the minutes. It is also clear that there was a lack of awareness in the local population of the illness and the need for contact tracing. It may be the case that there was a reluctance for people to come forward because of the stigma associated with TB or perhaps for other unexplored reasons. Whatever the factors involved, the initial management failed to contain the outbreak and cases with connections to the public house were still presenting with active disease over a decade later.

Phase 2 (October 2013-September 2015)

The outbreak control team was reconvened in October 2013 in response to five further cases of TB with links to the public house in Llwynhendy bringing the total at that stage to 14 cases. One of the new cases was a teaching assistant at a local comprehensive school. Eleven meetings were held in this phase until they appeared to peter out without a formal declaration of an end to the outbreak. As before, the team included environmental and public health, microbiology, and specialist nursing and medical support. On this occasion the meetings were chaired by an acting consultant in Health Protection.

Case definition

The case definition was widened to include any case of TB from the Carmarthenshire area with onset since 2009 and a VNTR profile of 32333. This definition may have been too broad given that microbiological intelligence relayed in the minutes suggested that there had been 115 cases, apparently unrelated, with a similar typing identified in England and Wales.

Contact tracing

At this point, it was realised that the contact screening from the outset had been inadequate, so plans were put in place to revisit and repeat the screening of the original contacts. The darts team were finally tracked down and agreed to co-operate. It was recognised that much of the social interaction between cases and the darts team may have extended to a second public house.

The OCT subsequently became aware of a case of TB in the local secondary school (Ysgol y Strade). Initially it was reasonably assumed that the school case must be related to the Llwynhendy outbreak, but the subsequent typing showed that the organism was unrelated. In retrospect, it may have been better at that point to hold a separate OCT for the school cluster because the school screening process continued to cause confusion when it was discussed alongside the Llwynhendy cases. There was also some concern that local resources may have been inadequate particularly regarding specialist nurses. At this juncture, Dr Carol Llewellyn-Jones agreed to take the lead role for the TB clinical service in Hywel Dda. There was now recognition that there was sustained transmission of TB in the community and further clinical cases with the Llwynhendy characteristic would continue to surface. It is of note that at this juncture, the services were dealing with six other cases/clusters of TB in Carmarthenshire.

At the time of the last OCT meeting in September 2015, a further two cases (one latent) with links to the public house had been identified but extensive contact tracing was deemed unnecessary because of the lack of close contacts. Although the Llwynhendy outbreak was not formally closed at this point, no further meetings occurred.

An interim, but not final, outbreak report for the first two phases was available to the panel. At that point, the outbreak included 19 cases of active disease though this number may have included some cases with

different typing that were not therefore related to the original index source case.

The Panel's view

In the second phase, public health management seemed to have improved with clearer actions, leadership and a recognition that the original contact tracing in phase 1 may well have been inadequate. It also became clear that there was continuing multi-source transmission of TB in Carmarthenshire with an organism that had allegedly spread into the area from England along the M4 corridor. Other cases and clusters with different strains were also occurring simultaneously in West Wales. The possibility that a community screening response would be required in future was considered at that point because the contemporary school outbreak in Llanelli may have been linked. This should, in retrospect, have been dealt with as a separate outbreak team. However, until the organism's strain was identified as different, the team were correct to assume that a link to Llwynhendy was highly likely. Cases with links to the pub were still presenting so it is not clear why the OCT meetings were discontinued in September 2015.

Phase 3 (November 2017- April 18)

The outbreak team was recalled for a further two meetings due to the occurrence of a new case with links to the public house via their parents both of whom had previously had TB. The case was further complicated because they had worked in a care home whilst symptomatic. The case had screened negative by tuberculin skin test three years earlier. TB screening was completed for the family and care home staff and residents. Wider screening was also considered but not pursued at this stage. No evidence of ongoing transmission was discovered so this was not pursued but GPs in the area were alerted and reminded to be vigilant.

The Panel's view

The response to the new case was handled correctly and documentation was clear. The ongoing risk of future cases was recognised and surveillance continued.

Phase 4 (November 2018- present)

The outbreak team was recalled in November 2018 because of three deaths associated with infection by the outbreak strain. One case, with no obvious direct link to the public house in Llwynhendy was a person with no significant prior illness but who died suddenly with sepsis without having started treatment for known pulmonary TB. The two other deaths in the area were people on treatment for TB but both had serious underlying disease (cardiac failure and lung cancer). In those two cases, TB was not listed on the death certificate as the primary cause of death. At this juncture 24 active cases were considered to be part of the outbreak centred on the public house. Three further cases with the same MIRU-VNTR typing but with no epidemiological link were not considered to be part of the outbreak. Five of the 24 cases were thought be responsible for onward transmission. A review of the outbreak resulted in the conclusion that the high level of onward transmission and prevalence of latent TB now justified widespread community screening which was subsequently commissioned. It was also agreed that the age cut off for treatment for latent TB be extended from 35yrs to 65yrs in line with the recently amended NICE guidelines. The last OCT meeting minutes to which we had access was in February 2022 at which the outbreak was summarised but not formally declared over. We understand that a further OCT meeting took place in September 2022.

The Panel's view

Outbreak control meetings in phases three and four were chaired by an experienced public health consultant. The documentation was now clear, with proposed actions defined and followed up in subsequent meetings. The contact tracing of active cases was thorough. The decision making and policy changes are all appropriate and the move towards community

screening was timely and correct both to assess the extent of the community risk and in order to allay public anxiety.

Community Screening

The OCT correctly took the view that to settle the concerns and to identify the extent of infection in the community, a population screening programme was necessary. This work was outsourced to an organisation called Find and Trace supported by Oxford Immunotec who were responsible for the phlebotomy and IGRA testing. The screened population included those who had not attended for previous contact tracing or had done so prior to the 2016 NICE guidance change. In addition, anyone with a link to a local public house in Llwynhendy between 2005 and 2018 was invited along together with anyone, not previously identified, who believed that they had had contact with someone with TB prior to their treatment.

Two community screening sessions were held, one in June and one in September 2019 in convenient settings. In the first session 1188 people had IGRA testing with 76 positive results (6.4%). At the second session 772 people were tested and 128 (16.6 %) were positive for latent TB. The majority (94%) of those screened were born in the UK. The prevalence of latent TB in both cohorts was substantially higher than the UK average. The strongest factor associated with a positive IGRA was frequenting a local public house in Llwynhendy in the period 2009-10. The difference between the positivity rates in the two screening sessions can be explained by the fact that more targeted invitations to come forward were issued in the second phase.

Approximately 300 identified contacts who did not come forward for the community sessions continue to be invited to the TB service clinics. It is not known how many of these remain to be assessed but we are assured that the catch up is on-going.

Clinical TB Service in Hywel Dda

At the beginning of the outbreak there was no formal or co-ordinated clinical TB service in Hywel Dda. Cases will have been dealt with as they presented by members of the respiratory team of consultants. At the time there was a lot of instability in the medical manpower due to organisational change and to the inability to recruit to permanent consultant posts. Contact tracing was undertaken by a general respiratory nurse though at the onset of the outbreak in Llwynhendy, nurses from Public Health Wales were drafted in to assist.

As a consequence of the outbreak, a funded session was established in 2014 with the appointment of Dr Llewellyn Jones as the lead physician for TB, assisted by her general respiratory nurse and based in Carmarthen. Clinics were held approximately every two weeks according to demand but less frequently if the consultant was on leave. In case of urgency, patients may also have been referred though the lung cancer pathway or via A&E and then referred on to the clinic after diagnosis. In 2019, further funding was found to appoint Kelly Goddard as the first dedicated TB nurse. At all times, contact tracing and home visiting has also been supported by PHW nurses. Dr Llewellyn Jones has now retired and her duties have been taken over by Dr Gareth Collier who continues with the same model of service.

Panel's view

There has been a significant improvement in the care of patients with TB and their contacts since the appointment of Dr Llewellyn Jones as lead clinician. She has developed the service and dealt with several outbreaks as well as Llwynhendy and continued to mop up the residual contacts from the community screening programme. There remain some resource issues which continue to hamper the team. One problem is the lack of annual leave cover which leaves the TB service exposed when the consultant or nurse is on leave. This can lead to a delay in starting treatment. Other shortfalls include the lack of formal administrative assistance, sufficient pharmacy support to allow DOT/VOT supervision and phlebotomy. We

understand that the latter has now been addressed by the appointment of a phlebotomist. Adequate and dedicated administrative support will also help to ensure an efficient service and take some pressure off the team.

Although the incidence of active TB in Hywel Dda is low, the workload is still significant by virtue of the ongoing contact tracing and supervision of treatment for latent TB. There are in addition, developing issues over refugee and immigrant populations as well as the emergence of drug resistance and non-tuberculous mycobacterial disease (NTM).

Review of the clinical cases

The panel were able to review the clinical records of 26 from a total 37 patients. Some notes were not available because patients were deceased with records destroyed or were resident outside Hywel Dda. All the cases we reviewed had pulmonary tuberculosis, eleven of whom had a positive smear and were therefore contagious. The duration of symptoms ranged from one week to seven months with a median of 133 days (the median delay in presentation in England is 79 days). In this instance, the highly infectious index case had symptoms for seven months prior to diagnosis. Once diagnosed, we found that appropriate treatment was generally prompt and completed. Eight of the outbreak cases had TB listed as a cause or association with death. Of the records the Panel were able to examine, the majority had TB as an incidental feature and had primarily died from other serious illness including cancer, cardiac disease, alcoholic cirrhosis and co-morbidity associated with immunosuppression. Only in one case was it clear that TB was the primary cause of death but in this instance, although diagnosis was relatively prompt, treatment was delayed by a short period. During this time, there was a temporary suspension of the TB service due to lack of annual leave cover. The subsequent clinical course for this patient, deteriorated surprisingly rapidly and may have been complicated by additional sepsis.

Clinical guidelines

There are no specific Welsh TB clinical guidelines for TB and recent NICE guidelines are not formally endorsed in Wales. In the absence of country-specific documents, the common practice has been to follow the BTS and subsequent NICE guidelines. There are repeated references in the minutes of the OCT meetings to the need for adherence to the contemporary versions of these guidelines. This is particularly relevant to management of latent TB where advice changed in 2016 to offer preventative treatment not only to those under 35 years but also to the 35-65 age group. The panel was persuaded that clinicians in Wales adopted the same guidelines as the rest of the United Kingdom.

Health Board and Public Health Wales interaction

The responsibility for the management of an outbreak of infectious disease lies initially with the Health Board and the local Director of Public Health. Public Health Wales provides oversight and practical support where necessary. These obligations are set out in the statutory establishment orders for both organisations from 2009. The first outbreak control policy from PHW was published in 2011 and the latest update in 2022. These policies are largely generic but do cover food and water-borne outbreaks in more detail. There is a PHW standard operating policy for TB case management published in 2017 but this does not cover OCT conduct. In early part of the outbreak, expert representatives from PHW were members of the initial outbreak control team but it appears as though their presence was not sustained through the later meetings of phase 1 and may not have contributed to all the decisions made. It appears that no senior representative from PHW or the local director of public health at the time were present for the final two meetings of Phase 1. Obviously, it is possible that communication was going on in the background by email or by other means. PHW nurses were helpfully deployed on the ground to help with contact tracing. In the later phases, the outbreak team was chaired by an

experienced PHW consultant (Dr Brendon Mason) and this was reflected in a substantial improvement in the management of the outbreak.

The Panel was puzzled by the absence of any reference to the outbreak in minutes of the meetings of either HDUHB or PHW Board until 2019. It appears that it was not until press interest in the fatality in 2018 and the community screening programme and a written complaint to PHW the following year that the outbreak was formally discussed at board level. It is possible that some discussion did take place within the executive team. The subsequent board discussion included the offer of some resource to HDUHB for the community screening. PHW were dealing with at least two other TB outbreaks and the beginning of the COVID pandemic at the time. The HDUHB Board minutes in January 2020 outlined the steps to be taken to contain the Llwynhendy outbreak. This included continuation of the screening offer, especially to children, the treatment of latent TB cases and an offer of BCG immunisation to those who tested negative if under 35 years of age.

PHW Internal reviews

Stimulated by a formal complaint to PHW about the failure to control the outbreak, an internal review was undertaken. This took the form of a brief examination of the relevant documents by the medical director and by an experienced non-executive director. This internal review was followed by two de-briefing sessions to audit the performance of PHW in the outbreak. The internal review identified failings in the initial public health response and raised questions about the interaction between PHW and the Health Board. In addition, there was some uncertainty about the involvement, or otherwise of Welsh Government in the process and the lack of a structured system to specifically manage outbreaks of TB disease and infection.

The de-brief sessions resulted in a number of practical recommendations to be taken forward, though the Panel wondered if any of these have been implemented. Many of these recommendations are endorsed by this Panel.

This internal review did not address the wider national issues about control of TB, for example by National Cohort Review or a National Plan for Wales.

Other reviews

The panel were grateful to Dr Brendon Mason who not only chaired the later phases of the OCT but also compiled several analyses of the outbreak. These included the epidemiology, the transmission risk and an investigation of the associated deaths. The analysis was particularly helpful in identifying the initial high risk of transmission from the index case (70% of close contacts and 20% of social contacts that were screened). This confirms the associated environment and the sputum smear status of the index case as a "super spreader" risk. This conclusion might have been reached much earlier in the outbreak.

The National Picture

Historically, respiratory disease has always been prominent in the experience of the people of Wales. The legacy of tuberculosis, miners lung disease and the association of respiratory disease with poverty has left a lasting impression. The Welsh Government has supported a Respiratory Health Delivery Plan since 2018. This includes a section on the better management of TB because although the rates of infection are lower in Wales, it appears as if the mortality rate is higher than elsewhere in the UK. The Delivery Plan has expanded the National Cohort Review Programme which has been running on an unofficial basis since 2012. The cohort review offers consensus on all cases derived from the UK enhanced surveillance system (ETS) and meets quarterly. It can also offer advice on dealing with drug resistance, new immigrant screening and management of difficult cases. The scheme now has representation from medical and nursing staff in all health boards, though not all have funded formal sessions for TB. HDUHB has been contributing to the cohort review since Dr Llewellyn Jones assumed her role in 2015.

One other product of the Delivery Plan has been a proposal for a Welsh National Plan for Tuberculosis, including a new policy for migrants. The

proposal, "Tuberculosis Strategy and Service Specification for Wales 2021-2026" was written by Dr Gwen Lowe (a PHW employee) on behalf of the Delivery Group. This document was submitted to the Welsh Government for consideration more than 12 months ago, but so far, no formal response has been received. In contrast, the NHS in England has had a formal collaborative (NHSE and UKHSA) strategy for the control of tuberculosis in place since 2015.

8. Conclusions

The outbreak of human tuberculosis, which was first identified in Llwynhendy in 2010, continues to cause concern now, more than a decade later. The relevant strain of MTB is not unique to the outbreak which was centred on a public house but has also been recorded elsewhere in the UK. The index case in the outbreak had suffered prolonged symptoms before diagnosis and was highly infectious in a social environment that would predictably have led to high levels of transmission. As a result, there have been at least 31(30 individuals) cases of active pulmonary TB and at least 300 cases of latent TB infection. Retrospective review of the available samples with culture and WGS typing identified 18 proven cases over the duration of the outbreak. Over the years, the outbreak response has resulted in the tracing of 663 individual contacts and a community screening programme, which tested 1950 people. The latter exercise demonstrated a surprisingly high level of TB infection in the local population (average 11%) which was highest in people who had historical contact with the public house in Llwynhendy or the index case. Although we cannot be certain that the high level of TB infection in the community is all related to the outbreak, it does suggest that there is a high risk of community outbreak in the future.

The pattern of TB in West Wales is different from the usual pattern seen in the UK. The cases that the panel have examined are predominantly UK born

people all of whom had pulmonary disease. This differs from the common presentation in urban Britain where most cases occur in the non-UK-born and about half of whom have TB outside the lungs. This difference in demography in West Wales may result in delays in diagnosis and therefore in increased transmission of disease until there is a higher level of medical and public awareness.

TB Background

Wales has low rates of TB that are generally confined to urban areas but despite the low incidence, the death rates are twice as high as England. The national rate of TB is falling but no figures are available beyond 2018. The incidence of active TB in Hywel Dda is very low but has continued to fluctuate. As explained above, the cases do not fit the same pattern as seen elsewhere in the UK. Continued vigilance is therefore required by health professionals and the public to guard against future outbreaks. We noted a reluctance amongst some contacts in the population caught up in the outbreak to co-operate with the contact tracing process.

Medical services environment at the onset of the outbreak

At the time of the outbreak the medical services were in flux during a period of service mergers and hospital re-arrangements. The respiratory service was struggling with consultant vacancies requiring locums to plug the gaps. In addition, there was no designated TB lead consultant or dedicated TB nurse to run a disease specific service.

Initial outbreak management

The initial outbreak management was inadequate. The cluster of cases was picked up promptly by microbiology and the first OTC meeting was timely but later meetings were held infrequently and seemed to lack a sense of urgency. The record keeping was poor and unstructured. The membership of the OCT was inconsistent and it appears as if the additional representation from PHW and the local DPH drifted away leaving the OCT short of experienced advice. It was clear quite early on that the index case was highly infectious yet contact tracing was limited to family and close

social contacts. The physical environment of the pub was highly conducive to respiratory transmission, but this appears to have been unexplored. There was a failure to understand the role of social interactions between customers in the public house in Llwynhendy and other public houses as well as a possible role of the travelling darts team in wider dissemination of TB disease and infection. The outbreak control team was terminated prematurely perhaps failing to appreciate the super spreader nature of the outbreak. There was also a failure to appreciate that a much wider contact tracing net was required amongst non-household contacts. It is possible that a contact tracing team more familiar with local behaviour patterns may have acted differently.

The appearance of further cases initiated a second phase of outbreak control meetings and the performance and record keeping improved. However, the OCT was complicated by the simultaneous and ultimately unrelated school outbreak. This may have resulted in a loss of focus on the original problem. There was recognition that further cases were likely to arise but, inexplicably, the meetings petered out without any arrangement either to continue or to close the outbreak.

The outbreak team was recalled when a further case led to a fatality. From that point on, the OCT meetings of phases 3 and 4 had adequate senior leadership and representation. It was realised eventually that a community screening exercise was required to explore the extent of the outbreak and to bring it under control.

Clinical case management

As previously mentioned, in Hywel Dda there was no formal TB service until 2014 and no dedicated TB nurse until 2019. The situation has now improved significantly with the leadership of Dr Llewellyn Jones and her successor, Dr Gareth Collier. Prior to her appointment, the cases were treated by a variety of respiratory consultants though as far as we can tell, the treatment was adequate and timely, once the diagnosis had been made.

There is concern that cases do still go unrecognised in the community because of the underlying lack of awareness amongst primary care staff and the public.

It was clear from our inspection of the records that there was a high level of co-morbid illness amongst people who developed TB. This may reflect the underlying health inequalities in the community. The people who died with a current or prior diagnosis of TB with one exception, had serious underlying illnesses that were the primary cause of death. In the one fatal case where TB was the primary cause of death, there were factors leading to a short delay of treatment.

Systemic factors

It was clear that HDUHB was responsible via the Director of Public Health for the initial management of the outbreak and delegated to the CCDC. The role of PHW was to provide oversight, expertise and additional resource when required. The first response to the outbreak was flawed and the responsibilities did not seem clearly defined. From the third phase, PHW seemed to have a stronger influence on events. Neither Board appeared to have knowledge of the outbreak until 2019. The internal reviews commissioned by PHW came to similar conclusions to this panel but could have done so earlier with heightened awareness from the beginning. In addition, we would have expected PHW to take a lead role in determining protocols and national policy for TB along the lines of the Health Security Agency in England. Instead, this seems to have been left to the specialty-led Delivery Group who have run the cohort review and proposed a national plan. PHW has had some involvement in the latter.

9. Recommendations

(1) The outbreak has not yet concluded and the high level of latent TB infection in the population implies further risk. This risk is heightened because the active disease in this population is

predominantly pulmonary and therefore more infectious. Although the level of active TB infection is low in West Wales, delayed presentation in unrecognised cases may lead to further outbreaks and deaths. The level of awareness amongst the public and their health care professionals must be therefore increased and maintained. This also applies to trainee health professionals.

(2) Any future outbreaks should be overseen by PHW from the outset with a TB -specific standard operating procedure for the conduct and recording of outbreak management. The current SOP and OCT policy needs to be updated in this respect. The latter needs to be developed alongside modern data analysis and WGS typing so that outbreaks are identified and contained. Comprehensive contact networks of all cases should be recorded electronically and plotted with social network analyses undertaken to ensure links between cases are uncovered quickly and easily.

(3) Funding should be identifiable ahead of time for outbreaks of infectious diseases so that such outbreaks can be managed in a timely and effective manner without the need for time-wasting discussion.

(4) The local TB service has improved but still has inadequacies. In particular, cross-cover arrangements need to be in place for annual, sick and study leave in order to prevent delays in treatment. Pharmacy and administrative support needs improvement. Succession planning for the TB Specialist Nurse also needs to be clear.

(5) At a national level, the Cohort Review Programme needs to be supported with adequate funding for each contributing health board.

(6) Welsh Government should support both the Cohort Review Programme and the proposal for a National Service Specification that includes the development of a TB pathway to tackle delayed diagnosis (e.g. investigating cough lasting longer than three weeks).

(7) Wales does not seem to be properly prepared for the challenges of new migrants, refugees, and the occurrence of future drug resistance. These factors should be included in a future TB plan supported and funded by Welsh Government.

Panel membership

Professor Michael Morgan (Chair)

Consultant respiratory physician, University Hospitals of Leicester NHS Trust. Honorary Professor, University of Leicester.

Alison Blake

Lead Nurse for Community TB service, Cornwall Partnership NHS Foundation Trust

Professor Graham Bothamley

Honorary Professor and Consultant Physician, Homerton University Hospital, Queen Mary University and London School of Hygiene and Tropical Medicine

Professor Onn Min Kon

Chair of the Joint Tuberculosis Committee, Consultant Physician, St Mary's Hospital, London

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TB Health Protection Nurse, National TB Unit, UK Health Security Agency.

Dr Sophia Makki

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Dr Esther Robinson

Head of TB Unit & Clinical Lead, National Mycobacterial Reference Service, UK Health Security Agency

Document list

OCT minutes November 2009- September 2022

HDUHB Board minutes

PHW Board minutes

HDUHB TB Operational Group minutes

Dr Brendon Mason's reports and analysis

PHW Internal Reports and De-briefs

Welsh Respiratory Delivery Group National Cohort Review reports

Proposal for a Tuberculosis Strategy and Service Specification for Wales 2021-2026

All Wales TB annual report 2019

Draft Outbreak reports 2011 & 2015

PHW Situation Summary 2022

Outbreak meeting attendance record

Community screening report

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Dr Brendon Mason

Dr Carol Llewellyn Jones

Dr Gareth Collier

Professor Kier Lewis

Kelly Goddard

Dr Ian Campbell

Brendon Scott & Prof Al Story

Dr Simon Barry

Dr Quentin Sandifer

Dr Mark Temple

An External Review of the Llwynhendy Tuberculosis Outbreak
Terms of Reference

1. Scope

1.1 An outbreak of *M. tuberculosis* (TB) centred on the Llwynhendy electoral ward in Carmarthenshire, West Wales was first declared in November 2010. Since then an outbreak control team (OCT) has been convened and stood down three times. In November 2018 an OCT was reconvened for the fourth time. This is now delivering a staged approach to community screening, which is ongoing.

1.2 The Boards of Public Health Wales and Hywel Dda University Health Board wish to examine whether the outbreak has been managed optimally including whether contact tracing should have been extended at an earlier stage, and whether the clinical care provided to cases was optimal, and if these affected the extent and impact of the outbreak.

1.3 Public Health Wales and Hywel Dda University Health Board have agreed to jointly commission an independent external review to examine these questions as well as to identify the lessons learned from the response to this outbreak and to provide assurance of the current arrangements.

1.4 The review will cover the management of the outbreak from November 2010, when first declared, until the present time (August 2021), to identify the actions that have been taken in response to lessons identified.

2. Purpose

2.1 The purpose of the Review is to examine:

- Whether the management of the outbreak since 2010 overall, and at each stage, was conducted in accordance with best practice guidance in place at the time of each phase of the outbreak (with reference to national strategies, strategies in other parts of the UK, WHO guidance, plans, guidelines and organisational protocols and procedures);

- The effectiveness of the respective involvement of Public Health Wales and Hywel Dda University Health Board in the control of the outbreak and treatment of latent or active TB cases at each stage (including the current phase) including the people and financial resources provided by both organisations in response to the outbreak to prevent disease transmission and treat identified TB disease;

- The governance arrangements (including reporting and escalation) for informing Teams and Boards of the outbreak and providing assurance to the Boards of each organisation;

- A review of any reported cases of: 1. People identified over the course of the outbreak who have died where the death certificate identified that TB contributed to or caused the death, and 2. People that have developed active TB;

- The effectiveness of any policy(ies) relevant to TB disease prevention, treatment and control including the management of outbreaks applicable in Wales in each phase of the outbreak and the reporting arrangements within Wales since the outbreak was first declared in 2010;

- The effectiveness of external expert advice sought and obtained including liaison with other organisations, for example, Public Health England (and UK Health Security Agency from October 2021) or the British Thoracic Society.

2.2 The review should identify lessons learned and make recommendations to Public Health Wales and Hywel Dda University Health Board for improvement. There may also be recommendations for other key stakeholders.

3. Reporting and Accountability

3.1 The Executive Medical Director at Public Health Wales and the Executive Medical Director at Hywel Dda University Health Board will be the joint Executive sponsors of the review and are accountable to their Boards for the delivery of the Reviewers' report(s).

3.2 The priority of both organisations at the present time is to continue to manage the outbreak and not distract attention or divert resources from that objective.

3.3 The sponsors would like the review to proceed at pace and are therefore looking to receive an interim Reviewers' report(s) by the end of February 2022 (indicative) with the view to have a preliminary discussion with the Chairs of the Boards and Chief Executives of both organisations prior to a final report being submitted to and presented at the respective Boards no later than May 2022, with an expectation of a report to QSIAC by the end of March.

3.4 The Executive sponsors will prepare a joint SBAR for the respective Boards to support the review panel's final report.

3.5 The Reviewer(s) may wish to establish short duration task and finish groups on specific matters of enquiry as and when necessary, for example, a mortality review group and both organisations will give reasonable consideration to requests for any associated necessary resources.

3.6 The Review Project team will report regularly (monthly) on progress of the review to the Executive Sponsor and Executive Team in each organisation.

3.7 If, in the course of the Review, matters are identified that require immediate and urgent action on grounds of public health or quality and safety of clinical care, then these will be raised, in the first instance, with the Executive Sponsors of the Review to determine whether urgent actions are required.

4. Membership of the review team

4.1 The Reviewers are expected to include:

- A senior public health specialist with expertise in health protection including outbreak control and ideally with demonstrable knowledge of tuberculosis as a public health issue.
- A senior respiratory medicine specialist with expertise in tuberculosis disease.
- A respiratory nurse specialist with expertise in tuberculosis disease.
- A senior microbiologist with expertise in TB diagnosis and expertise in public health microbiology.
- Lay Member: An independent lay representative from a national organisation that has an interest in the treatment and control of tuberculosis and patient outcomes.

The review panel will be chaired by Professor Mike Morgan, previously NHS England's National Clinical Director for Respiratory Disease.

5. Resources to support the review

The commissioning organisations will agree a reasonable request from the reviewers for the resources, human and otherwise, needed to deliver the review. It is expected that this will include access to relevant premises and facilities to conduct necessary activities (meetings etc.); administrative support to assist document retrieval and management, arranging interviews, and the preparation of (a) report(s); retrieval and preparation of case records to support a mortality review; and project management to deliver the review.

A Project team will be established to support the review panel. The Project team will be led by a Project manager and will include administrative support, Communications and Information and Communications Technology. The Chair of the Review Panel will work closely with the Project Team to ensure adequate support to the review and review panel members.

6. Communications and publication of review findings

6.1 The review is undertaken as part of the legal duty of candour for Public Health Wales and Hywel Dda University Health Board and accordingly, the communication and dissemination of the findings will adopt an open and transparent approach.

6.2 A joint Communications Strategy will be agreed by both Public Health Wales and Hywel Dda University Health Board, that will define the end-to-end process from the initiation of the review to the publication of the findings.

6.3 The Communication Strategy will include consideration of the needs of key stakeholders, including members of the public, individuals and families directly affected, Welsh Government, Health Boards, Community Health Councils and Local Authorities.

6.4 A joint Communications Plan will include details on plans for publication, including indicative timelines for public meetings and meetings with those directly affected. Where required, earlier contact will be made with individuals and families affected.