



## **Drug-related infectious diseases**

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Tuesday 24th October 2017

### Basic (Case) Reproduction Rate "All you need to know to design interventions"





Number of secondary infections produced by a typical case of an infection in a population that is totally susceptible

### **Basic Reproduction Rate** What it predicts





### **Drug Related Infections** Public Health Priorities



- HIV
- Hepatitis C
- Hepatitis B
- Tuberculosis
- Anthrax
- Botulism
- Other bacterial infections



## Hepatitis C – epidemiological overview



- 130–170 million persons (2%–3% of the world's population) chronically infected with HCV
  - Highest prevalence in Africa and Central and East Asia (>3% prevalence)
  - Prevalence in Europe ranges from 0.1% in Belgium, Ireland and the Netherlands to 8.8% in Italy
- Incidence in developed countries declining
- 27% of cirrhosis and 25% of hepatocellular carcinoma attributed to HCV
- 350 000 deaths/year





### **Routes of Transmission**

Contact with blood of an infected person primarily through:

Sharing of contaminated needles, syringes, or other injection drug equipment

Less commonly through:

- Sexual contact with an infected person
- Birth to an infected mother
- Needlestick or other sharp instrument injuries



### Symptoms of acute infection

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Gray-colored bowel movements
- Joint pain
- Jaundice





### **Incubation period**

• 14 to 180 days (average: 45 days)

### **Health impact**

- 20%–30% of newly infected persons develop symptoms of acute disease. Those who do develop acute illness usually recover with no lasting liver damage.
- 75%–85% of newly infected persons develop chronic infection
- ♦ 60%–70% of chronically infected persons develop chronic liver disease
- ♦ 5%–20% develop cirrhosis over a period of 20–30 years
- $\$  1%–5% will die from cirrhosis or liver cancer



### Treatment

#### Acute disease:

• Antivirals and supportive treatment

#### **Chronic disease:**

- Regular monitoring for signs of liver disease progression;
- New direct acting antiviral medications offer shorter durations of treatment and increased effectiveness
- Over 90% of patients who complete direct acting antiviral medications treatment are cured
- No lasting immunity after treatment

### Vaccine

• There is no vaccine available against hepatitis C

## Rate of all reported hepatitis C cases across EU/EEA countries, 2006-2015





Source: Country reports from: Austria, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

## Rate of reported hepatitis C cases in EU/EEA by country, 2015\*





\*Countries included if their surveillance systems captured data on both acute and chronic cases. Source: Country reports from: Austria, Bulgaria, Croatia, Czech Republic, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Iceland, Ireland, Italy, Latvia, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

# anti-HCV prevalence in the adult general population in the EU/EEA, 2005-2015





### **Reported transmission category for acute and chronic hepatitis C cases, 2015**



Source: Country reports from: Austria, Denmark, Estonia, Hungary, Ireland, Italy, Latvia, Malta, Netherlands, Portugal, Romania, Slovakia, Slovenia, and the United Kingdom.

## Injecting drug use and hepatitis C

CONTRACTOR

Injecting drug use is central to the hepatitis C epidemic in Europe Anti-HCV prevalence among PWIDs on average 50 times greater than the general population (Hahné et al., 2013)

> Percent 100 100 80 80 **Anti-HCV** prevalence (%) among PWIDs 60 60 in the European Union, Norway and Turkey, 2013–14 40 40 20 20 Ô 0 Malta Cyprus Greece Germany Finland Estonia ithuania Slovenia Slovakia Croatia Turkey ungary Italy Austria Norway Bulgaria Latvia ortugal Belgium **United Kingdom** Vethenlands Sweden Zech Republic Samples with national coverage Samples with sub-national coverage

## Hepatitis B – epidemiological overview

- 240 million persons (3% of the world's population) estimated to be chronically infected with HBV
  - Highest prevalence in Africa and East Asia (5-10% prevalence)
  - Prevalence in Europe ranges from 0.1% in Ireland to 4.4% in Romania
- 30% of cirrhosis and 53% of hepatocellular carcinoma attributed to HBV
- 780 000 deaths/year





### **Routes of Transmission**

Contact with infectious blood, semen, and other body fluids primarily through:

- Sexual contact with an infected person
- Birth to an infected mother
- Sharing of contaminated needles, syringes, or other injection drug equipment
- Needlesticks or other sharp instrument injuries



### Symptoms of acute infection

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Gray-colored bowel movements
- Joint pain
- Jaundice





### **Incubation period**

• 45 to 160 days (average: 120 days)

### **Health impact**

- 30%–50% of persons > 5 years develop symptoms of acute disease
- Symptoms less common in children and immunosuppressed
- Most persons with acute disease recover with no lasting liver damage; acute illness is rarely fatal
- Among unimmunized persons, chronic infection occurs in 6%–10% of older children and adults
- Much higher rates of chronic infection in unimmunised infants and children
- ✤ 15%-25% of chronically infected persons develop chronic liver disease, including cirrhosis, liver failure, or liver cancer



### Treatment

#### Acute disease:

• No medication available; best addressed through supportive treatment

#### **Chronic disease:**

- Regular monitoring for signs of liver disease progression;
- some patients are treated with antiviral drugs

### Vaccine

- Vaccine available against hepatitis B for adults, children and infants
- Lifelong immunity following first full course of vaccination (for most)
- Vaccine (+/- immunoglobulin) can be used to prevent infection postexposure (should be given as soon as possible after exposure)

## Rates of acute and chronic hepatitis B cases in EU/EEA countries, 2006-2015



Source: Country reports from: Austria, Bulgaria, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom\*. \* Note that UK data exclude Scotland.

## Rate of reported acute hepatitis B cases in EU/EEA by country, 2015\*





#### \*Data for UK exclude Scotland

Source: Country reports from: Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom

### Rate of reported chronic hepatitis B cases in EU/EEA by country, 2015\*





#### \*Data for UK exclude Scotland

Source: Country reports from: Austria, Denmark, Estonia, Finland, Iceland, Ireland, Latvia, Luxembourg, Malta, the Netherlands, Norway, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom



Source: Country reports from: Austria, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom\*. \* UK data exclude Scotland.

## Hepatitis B & C: Epidemiological Summary



- High numbers of newly diagnosed hepatitis B and C cases
  - Hepatitis C more commonly reported than hepatitis B
  - Chronic cases dominate across both diseases
  - Marked variation between countries
- For Hepatitis B:
  - a decrease in acute cases
  - a rise in newly reported chronic infections
- Hepatitis C:
  - strong north-south geographical trend
- Transmission routes for hepatitis B differ from hepatitis C, and for hepatitis B these routes vary by disease status
- Imported cases form a significant proportion of newly reported cases, especially for hepatitis B

### Key populations: range of prevalence estimates from EU/EEA countries, 2005 -2015





#### Source: ECDC, 2016



### **Routes of Transmission**

Contact with blood of an infected person primarily through:

- Sexual contact with an infected person
- Sharing of contaminated needles, syringes, or other injection drug equipment (4% of HIV infections in EU/EEA 2015)
- Birth to an infected mother
- Transfusion, needlestick or other sharp instrument injuries



### Symptoms of acute infection

- Flu-like illness 2-6 weeks after HIV infection, which lasts for a week or two.
- After these symptoms disappear, HIV may not cause any symptoms for many years
- Many people with HIV don't know they're infected

### HIV



### **Health impact**

- Without treatment HIV infection progressively damages the immune system
- Average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype
- ✤ Progressive immune system damage results in AIDS
- ✤ increased risk of life-threatening infection, cancer or wasting disease.
- ⇔ without treatment, people with AIDS typically survive about 3 years.

### HIV



### Treatment

## Antiretroviral therapy (ART)/ highly active antiretroviral therapy (HAART)

HIV Nucleon de deservet carrection de unit initiations the virus from reproducing, allowing the immune system to repair itself and prevent further damage. A complete of the drugs is used because HIV can quickly adapt and become resistant.

• Non-nucleoside reverse transcriptase inhibitors Usually register war-hake yet been diagnosed with HIV take between one protected in the form (PIs).

Treating and entrice the sound of virus in the blood to undetectable levels tegrase inhibitors.

### Vaccine

• There is no vaccine available against HIV

# HIV diagnoses, by mode of transmission, 1991-2014, EU/EEA





Data is not yet fully adjusted for reporting delay. Cases from Estonia and Poland excluded due to incomplete reporting on transmission mode during the period; cases from Italy and Spain excluded due to increasing national coverage over the period.

#### Source: TESSy, ECDC/WHO (2016)

### HIV diagnoses fall, but localised outbreaks show vulnerability

#### Newly diagnosed HIV cases related to injecting drug use

Cases in the European Union

### Patients receiving opioid substitution treatment (OST)



- Injecting-related HIV notifications in EU reach lowest number
- EMCDDA and ECDC monitor prevalence, risk behaviour, interventions
- Outbreaks in Greece and Romania in 2011 trigger EU-wide risk assessments and country missions
- Multi-indicator analyses for policy support



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### Five-fold increase in drug related HIV cases in Glasgow THE IMPACT OF THE GLOBAL FUND'S WITHDRAWAL ON HARM REDUCTION

PROGRAMS

A CASE STUDY FROM BULGARIA EURASIAN HARM REDUCTION NETWORK USAID-FUNDED HEALTH POLICY PROJECT

RAPID COMMUNICATIONS

Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015

C Giese <sup>12</sup>, D Igoe <sup>2</sup>, Z Gibbons <sup>3</sup>, C Hurley <sup>4</sup>, S Stokes <sup>3</sup>, S McNamara <sup>3</sup>, O Ennis <sup>4</sup>, K O'Donnell <sup>2</sup>, E Keenan <sup>3</sup>, C De Gascun <sup>56</sup>, F Lyons <sup>7</sup>, M Ward <sup>4</sup>, K Danis <sup>18</sup>, R Glynn <sup>4</sup>, A Waters <sup>5</sup>, M Fitzgerald <sup>4</sup>, on behalf of the outbreak control team <sup>9</sup>

# Percentage of HIV diagnoses, by route of transmission, 2015, EU/EEA





Source: ECDC/WHO (2016)

## Percentage of new HIV diagnoses with known mode of transmission, EU/EEA, 2015



Source: ECDC/WHO (2016)

Unknown mode of transmission is excluded from proportions presented here.

## HIV prevalence among people who inject drugs, 2011-2013





Source: ECDC/EMCDDA (2015); Dublin monitoring report on PWID

#### Late diagnosis of HIV among PWID is common New HIV diagnoses, by CD4 cell count per mm<sup>3</sup> at diagnosis and transmission mode, EU/EEA, 2015





Source: ECDC/WHO (2016)

36

# Estimated proportion of all PLHIV who are virally suppressed, WHO European Region





Source: ECDC, Preliminary data reported in 2016 as part of Dublin Declaration reporting; only countries with data on PLHIV and viral suppression measures are included in the map and the regional average.

# Legal and Policy Barriers to HIV test provision and uptake

Out of 48 countries in Europe and Central Asia, how many reported that unfavourable laws and policies limit provision and uptake of HIV testing services among injecting drug users? Out of 48 countries in Europe and Central Asia, how many reported that they had laws and policies that allow provision of needle and syringe programmes in prison settings?

• A	3	• A	5
■ B	7	■ B	10
• C	13	• C	20
■ D	27	■ D	30

#### Number of countries reporting that unfavourable laws and policies limit provision and uptake of HIV testing services among key populations, 2016



ECDC EVIDENCE BRIEF: HIV and laws and policies in Europe, May 2017

### **Countries reporting that unfavourable laws and policies limit provision and uptake of HIV prevention services among key populations, 2016**





ECDC EVIDENCE BRIEF: HIV and laws and policies in Europe, May 2017

# Number of countries reporting laws and policies that allow HIV prevention intervention for people who inject drugs, 2016



ECDC EVIDENCE BRIEF: HIV and laws and policies in Europe, May 2017

### **A Tale of Two Cities**







## What works to prevent infections among people who inject drugs?

### The joint ECDC/EMDDA guidance project

## Process of guidance development



European Monitoring Centre for Drugs and Drug Addiction

- Started September 2010
- Systematic review of the literature for prevention interventions
  - University of Strathclyde; Scottish National Health Service; University of Bristol; LSHTM
- Guidance written by ECDC and the EMCDDA
- Review and input from a technical advisory expert group
- Guidance launched October 2011 at the EMCDDA

What works to prevent bloodborne infections among people who inject drugs?



European Monitoring Centre for Drugs and Drug Addiction

- Thousands of studies about needle and syringe programmes (NSP)
- Hundreds of studies about opioid substitution treatment (OST)
- Lots of politics and controversy around delivery of these interventions

#### What works to prevent HIV and hepatitis C among people who inject drugs?



European Monitoring Centre for Drugs and Drug Addiction

#### Review-level evidence for the effectiveness of <u>opioid substitution</u> <u>treatment (OST) and needle and syringe programmes (NSP)</u>

	Level of evidence for OST	Level of evidence for NSP
Reduced injecting risk behaviour	++	++
<b>Reduced HIV transmission</b>	++	+
<b>Reduced HCV transmission</b>	+	?

Palmateer 2010; Cochrane review 2009 (Mattick et al); ECDC and EMCDDA 2011

#### **European guidance on prevention of infections** among people who inject drugs **Comprehensive Guidance** document Based on evidence and fully referenced (50 pages) MCDDA and ECDC GUIDAN Guidance "in brief" Condensed recommendations (8 pages) Two part evidence assessment Area and Dreet 1. Needle and syringe programmes and other interventions for preventing hepatitis C, HIV and injecting risk behaviour (144 pages) iteical Attes 2. Drug treatment for preventing hepatitis C, HIV and injecting risk behaviour (62 pages) Available at: www.ecdc.europa.eu

### Seven key interventions





- INJECTION EQUIPMENT
- VACCINATION
- DRUG DEPENDENCE TREATMENT
- TESTING
- INFECTIOUS DISEASE TREATMENT
- HEALTH PROMOTION
- TARGETED DELIVERY OF SERVICES

### COMBINE THESE KEY INTERVENTIONS TO ENHANCE PREVENTION SYNERGY AND EFFECTIVENESS

### **Latest Evidence Review: HCV** Quantitative Findings, September 2017



#### ADDICTION

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Review

Needle syringe programmes and opioid substitution therapy for preventing HCV transmission among people who inject drugs: findings from a Cochrane Review and metaanalysis

Lucy Platt ⊠, Silvia Minozzi, Jennifer Reed, Peter Vickerman, Holly Hagan, Clare French, Ashly Jordan, Louisa Degenhardt, Vivian Hope, Sharon Hutchinson, Lisa Maher, Norah Palmateer, Avril Taylor, Julie Bruneau,

Matthew Hickman

Accepted manuscript online: 11 September 2017 Full publication history

DOI: 10.1111/add.14012 View/save citation



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## BRISTOL Implications of Evidence Review

- strong consistent evidence that OST reduces HCV transmission
- weaker evidence for high coverage NSP
  - more heterogeneity
  - NSP highly cost effective/ cost saving
- corroborates importance of combining interventions (NSP and OST)
  - Model evidence that OST/NSP enhance HCV TasP & minimize re-infection

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COMBINATION PREVENTION SCALE-UP: 10 YEAR RELATIVE PREVALENCE REDUCTIONS WITH NO BASELINE COVERAGE OF OST/NSP AND USING DAAs



- Dark red: modest (<20%) impact, high HCV
- Orange: ~50% impact
- White: >80% impact
- >40% reduction requires HCV
   What does this analysis tell us?
   OST&NSP increases benefit of HCV treatment

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Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, and Vickerman P. C. Clinical Infectious Diseases 2013

### University of BRISTOL IN 20%/40% CHRONIC PREVALENCE SETTING, CONSIDER PRIORITIZING BY RISK STATUS



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# University of BRISTOL Implications of economic and modelling studies – mixture of evidence

- Empirical evidence OST/NSP reduces HCV
  - NSP & OST highly cost-effective
  - Models suggest that: OST/NSP avert HCV transmission & increase impact of HCV TasP
- Dynamic and Economic Models show that:
  - HCV treatment scale-up critical for HCV prevention
  - Early treatment of PWID cost-effective
  - Case-finding cost-effective because of prevention benefit
- No observed evidence (yet) of HCV TasP (in PWID)

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## Tuberculosis

- Cough
- Fever
- Night sweats
- Loss of appetite
- Weight loss
- Skin lesions
- Bone (spine) disease
- Meningitis
- Latent TB Infection (LTBI)
- Treatment requires combinations of drugs over many months



## Some questions about TB



What proportion of the world is infected with TB?

• A 0.1%

How many EU/EEA countries have low TB incidence?

- A 5
- B 13 B 2%
- C 23%
- D 58%

- C 22
- D 27

## **TB notifications, EU/EEA, 2015**



60 195 TB cases in 30 EU/EEA countries Notification rate of 11.7 per 100 000 population (range 2.1–76.5)



Not reporting



# Multidrug-resistant TB (MDR TB), EU/EEA, 2015



**4.1%** of TB cases with DST\* results were multidrug-resistant (range 0–21.2%)





Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe. TB surveillance and monitoring in Europe, 2017

\* DST – drug susceptibility results reported for at least isoniazid and rifampicin

## **TB/HIV co-infection, EU/EEA, 2015**





Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2017

\* Among countries reporting HIV status for at least 50% of TB cases

### Tuberculosis, injecting drug use and integrated HIV-TB care: a review of the literature



- Latent TB infection prevalence was high and active disease more common among HIV-positive PWID.
- Co-location of TB services with NSP and opioid substitution therapy (OST), combined with incentives, consistently improved TB screening and prevention uptake
- Small-scale combined TB treatment and OST achieved good adherence in diverse settings
- Successful interventions involved collaboration across services; a clientcentred approach; and provision of social care
- No peer-reviewed studies described models of integrated HIV-TB care for PWID but grey literature highlighted key components:
  - co-located services, provision of drug treatment, multidisciplinary staff training
  - Remaining barriers: staffing inefficiencies, inadequate funding, police interference, and limited OST availability

Grenfell P, et al. Tuberculosis, injecting drug use and integrated HIV-TB care: a review of the literature. Drug Alcohol Depend. 2013 May 1;129(3):180-209.

### Anthrax

(caused by Bacillus anthracis bacterium)

#### Skin lesions (eschar)

- rarely fatal if treated
- ≈20% fatality if untreated
- Injection anthrax
  - Fever and chills
  - A group of small blisters or bumps that may itch, appearing where the drug was injected
  - A painless skin sore with a black center that appears after the blisters or bumps
  - Swelling around the sore
  - Abscesses deep under the skin or in the muscle where the drug was injected

### Pulmonary anthrax (progression from flu-like illness

to respiratory distress, shock and death)

- Late stages ≈90% fatal
- Early treatment reduces fatality rate to below 50%



### Anthrax







JOINT ECDC AND EMCDDA RAPID RISK ASSESSMENT

Anthrax cases among injecting drug users Germany, June-July 2012 Update, 6 July 2012

#### Main conclusions and recommendations

As of 4 July 2012, three cases of anthrax among injecting drug users (IDUs) have been reported from Germany: two from Regensburg, Bavaria and one from Berlin. All three cases had onset of symptoms in June 2012 and one case has died. The first two cases are likely linked through exposure to heroin contaminated by a most likely identical *Bacillus anthracis* strain (based on molecular typing results). The link of the third case, though probable, needs to be confirmed. The geographical distribution of the contaminated heroin is unknown at this time, but it is possible it has the same source as the contaminated heroin incriminated in the 2009/2010 outbreak in Scotland (with cases also reported from Germany and England). The risk of exposure for heroin users in Germany and other countries is presumably still present and therefore it is not excluded that additional cases among IDUs will be identified in the near future.

### Anthrax





### Botulism

(caused by paralysis-inducing toxin of Clostridium botulinum bacteria)



- Risk of getting wound botulism increased by use of black tar heroin, "skin popping" or "muscle popping" (or "muscling")
- Heating ("cooking") heroin will not kill the botulism pathogen

Symptoms and signs (**NB** some can be mistaken for opioid overdose)

- Double and/or blurred vision
- Drooping eyelids
- Slurred speech
- Difficulty swallowing
- Dry mouth
- Muscle weakness
- Difficulty breathing
- Paralysis
- Treated with antitoxin and antibiotics
- Recovery takes weeks to months
  ≈ 5% of patients die

## ecce



Europeen Monitoring Centre for Drugs and Drug Addiction





Wound botulism in people who inject heroin: Norway and the United Kingdom

14 February 2015

#### Main conclusions and options for action

Since December 2014, and as of 10 February 2015, 23 cases of botulism have been reported in Norway (eight cases) and Scotland (15 cases), affecting people who inject drugs (PWID). All the reported cases used heroin, and it is assumed that the source of the infections is contaminated heroin. The batch or batches of the heroin suspected of being contaminated with the spores of *Clostridium botulinum* have so far not been identified. It is therefore not possible to estimate the volume and distribution of contaminated heroin. However, the clustering of the cases in time and place suggest that the 23 cases could be linked to heroin from a common contaminated batch.

People who inject drugs are known to be at risk of wound botulism. Guidance on drug treatment and prevention and control of infections among people who inject drugs has been issued by ECDC and the EMCDDA in 2011 [1]. No person-to-person transmission has ever been reported.

The following measures are relevant for mitigating the risk of more cases of wound botulism in the EU/EEA Member States:

### **Botulism**

### **Other bacterial infections** Streptococci and Staphylococci

- Common cause of skin and wound infections
- Can give rise to serious complications:
  - kidney damage
  - heart valve damage
  - necrotising fasciitis ("flesh eating disease")
  - Blood stream infection with toxic shock
- Treated with antibiotics (but can be resistant e.g. MRSA)



### **Bacterial Infections Associated with Exposure to Injecting Drug Use, UK 2005-15**



Bacterial Infection	Total Reports Associated with IDU, UK, 2005-2015
Anthrax	60
Botulism (wound)	133
Group A Streptococci	228
Staphylococcus aureus (MSSA)	1199 (*)
Staphylococcus aureus (MRSA)	262
Tetanus	11

\* 2011-2015 data only

### **Bacterial Infections Associated with Exposure to Injecting Drug Use, UK 2005-15**



### Basic (Case) Reproduction Rate "All you need to know to design interventions"





Number of secondary infections produced by a typical case of an infection in a population that is totally susceptible

- Vaccination
- Condoms
- Injecting behaviour
- Behavioural
  interventions
- OST/NSP
- Vaccination

• Treatment

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## Thank you!



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