This document represents a synopsis of key issues and major discussion points arising from the Public Health Infections Research workshop held in December 2009. The outcomes of the workshop will inform the strategy document prepared for consideration by OSCHR.

1 BACKGROUND

Public health infections research is one of four priority areas identified under the Office for the Strategic Coordination of Health Research (OSCHR) public health work stream. The National Institute for Health Research (NIHR) has been tasked with leadership of the development of a public health infection strategy and the Medical Research Council (MRC) is working with NIHR on its development.

The primary aim of the strategy is to deliver a vision for an integrated national approach to infectious disease research that reflects the public health needs of the UK and also the relative strengths of the UK health research community. The objective is to provide a clear statement of the research opportunities in the field to inform funding priorities and policy development.

To achieve this, a four phase review process will engage with relevant experts and stakeholders in the UK infection research community and gather views on what the key research questions of the future might be and how they might be tackled. A Scientific Advisory Group has also been convened, to have oversight of the process, chaired by Professor Jon Friedland (membership in Appendix 1).

The review process leading to the development of a strategy will involve:

**Phase I:** scoping exercise and production of a landscaping document analysing the major public health and infectious disease publications which have been produced over the last ten years (Appendix 2).
Phase II: consultation with scientific leaders in infections research to gather views on what the key public health infection priorities are in the UK.

Phase III: a workshop to engage with the infectious disease research community.

Phase IV: development of the final public health infections research strategy and dissemination to all stakeholder groups.

**PHASE III WORKSHOP**

*Aims of the workshop:*

- To discuss the needs and opportunities in public health infections research
- To define key research areas and questions that should form strategic priorities within the OSCHR framework
- Advise on how the identified research priorities might be taken forward

**METHODOLOGY**

Infectious disease experts spanning a range of disciplines were identified in consultation with members of the Scientific Advisory Group, MRC and NIHR staff, and invited to attend the workshop. In total 60 leading UK scientists (both academic and industrial) took part in the two day workshop (Appendix 3 for attendee list and meeting agenda).

The workshop was structured around an opening session where ‘spotlight’ reviews of potential research target areas were given by invited speakers. These were followed by a series of break out group discussion sessions whose remit was to consider the needs and opportunities in public health infectious disease research and to refine these into strategic priorities within the OSCHR framework. The workshop followed the following format:

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This report summarises the major discussion points and outcomes arising from each stage of the workshop.
2 WORKSHOP SYNOPSIS

2.1 Introduction

The workshop commenced with a presentation describing the work of the public health infections research review to date (Appendix 4). The presentation explained that through the work of the Scientific Advisory Group and the initial landscaping exercise (Phase I), five recurrent infectious disease priorities had been highlighted as posing a significant public health burden in the UK.

For each disease area an expert in the field was identified and invited to give a presentation at the workshop addressing the following main points:

1. The nature of the public health threat/challenge
2. UK research strengths
3. UK weaknesses and needs
4. Possible research priorities

The five disease areas identified and introduced were:

- Healthcare associated infections (Professor Alison Holmes)
- Antimicrobial resistance (Professor Brian Duerden)
- Emerging and resurgent infections (Professor Neil Ferguson)
- Sexually transmitted infections and HIV (Professor Graham Hart)
- Severe infections: GI, CNS and respiratory infections (Professor David Dockrell)

The full set of presentations from the workshop can be found in Appendix 5. The following summarises the main points addressed in each presentation.

Healthcare associated infections (Appendix 5a)

1. The public health threat/challenges
   - Scope includes all healthcare, not just acute care, and involves healthcare staff/workforce as well as patients
   - Critical component in addressing the problem of antimicrobial resistance
   - World Health Organization priority and a Global Challenge of major societal and political interest
- Opportunities for prevention exist, often through relatively simple solutions

2. **UK research strengths**
   - Large research collaborations are already being undertaken (e.g. UK Clinical Research Collaboration (UKCRC) Translational Infection Research Initiative) and considerable investment has already been made

3. **UK weaknesses and needs**
   - Need to build capacity in healthcare economics
   - Need for better surveillance/better use of collected data
   - Low levels of prevention and health services research
   - Opportunities for cross-boundary research across the healthcare sector and multidisciplinary research approaches are missed

4. **Possible research priorities**
   - Improved understanding of the natural history of pathogens and modes of transmission
   - Improved surveillance of existing and potential new pathogens
   - Technological innovation: development of new, rapid screening and diagnostic kits; intelligent healthcare environment design
   - Development of new treatments (e.g. vaccines against hospital infections)
   - Patient management and behavioural interventions

**Antimicrobial resistance (Appendix 5b)**

1. **The public health threat/challenges**
   - Importance of antimicrobial resistance was recognised 40 years ago yet it is still acknowledged as a major priority and relatively little progress has been made, the pipeline for new antimicrobials is very poor

2. **UK research strengths**
   - Significant investment and research has been undertaken

3. **UK weaknesses and needs**
   - Need for new antimicrobial agents
- Need to understand resistance mechanisms and to preserve the use of existing agents as far as possible
- Need to explore alternative approaches (e.g. immune stimulation/modulation, promotion of flora)
- Surveillance, including antibiotic prescribing and outcome data

4. Possible research priorities
- Identification of new antimicrobial agents and how to use them
- Circumvent resistance
- Improve the evidence base for changing practice

Emerging and re-emerging infections (Appendix 5c)

1. The public health threat/challenges
- Pandemic: global epidemic of a new disease – the effect on society can be profound
- Often starts with a zoonosis mutating to be transmissible (e.g. influenza, HIV, SARS)
- Risk may be increasing due to habitat encroachment, higher human/livestock densities
- Re-emerging infections represent a fundamentally different challenge to emerging infections as they involve known agents; generally predictable (e.g. dengue fever)

2. UK research strengths
- ‘Tropical medicine’ strong research
- Reference centre for veterinary medicine
- Virology: good basic research and clinical research
- Epidemiology and modelling
- Healthcare and public health: surveillance good due to centralised public health service

3. UK weaknesses and needs
- Virus diagnostics/discovery: in particular integrated with field studies
- Limited integration of veterinary and human virology and epidemiology
- High global connectivity
- Rapidity of commissioning/implementing real-time clinical research
- Connectivity across government in a public health crisis
- Public – private partnerships in public health crisis (e.g. rapid engagement of pharmaceutical industry in a public health crisis)

4. Possible research priorities
- Characterise threats and reservoirs
- Sustainable surveillance – benefit sharing with developing countries
- Quantitative understanding of predictors of emergence
- Genetic determinants of transmissibility, virulence and species for major threats
- Compound screening, development of generic antivirals and vaccine technologies, rapid manufacturing facilities
- Protocols for ultra-rapid clinical research and development and emergency use authorisation of novel treatments/vaccines
- Behavioural/social science research on risk communication, compliance in a public health emergency
- Rapid response research

Sexually transmitted infections and HIV (Appendix 5d)

1. The public health threat/challenges
   - A changed sexual health/HIV paradigm has emerged

2. UK research strengths
   - Good surveillance: trends, populations, new and emerging infections
   - Leadership in well-phenotyped patient cohorts in HIV: natural history; toxicity and resistance; guideline development
   - High quality and timely observational studies
   - Trials expertise for global health – use for UK prevention and treatment?

3. Possible research priorities
   - Reduction in STI/HIV incidence, including wider and improved diagnosis
   - Behaviour of populations and strategies to reduce risk behaviour
   - Ecology of organisms: basic public health science (e.g. pathogenesis, epidemiology, surveillance resistance)
   - Prevention, in particular primary prevention (e.g. social marketing) and secondary (e.g. early diagnosis and treatment) strategies
Severe infections (Appendix 5e)

1. The public health threat/challenges
   - Respiratory infections including: pneumonia; influenza; viral respiratory tract infections e.g. Respiratory Syncytial Virus
   - Gastrointestinal infections: including invasive salmonella; healthcare associated infections such as Clostridium difficile; E. coli O157; economic costs due to closure of schools, hospital wards e.g. noravirus
   - Neurological infections e.g. meningitis; pneumococcal meningitis
   - Severe infections are a leading cause of death, in particular in children and other vulnerable groups

2. UK research strengths
   - Epidemiology e.g. Health Protection Agency networks, public health system, infection control
   - Microbiology: genome sequencing, molecular microbiology
   - Host factors: genetics of susceptibility; innate immunity
   - Modelling
   - Translation: vaccinology; UK Clinical Research Networks (UKCRN)

3 & 4. UK weaknesses and needs/research priorities
   - Containment of antimicrobial resistance (e.g. Acinetobacter baumanii in HCAI pneumonia)
   - Vaccine efficacy in select groups
   - Rapid diagnostics to identify microbial or host signatures
   - Immunomodulatory therapy (e.g. inability to deliver in sepsis)

2.2 Breakout Group Discussion Session 1

The workshop attendees were split into five break out groups with participants mixed across a range of different research areas and disciplines. To stimulate discussion a matrix was developed to explore potential strategic research areas and interactions, this is shown in Figure 1 below. Each group was asked to consider the following questions:
   - What are the key needs and opportunities in public health research in terms of impact on health, scientific progress, the economy or society?
   - Are the major needs reflected within the three dimensional matrix?
Figure 1. 3-D Strategy Matrix

The major points from all the discussions are summarised below:

**Needs and opportunities in public health infection research**

- Target vulnerable groups across the life course, including the very young and very old
- Focus on high risk populations e.g. drug users, migrants, prisoners
- Development of new treatment strategies e.g. antimicrobials, alternatives to antimicrobials, to combat HCAIs and severe and emerging infections
- Innate immunity: what keeps people well, use this knowledge as a basis for new preventative and treatment modalities
- Development of new research methodologies e.g. link genotype to phenotype; modelling
- Development of new technologies: early diagnosis, rapid diagnosis, infrastructure, hospital design, point of care diagnostics
- Chronic infections: an unrecognised need
- Preparedness for pandemics/outbreak control
- Development of cohorts and evaluation of outcomes e.g. for acute infections cohorts would not need to be long term
• Behaviour and prevention: social interventions; prevention of new chronic infections; identify undiagnosed individuals; how to reach difficult groups; understand how people take medicines (e.g. vaccine uptake, self management of infections, antibiotic use)

• Promotion of science-led partnership to tackle key research priorities, including joined up working with government agencies, academia-industry partnerships and the interface of animal and human infections

2.3 Review and Synthesis of Discussions
The groups’ discussions raised a number of key points in relation to the development of the overall strategy:

• The five identified target disease areas were agreed by the group to be important, but recognised to have significant overlap with each other. The disease areas do not, however, catch all infections of public health importance e.g. chronic infections

• Across all the disease areas there are a number of ‘cross-cutting’ themes which represent a broader range of opportunities for a research agenda which addresses the breadth of the public health burden

• The research strategy should harness the strengths of fundamental (basic) research to address the need to improve human health

The recurrent priority areas to come out of the discussions therefore led to a radical reworking of the discussion matrix (Figure 1). Rather than focusing a research strategy on the previously identified five disease areas, it was proposed that the public health infections research agenda should be tackled through three major strategic research approaches which cut across the target research areas:

1. Research tools and technologies which address and determine phenotype/genotype
   - Diagnostics
   - Molecular epidemiology
   - Stratified clinical trials/experimental medicine – modelling
2. Research capabilities
- A research culture that can and will identify cases at point of care
- Development of cohorts and evaluation of outcomes

3. Alternative approaches/Novel paradigms
- Understanding resilience to infection
- Develop non-pathogen specific treatment- e.g. modulation of inflammatory response, innate immunity, etc
- New therapeutic uses for monoclonal antibodies
- Renewed effort for new antimicrobials
- Treatment as prevention (for chronic infection inc HIV)

2.4 Break out Group Discussion Session 2
With the proposed new Strategic Research Approaches identified, the workshop attendees were again split into five groups and tasked to identify what the key overarching research questions are that should be addressed. The following summarises the main priorities which emerged from the discussions.

Key overarching research priorities:
- Improve the diagnosis and detection of infectious agents and relate this to treatment and outcomes
- Increase and broaden interventions used against infectious diseases e.g. new vaccines, development of novel antimicrobials, use of information technology for surveillance
- Population level studies of infection to understand behavioural influences on health outcomes
- Understand the basis of transmission during outbreaks through applying molecular tools
- Understand and control chronic infections
- Develop the capacity to monitor public health in real-time
- Rapid response to new infections and threats
- Capacity to use novel technologies (e.g. host pathogen genetics, molecular diagnostics, epidemiology, e-health, data linkage)
- Target groups where the public health need is the greatest:
burden of disease in terms of morbidity and mortality falls on the very young and elderly
- vulnerable groups (e.g. disadvantaged, recent migrants)
- New systems and developing material cohorts
  - How safe are our hospitals? How safe are interventions in our hospitals?
- Understand host response and resilience to infection

3. Overall conclusions
The workshop concluded with a general discussion summarising the key issues and points raised during the meeting.
- Infectious disease research is of fundamental importance to the health of the UK population, numerous reviews over the last ten years had advocated a variety of initiatives but there remained a lack of clarity on research priorities and how they might be addressed
- Preparedness for outbreaks remains a vital capability for the UK, and for the UK in relation to global health: there was a need to develop the capacity to respond quickly when an outbreak occurs
- This included the capability for real-time clinical and behavioural research and public health surveillance
- There needed to be a focus on renewing efforts to develop and utilise novel technologies and approaches, both in detecting infection (rapid or point of care diagnosis) and defining host /pathogen relationships.
- Understanding the host response, including resilience, vaccine efficacy, response to treatment and adverse effects
- The development of novel or alternative treatment strategies, focussing in particular on non-pathogen specific approaches, such as reducing inflammation or promoting innate immunity or the natural flora
- The development of new prevention strategies: understanding and targeting transmission at a variety of levels (zoonosis, hospital setting, community level), encouraging behavioural change, or combining rapid diagnosis with treatment.
- To focus on where the problems lie: safety of vulnerable groupings
- The need to embrace the ‘one-medicine agenda’ (e.g. importance of zoonoses) and to collaborate with a broader range of stakeholders across a range of disciplines
4. Next steps

The outcomes and discussion points from the workshop will be further discussed and refined in consultation with the Public Health Infections Scientific Advisory Group to develop an integrated national strategy for infectious disease research.

5. Appendices

Appendix 1 Membership of the Public Health Infections Scientific Advisory Group

Appendix 2 Public Health Infection Research Review and Figure 1: Timeline of selected public health infectious disease publications and reviews: 1998–present

Appendix 3 Agenda of Public Health Infections Research Strategy Workshop held on 16th & 17th December 2009 and Attendees’ list

Appendix 4 Introductory presentation: Aims of the Workshop and Setting the Scene

Appendix 5 Presentations on Needs and Opportunities in Public Health Infections Research
   5a Health Care Associated Infections
   5b Antimicrobials: the public health challenge of antibacterial resistance
   5c Emerging and resurging infections
   5d STI & HIV research for Improved Population Sexual Health
   5e Severe infections: respiratory, CNS and gastrointestinal
# Public Health Infections Scientific Advisory Group Membership

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1 BACKGROUND AND PURPOSE OF THE REVIEW
In February 2009 the Medical Research Council and Department of Health, through the Office for the Strategic Coordination of Health Research (OSCHR), initiated a strategic review of public health infectious disease research in the UK.

The primary aim of the review is to deliver a vision for an integrated national approach to infectious disease research that reflects the public health needs of the UK and also the relative strengths of the UK health research community.

To achieve this, the review process will engage with relevant experts and stakeholders in the UK infection research community and gather views on what the key research questions of the future might be and how they might be tackled. Specifically, the review will involve a four phase process:

**Phase I**: scoping exercise and production of a review document analysing the major public health and infectious disease publications which have been produced over the last ten years.

**Phase II**: consultation with scientific leaders in infection research to gather views on what the key public health infection priorities are in the UK.

**Phase III**: a workshop to engage with the infectious disease research community.

**Phase IV**: development of the final public health infection research strategy and dissemination to all stakeholder groups.

This document represents the outcome of Phase I and its purpose is to summarise the infectious disease issues and research priorities highlighted in major government publications and reviews published over the last ten years. Furthermore, the background information contained within the review will provide a framework for the phase II expert consultation exercise.
PHASE I LITERATURE REVIEW

Scope of the review
The public health infection research review has focused exclusively on human infectious diseases of public health relevance to the UK population. Zoonoses were included due to their relevance to human health\(^1\). The review does not include the broad area of immunology or animal and plant infectious diseases.

Public health was defined as ‘the science and art of preventing disease, prolonging life and promoting health through the organised efforts of society\(^2\). This definition was described in the Public Health in England report by Sir Donald Acheson in 1988, and it is widely recognised as reflecting the essential focus of modern public health\(^2\).

Infectious diseases were defined as diseases which result from transmissible agents including bacteria, viruses, parasites, fungi and prions\(^1,3\).

Methodology
The literature review was conducted as a desk-based consultation exercise. The aims were to assess the current state of the UK public health infection landscape, identify the major infectious disease problems and categorise them into broad priority areas, and to highlight any research priorities described in previous reports. To achieve this, the approach taken was to research, analyse and review all the major public health infection reviews, reports and strategy documents published over the last ten years. The sources of evidence reviewed included:

- Government White papers
- House of Lords Select Committee reviews
- Health Protection Agency publications including disease surveillance reports, annual reviews
- House of Commons Health Committee reviews
- Reviews from major funding bodies including the Wellcome Trust, the Biotechnology and Biological Sciences Research Council (BBSRC), the Medical Research Council (MRC), UK Clinical Research Collaboration (UKCRC)
- Department of Health publications including Chief Medical Officer reports, national strategy documents, annual reviews
- Foresight Infectious Diseases Project reports
- Expert panel/committee publications including annual reports, minutes of meetings
- Other relevant reports, committee minutes and peer-reviewed scientific papers
A full list of the evidence reviewed in this project may be found in Appendix I. Furthermore, in order to provide an overview of the evidence reviewed and its significance to public health infection priorities today, a detailed timeline summarising the publication dates of the major review documents is illustrated in Figure 1.
2 INFECTIOUS DISEASES IN THE UK

‘Complacency is perhaps the cardinal sin for those charged with protecting public health. Infectious diseases, once thought conquered, are always marshalling their forces ready to strike back in the face of reduced vigilance. Recent years have demonstrated the remarkable potential for nature to generate new threats particularly when major changes are taking place in the human habitat and behaviour’.

Sir Liam Donaldson, Chief Medical Officer writing in the Journal of the Royal Society for the Promotion of Health 2001: 146-151

Background
Throughout history, infectious diseases have posed a major threat to human health, wellbeing and survival\(^2,3\). In the late nineteenth and early twentieth centuries considerable progress was made in tackling infectious disease epidemics through major sanitary reforms\(^2\). Clean water, improved sanitation, a reduction in overcrowding and nutritional improvement served to dramatically reduce the death rates\(^2\). In the twentieth century the introduction of vaccination programmes, antibiotics and new drugs further reduced the number of deaths and by the late 1960s there was optimism that infectious diseases were under control and would no longer pose a threat to human health\(^2,4\).

This optimism was unfortunately misplaced\(^2,4\). New threats from previously unidentified pathogens such as human immunodeficiency virus (HIV) and severe acute respiratory syndrome (SARS) have emerged; diseases previously thought to be under control such as tuberculosis have shown a resurgence in incidence; and antimicrobial resistance has arisen as a global health problem\(^2,4,5\).

The burden of infectious disease
Infectious diseases are estimated to account for about a quarter of all deaths worldwide, approximately 13 million each year\(^6\), with the five main causes of death being lower respiratory tract infections, HIV, diarrhoeal diseases, tuberculosis and malaria\(^4,6\). Furthermore, infectious diseases are responsible for over a quarter of the world’s morbidity, as measured by disability-adjusted life years (DALYs)\(^4\).

In the UK, infectious diseases represent a significant burden, constituting the top four reasons for primary care consultations and being implicated as a causal factor in about 10% of all deaths\(^5\). The annual cost of treating infectious diseases in England has been
estimated to be around £6 billion per year, with primary care bearing the greatest burden of the cost at £3.5 billion per annum\(^5\) (Figure 1).

**Figure 1. Estimated annual cost of treating infections in England (£)\(^5\)**

![Diagram showing the cost of treating infections in England](image)

### The nature of the disease threat

The evidence base reviewed for this project was used to determine the nature of the current public health infectious disease threat in the UK (see Appendix I). On the basis of the recurrent issues and priorities mentioned in the reviewed documents, five broad categories of disease emerged as posing significant threats to human health:

- Healthcare associated infections
- Antimicrobial resistance
- Emerging infections
- Sexually transmitted infections and HIV
- Acute respiratory infections

In the chapters that follow the public health importance of each of these categories is described in terms of the burden of the disease, the nature of the disease threat and the microorganisms responsible. In addition, a summary of the research priorities identified in previous reviews is presented as a publication timeline in order to stimulate thinking about where the possible research priorities of the future may lie.
3 HEALTHCARE ASSOCIATED INFECTIONS (HCAI)

Background
Healthcare Associated Infections (HCAIs) are widely recognised as making a significant contribution to the overall burden of infectious diseases in the UK. Identified as one of the areas needing intensified control measures in the Chief Medical Officer’s infectious disease strategy for England, Getting Ahead of the Curve, a set of national priorities for healthcare associated infection were subsequently described in the Chief Medical Officer’s report Winning Ways: working together to reduce hospital healthcare associated infection in England.

Key points about Healthcare Associated Infections:
- At any one time 8 per cent of hospital patients has an infection caught in hospital
- The effects of HCAIs range from discomfort for the patient, to prolonged or permanent disability and in a small number of cases, death
- There are at least 300,000 hospital acquired infections a year
- They are estimated to cost the NHS around £1 billion a year
- The old and young and those with compromised immune systems are most at risk
- The two strongest risk factors are the degree of underlying illness and the use of medical devices or invasive diagnostics
- Concern surrounds the increasing number and frequency of infections resistant to common antibiotics
- With good infection control practice and careful hygiene measures it has been estimated that around 15 – 30% of infections could be avoided

Over the last decade, the increasing prevalence of HCAIs and a number of high profile outbreaks have fuelled a considerable amount of public concern and intense political pressure. Considerable investment, improved hygiene measures, increased surveillance and performance management have contributed to start to improve the situation, but tackling healthcare associated infections through improving cleanliness remains a key national priority for the NHS as re-emphasised in the NHS Operating Framework for 2009-10.
The nature of the disease threat

Healthcare Associated Infections can be defined as infections which occur as a result of healthcare interventions, either in patients undergoing an intervention, or in healthcare workers involved in the interventions\(^1\). They can arise from a wide range of microorganisms (bacteria, fungi, protozoa, viruses) which in turn can cause a range of different diseases. The most common are those affecting the lower respiratory tract including pneumonia, gastrointestinal system, the urinary tract, surgical wounds and skin and soft tissue\(^4\) (Figure 1).

![Figure 1. Types of Healthcare Associated Infections](image)

Source: Third National Prevalence Survey of HCAI in acute hospitals in 2006\(^4\).

Infections result from a complex interplay between the microorganism, the patient and the environment, where factors such as the virulence or transmissibility of the organism, the vulnerability of the patient (immune-compromised, age, frailty) and infection hazards associated with the environment interact\(^9\).

The microorganisms involved in HCAI can arise from either the patient themselves (endogenous infection) or from other patients or healthcare workers (cross-infection), with spread occurring by contact (hands, clothing, equipment etc) or airborne routes\(^9\). It is important to note that not all HCAI can be eliminated and the aim of infection control should be to minimise the number of infections.
Microorganisms responsible for HCAI
The Department of Health has given high priority to reducing healthcare associated infections\textsuperscript{10,11} and have specifically targeted Meticillin Resistant \textit{Staphylococcus aureus} (MRSA) and \textit{Clostridium difficile} in their HCAI Strategy for 2008, \textit{Clean, Safe Care}\textsuperscript{12}.

\textbf{Meticillin Resistant \textit{Staphylococcus aureus} profile}

- About 30\% of the healthy population have some type of \textit{S. aureus} living naturally on their skin or in their nose\textsuperscript{12}
- Increases length of hospital stay by 10 additional days, impacting on the cost burden\textsuperscript{12}
- In 2007 a total of 1,517 death certificates mentioned MRSA, while 433 gave it as the underlying cause of death\textsuperscript{13}
- Transmitted mainly through contact with colonised skin or contaminated equipment\textsuperscript{12}
- Key risk of serious bloodstream infection is through piercing of skin (e.g. cannula, open wounds)\textsuperscript{12}
- In 2004 the Government set a target for a 50\% reduction in MRSA bacteraemia (bloodstream infection by MRSA) by 2008, which surveillance data indicates has been achieved\textsuperscript{9,11}

\textbf{Clostridium difficile profile}

- Bacterium which lives in gut of about 3\% of healthy adults in England\textsuperscript{12}
- Causes diarrhoea, which can be very severe and occasionally life threatening\textsuperscript{12}
- On average, increases hospital stay by 21 days\textsuperscript{12}
- In 2007 a total of 7,916 death certificates mentioned \textit{C. difficile}, with 3,875 recording it as the underlying cause of death\textsuperscript{14}
- Transmitted through contact with spores from infected faeces, or contact with contaminated environment and equipment\textsuperscript{12}
- Spores survive well in the environment\textsuperscript{12}
- Screening for colonised patients is inappropriate\textsuperscript{12}
- High profile failings at Stoke Mandeville Hospital and Maidstone and Tunbridge Wells NHS Trust
- New Government target to reduce infection numbers by 30\% by 2011
- World’s first vaccine against \textit{C. difficile} entered clinical trials in March 2009. The vaccine is owned by Sanofi Pasteur, and was originally developed by Cambridge based biotech firm Acambis.
In addition to MRSA and C. difficile it is important not to lose sight of the many other microorganisms which have the potential to cause harm and severe disruption such as norovirus and other emerging HCAI pathogens such as Acinetobacter baumannii, glycopeptides-resistant enterococci (GRE), Candida spp, coagulase negative staphylococci and multi-resistant gram negative rods\textsuperscript{9}.

**Norovirus profile\textsuperscript{9}**

- Most commonly detected pathogen both in sporadic cases and outbreaks of gastroenteritis
- Not serious, short-lived infection but uncomfortable
- Highly infectious
- Wintertime seasonality
- Outbreaks affect healthcare facilities globally, and cause massive disruption to provision of care
- Main control is through ward closure which in epidemic years may cost NHS inpatient services in excess of £100 million
- Virus is evolving and the emergence of variants that escape population immunity are associated with epidemic seasons
- No national reporting scheme for surveillance

Furthermore, the results of the third prevalence survey of HCAI in acute NHS Trusts\textsuperscript{4} (Figure 4) indicates the common areas of infection risk, which clearly warrant further attention and infection control management.

**Key points surgical site infections (SSI)\textsuperscript{9}**

- Account for 14\% of all HCAIs
- Associated with considerable morbidity
- On average SSI double length of hospital stay
- S. aureus is the most common microorganism causing SSI and MRSA accounts for 64\% of these infections
- Work is under way to extend surveillance of SSI to include the period after discharge from hospital.

Finally, the Steering Group on HCAI in their final report\textsuperscript{15} highlighted the importance of broadening the current UK surveillance measures to include the following microbes of emerging public health importance:

- Panton Valentine Leukocidin-positive (PVL) *Staphylococcus aureus*, which has caused widespread problems in other countries such as the USA.
• *Acinetobacter* spp, traditionally an opportunistic pathogen, these bacteria will have an increasing role to play as patients vulnerable to infection through their illness or treatment grows⁹.
• ESBL (Extended-Spectrum Beta-Lactamase)-producing *E. coli* are antibiotic-resistant strains of *E. coli* (resistant to cephalosporin antibiotic).

**Healthcare Associated Infection research priorities**

The Chief Medical Officer’s Report, *Winning ways*³ identified the importance of high quality Research and Development as a means of ensuring that technological breakthroughs in prevention and control are rapidly translated into patient benefit. The report included a number of research priorities for HCAI (Table 1). Further research priorities were identified in a UKCRC Challenge Workshop on HCAI and antimicrobial resistance in 2007¹⁷. The workshop was sponsored by the Medical Research Council and Department of Health and engaged key research communities with the issue of HCAI and antimicrobial resistance. The primary aim was to identify major research issues and discuss responses which could make a significant clinical and public health impact (Table 1).

**Drug and vaccine development**

The Chief Medical Officer’s infectious disease strategy, *Getting Ahead of the Curve*, identified the need for research to be conducted to develop new drugs and vaccines to combat and prevent healthcare associated infections². This was reemphasised in the Department of Health’s healthcare associated infection action plan, *Winning ways*, which called for further research to determine the feasibility of vaccines to prevent HCAI³ (Table 1).
Table 1: Timeline summarising HCAI research priorities identified in previous reviews and reports

<table>
<thead>
<tr>
<th>Major review (author/title)</th>
<th>Date</th>
<th>Research priorities/ recommendations</th>
<th>Achieved/outcome</th>
</tr>
</thead>
</table>
| Department of Health:       | 2002 | - Formulate an action plan to identify HCAI disease priorities  
                            |       | - Research to develop new drugs and vaccines to combat and prevent HCAI  
                            |       | Action plan published in 2003 *Winning ways: working together to reduce HCAI* |
| Getting Ahead of the Curve² |      |                                      |                  |
| Department of Health:       | 2003 | - Formulation of a national research strategy to address gaps in current scientific and clinical knowledge about how to reduce healthcare associated infections  
                            |       | - Explore and exploit the potential of molecular methods to improve infection control  
                            |       | - Research funding partners to contribute to an integrated research programme  
                            |       | - Establish a research network for healthcare associated infection  
                            |       | - Wider use of epidemiological modelling techniques to assess HCAI control strategies  
                            |       | - Establish a rapid review process to assess new procedures and products for which claims of effectiveness are made of their ability to prevent or control HCAI  
                            |       | - Determine the feasibility of vaccines to prevent HCAI  
                            |       | UKCRC translational research initiative  
                            |       | HCAI Research Network established in 2006, management of the initiative was contracted to the Richard Wells Research Centre, Thames Valley University London.  
                            |       | Rapid review panel was set up in 2004 to review new HCAI related technologies¹² |
| Winning ways: working       |      |                                      |                  |
| together to reduce HCAI³    |      |                                      |                  |
| **UK Clinical Research Collaboration (UKCRC): UKCRC challenge workshop on HCAI and antimicrobial resistance**<sup>17</sup> | **2007** | - Link basic and applied research in the area of healthcare associated infections to deliver improvements in clinical care  
- Complex intervention studies as a methodological assessment of clinical interventions  
- Develop and deliver improvements in health systems research  
- Promote and support multi-disciplinary research  
- Develop new diagnostic tools for use at point of care  
- Better assessment of the impact of behaviour of both patients and practitioners on the incidence and control of HCAIs and antimicrobial resistance  
- Public engagement at all levels from local issues to development of national research priorities |
| --- | --- | --- |
| **Department of Health: Clean, safe care**<sup>12</sup> | **2008** | - High priority given to reducing healthcare associated infections, specifically targeting MRSA and *C. difficile*  
- Innovation priorities set for designing better hospital equipment and furniture |
4 ANTIMICROBIAL RESISTANCE

Background
Antimicrobial resistance is a growing and serious threat to the treatment and control of infectious diseases worldwide\(^1\). In the UK, the nature and significance of the threat was illustrated in reports from the House of Lords Science and Technology Select Committee\(^2,3\) and in the Standing Medical Advisory Committee’s report, *The Path of Least Resistance*\(^4\). Combating the increasing prevalence of antimicrobial resistance has become a major public health priority in the UK\(^4,5,6,7,8\) and a *UK Antimicrobial Resistance Strategy* action plan was launched in 2000\(^6\).

<table>
<thead>
<tr>
<th>Key points about Antimicrobial Resistance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ranked in the top three future risks to human health in the Foresight Infectious Diseases project(^14)</td>
</tr>
<tr>
<td>- It is not a new phenomenon; shortly after penicillin came into widespread use, a resistant strain of <em>Staphylococcus aureus</em> emerged(^9)</td>
</tr>
<tr>
<td>- Naturally occurring phenomenon(^4,7)</td>
</tr>
<tr>
<td>- Increases clinical complications, length of hospital stay and adds to costs(^4)</td>
</tr>
<tr>
<td>- Alternative drugs may be more toxic, less effective or more expensive(^4)</td>
</tr>
<tr>
<td>- Often associated with Healthcare Associated Infections (HCAI) such as the high profile Meticillin Resistant <em>Staphylococcus aureus</em> (MRSA), but it also includes community infections e.g. <em>Streptococcus pneumonia</em>, <em>Nesseria gonorrhoeae</em></td>
</tr>
<tr>
<td>- Resistance to a single type of drug is problematic; but bacteria can pick up many resistance genes, eventually acquiring resistant to multiple antibiotics</td>
</tr>
<tr>
<td>- Multidrug resistance may lead to some conditions becoming untreatable (^4)</td>
</tr>
<tr>
<td>- Development of new antimicrobials is limited(^4)</td>
</tr>
</tbody>
</table>

The emergence of so called ‘super bugs’ resistant to multiple antibiotics has attracted much media attention and public concern. The importance of measures to control antimicrobial resistance was reemphasised by the Chief Medical Officer in the infectious disease strategy for England, *Getting Ahead of the Curve*\(^7\), and the prudent use of use of antibiotics was identified as a key mechanism for combating the escalating problem in *Winning Ways*\(^8\). Recent public health programmes have been aimed at decreasing the
unnecessary use of antimicrobials\textsuperscript{10} and the Department of Health have re-launched their awareness campaign in 2009 to encourage more prudent use of antibiotics\textsuperscript{11}.

Table 1. UK use of antibiotics

<table>
<thead>
<tr>
<th>Where antibiotics are used</th>
<th>Types of use</th>
<th>Questionable use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human use (50%)</td>
<td>20% hospitals</td>
<td>20 – 50% unnecessary</td>
</tr>
<tr>
<td></td>
<td>80% community</td>
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<tr>
<td>Agricultural use (50%)</td>
<td>20% therapeutic</td>
<td>40 – 80% questionable</td>
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<tr>
<td></td>
<td>80% prophylactic / growth promotion\textsuperscript{*}</td>
<td></td>
</tr>
</tbody>
</table>


\textsuperscript{*}Use of antibacterials for growth promotion in animals was banned EU-wide in 2006.

The nature of the disease threat

Antimicrobial resistance describes the ability of a microorganism (bacteria, virus, fungi or protozoa) to resist the action of antimicrobial drugs\textsuperscript{13}. The development of resistance is a natural phenomenon, arising through natural selection\textsuperscript{1,4}. Antimicrobial resistance may arise by genetic mutations, by incorporating genes from other organisms or by natural selection of inherently resistant organisms\textsuperscript{4,14}. Resistance can occur by one of three routes: altering the molecule targeted by the antimicrobial agent, or using an alternative; deactivating the antimicrobial agent; or stopping the antimicrobial agent from entering the organism, or pumping it out.

Resistance can emerge extremely rapidly (e.g. Figure 1)\textsuperscript{14}, and multiple resistant organisms are increasingly common e.g. multiple resistant Meticillin Resistance \textit{Staphylococcus aureus}, glycopeptides resistant enterococci, and penicillin resistant \textit{Staphylococcus pneumoniae}\textsuperscript{8}. The extent of bacterial resistance is illustrated in Table 2.

The emergence of antimicrobial resistance is a complex problem driven by many interconnected factors, in particular the use and misuse of antimicrobial agents\textsuperscript{1}.

Factors contributing to antimicrobial resistance:

- Misuse of antimicrobials such as the widespread use of antibiotics in situations where they are unnecessary (e.g. treating viral sore throats)\textsuperscript{7,14}
- Inclusion of antibiotics as a growth promoter in animal feed\textsuperscript{4}
Figure 1. Ciprofloxacin resistance in *E. coli* bacteraemia


Table 2. The extent of bacterial resistance in the UK

<table>
<thead>
<tr>
<th></th>
<th>Penicillin</th>
<th>Cephalosporins</th>
<th>Carbapenems</th>
<th>Tetracycline</th>
<th>Chloramphenicol</th>
<th>Aminoglycosides</th>
<th>Quinolones</th>
<th>Trimethoprim</th>
<th>Fusidic acid</th>
<th>Erythromycin</th>
<th>Glycopeptides</th>
<th>Rifampicin</th>
<th>Ethambutol &amp; isomiazid</th>
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<td>MRSA</td>
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<td>Enterococci</td>
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<td><em>S. pneumoniae</em></td>
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<td>Viridans streps</td>
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<td><em>E. coli</em></td>
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<td>Klebsiella spp</td>
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<td>Pseudomonas</td>
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<td>Acinetobacter</td>
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<td><em>N. meningitidis</em></td>
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<td><em>N. gonorrhoeae</em></td>
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<td><em>H. influenzae</em></td>
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<td><em>M. tuberculosis</em></td>
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</tbody>
</table>

- Inherently resistant
- Acquired resistance in <20% of isolates
- Acquired resistance in >20% of isolates
- Acquired resistance unknown

* Resistance emerges rapidly by mutation

As the number of microorganisms resistant to antimicrobials increases, concern has risen as to whether there are the new compounds in the drug discovery pipeline to address the problem\textsuperscript{4,15}. Over the last 20 years the number of new antibiotic compounds licensed for use in the UK has declined, with only three new classes of antibiotics licensed in the last five years (Figure 2)\textsuperscript{16}. New antimicrobial classes are emerging, such as the oxazolidinones and the lipopeptides\textsuperscript{9}, but there are acknowledged gaps in the development of effective agents against Gram-negative bacteria such as \textit{Pseudomonas}, \textit{Acinetobacter} \textsuperscript{9}.

\textbf{Figure 2. Number of new antibiotic licenses in the UK}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig2.png}
\caption{Number of new antibiotic licenses in the UK}
\end{figure}

Redrawn from: 150 years of the Annual Report of the Chief Medical Officer 2008\textsuperscript{16}.

\textbf{Microorganisms with antimicrobial resistance}

In the UK, the threat of antimicrobial resistance has primarily focused on HCAI\textsuperscript{14}, and the Department of Health have specifically targeted Healthcare Associated Infections such as MRSA in their HCAI Strategy for 2008, \textit{Clean, Safe Care}\textsuperscript{17} (see chapter 3).

Within the hospital environment other opportunistic pathogens are increasingly becoming problematic due to their inherent or acquired resistance, the selective pressures of the hospital environment, and the number of immunocompromised patients who are susceptible to infection within a small locale\textsuperscript{4}: For example, hospital acquired Gram negative rods, such as \textit{Enterobacter} spp, \textit{Klebsiella} spp, \textit{Pseudomonas} spp and \textit{Acinetobacter} spp, are causing infection problems within intensive care units\textsuperscript{4,9}. The problem is exacerbated as there are few new antimicrobial agents either available or under development which target Gram negative bacteria resulting in a proportion of infections being untreatable\textsuperscript{9}.
Antimicrobial resistance is not only confined to hospitals, but is emerging in community pathogens such as *Streptococcus pneumonia* and *Neisseria gonorrhoeae* which have shown increased resistance to penicillin and have accumulated resistance to other antibacterial agents. In addition, multidrug resistant *Mycobacterium tuberculosis* is a major concern, as tuberculosis is currently undergoing resurgence in prevalence in the UK with 8,000 new cases reported in 2007\textsuperscript{10,18}.

**Escherichia coli profile**

- Most frequent cause of bacteraemia in 2007 with ~22,000 cases reported\textsuperscript{10,18}
- Major cause of urinary tract infections\textsuperscript{18}
- Since 2003 new highly antibiotic resistant strains have emerged and become widespread in England and parts of Northern Ireland: so-called extended spectrum β lactamase (ESBL) producing strains\textsuperscript{19}
- ESBL-producing *E. coli* produce enzymes capable of destroying and conferring resistance to antibiotics\textsuperscript{19}
- ESBL strains are resistant to multiple antibiotics, including two of the most important and widely used classes, penicillins and cephalosporins\textsuperscript{19}
- Serious infections with ESBL-producing *E. coli* now require treatment with carbapenems, the last line of defence\textsuperscript{19}
- Infections with ESBL strains occur both in community and hospital environments\textsuperscript{19}

**Neisseria gonorrhoeae profile**

- Second most common bacterial sexually transmitted infection in the UK, with a total of 18,710 uncomplicated infections diagnosed in GUM clinics in 2007\textsuperscript{20}
- Infection tends to be concentrated in core prevention groups: young adults, men who have sex with men, and black ethnic minority groups\textsuperscript{21}
- If untreated, infection in women can lead to chronic pelvic pain, pelvic inflammatory disease, ectopic pregnancy and infertility\textsuperscript{21}
- Effective treatment is complicated by the ability of *Neisseria* to develop antimicrobial resistance\textsuperscript{21}
- Resistance has emerged to the fluoroquinolone ciprofloxacin, as a result it is no longer recommended as first line therapy\textsuperscript{21}
- Rising resistance to penicillin (from 9.5% in 2006 to 24% in 2007) and tetracycline (from 37% in 2006 to 60% of isolates in 2007) is also notable\textsuperscript{20}
- Cephalosporins (ceftriaxone or cefixime) are currently recommended as first line therapy\textsuperscript{21}; in 2007 for the first time two isolates were categorised as exhibiting decreased susceptibility to cefixime\textsuperscript{20}
It is important to note that antimicrobial resistance is not only limited to bacterial species, but it is also emerging in antiviral treatments (e.g. *Herpes* viruses, Human Immunodeficiency Virus (HIV)*⁴, Hepatitis B*⁴ and influenza*¹⁰), and in antifungal treatments (e.g. *Candida* spp)*¹⁴. The problem is exacerbated due to the few antiviral and antifungal treatments which are currently available*⁴.

**Antimicrobial resistance research priorities**

The Standing Medical Advisory Committee Report⁴, *The Path of Least Resistance*, recognised the enormous potential within the public sector for research to tackle the problem of antimicrobial resistance and highlighted several key aspects for further research and investment (Table 3). Further research priorities were identified in the Department of Health’s *UK Antimicrobial Resistance Strategy and Action Plan*⁶ which aimed to minimise the morbidity and mortality due to antimicrobial resistant infection, and to maintain the effectiveness of antimicrobial agents (Table 3).

**Drug and vaccine development**

The development of new products to tackle antimicrobial resistance and to improve the detection and identification of infectious disease were identified as key research areas in the Foresight *Infectious Diseases project*¹⁴ and the Chief Medical Officer’s infectious disease strategy, *Getting Ahead of the Curve*⁷. Furthermore, the World Health Organisation has identified antimicrobial drug resistance as one of its highest priority gaps for drug development, suggesting that action is needed to stimulate basic and applied research and development of new antibiotic drugs and to explore the potential of alternative approaches such as vaccines to reduce the future impact of resistance*¹⁵.

The future development of new antimicrobial agents is, however, uncertain due to the lower return on investment for pharmaceutical companies when compared to the development of other drugs*¹⁶. The Chief Medical Officer for England in his report, *150 Years of the Chief Medical Officer’s Annual Report*, called for consideration to be given to this problem through promoting novel ways of stimulating research and development into new antibiotics, including public-private partnerships*¹⁶.*
### Table 3: Timeline summarising antimicrobial resistance research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Major review</th>
<th>Date</th>
<th>Research priorities/ recommendations</th>
<th>Achieved/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing Medical Advisory Council: The Path of Least</td>
<td>1998</td>
<td>- Encourage the development of strategies to minimise the use of antimicrobials</td>
<td></td>
</tr>
<tr>
<td>Resistance⁴</td>
<td></td>
<td>- Improve understanding of incidence and development of resistance in bacteria isolated from food producing animals</td>
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<tr>
<td></td>
<td></td>
<td>- Investigation into the factors driving antimicrobial resistance</td>
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<td>- Basic molecular research on the mechanisms of resistance and its spread</td>
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<td>- Mathematical modelling of resistance</td>
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<tr>
<td></td>
<td></td>
<td>- Development of new antimicrobial agents; encouragement of industrial investment</td>
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<td></td>
<td>- Geographical information systems</td>
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<td>- Links between prescribing and resistance at individual and population levels</td>
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<td>- Factors leading to inappropriate prescribing</td>
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<td>- Development and assessment of computerised decision-support systems in hospitals</td>
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<td>- Raising the profile of research on the epidemiology and basis of antimicrobial resistance</td>
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<td>- Addressing the skills gap in microbiology research through training the next generation of PhD and postdoctoral researchers</td>
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<tr>
<td>Source</td>
<td>Year</td>
<td>Research Priorities</td>
<td></td>
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<td>-----------------------------------------------------------------------</td>
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</tr>
</tbody>
</table>
| Department of Health: UK Antimicrobial Resistance Strategy and Action Plan | June 2000 | - Basic research into the mechanisms of resistance and its spread  
- Drivers of resistance and effects of interventions  
- Research to support development of surveillance and surveillance data analysis  
- Applied research to further investigate risk factors, clinical impact and best practice for control in the UK  
- Optimum dosing and duration of antimicrobials  
- Clinical research into what was prescribed and why, to inform clinical prescribing practice  
- Rapid affordable diagnostics and susceptibility tests  
- Use of delayed prescriptions |
| WHO: Global Strategy for Containment of Antimicrobial Resistance       | 2001 | - Research to address the knowledge gaps in understanding antimicrobial resistance  
- Research and development of new drugs; support for industry to develop new antimicrobial agents and vaccines |
| Department of Health: Getting ahead of the curve                      | 2002 | - Development of new drugs and vaccines to combat and prevent infection |
| WHO: Priority medicines for Europe and the rest of the world           | 2004 | - Development of new antimicrobial agents against resistant pathogens  
- Development of rapid diagnostic tools to prevent inappropriate prescribing  
- Vaccines for specific infections to prevent need for antibiotics |
<table>
<thead>
<tr>
<th>Institution</th>
<th>Year</th>
<th>Research Areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foresight infectious diseases project[^14]</td>
<td>2006</td>
<td>- Vaccine development</td>
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<td>- Diagnostics for identification of pathogens to reduce uncertainty and permit the more precise prescribing of antimicrobials</td>
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<td>- New methods to distinguish between viral and bacterial infections</td>
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<td>- Support industry innovation in drug development</td>
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<td></td>
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<td>- Exploit new technologies for identification and validation of molecular targets and drug discovery</td>
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<td></td>
<td></td>
<td>- Microbial population biology and ecology of resistance, to improve understanding of mechanisms of resistance and its spread</td>
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<td>- Basic science to understand and exploit essential genes</td>
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<td>- Improving and expanding training, including continuing training of health personnel</td>
</tr>
<tr>
<td>Department of Health: 150 years of the Annual report of the Chief Medical Officer[^16]</td>
<td>2009</td>
<td>- Stimulate research and development of new antibiotics including public-private partnerships</td>
</tr>
</tbody>
</table>
5 EMERGING INFECTIONS

Background
The considerable potential of emerging infections to cause serious public health and socio-economic impacts has been illustrated globally over the past thirty years through infections such as Human Immunodeficiency Virus (HIV), Severe Acute Respiratory Syndrome (SARS), new variant Creutzfeld-Jakob disease and Influenza A strain H5N1, H1N1, and H1N1.

In the UK, the Chief Medical Officer’s infectious disease strategy, Getting Ahead of the Curve, describes emerging infections as an ever-present threat and recommended that ‘to successfully combat the threat posed by new and emerging infectious diseases, the key is a strong surveillance system underpinned by good clinical reporting and specialist laboratory facilities’.

The UK Government responded to the recommendations of the Chief Medical Officer by: formally creating the Health Protection Agency to research and organise planning for biological, chemical and health emergencies; and establishing the National Expert Panel on New and Emerging Infections, to assess the threat of new and emerging infectious diseases.

The nature of the disease threat
An emerging infection can be defined as either a newly recognised, clinically distinct infectious disease, or a known disease whose reported incidence in a place or population has increased over the past two decades.
Emerging infections can develop from microorganisms that:
- were previously unknown or unrecognised (e.g. HIV/AIDS, SARS)
- have evolved more virulent strains (e.g. *Escherichia coli* 0157)
- were previously well-controlled, but have re-emerged after a significant decline in their incidence (e.g. tuberculosis, drug resistant bacteria)
- had been believed to cause infection only in animals (e.g. vCJD)
- have been discovered to be responsible for causing a previously known disease e.g. causing a long term (chronic) disease

Over the last thirty years, over 40 'new' human pathogens have been recorded (Table 1) and the majority of these had zoonotic origins. Zoonoses are infections which are naturally transmissible from vertebrate animal hosts to humans; over 400 known animal diseases are considered zoonotic. The animal host can either be the primary source of the infection such as rabies, West Nile Virus and transmissible spongiform encephalopathies, or the point source of a 'species jump', with onward transmission through human-to-human contact such as with Ebola and yellow fever.

Emerging infections can be caused by viruses, bacteria, prions, rickettsia, fungi, protozoa and helminths and a broad range of transmission routes have been identified including aerosols, vectors (mainly mosquitoes or ticks) or through sexual activity.

<table>
<thead>
<tr>
<th>Factors contributing to the spread of emerging infections:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• International travel and trade</td>
</tr>
<tr>
<td>• Changes in land use, agriculture and urbanisation</td>
</tr>
<tr>
<td>• Human encroachment on remote areas leading to contact with uncharacterised zoonotic diseases</td>
</tr>
<tr>
<td>• Societal and demographic change</td>
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<tr>
<td>• Poverty and social inequality</td>
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<tr>
<td>• Hospitals and medical procedures</td>
</tr>
<tr>
<td>• Food production and water supplies</td>
</tr>
<tr>
<td>• Intensification of agriculture and livestock keeping</td>
</tr>
<tr>
<td>• Breakdown in public health measures</td>
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<tr>
<td>• Human susceptibility to infection</td>
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<tr>
<td>Year</td>
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<td>2008</td>
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</tbody>
</table>
Examples of emerging infections
The Department of Health identified emerging and re-emerging infections, such as HIV/AIDS (chapter 6), influenza, hepatitis B, hepatitis C and tuberculosis as significant threats to health in its infectious disease strategy for England, Getting Ahead of the Curve¹.

Influenza
Influenza is a respiratory tract infection caused by the influenza virus²². Influenza viruses constantly evolve, through gradual year on year changes (antigenic drift due to the inherent instability of the virus) to cause annual cycles of infection, so called seasonal influenza (chapter 7)¹,²²,²³,²⁴. In addition, the virus can undergo a more radical change (antigenic shift resulting from the recombination of two or more different strains affecting different species or through mutation without recombination²²,²⁴), creating a new strain to which the population has little or no immunity¹. This form has the potential to cause a worldwide epidemic (pandemic)²² and has been the subject of much scientific and media interest.

Pandemic influenza is a natural phenomenon, which occurs on average two to three times each century¹; in the last century pandemics occurred in 1918-1919, 1957-58 and 1968-69¹. The World Health Organization has warned that an influenza pandemic is inevitable and imminent²⁴ and the Chief Medical Officer for England stated that most experts believe that it is a matter of when, not whether, another influenza pandemic will strike¹,²⁴.

For pandemic influenza to occur, three conditions must be met²²:
- A novel virus subtype must emerge to which the general population will have little or no immunity
- The virus must be capable of replicating in humans and causing serious illness
- The new virus must be efficiently transmitted from one human to another

The UK Government have made combating an influenza pandemic one of its top emergency planning priorities²⁵ and the Department of Health has established a Scientific Advisory Committee on Pandemic Influenza, to advise on the scientific evidence base for health-related pandemic influenza policies. The UK health departments have also developed a national contingency plan, Pandemic flu: a national framework for responding to influenza pandemic 2007²⁶.
Pandemic influenza

- Occurs when a new highly infectious strain of influenza appears to which the population has little or no immunity\(^1\)
- Strains of pandemic influenza vary widely in virulence\(^22\)
- 1918-1919 pandemic known as ‘Spanish flu’ was one of the most deadly events in human history with an estimated 20-50 million people killed\(^4,22\)
- Experts have predicted that the next pandemic may result in between 2-50 million deaths\(^24\)
- UK contingency plan assumes 25% of population will be affected with over 50,000 deaths\(^22\)
- World Bank have estimated that a moderate influenza pandemic could cost the global economy $2 trillion\(^27\)

International concern has been raised in recent years over the emergence of two novel influenza strains: a highly pathogenic avian influenza A subtype H5N1\(^{22,23,24,28}\), and a novel strain of swine influenza A H1N1\(^29\). A scientific paper prepared for the Scientific Advisory Group on Pandemic Influenza concluded that the likelihood of H5N1 or any other virus developing pandemic potential could not be quantified\(^23\), and both H5N1 and H1N1 remain under close surveillance by the World Health Organization\(^30\).

Tuberculosis

Tuberculosis has re-emerged as a major international health problem\(^1\) with approximately nine million new cases and two million deaths reported in 2006\(^18\). The resurgence in some parts of the world has been fuelled by an increase in the number of immunocompromised individuals (through HIV infection) and the emergence of multidrug resistant strains of *Mycobacterium tuberculosis*\(^1\). In the UK, its re-emergence over the last two decades has been accompanied by a significant change in its epidemiology\(^1,19\). Combating the increased prevalence of tuberculosis in England was identified as a priority in *Getting Ahead of the Curve*\(^1\), and in 2004 the Chief Medical Officer published an action plan, *Stopping Tuberculosis in England*, which outlined measures to control and eliminate tuberculosis\(^19\).
Chronic diseases
In recent years, a number of known chronic diseases have been identified as having an infectious origin, for example peptic ulcer disease (*Helicobacter pylori*), cervical cancer (human papillomavirus) and liver cancer (hepatitis B and C viruses).1

Tuberculosis profile
- Caused by bacteria belonging to the *Mycobacterium tuberculosis* complex.20
- A total of 8,417 cases of tuberculosis were reported in the UK in 2007, over 90% of cases were in England.20
- Every year there are around 350 deaths from TB in England and Wales.19,21
- Highest burden of disease is in urban areas, with 39% of cases reported in London.20
- Majority of cases occurred in young adults (15 to 44 years) and among those born outside UK.20
- Leading cause of death in people with HIV.2
- Globally multidrug resistant TB has emerged, which is more difficult and expensive to treat. In England 7.4% were resistant to at least one first line drug, 6.8% were isoniazid resistant, 1.2% were multidrug resistant.20
- The current detection rate for active tuberculosis is low. Accurate, rapid robust tools are needed to distinguish between exposure, infection and disease.2

Chronic diseases
In recent years, a number of known chronic diseases have been identified as having an infectious origin, for example peptic ulcer disease (*Helicobacter pylori*), cervical cancer (human papillomavirus) and liver cancer (hepatitis B and C viruses).1.
Recognising the importance of this emerging area, the Chief Medical Officer identified chronic diseases as a key priority in his infectious disease strategy, *Getting Ahead of the Curve*¹. The list of potential links between infectious agents and chronic diseases is growing (Table 2) and the Chief Medical Officer recommended that a research strategy should be developed to establish and validate the casual associations between infectious agents and chronic diseases¹.

**Table 2. Links between infectious agents and chronic diseases**
Table redrawn from: *Getting Ahead of the Curve*¹

<table>
<thead>
<tr>
<th>Microorganism or infection</th>
<th>Chronic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Heliobacter pylori</em></td>
<td>Duodenal ulcer and gastric mucosa associated lymphoid tissue lymphoma</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)</td>
<td>Cervical carcinoma</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em></td>
<td>Dental caries</td>
</tr>
<tr>
<td><em>E. coli</em> O157</td>
<td>Haemolytic uraemic syndrome and chronic renal failure</td>
</tr>
<tr>
<td>Hepatitis B (HBV)/ Hepatitis C (HCV)</td>
<td>Liver cancer and cirrhosis</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>Burkitts lymphoma and nasopharyngeal</td>
</tr>
<tr>
<td>Disease</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>JC virus</td>
<td>Progressive multi-focal leucoencephalopathy</td>
</tr>
<tr>
<td>Human herpes virus type 8 (HHV8)</td>
<td>Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Human T-cell Lymphotropic virus 1 (HTLV-1)</td>
<td>Adult T-cell leukaemia and tropical spastic</td>
</tr>
<tr>
<td>Clonorchis sinensis</td>
<td>Cholangiocarcinoma</td>
</tr>
<tr>
<td>Schistosoma haematobium</td>
<td>Squamous cell carcinoma of the bladder</td>
</tr>
</tbody>
</table>

### Possible links

- **Chlamydia pneumoniae**, **Helicobacter pylori**, herpes simplex virus 2, Epstein-Barr virus and chronic periodontal infection: Coronary heart disease
- Mycobacterium avium subsp. Paratuberculosis: Crohn’s disease
- Propionibacterium acnes: Sciatica
- Yersinia spp. Salmonella spp., Campylobacter spp and Chlamydia trachomatis: Reactive arthritis
- Klebsiella pneumoniae: Ankylosing spondylitis
- Proteus mirabilis: Rheumatoid arthritis
- Mycobacteria: Sarcoidosis
- Carious dental infection: Endocarditis
- HPV: Squamous cell carcinoma of the skin in immunosuppressed patients
- Anaerobic bacterial metabolites: Cancer of the bowel
- Schistosoma spp: Carcinoma of the prostate
- Bacterial vaginosis: Birth prematurity

### Hypothesised on the basis of epidemiology or infection triggers

- Viruses: Juvenile diabetes
- Infectious triggers: Rheumatoid arthritis
- Infection: Multiple sclerosis
- Childhood or adolescent infection: Childhood leukaemia
- Viral infections: Chronic fatigue syndrome

### Zoonotic infections

The Foresight Infectious Diseases project stated that in the UK the major threat of zoonotic transmission is from Transmissible Spongiform Encephalopathies (TSEs) and food-borne diseases arising from faecal contamination from animals\(^2\). In recent years high profile food-borne infections in the UK have included: major food poisoning outbreaks in Lanarkshire (1996)\(^1\) and South Wales (2005) caused by Verocytotoxin-producing *Escherichia coli* (VTEC) 0157; and the emergence and identification of Bovine...
Spongiform Encephalopathy (BSE) in cattle and the consequent new variant CJD\textsuperscript{32}. The annual cost of food-borne zoonotic diseases in UK has been estimated at £750 million\textsuperscript{2}.

**variant Creutzfeldt-Jacob Disease (vCJD)**
- Rare and ultimately fatal degenerative brain disease, caused by a build-up of an abnormal form of a naturally occurring prion protein\textsuperscript{32,33}
- Member of the Transmissible Spongiform Encephalopathies (TSE) disease group\textsuperscript{32,33}
- There are several types of CJD in humans, the most common being sporadic CJD. In 1996 the UK National CJD surveillance unit identified a new form which infects mostly young adults, variant CJD\textsuperscript{33}
- New variant CJD is strongly linked to exposure through food to BSE in cattle\textsuperscript{32}
- Significant economic impact on the UK, despite the relatively few cases to date; cost of treating each vCJD patient $\sim$£45,000\textsuperscript{9}
- By 2009, a total of 169 cases had been reported, with 164 deaths\textsuperscript{34}
- No treatment or simple non-invasive test available\textsuperscript{33}

**Future emerging infections?**
The Chief Medical Officer for England described the ability of infectious agents to emerge in an unexpected and unpredictable manner in *Getting Ahead of the Curve*\textsuperscript{1}, and used the example of the emergence of West Nile Virus (WNV) in the United States. In his annual report in 2002, the Chief Medical Officer described the three main factors which would need to occur for WNV to become endemic in the UK and recommended enhanced surveillance of the disease and the need for a WNV contingency plan\textsuperscript{35}, which was subsequently published in 2004\textsuperscript{36}. Other emerging zoonotic diseases with published guidelines for their management and control include Hendra virus and Nipah virus\textsuperscript{37}. 
Emerging infection research priorities
The Chief Medical Officer for England identified combating the threat of emerging infectious diseases as a key priority in his infectious diseases strategy for England\(^1\), and underlined the importance of strong surveillance systems and good clinical reporting practices (Table 3).

Pandemic influenza research priorities
To ensure that the UK is prepared to respond to influenza pandemic, the Department of Health have established a Pandemic Influenza Programme. The programme comprises several workstreams called Pandemic Influenza Groups (PIG), one of whom conducted a research gap analysis in 2008. The Research Pandemic Influenza Group’s report acknowledged that a great deal of pandemic influenza research is currently underway in the UK, and went on to identified research priorities over a large range of sciences and development stages, appropriate to a whole range of different funders\(^40\).

Tuberculosis research priorities
The action plan from the Chief Medical Officer, Stopping Tuberculosis in England, included leading edge research as one of its ten action points with the aim of increasing our understanding of TB and its control; improving the evidence base for its control; and developing better tools for its diagnosis, treatment and prevention\(^19\) (Table 3).

West Nile Virus (WNV)
- Member of the Flavividae family which includes other viruses such as yellow fever, dengue fever and Japanese encephalitis\(^36,38\)
- Zoonotic arbovirus transmitted between animals and humans by mosquitoes\(^36\)
- First isolated in 1937 in Uganda and was confined to the old world until the end of the century when it was reported in Europe and then appeared unexpectedly in the US in 1999\(^1,36,38\)
- Endemic in the US by 2002 with over 4,000 reported infections and 284 deaths in 2004\(^36\)
- Department of Health has set up a contingency plan to deal with WNV\(^36\)
- Ongoing surveillance in England and Wales of humans, horses, mosquitoes and dead birds\(^36,39\)
- UK risk assessed as low, but continued surveillance has been recommended\(^9\)
**TSE research**

The five main funders of TSE research, the Department of Health, the Department for Environment, Food and Rural Affairs (Defra), the Food Standards Agency, the Biotechnology and Biological Sciences Research Council and the Medical Research Council currently spend more than £29 million per year in this field and have published a revised research strategy for 2009 – 1141.

**Drug and vaccine development**

The development of new products to tackle infection and to improve the detection and identification of emerging infectious diseases were identified as key research areas in the Foresight *Infectious Diseases project*42, and the Chief Medical Officer’s infectious disease strategy highlighted the importance of research into new drugs, diagnostics, vaccines and treatment for tuberculosis and influenza1. The World Health Organisation has identified pandemic influenza as one of its highest priority pharmaceutical gaps42.
### Table 3: Timeline summarising emerging infection research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Major review</th>
<th>Date</th>
<th>Research priorities/ recommendations</th>
<th>Achieved/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General emerging infection research priorities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Department of Health Getting Ahead of the Curve¹</td>
<td>2002</td>
<td>- Surveillance systems that provide the comprehensive coverage necessary to detect new or unusual disease presentations or changes in the occurrence or profile of microorganisms</td>
<td>Health Protection Agency formed on 2 April 2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Strengthen clinical reporting</td>
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<tr>
<td></td>
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<td>- Use surveillance data, especially on information gaps in the population’s immunity, to anticipate outbreaks or epidemics</td>
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<td></td>
<td></td>
<td>- Coordinate specialist laboratory facilities to enable microorganisms to be assessed and profiled in a standard manner</td>
<td>Health Protection Agency formed on 2 April 2003</td>
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<tr>
<td></td>
<td></td>
<td>- Establish a national source of expertise in assessing the threat from new and emerging infections</td>
<td>National Expert Panel on New and Emerging Infections formed and first meeting held on 25 November 2003</td>
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<tr>
<td></td>
<td></td>
<td>- Create a mechanism to rapidly produce a specification for new control measures (e.g. drugs, vaccines) when new problems emerge</td>
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<tr>
<td>Foresight Infectious diseases project²</td>
<td>2006</td>
<td>- Maintain strong international links with agencies in other countries with responsibility for infectious disease surveillance and control policies</td>
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<tr>
<td></td>
<td></td>
<td>- Establish a national source of expertise in assessing the threat from new and emerging infections</td>
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</table>
Table 3: Timeline summarising emerging infection research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Research Priorities</th>
</tr>
</thead>
</table>
| 2004       | WHO Priority Medicines for Europe and the World\(^{42}\)               | High priority pharmaceutical gap with the following research priorities:  
- Behavioural responses  
- Diagnostics  
- Support systems |
| 2006       | Royal Society and the Academy of Medical Sciences. Pandemic influenza: science to policy\(^{43}\) | - Examine areas where further research could be funded such as basic avian influenza research and avian immunology  
- Encourage research in the development and evaluation of novel antivirals for influenza, in both industry and academia. Develop public-private partnerships between academia and industry.  
- Many young children are immunologically naive to influenza and further research is needed on the characteristics of primary immune responses and the safety and efficacy of the use of seasonal and... |
Table 3: Timeline summarising emerging infection research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Source</th>
<th>Date</th>
<th>Research Priorities</th>
</tr>
</thead>
</table>
| Royal Society and the Academy of Medical Sciences. Pandemic influenza: report of follow-up symposium | 2007 | - Make samples of the H5N1 vaccines available to the research community and that the MRC solicits high-quality research applications specifically to analyse these vaccines  
- Improve understanding of cellular, innate and adaptive immune responses in protection from disease and determining disease severity  
- Develop standardised clinical assay methods for evaluation of pre-pandemic and pandemic vaccines  
- Conduct research to identify which infection control measures and non-pharmaceutical interventions, such as personal protective equipment and social distancing methods are likely to have the greatest impact during a pandemic |
| Department of Health Pandemic Influenza Group report                   | 2008 | - Further research and development on avian vaccines  
- Create a mechanism to rapidly produce a specification for new control measures (e.g. drugs, vaccines) when new infectious disease problems emerge  
- New products to tackle infection and improve the detection and identification of infectious diseases |
Table 3: Timeline summarising emerging infection research priorities identified in previous reports and reviews

Research gaps were categorised into the following cross-discipline priority areas:
- Determinants of transmissibility
- Mechanisms of transmission
- Transmission by setting and impact of interventions
- Determinants and mechanisms of pathogenicity
- Vaccines and their use
- Antivirals and their use
- Models and operational toolkits

<table>
<thead>
<tr>
<th><strong>Tuberculosis research priorities</strong></th>
<th>2004</th>
<th>Department of Health Stopping Tuberculosis in England[^19]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>- Increase understanding of TB and its control</td>
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<td></td>
<td></td>
<td>- Improve the evidence base for its control</td>
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<tr>
<td></td>
<td></td>
<td>- Develop better tools for its diagnosis, treatment and prevention</td>
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<tr>
<td></td>
<td></td>
<td>- Formulate a TB research strategy to fill evidence gaps within the fields of: better drugs, diagnostics and management; service delivery; risk factors; latent TB infection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Chronic diseases research priorities</strong></th>
<th>2002</th>
<th>Department of Health Getting Ahead of the Curve[^1]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>- Formulate a research strategy aimed at establishing the causal associations between infectious agents and chronic diseases</td>
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<tr>
<td></td>
<td></td>
<td>- Increase clinical awareness and professional education where there is an established link</td>
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<td>Not published</td>
</tr>
</tbody>
</table>

[^19]: Not published
Table 3: Timeline summarising emerging infection research priorities identified in previous reports and reviews

| Department of Health Hepatitis C Strategy for England | 2002 | - Survival of hepatitis C virus: research is needed to identify methods for effectively rendering injecting equipment safe using readily available products e.g. household bleach |
| | | - Mother to baby transmission: uncertainty surrounding vertical transmission from mother to baby; research needed to determine if elective caesarean section or other obstetric interventions reduce the risk of transmission during pregnancy and/or childbirth |
| | | - Modelling the effectiveness of different prevention activities |
| | | - Behavioural research: research into ‘prevention of initiation to injection’ is needed to inform harm reduction work. |
| | | - Complementary and alternative medicine: research evidence is needed from large and well designed studies to evaluate the effectiveness of this in the management of hepatitis C |
6 SEXUALLY TRANSMITTED INFECTIONS AND HIV

Background
Sexually Transmitted Infections (STIs) including human immunodeficiency virus (HIV) constitute a major public health infectious disease problem both globally and in the United Kingdom. Recognising the urgent need to address the rising prevalence of STIs and HIV the Department of Health published England’s first sexual health strategy, Better Prevention, Better Services, Better Sexual Health: The National Strategy for Sexual Health and HIV in 2001. Setting out an ambitious ten year programme to combat sexual ill health and service delivery, it placed sexual health firmly on the public health agenda.

Key points about Sexually Transmitted Infections:
- Identified as one of eight major threats to human health in the immediate future in the Foresight infectious diseases project
- The cost to the NHS of STIs excluding HIV based on initial appointments and follow up visits is approximately £165 million per annum
- The annual cost of treating those infected with HIV has been estimated to be £400 million, with the cumulative lifetime treatment costs predicted to exceed £5 billion by 2007
- One in ten of the UK population have at some point had an STI
- 400,000 new STI episodes were diagnosed in genitourinary medicine clinics in 2007
- Sexually transmitted infections remain one of the most important causes of illness due to infectious disease among young people (aged between 16 to 24 years)
- There were over a million sexual health screens carried out in genitourinary medicine clinics in the UK in 2007

The public health importance of sexually transmitted infections and HIV was reiterated by the Chief Medical Officer in his infectious disease strategy, Getting Ahead of the Curve, and by the House of Commons Select Committee on Health, who described the state of sexual health in the UK as 'in crisis'. In 2004, the Government’s White paper, Choosing Health: Making Healthier Choices Easier, gave further prominence to tackling the nation’s sexual health and set out specific commitments including improving access.
to genitourinary medicine (GUM) clinics, the National Chlamydia Screening Programme and sexual health advertising campaigns\textsuperscript{12}.

Despite some notable progress and improvements in the provision of clinical services in recent years\textsuperscript{4}, the nature and scale of sexual ill health and inequalities in England today are still of grave concern\textsuperscript{7}. Over the last ten years there has been a steady increase in the number of newly diagnosed STIs at GUM clinics\textsuperscript{4,7,9,13} (Figure 1), with increased testing, more sensitive diagnostic methods and changes in sexual behaviour all contributing to the rising trend (HOC 2002, HPA 2008d).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Sexually Transmitted Infection diagnoses in GUM clinics: 1998-2007}
\end{figure}

Improving the sexual health of the nation therefore remains a public health priority and it was recommended as one of six priority commissioning goals for the NHS in the review, \textit{High Quality Care for All: NHS Next Stage Review}\textsuperscript{14}.

\textbf{The nature of the disease threat}

Sexually transmitted infections are infections whose predominate route of transmission is through sexual intercourse\textsuperscript{1,15}. They are mainly caused by bacteria, viruses and protozoa\textsuperscript{1} and can be asymptomatic in their presentation\textsuperscript{15}. If a person does present with symptoms, they may include increased discharge, pain or ulceration\textsuperscript{15}. Left undiagnosed
and untreated STIs may result in serious complications in later years\textsuperscript{15} and can cause considerable reproductive morbidity including pelvic inflammatory disease, ectopic pregnancy, infertility, cervical cancer and even death\textsuperscript{1,2,3}. As well as the physical impact, significant psychological morbidity is also associated with the perceived stigma of sexually transmitted infections\textsuperscript{1}.

In the UK, the most common STIs are chlamydia, genital warts, genital herpes and gonorrhoea\textsuperscript{9} (Figure 2), with chlamydia and genital warts accounting for over half of all new STIs diagnoses at GUM clinics in 2007\textsuperscript{9,13}.

**Figure 2. New STI diagnoses made at GUM clinics in 2007**

![Pie chart showing the distribution of new STI diagnoses in 2007. Chlamydia infection (uncomplicated and complicated) is the largest category at 31.6%, followed by genital warts at 25.5%, genital herpes simplex at 6.7%, gonorrhoea (uncomplicated and complicated) at 6.5%, new HIV diagnosis at 4.8%, infectious syphilis at 2.6%, and other at 1.7%. Non-specific genital infection (uncomplicated and complicated) is the smallest category at 0.7%.]

Source: Health Protection Agency. All new STI episodes seen at GUM clinics in the UK: 1998-2007\textsuperscript{9}.

The *National Strategy for Sexual Health and HIV* recognised that STIs are not equally distributed throughout the UK population and highlighted that significant inequalities in sexual health exist between different groups\textsuperscript{5}. The highest burden of sexually transmitted infections is borne by young people (aged 16-24 years), men who have sex with men, and black and minority ethnic groups\textsuperscript{4,5,10,16,17}. There is also a strong link between social deprivation and STIs\textsuperscript{5}. The *National Strategy for Sexual Health and HIV* formulated initiatives targeted towards these priority prevention groups\textsuperscript{5}, but despite positive developments, efforts to reduce HIV and STI transmissions have not succeeded\textsuperscript{4}. 
Key points for STI target prevention groups

- **Young people aged 16-24 years**: carry the greatest STI burden and although they represented only 12% of the UK population they accounted for nearly half of all diagnoses in GUM clinics in 2007: 65% of all chlamydia (79,557 of 121,986); 55% of all genital warts (49250 of 89,838); 50% of gonorrhoea (9,410 of 18710); 11% of all new HIV diagnoses\(^{10,13}\).

- **Men who have sex with men**: in 2007, an estimated 32,000 were living with either diagnosed and undiagnosed HIV\(^{16}\); accounted for 41% of all new HIV diagnoses in 2007\(^{16}\); increasing incidence of most STIs has been observed\(^{4,16,18}\) which not only indicates unsafe sex but sets markers for possible HIV infection\(^{11}\).

- **Black African communities**: in 2007 there were 2,691 new HIV diagnoses, representing 40% of all new diagnoses in UK, most of which were almost certainly acquired in sub-Saharan Africa\(^{17}\).

Examples of sexually transmitted infections

The *National Strategy for Sexual Health and HIV*\(^{4,5,6,7}\) set out an ambitious 10 year-programme to tackle sexual ill-health, reduce HIV transmission and modernise sexual health services in England. High priority was given to reducing the incidence of *Neisseria gonorrhoeae* (chapter 4), *Chlamydia trachomatis* and HIV, targets which were reiterated in the Government’s White paper, *Choosing Health* in 2004\(^{5,12}\).

**Chlamydia trachomatis profile**

- Genital chlamydia infection is the most commonly diagnosed bacterial STI in UK GUM clinics\(^{9,13}\).
- Infection is asymptomatic in at least 70% of women and 50% of men\(^{4}\), consequently in the absence of screening a significant pool of infection will remain undiagnosed\(^{2}\).
- If left untreated the sequelae are severe and can cause pelvic inflammatory disease, ectopic pregnancy and tubal infertility\(^{4}\).
- Since 2003 there has been a proactive policy in England the National Chlamydia Screening Programme (NCSP), aimed at sexually active young people aged under 25\(^{4}\).
- The most common STI in young people (aged 16-24 years): the NCSP performed 270,729 screens in 2007, of which 9.5% women and 8.4% of men tested positive for chlamydia\(^{10}\).
In the 25 years since HIV/AIDS was first recognised HIV-1 has emerged from an unrecognised pathogen to one of the world’s major killers\(^3\), causing over two million deaths worldwide in 2007 alone\(^9\). In the UK, HIV continues to be one of the most important communicable diseases, with high treatment and care costs, serious morbidity and significant mortality\(^1\).

**HIV profile**

- In 2007, the UK had an estimated 77,400 HIV infected persons, of whom 28% did not know that they were infected\(^18\)
- Number of cases of HIV being diagnosed each year is rising and reached 7,734 in 2007, with a similarly high figure in each year since 2003\(^18\)
- Late diagnosis is an important determinant of morbidity and mortality: 31% of cases were classed as late diagnosis in 2007\(^18\)
- The annual cost of treating those infected with HIV has been estimated to be £400 million, with the cumulative lifetime treatment costs predicted to exceed £5 billion by 2007\(^8\)
- HIV and its associated immunodeficiency is a potent driver of tuberculosis\(^11\)
- No cure or vaccine is currently available for HIV/AIDS\(^11\)
- The *National Strategy for Sexual Health and HIV* set a target for reducing the number of number HIV diagnoses by 25% by 2007, which has not been achieved\(^4\)

Other microorganisms responsible for contributing to the overall burden of sexually transmitted infections include genital human papillomavirus (genital warts), genital herpes simplex and re-emerging pathogens such as a bacteria-like spirochete *Treponema pallidum* subspecies *pallidum* (infectious syphilis)\(^3,4,11,22\), which has exhibited a substantial rise in numbers over the last ten years (139 episodes in 1998 to 2,680 episodes in 2007)\(^9\).
Sexually transmitted infections and HIV research priorities

In 2001, the national strategy for sexual health and HIV, Better prevention, better service, better sexual health, highlighted the need for research and a strong evidence base with regard to health promotion and planning services for HIV/AIDS and STIs. The strategy proposed two broad areas for future research: prevention, information provision and determinants of risk; research into interventions (Table 1). Following a consultation phase, the research priorities for the sexual health strategy were further refined and described in the implementation action plan (Table 1). The importance of improving the evidence base was further emphasised through the Government’s initiative Choosing Health.

Drug and vaccine development

The development of new drug treatments for STIs and support towards the international effort to develop a safe and effective HIV vaccine were identified as key research priorities in the national sexual health strategy5,6, and were reiterated in the Chief Medical Officer’s infectious disease strategy in 200211. In addition, the Foresight Infectious Diseases project highlighted the need to actively support research into the development of rapid diagnostic tests for a range of STIs and also to measure the immunological function or viral load in patients diagnosed with HIV3 (Table 1).
Table 1: Timeline summarising sexual health and HIV research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Major review</th>
<th>Date</th>
<th>Research priorities/ recommendations</th>
<th>Achieved/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department of Health: Better prevention, better services, better sexual health - The national strategy for sexual health and HIV⁵</td>
<td>2001</td>
<td>- Promote research into new drug treatments</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- Supporting international effort to develop a safe, effective and affordable vaccine</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Prevention, information provision and determinants of risk</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- links between drugs, sex and alcohol and the identification of effective interventions</td>
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<td></td>
<td></td>
<td>- better understanding of the sexual networks, health seeking behaviour and risk behaviour of targeted groups</td>
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<tr>
<td></td>
<td></td>
<td>- the impact of combination therapies for HIV on behaviour, and the potential for complacency and unsafe sex in uninfected groups at risk and those already infected</td>
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<td></td>
<td></td>
<td>- the impact of ethnicity, deprivation, and other socio-economic factors in sexual health</td>
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<td></td>
<td></td>
<td>- best practice in condom promotion, including the most effective use of free condom distribution</td>
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<td></td>
<td></td>
<td>- effective microbicides and an affordable HIV vaccine, and how their use could be integrated into other HIV prevention and health promotion activities</td>
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<tr>
<td></td>
<td></td>
<td>Interventions</td>
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<tr>
<td></td>
<td></td>
<td>- barriers preventing access to services, especially within targeted groups</td>
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<tr>
<td></td>
<td></td>
<td>- a better understanding of why young men do not access services, and evaluation of innovative methods for engaging them in sexual and reproductive health</td>
<td></td>
</tr>
<tr>
<td>Department of Health: National strategy for sexual health implementation action plan&lt;sup&gt;6&lt;/sup&gt;</td>
<td>2002</td>
<td>Proposed a review the content of the joint MRC and DH research programme to support the implementation of the sexual health and HIV strategy</td>
<td>Sexual Health and HIV Research Strategy Committee formed; 28 research projects were commissioned (2003-2007)&lt;sup&gt;7&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td>- interventions; effectiveness of new models of care for improving sexual health outcomes</td>
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<td></td>
<td></td>
<td>- improving partner notification within clinics and the community</td>
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<td></td>
<td></td>
<td>- evaluating and improving the uptake of sexual health screening services in non-specialist settings, especially for Chlamydia</td>
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<tr>
<td></td>
<td></td>
<td>- developing and evaluating surveillance mechanisms to meet new service configurations</td>
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<tr>
<td></td>
<td></td>
<td>Research priorities:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- Improve knowledge of the link between social exclusion and poor sexual health including HIV</td>
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<td></td>
<td></td>
<td>- Determinants of risk taking and identification of effective risk reduction strategies</td>
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<td></td>
<td></td>
<td>- Build capacity to develop better evidence on sexual health and African communities</td>
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<tr>
<td></td>
<td></td>
<td>- Evaluation of the effectiveness and cost effectiveness of existing and new models of care for improving sexual health outcomes</td>
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<tr>
<td></td>
<td></td>
<td>- Research to improve the effectiveness of partner notification within clinics and the community</td>
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<td></td>
<td></td>
<td>- Keep abreast of the development of effective microbicides and an affordable HIV vaccine</td>
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</tbody>
</table>
Table 1: Timeline summarising sexual health and HIV research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Author/Report</th>
<th>Year</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department of Health: Getting Ahead of the Curve</td>
<td>2002</td>
<td>Implementation of National Strategy for Sexual Health and HIV to modernise sexual health and HIV services over the next 10 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Contribute to international research to develop a vaccine against HIV infection</td>
</tr>
<tr>
<td>House of Commons Health Committee: Sexual health</td>
<td>2003</td>
<td>Develop the long term evidence base for sexual health and support research into HIV/AIDS</td>
</tr>
<tr>
<td>Foresight infectious diseases</td>
<td>2006</td>
<td>HIV tests to measure immunological function or viral load in order to determine whether treatment should be initiated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Development of cheap, rapid and reliable tests for specific STIs as most STIs are asymptomatic</td>
</tr>
</tbody>
</table>
7 ACUTE RESPIRATORY INFECTIONS

Background
Acute respiratory infections are the leading cause of acute illness worldwide\textsuperscript{1,2} and are the most important cause of mortality in infants and young children, accounting for about two million deaths each year\textsuperscript{3}. Identified in the UK as posing the greatest burden of all infectious diseases in the Health Protection Agency’s burden of disease report, *Health Protection in the 21\textsuperscript{st} Century*\textsuperscript{4}, acute respiratory infections were listed in the Foresight infectious diseases project as one of eight major threats to human health in the immediate future\textsuperscript{5}.

<table>
<thead>
<tr>
<th>Key points about Acute Respiratory Infections:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Identified as one of the most important infectious disease categories both in terms of cost and prevalence\textsuperscript{4}</td>
</tr>
<tr>
<td>• Respiratory infections cause on average 35,157 deaths per year, 95% of which are in the elderly\textsuperscript{4,6}</td>
</tr>
<tr>
<td>• Primary care bears the greatest burden of respiratory infections: approximately 5.5 million GP consultations a year are attributed to respiratory infections, costing approximately £170 million\textsuperscript{4}</td>
</tr>
<tr>
<td>• Account for over 100,000 hospital admissions per year\textsuperscript{4,5}</td>
</tr>
<tr>
<td>• Lower respiratory tract infections and pneumonia account for 19.9% of Healthcare Associated Infections\textsuperscript{7}</td>
</tr>
<tr>
<td>• Source of widespread concern because they have the potential to cause problems on a global scale, for example, the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003 caused less than 1000 deaths, but cost the global economy an estimated US$10-30 billion\textsuperscript{5}</td>
</tr>
</tbody>
</table>

The severity of the public health threat posed by acute respiratory infections has been illustrated in recent years through the emergence of pathogens such as Severe Acute Respiratory Syndrome (SARS) and avian influenza\textsuperscript{5,8}. The importance of strong national and international surveillance systems to manage and control such epidemic and pandemic threats formed a key component of the Chief Medical Officer’s infectious disease strategy, *Getting Ahead of the Curve*\textsuperscript{6,9}, and has been recognised in the UK Government’s global health strategy, *Health is Global*\textsuperscript{10}. In addition to emerging and pandemic disease threats, acute respiratory infections form a significant component of other national health priorities as a major contributor to Healthcare Associated
Infections\textsuperscript{4,5,7,11–14} (chapter 3) and due to the increasing prevalence of respiratory pathogens with antimicrobial resistance\textsuperscript{6,11,15–17} (chapter 4).

**The nature of the disease threat**

Acute respiratory infections are a complex group of conditions which can be classified anatomically as either upper or lower respiratory tract infections. Upper respiratory tract infections are common, rarely life threatening diseases affecting the nose, throat, larynx and trachea and include diseases such as the common cold, tonsillitis, sore throat, sinusitis and laryngitis\textsuperscript{1,2,15}. Lower respiratory tract infections affect the bronchi, bronchioles and alveoli, and they are responsible for more severe illnesses such as influenza, pneumonia and bronchiolitis\textsuperscript{1,2,5,18}.

Respiratory infections are caused by a range of different endemic and epidemic viral and bacterial pathogens\textsuperscript{5} and can result in a wide spectrum of illnesses\textsuperscript{4}. They are commonly transmitted by airborne droplets or nasal secretions and are often seasonal in their activity, tending to circulate at higher levels in winter months\textsuperscript{4}. The populations most at risk of developing a fatal respiratory disease are the very young, the elderly and the immunocompromised\textsuperscript{1,2}.

The biology and epidemiology of acute respiratory infections have several features that increase their potential to cause serious public health problems\textsuperscript{5}:

- A rapid time course of infection, with incubation periods of a few days and recovery over a similar time period
- Not all infected persons will develop symptoms that are severe enough to be reported, potentially allowing extensive transmission in the general population
- Transmission potential in the general population may be high
- Effective protection or treatment through vaccines or drugs may not be immediately available once an outbreak is detected

The Health Protection Agency has estimated the burden of respiratory infections in the England and Wales through an analysis of NHS direct calls, primary care consultations and hospital admissions\textsuperscript{4} (Table 1). It is important to note that estimating the true burden of respiratory infections is incredibly difficult due to problems in data collection as many GP consultations are non-specific and cases are never confirmed through laboratory tests\textsuperscript{4}.
Table 1. Annual mean number of events attributable to respiratory pathogens, England and Wales

<table>
<thead>
<tr>
<th></th>
<th>Streptococcus pneumonia</th>
<th>Respiratory Syncytial Virus (RSV)</th>
<th>Influenza A &amp; B</th>
<th>Mycoplasma pneumonia</th>
<th>Rhinovirus</th>
<th>Rate per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calls to NHS direct</td>
<td>36,704</td>
<td>13,340</td>
<td>20,975</td>
<td>-</td>
<td>2,430</td>
<td>140</td>
</tr>
<tr>
<td>GP consultations</td>
<td>1,669,265</td>
<td>1,110,898</td>
<td>1,430,121</td>
<td>654,630</td>
<td>586,234</td>
<td>10,500</td>
</tr>
<tr>
<td>Hospital admissions</td>
<td>68,354</td>
<td>35,540</td>
<td>9,967</td>
<td>1,997</td>
<td>-</td>
<td>223</td>
</tr>
</tbody>
</table>


Microorganisms responsible for respiratory infections

In the UK, the threat posed by acute respiratory infections has primarily focused on the pandemic potential of influenza: the UK Government has made combating influenza one of its top emergency planning priorities; the Department of Health have established a Scientific Advisory Committee on Pandemic Influenza; and the UK health departments have developed a national pandemic flu contingency plan (chapter 5).

Seasonal influenza also has a significant public health impact, with over 1.4 million GP consultations per year, affecting 10-15% of the UK population, causing an estimated 5-25,000 deaths per year. Influenza is second only to Streptococcus pneumonia as the leading burden of respiratory disease, with Respiratory Syncytial Virus carrying a significant burden of infection in the very young and the elderly.

Respiratory Syncytial Virus (RSV) profile

- Enveloped RNA virus in same family as human parainfluenza viruses and mumps and measles viruses
- Causes a mild respiratory infection in most people, but in some people it can cause pneumonia or even death
- Leading cause of lower respiratory tract infections in infants and young children
- Commonest cause of severe respiratory illness such as bronchiolitis (inflammation of the bronchioles) in children under 2
- Commonest cause of hospital admissions due to acute respiratory illness in young children: 28 per 1000 hospital admissions in children aged under 1 in England
- Causes severe respiratory illness in elderly people and outbreaks have been shown to be associated with higher death rates
- No vaccine is currently available
It is important to also consider acute respiratory infections in terms of clinical syndrome, as lower respiratory tract infections such as pneumonia and bronchiolitis are of great concern worldwide. Pneumonia is an inflammation of the lung tissue which is usually caused by an infectious agent. A wide range of viral and bacterial pathogens have been implicated in causing pneumonia, with a small range of key pathogens causing most cases (Table 2).

**Table 2: Common causes of pneumonia in different healthcare settings in order of incidence**

<table>
<thead>
<tr>
<th>Outpatients</th>
<th>Inpatients</th>
<th>Intensive care unit</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td><em>Mycoplasma pneumoniae</em></td>
<td>Legionella spp</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td><em>Chlamydia pneumoniae</em></td>
<td><em>Haemophilus influenza</em></td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td><em>Haemophilus influenza</em></td>
<td>Gram negative bacilli</td>
</tr>
<tr>
<td>Respiratory viruses*</td>
<td>Legionella spp</td>
<td><em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>Respiratory viruses*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*Influenza A and B, adenovirus, RSV, parainfluenza
Pneumonia is often divided into two main types: community-acquired pneumonia and hospital-acquired pneumonia. Community-acquired pneumonia poses a significant public health threat: with an annual incidence of 5-11 per 1000 adult population\textsuperscript{31}, it is the fifth leading cause of death in the UK\textsuperscript{32}. Hospital-acquired pneumonia also represents a major problem as it is the third (13.9\%) most common type of healthcare associated infection in the UK\textsuperscript{7}.

**Acute respiratory infection research priorities**
Acute respiratory infections, with the exception of pandemic influenza (chapter 5), have not been the subject of any major governmental reviews over the last ten years, despite their significant disease burden. Table 3 summarises the acute respiratory infection research priorities highlighted in the Foresight infectious diseases project report\textsuperscript{3} and the Chief Medical Officer’s infectious disease strategy *Getting Ahead of the Curve*\textsuperscript{8}.

**Drug and vaccine development**
The Chief Medical Officer in the infectious disease strategy, *Getting Ahead of the Curve*, highlighted the need to develop a vaccine against Respiratory Syncytial Virus, which is a significant cause of morbidity and mortality in adults as well as in children\textsuperscript{8}.
Table 3: Timeline summarising acute respiratory infection research priorities identified in previous reports and reviews

<table>
<thead>
<tr>
<th>Major review</th>
<th>Date</th>
<th>Research priorities/ recommendations</th>
<th>Achieved/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department of Health: Getting Ahead of the Curve</td>
<td>2002</td>
<td>- Research and investment to bring forwards the development of a vaccine against Respiratory Syncytial Virus</td>
<td></td>
</tr>
<tr>
<td>Foresight Infectious Diseases Project</td>
<td>2006</td>
<td>- Characterised by their capacity for rapid spread, this puts a premium on speed of detection and diagnosis</td>
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<tr>
<td></td>
<td></td>
<td>- Development of technology to detect infection in asymptomatic individuals</td>
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<tr>
<td></td>
<td></td>
<td>- Development of special technology to screen people in areas of high throughput, to monitor and arrest disease spread</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 1

References: evidence reviewed

Chapter 1


Chapter 2


14. Office for National Statistics (2007b) Number of death certificates which mentioned Clostridium difficile, or recorded Clostridium difficile as the underlying
www.statistics.gov.uk/downloads/theme_health/Counts_CDiffl.xls


Chapter 4


Chapter 5


Chapter 6


Chapter 7


Figure 1: Timeline of selected public health infectious disease publications and reviews: 1998-present

Abbreviations
DH: Department of Health
HPA: Health Protection Agency
HoL: House of Lords Science and Technology Select Committee
NAO: National Audit Office: report by the Comptroller
Roy Soc: Royal Society
RS AMS: Royal Society and Academy of Medical Sciences
UKCRC: UK Clinical Research Collaboration
Public health infections research is one of the four priority areas identified under the Office for Strategic Coordination of Health Research (OSCHR) public health work stream. NIHR has been tasked with leadership of the public health infection strategy and MRC is working with NIHR on its development.

The strategy seeks to deliver an integrated, national vision for public health infection research that reflects the public health needs and strengths of the UK research community. The objective is to provide a clear statement of the research opportunities in the field in order to inform funding priorities and to inform policy development at national and international levels.

The workshop aims to discuss and form consensus on research needs, opportunities and strategic priorities in public health infections research in a broad stakeholder setting involving experts across the field from basic science, clinical infectious disease, epidemiology, primary care and public health, through to policy development and implementation. The outcomes of the workshop will inform the strategy document prepared for consideration by OSCHR.

**AGENDA**

**Day 1: Wednesday 16th December**

13:00 -14:00 Registration and Lunch

**Introductory Session**

Chair: Dr Russell Hamilton, NIHR

14:00 – 14:10 **Welcome and Introductions**
Sir Leszek Borysiewicz, MRC
Dr Russell Hamilton, NIHR

14:10 – 14:20 **Setting the Scene and Aims of the Workshop**
Professor Jonathan Friedland, Imperial College

**Session 1: Framework for Public Health Infections Strategy**

Chair: Professor Jonathan Friedland, Imperial College

14:20 -15:35 **Needs and Opportunities in Public Health Infections Research**

**Health Care Associated Infections (10’+5’)**
Professor Alison Holmes, Imperial College

**Antimicrobials: Development, Use, Resistance (10’+5’)**
Professor Brian Duerden, Department of Health

**Emerging and Resurgent Infections (10’+5’)**
Professor Neil Ferguson, Imperial College

**Sexually Transmitted Infections and HIV (10’+5’)**
Severe infections - respiratory, GI, CNS (10’+5’)
Professor David Dockrell, University of Sheffield

15:35 – 15:50 Coffee
15:50 - 16:50 The Matrix Challenge: Scope, Structure, Composition & Priorities
   Chair: Dr Wendy Ewart, MRC
   Introduction
   Dr Wendy Ewart, MRC
   Group Discussion
   5 parallel break out groups across research interests and disciplines

16:50 – 17:00 Break
17:00 – 18:00 Feedback from break out groups and discussion
18:00 – 19:00 Drinks Reception
19:00 Dinner

Day 2: Thursday 17th December

Session 2: Priorities in Public Health Infections Research
Chair: Sir Leszek Borysiewicz, MRC

9:00 - 9:15 Review of Day 1
   Dr Wendy Ewart, MRC

9:15- 10:30 Making the Matrix Work: Definition of Priorities & Delivery
   Introduction
   Dr Wendy Ewart, MRC
   Group Discussion
   5 re-structured break out groups across research interests and disciplines

10:30 – 11:00 Coffee
11:00 – 12:15 Feedback from Break Out Groups and Discussions
12:15 – 12:30 Concluding Remarks and Next Steps
   Sir Leszek Borysiewicz, MRC
   Professor Jonathan Friedland, Imperial College

12:30 Lunch
## Public Health Infections Workshop

### Attendees list

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Janet Allen</td>
<td>Biotechnology and Biological Sciences Research Council</td>
</tr>
<tr>
<td>Professor Jeff Almond</td>
<td>Sanofi Pasteur</td>
</tr>
<tr>
<td>Professor Daniel Altmann</td>
<td>Imperial College London</td>
</tr>
<tr>
<td>Professor David Armstrong</td>
<td>King’s College London</td>
</tr>
<tr>
<td>Sir Leszek Borysiewicz</td>
<td>Medical Research Council</td>
</tr>
<tr>
<td>Dr Meredith Bradbury</td>
<td>Technology Strategy Board</td>
</tr>
<tr>
<td>Professor William Carman</td>
<td>University of Glasgow</td>
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<tr>
<td>Professor Mary Collins</td>
<td>University College London</td>
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<tr>
<td>Dr Lloyd Czaplewski</td>
<td>Biota Europe Ltd</td>
</tr>
<tr>
<td>Professor David Dockrell</td>
<td>University of Sheffield</td>
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<tr>
<td>Professor Gordon Dougan</td>
<td>Sanger Institute</td>
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<tr>
<td>Professor Brian Duerden</td>
<td>Department of Health</td>
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<tr>
<td>Professor Tom Evans</td>
<td>University of Glasgow</td>
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<tr>
<td>Dr Wendy Ewart</td>
<td>Medical Research Council</td>
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<td>Professor Neil Ferguson</td>
<td>Imperial College London</td>
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<tr>
<td>Professor Roger Finch</td>
<td>University of Nottingham</td>
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<tr>
<td>Professor John Frank</td>
<td>University of Edinburgh</td>
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<tr>
<td>Professor Jonathan Friedland</td>
<td>Imperial College London</td>
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<tr>
<td>Professor Noel Gill</td>
<td>Health Protection Agency</td>
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<tr>
<td>Dr Pat Goodwin</td>
<td>Wellcome Trust</td>
</tr>
<tr>
<td>Professor George Griffin</td>
<td>St Georges University</td>
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<tr>
<td>Professor Andy Hall</td>
<td>London School of Hygiene and Tropical Medicine</td>
</tr>
<tr>
<td>Dr Russell Hamilton</td>
<td>National Institute for Health Research</td>
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<td>Professor Graham Hart</td>
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<td>Dr Alan Hay</td>
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<td>London School of Hygiene and Tropical Medicine</td>
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<td>Professor Andrew Hayward</td>
<td>University College London</td>
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<td>Professor Michael Malim</td>
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<td>Professor Jane McKeating</td>
<td>Birmingham University</td>
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<td>Dr Penny Wilson</td>
<td>Technology Strategy Board</td>
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<td>Professor Douglas Young</td>
<td>Imperial College London</td>
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Background and purpose of review

NIHR has been tasked with leadership of the public health infection strategy by OSCHR, MRC has been working with NIHR to develop this strategy.

Aim:
To deliver an integrated, national vision for public health infection research that reflects the public health needs and strengths of the UK research community.

Objective:
To provide a clear statement of the research opportunities in the field of public health infection research in order to inform funding priorities and to inform policy development in this area at national and international levels.

Four phase process:

Phase I – landscaping exercise

Main activities:
1. Literature review
   Major government publications, House of Lords Select Committee Reports, Department of Health publications, reviews of research areas, relevant websites, statistics etc.
2. Identification of ‘top 5’ research priority areas
   • Healthcare associated infections
   • Antimicrobial resistance
   • Emerging infections
   • Sexually transmitted infections including HIV
   • Acute respiratory infections
3. Preparation of landscape document

Phase II – survey of experts

• Questionnaire sent to 64 diverse experts along with landscaping document
• 11 responses though 4 of these represented consensus from groups (eg HPA, DH, Imperial)
Phase II – Scientific Advisory Group mtg  
18 September 2008

- Review by Strategy Advisory Group of questionnaire results and the research priority areas identified
- Consolidation into 3-dimensional strategy framework/matrix for wider discussion at workshop

Phase III - Workshop

**Aims of Workshop**

- To discuss needs and opportunities in public health infections research – refine the 3-D Matrix
- To define key research areas and questions that should form strategic priorities within the OSCHR framework – populate the 3-D Matrix
- Advise on how identified research priorities might be taken forward
  - Funding mechanisms
    - Focus, large v small, NIHR v + MRC
  - Roles of different institutions
    - Teaching Hosp, DGH, Universities, HPA etc

Phase IV - Next steps

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tr>
<td>Dec 2009/Jan 2010</td>
<td>Formulation of strategy document in light of workshop discussions</td>
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<tr>
<td>Late Jan 2010</td>
<td>Review of strategy document by Scientific Advisory Group</td>
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<tr>
<td>March 2010</td>
<td>Present Public Health Infections to OSCHR</td>
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<tr>
<td>April/May 2010</td>
<td>Publication and dissemination to key stakeholders</td>
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</table>
Health Care Associated Infections
A Holmes

Key strengths
• Weaknesses and needs
• Opportunities across the breadth of field
• Possible research priorities

Consider scope
• All healthcare associated - not just acute care
• Includes staff and workforce
• Developed and developing world
• Includes children and neonates
• Need to engage broad research experience
• Results of Consultation on priorities using UKCRC coding:
  – Emphasis on aetiology, detection, screening, and diagnosis, and development of treatment and therapeutic interventions.
  – Only 4.2% on ‘code 3’ (prevention).
  – No responses in ‘code 6’ (health services research).

Consider marked reductions in MRSA BSIs

Key strengths
• There is the will and the political and public interest and support for research and action
• The burden of disease
• It is where emergence happens and intelligence needed
• Opportunities for true synergistic research partnerships... engineering, materials, design, management, organisational, policy, architecture, human factors, behavioural
• Societal impact
• Crosscutting quality improvement benefit in healthcare
• Infection control critical in addressing antibiotic resistance
• Potential for rapid impact
• Part of patient safety agenda, quality improvement agenda, innovation agenda...
• Increasing interest on analysis of national strategies and policy
• WHO priority
  – Validated and standardized prevention strategies have been shown to reduce HCAI
  – At least 50% of HCAI could be prevented
  – Most solutions are simple and not resource-demanding and can be implemented in developed, as well as in transitional and developing countries
• Global challenge

Weaknesses and Needs.
• Collaborative opportunities missed, expertise engagement too narrow
• Poor surveillance. Poor use of data
• Poor data from developing world
• Needs cross boundary, whole healthcare economy approach
• Much organism specific research etc little applied research on implementation, sustainability, organisational development, behaviour and resilience, human factors etc
• Poor economic models
• Syndemic research poorly developed

Gerberding, J. L. JAMA 2005;294:1403-1406

Key Challenges to Transform Health Protection Research
Opportunities across the breadth of the field

- Opportunities for broad engagement of expertise and partnerships e.g. UKCRC CIPM- 4 interlinking workstreams
  WS1: Embedding infection prevention within NHS organisational structures – (i) implementation and adoption of innovation (ii) infection prevention and antibiotic prescribing behaviours- changing and sustaining
  WS 3: Developing and utilising infection surveillance schemes across the whole health care economy.
  - Identifying patterns of risk - syndromic surveillance - more sophisticated use of existing datasets
- Involving business and management school, social marketing, organisational psychology, academic data management

Possible research priorities

Common Research Questions across all diseases:
- Improved understanding of natural history of pathogens and modes of transmission
- Need for improved surveillance of existing and potential new pathogens (not just organism specific, need to include patterns of disease)
- The development of new rapid diagnostic kits
- The development of new treatments

Possible research priorities HCAI

ARHAI highlighted:
- The environment (including patient environment but also encompass estates, buildings, facilities etc.)
  Includes organisations, systems, choice architecture
- Technological innovation (including rapid testing screening and diagnostics)
  Includes research into device design
- Patient management (including care technology, infection prevention practice)
Possible research priorities HCAI

ARHAI research focus session on priorities presentations:
- Methods of patient isolation and/or cohorting impact on HCAI and the control of antibiotic resistant organisms
- Bacterial vaccinations against hospital infections
- Multidisciplinary applied research on infection prevention and antibiotic prescribing addressing:
  - Implementation and adoption of innovation (processes and technologies)
  - Behavioural interventions (at multiple levels, and sustained)

Behavioural Interventions

- Behavioral interventions: Developing systems that address human factors (decision aids, desired action is the default, habits and patterns used in design, process clearly specified, takes advantage of pathways).
  
  Pronovost et al. HSR 41:4 1599-1617

Behavioural Interventions

- Behavioral interventions: Developing systems that address human factors (decision aids, desired action is the default, habits and patterns used in design, process clearly specified, takes advantage of pathways).

  Rear R 2006 HSR 41.4,1677-89, Pronovost et al HSR 41:4 1599-1617

Behavioural Interventions

- Behavioral interventions: Developing systems that address human factors (decision aids, desired action is the default, habits and patterns used in design, process clearly specified, takes advantage of pathways).

  Pronovost et al HSR 41:4 1599-1617

Behavioural Interventions

Social marketing strategies are being investigated and developed to promote identified behaviours in infection prevention and in antibiotic prescribing practice in the selected targeted populations

- Little done in the acute setting
- Campaigns often used researched and evaluated so evidence of effectiveness or sustainability of impact is scant

Social marketing strategies are being investigated and developed to promote identified behaviours in infection prevention and in antibiotic prescribing practice in the selected targeted populations

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Social marketing strategies are being investigated and developed to promote identified behaviours in infection prevention and in antibiotic prescribing practice in the selected targeted populations

In addition.......

- Design of healthcare, systems, and organisational issues
  - understanding resilience, the use of indicators and managing complexity
- Cross boundary research approaches for HCAI, antibiotic prescribing, and surveillance
- Better understanding of health economics
- Need for shared international research on policy, strategy and organisational contexts and a global understanding
Antimicrobials: the public health challenge of antibacterial resistance

Professor Brian I. Duerden CBE
Inspector of Microbiology and Infection Control
Department of Health, London

...resistance to antibiotics constitutes a major threat to public health

Antimicrobials
- Antibacterials (antibiotics)
- Antifungals
- Antivirals

Concerns about resistance
- Treatment failures
  - In initial empiric treatment
  - In all treatments, i.e., no effective agents
- Clinical cost to patients
  - Prolonged illness; death
- Use of more toxic agents
- Cost – empiric and specific agents
- Side effects of broad-spectrum agents
  - C. difficile
- Unregulated and indiscriminate use of antimicrobials

Resistance problems in clinical practice
- M. tuberculosis – MDRTB; XDRTB
- MRSA
- ESBL-producing E. coli
- Carbapenemase-producing Gram –ves
  - Klebsiella, Enterobacter, E. coli
  - Acinetobacter; Pseudomonas
- Glycopeptide resistant enterococci
- N. gonorrhoeae
- Pen-R pneumococci

Public health responses
- Strategy
- Surveillance
- Practice
- Research
- Education
Strategy - 40 years of reports
- Swann Report – animals & vet. med. 1969
- House of Lords
  - Antibiotic resistance 1998
  - …………… Revisit 2001
  - Fighting infection 2003
- Standing Medical Advisory Committee
  - Path of Least Resistance 1998
- Chief Medical Officer
  - Getting Ahead of the Curve 2002
  - Winning Ways 2003

UK Strategy to combat antimicrobial resistance - 2000
- Conservation
  - Make best use of what we have
  - Reduce the pressure for resistance
1. Surveillance
   - Resistant organisms; illness; usage
2. Prudent use
   - Human; veterinary; animal husbandry
3. Infection control

Specialist Advisory Committee on Antimicrobial Resistance  2001-7
- Research funding
- Antimicrobial pharmacist project
- Surveillance – still to be fully achieved!
  - Resistance; Prescribing; Clinical outcome
- EU intergovernmental conference
  - Technology; need for new agents
- Public education
- Professional education

ARHAI 2007 -
- Advisory Committee on
  Antimicrobial Resistance and Healthcare Associated Infection

Public health policy outputs
- Overarching report 2007
  - Antimicrobial usage
  - Bacterial resistance
    - i.e., surveillance in man and animals
- Professional education
- Prudent prescribing
- Public education
  - i.e., how to change practice

HCAI : 2004-09
- MRSA and C. difficile
  - Plus Acinetobacter, ESBL-E. coli
- Antibiotic selection promotes all HCAI
- Antimicrobial stewardship guidance
- Code of Practice; Health Act 2006
  - Health and Social Care Act 2008
Code of Practice for Infection Prevention and Control

- Management & organisation
- Antimicrobial formulary & prescribing policy
  - Implemented
  - Audited
- Staff/workforce
  - Training to deliver the protocols
  - Appraisal

Science to inform the responses

- Antibacterial agents
  - Targets; mode of action; new drugs
- Antimicrobial resistance
  - Mechanisms; spread
- Surveillance
  - Resistance; antibiotic usage; clinical outcome
- Alternatives and adjuvants

Research

- 2004 -8 DH programme: 14 projects
  - Mechanisms & mutations  3
  - Isolation & infection control  2
  - Public education & practice  1
  - Laboratory testing  1
  - Surveillance  4
  - Environmental organisms  2
  - Antifungal use & resistance  1

New antibacterial agents

- Why so few?
  - Easy targets cracked, i.e., difficult science
  - Law of diminishing returns
  - Cost – poor financial return
  - Short time before resistance develops

- We need
  - Focus on novel agents
  - Better use of those that are found

Swedish Presidency Initiative

- Innovative incentives for [new] effective antibiotics
  - Stockholm Conference Sept 2009
  - London Seminar November 2009
  - Council Conclusion – December 2009
  - Commission action plan within 24 months

Antibiotic resistance research

- Resistance mechanisms
- Selection and transmission
- Genetics
- Blocking mechanisms
- Means to prevent/delay – conservation
- Synergy
**Surveillance**

- Resistance (current sources)
  - Blood culture data (HPA CoSurv)
  - Reference laboratories (Referred isolates)
  - Routine diagnostic data (HPA AmSurv)
- Antibiotic prescribing data
  - Primary care (by prescription)
  - Secondary care – inadequate (not patient specific)
- Outcome data

*Does prudent prescribing result in less resistance and better outcomes?*

**Alternatives and adjuvants**

- Make current agents more effective
  - Block resistance
  - Enhance activity
- Immune stimulation/modulation
  - Promote immune responses
- Promote the normal flora
  - Prebiotics, probiotics

**Research for the future**

- New agents
  - And how to use them
- Circumvent resistance
- Improve the evidence base for changing practice
5c Emerging and re-surging infections

Neil Ferguson
MRC Centre for Outbreak Analysis and Modelling
Faculty of Medicine
Imperial College

Introduction

- Public health challenges
- Strengths/weaknesses
- Priorities

The threat

- Pandemic = global epidemic of a new disease.
- Starts with a zoonosis mutating to be transmissible.
  - Influenza and HIV/AIDS
  - SARS – near-pandemic.
  - H5N1/Nipah/VHFs/???... – the next pandemic?
- Can profoundly affect society.
- Risk may be increasing – encroachment on habitats, higher human/livestock densities...

Public health challenges

- Predict:
  - Characterise zoonotic pathogens.
  - Identify specific threats.
  - Understand predictors of emergence.
- Prepare:
  - Improve surveillance
  - Pre-screen antimicrobial agents
  - Rapid production capacity
- Detect:
  - Innovative surveillance (e.g. GPHIN).
  - Rapid in-country diagnostics.
- Respond:
  - Real-time characterisation (virological, clinical, epidemiological).
  - Healthcare system (and societal) resilience.
  - Real-time clinical research (and EUAs).

Re-emerging infections

- Fundamentally different challenge.
- Known agents.
- Generally predictable (e.g. dengue and climate change).
- But may bring ‘global health’ home to roost.

UK strengths

- Global reach:
  - ‘Tropical medicine’ strong.
  - Reference centre for veterinary medicine.
  - Good representation in WHO.
- Virology:
  - Good basic virology.
  - Good clinical virology in some areas.
- Epidemiology:
  - Strong player in epidemiology and modelling.
- Healthcare/public health:
  - Surveillance can benefit from centralised nature of healthcare and emergency response.
<table>
<thead>
<tr>
<th>UK weaknesses</th>
<th>Priorities</th>
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<tr>
<td>• Virus discovery/diagnostics (esp. integrated</td>
<td>• Characterising potential threats and reservoirs.</td>
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<td>with field studies).</td>
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<tr>
<td>• Limited integration of veterinary and human</td>
<td>• Sustainable surveillance – benefit sharing with developing</td>
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<tr>
<td>virology and epidemiology</td>
<td>countries, novel detection &amp; identification technologies.</td>
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<tr>
<td>• Very high global connectivity (we get things</td>
<td>• Quantitative understanding of predictors of emergence.</td>
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<td>first).</td>
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<tr>
<td>• Rapidity of commissioning/implementing real-</td>
<td>• Understanding the genetic determinants of transmissibility,</td>
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<tr>
<td>time clinical research.</td>
<td>virulence and species specificity for major threats.</td>
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<tr>
<td>• Connectivity across government in a public</td>
<td>• Compound screening, development of ‘generic’ antiviral and vaccine</td>
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<td>health crisis.</td>
<td>technologies, rapid manufacturing facilities.</td>
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<td>• Public-private partnerships in a public health</td>
<td>• Quantifying effectiveness of non-pharmaceutical interventions for</td>
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<td>crisis (rapid engagement of Pharma).</td>
<td>different pathogens.</td>
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<td>• Protocols for ultra-rapid clinical R&amp;D and emergency use</td>
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<td>authorisation of novel treatments/vaccines.</td>
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<td></td>
<td>• Behavioural/social science research on risk communication,</td>
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<td>improving population compliance and maintaining resilience in a</td>
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<td>public health emergency.</td>
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5d STI & HIV Research for Improved Population Sexual Health

Public Health Infections Research Strategy Workshop:

STI & HIV Research for Improved Population Sexual Health

Professor Graham J Hart PhD

STI/HIV PREVENTION - A changing paradigm

Behaviour of individuals

STI/HIV incidence/prevalence

Biology of organism

Behaviour of populations

Socio-economic and demographic environment

STI/HIV incidence/prevalence

Ecology of organisms

PREVENTION

Time

STI/HIV PREVENTION - A changing paradigm

Behaviour of populations

Socio-economic and demographic environment

STI/HIV incidence/prevalence

Ecology of organisms

PREVENTION

Time

Estimated number of adults (15-59 years) living with HIV (both diagnosed and undiagnosed) in the UK: 2008

Diagnosed

Undiagnosed

Total = 77,550 (73,000 - 83,300)

Excludes 5,450 HIV infections among individuals outside the 15-59 years age range

6,550

4,550

1,200

550

450

150

2,150

2,250

4,050

2,850

8,950

0

10,000

20,000

30,000

40,000

50,000

60,000

70,000

80,000

90,000

100,000

Estimated number of adults (15-59 years) living with HIV (both diagnosed and undiagnosed) in the UK: 2008

Heterosexual

men born in Africa

Heterosexual

women born in Africa

Heterosexual

men born in UK/elsewhere

Heterosexual

women born in UK/elsewhere

Injecting drug user men

Injecting drug user women

STI/HIV PREVENTION - A changing paradigm

Behaviour of populations

Socio-economic and demographic environment

STI/HIV incidence/prevalence

Ecology of organisms

PREVENTION

Time
### Number of New Diagnoses of Selected STIs, GUM Clinics, United Kingdom: 2008

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<tr>
<td>Chlamydia</td>
<td>123,018</td>
<td>1%</td>
<td>116%</td>
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<tr>
<td>Genital warts</td>
<td>92,525</td>
<td>3%</td>
<td>29%</td>
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<tr>
<td>Genital herpes</td>
<td>28,957</td>
<td>10%</td>
<td>65%</td>
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<tr>
<td>Gonorrhoea</td>
<td>16,629</td>
<td>-11%</td>
<td>1%</td>
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<tr>
<td>Syphilis</td>
<td>2,524</td>
<td>-4%</td>
<td>1,032%</td>
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### Strategic Priorities: STI/HIV Incidence

- Improved methods of determining incident HIV infection
- How to reduce the undiagnosed fraction
- What factors are associated with reductions/increases in some STIs and not others
- Innovation in point of care testing (POCT), rapid diagnostics & communication technology
- Control of common STIs (Chlamydia; HPV) & relation to long term (reproductive) health

### STI/HIV Prevention - A Changing Paradigm

#### Behaviour of Populations

#### Socio-economic and Demographic Environment

#### Prevention

#### STI/HIV Incidence/Prevalence

#### Ecology of Organisms

### Time

### National Survey of Sexual Attitudes & Lifestyles

#### Percentage Distribution of Heterosexual Partners: Lifetime, by Gender, 1990 & 2000

### Gay Men’s Sexual Health Survey: Sexual Behaviour from 1996-2008
**Diagnoses of syphilis in GUM clinics by sex: England & Wales; Scotland**

- Scotland - Men
- Scotland - Women
- England and Wales - Men
- England and Wales - Women

**AIDS first recognised**

- Scotland - Men
- Scotland - Women
- England and Wales - Men
- England and Wales - Women

---

**Strategic Priorities: Behaviour of populations**

- Social and behavioural factors underlying increases in risk behaviour
- Clinical (individual) and community (population) level interventions to reduce risk behaviour
- Re-established (syphilis), new (LGV) & emerging (Hep C) STIs particularly in high risk groups
- Translational public health: from trial efficacy to population effectiveness

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**STI/HIV PREVENTION - A changing paradigm**

**Behaviour of populations**

**PREVENTION**

**Ecology of organisms**

**STI/HIV incidence/prevalence**

Socio-economic and demographic environment

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**STI/HIV PREVENTION - A changing paradigm**

**Behaviour of populations**

**PREVENTION**

**Ecology of organisms**

**STI/HIV incidence/prevalence**

Socio-economic and demographic environment

---
Ciprofloxacin resistance (≥1mg/l) in gonorrhoea, by sexual orientation, England & Wales: 2004-2008

Phylogenetic tree of sequences closely linked to at least one other (N = 402)

Clusters with 10 members are shown in red
Letters indicate the position of identified clusters

Strategic Priorities: Ecology of organisms

- Basic public health science: pathogenesis, epidemiology, surveillance, resistance
- Early identification of sexual networks associated with ‘outbreaks’ of resistant organisms
- Modelling the impacts of increased susceptibility, infectivity and transmission

STI/HIV PREVENTION - A changing paradigm
Strategic Priorities: Prevention

- Primary, secondary and tertiary prevention
- Evaluating the impacts of generalised and targeted social marketing
- New and emerging prevention technologies
  - Circumcision
  - Pre-exposure prophylaxis
  - Vaginal/rectal microbicides
- Primary Care: Management of HIV/addressing other health needs in an ageing cohort

Recent Investments:
DH/MRC Sexual Health & HIV Research Strategy Committee

2002 – 2007
PRP allocates £1m per annum for co-funded programme of research to support the National Sexual Health & HIV Strategy

SHHRSC issues 4 Highlight Notices
150 submissions
28 funded

2007 -
NIHR: increasing support for STI/HIV research

Achievements

- Strategic overview of research priorities
- Targeted funding to address specific gaps in knowledge
- Increased evidence base for improved STI/HIV prevention and control
- Methodological development
- Dissemination of evidence to HCWs & service providers
- Investment in capacity building & development of early career researchers in sexual health/HIV

UK Strengths

- Exceptionally good surveillance – trends; populations; new & emerging infections
- Leadership in well-phenotyped patient cohorts in HIV: natural history; toxicity & resistance; guideline development
- High quality & timely observational studies
  - NATSAL
  - MSM
  - UK Africans
- Trials expertise for global health – UK prevention & treatment?

Combined Strategies for Effective STI/HIV Control

- **PRIMARY PREVENTION**
  - Behavioural: Social Marketing
  - Biomedical: Vaccines (HPV, Hep B)
  - Microbicides
  - Circumcision
  - PreP

- **EARLY DIAGNOSIS**
  - Screening & treating high-risk populations for STIs
  - Reducing undiagnosed HIV

- **TREATMENT**
  - Infectivity/transmission
  - Health service delivery
CONCLUSION

• Changed sexual health/HIV paradigm

• Recent investments have established a strong evidence base & cadre of skilled researchers

• New opportunities exist in primary prevention, early diagnosis & treatment – respectively, & in combination

• Future research agenda should build on UK competitive advantage in sexual health & HIV

Acknowledgements

Professor Anne Johnson
Dr Pam Sonnenberg
Severe infections: respiratory, CNS and gastrointestinal

David Dockrell
Wellcome Senior Clinical Fellow
University of Sheffield

Severe respiratory infections

- Pneumonia a leading cause of death at all ages, direct and indirect (2 million children p.a).
- Pneumococcal disease one of four leading causes of infectious disease-related death.
- Emerging infections: community-acquired meticillin Staph. aureus and health-care-associated infections
- Burden of viral respiratory tract infections e.g. RSV, IAV (Sur attack rate 13%)
- Significant impact at extremes of age, the immunocompromised and those with pre-existing lung disease

Severe gastro-intestinal infections

- Global dimension, second leading cause of infant mortality.
- Invasive salmonellosis a major problem in immunocompromised groups
- Health care associated infections e.g. Clostridium difficile infection
- Morbidity E. coli O157
- Economic costs e.g. Noravirus school, ward closures etc.

Severe neurological infections

- Meningococcal disease an important cause of death in children/young adults.
- Pneumococcal meningitis, HSV encephalitis major problems in the elderly
- Emerging viral infections e.g. West Nile Virus
- Global dimension with burden greatest where resources least equipped to deal with consequences e.g. TB meningitis, Meningococcal African outbreak in 2002 1/4 million cases

Strengths

- Epidemiology
  - HPA Networks
  - Public health system
  - Infection control
- Microbiology
  - Genome sequencing
  - Molecular microbiology

- Host factors
  - Genetics of susceptibility
  - Innate and adaptive immunology
- Modeling
- Translation
  - Test evaluation e.g. Colindale
  - Vaccinology
  - NHS, UKCRN
**Strengths**

- Global perspective
- Structures and links with developing countries
- Charities
- Wellcome Trust, MRC

**Weaknesses/Opportunities**

- Difficulty containing evolution of antimicrobial resistance e.g. Acinetobacter baumanii in HCAI pneumonia
  - Need novel approaches
- Vaccine efficacy in select groups
- Rapid diagnostics
  - Application of ‘omics’ technologies to identify microbial or host signatures of infection
- Immunomodulatory therapy
  - Inability to deliver immunomodulatory therapy in sepsis

**Vaccine challenges**

- Replacement
  - Serotypes
  - Species
- Burden of disease by vaccine resistant strains
- Microbial evolution
- Vaccine resistant populations
  - Immunocompromised hosts
  - Elderly

**Alternative approaches**

- Colonisation
- Severe infection
- Clinical infection
- Sub-clinical infection
- Vaccination
- Antimicrobials
- Immunomodulatory therapy
- Anti-inflammatory therapy
- Host response

**Genetics**

- Susceptibility to disease
- Severity of disease
- Response to therapy
- Side effects of therapy

**Clinical translation**

- Balancing research ethos with conflicting demands within the NHS
- Commitment to research positions
  - Training fellowships
  - Academic medicine
- Limited centres able to perform Phase I/II proof–of–concept, first in man studies, ethics
- Many patients live in areas remote from centres of excellence/ regional resources
Underpinning biomedical science

- Pipeline for diagnostics and therapeutics
- Investment in future clinical care
- Needs long term commitment
- Infrastructure
- Non-clinical biomedical scientist career structure
- Need to co-ordinate and join up basic and clinical science
- Benefits extend beyond health care but also into economy through vibrant biotechnology industry