# Written Supplementary evidence by Dr Josh Jones, UK Phage Therapy (00045)

## EXECUTIVE SUMMARY

1. Considering just diabetic foot and hip/knee infections – using licensed phage therapy products **the NHS could save an estimated £179.7 million per year.** This is an underestimate of potential savings and further significantly underestimates the potential savings as only three types of infection are considered.
2. The potential savings for just these three types of infections will outweigh the cost of initial capital investment (£50-75 million).
3. Total savings to the NHS will be significantly higher when the impact of phage therapy in other infection types is considered (e.g. respiratory, urinary, surgical site, sepsis etc.).
4. Regardless of whether for licensed or unlicensed use, all phages produced for clinical use in the UK must be made in accordance with Good Manufacturing Practice. This should remain the case.
5. Once established, it could take around 1-4 weeks to manufacture a batch of GMP phages at an estimated cost of £5,000 per phage production run and one-off annual fixed costs of £50,000.

## Q1: TO WHAT EXTENT DO UNLICENSED MEDICINES POLICIES VARY BETWEEN NHS TRUSTS?

- All NHS Trusts/Boards can use unlicensed medicines.
- The principles of the governance of unlicensed medicines are similar between Trusts.
- There is variation in the precise mechanics of the governance structures.
- Unlicensed medicines policies are able to move on clinically relevant time scales.
- It is appropriate that individual Trusts take responsibility for their own local use of unlicensed medicines.

## Q2: HOW MUCH COULD PHAGE THERAPY SAVE THE NHS?

The answer to this depends on whether phage therapy is being considered in an unlicensed or licensed capacity. For the former, it is difficult to estimate the savings that could be delivered by phage therapy. Therefore, this summary will examine licensed phage therapy for a selection of infection types where cost and prevalence data are more readily available. The total savings estimated here will be an underestimation as many more infection types are not covered. This summary will take a bottom-up approach, starting from potential savings per patient.

## 1) SAVINGS FROM DIABETIC FOOT INFECTION

### THE SCALE OF THE PROBLEM

According to the National Diabetes Foot Care Report[1], between 2017 and 2020 in England:

- There were 7,957 major and 21,738 minor amputations for diabetes = 190 amputations/week.
- 97,175 patients had a hospital admission for foot disease, 34% had more than one admission.
- The major amputation rate was 1.82 times higher in the most vs. the least deprived areas.

### THE COST OF THE PROBLEM

- The NHS spent an estimated £837 to £962 million on diabetic foot care in 2014-15[2]
- It has been estimated that £1 in every £140 is spent on diabetic foot care[3]
- Almost 1% of the entire NHS budget goes on diabetic foot care[2]

### PHAGE THERAPY: POTENTIAL SAVINGS

In 2014-15 in England there were[2]:

| | | |
|---|---|---|
| 3016 major amputations | av. tariff cost* £8,213 | Total annual cost £24.8 million |
| 4015 minor amputations | av. tariff cost* £4,211 | Total annual cost £16.9 million |

**The NHS tariff is the set amount that NHS Trusts are reimbursed for clinical activities, in this case surgical costs.*

Diabetic foot amputations principally occur due to vascular disease and/or infection[4].

Over half of diabetic foot patients may have an infection[5]. For the purposes of modelling, we will assume that 50% of amputations are secondary to infection.

Phage therapy has been estimated to be 69.7% effective in the treatment of DFIs[6].

### NHS TARIFF SAVINGS

Prevention of 69.7% of half of annual amputations by phage therapy could save:

| | |
|---|---|
| Major amputations | £8,632,487 |
| Minor amputations | £5,892,147 |
| TOTAL ANNUAL SAVINGS | £14,524,634 |

This excludes other significant care costs, e.g. outpatient care, hospital admission or post-op care.

### OUTPATIENT CARE SAVINGS

The annual costs of outpatient diabetic foot care have been estimated to be £564.16 million[2].

Conservatively and crudely assuming that 25% of costs are secondary to infection, then preventing 69.7% of those costs would save £98.3 million annually.

### POST-AMPUTATION CARE SAVINGS

The cost of lifetime post-amputation care is significant. The total lifetime cost to the NHS of post-amputation care for diabetic amputees in England in 2014-15 has been estimated to be £20.8 million[2].

Assuming 50% of post-op patients had an amputation secondary to an infection and a phage therapy success rate of 69.7%, phage therapy could save £7.25 million annually.

### TOTAL ANNUAL SAVINGS – DIABETIC FOOT INFECTION

**Potential annual savings from phage therapy for diabetic foot infection: £120 million**

*This is an underestimate because:*

- *It excludes costs of antibiotics, imaging, costs associated with admission, mental health impacts etc.*
- *It excludes the wider costs to society and the economy. For many, amputation means loss of house or job, perhaps the need for care and state support.*
- *The success rate of phage therapy is likely greater than 69.7%, which is based on 43 DFI patients[6]. A systematic review of phage therapy in general, including 2,241 cases, estimated that 78.8% of patients had clinical improvement[7].*

## 2) SAVINGS FROM INFECTED JOINT REPLACEMENTS

### INFECTED HIP REPLACEMENTS

The cost of surgery for an infected hip replacement has been estimated to be £42,000 per patient[8].

Between 2015 and 2020 there were an average of 1,361 operations for infected hip replacements per year[9], at a total estimated cost of £57.2 million.

The efficacy of phage therapy in prosthetic joint infection has been estimated to be 57%[10].

**Potential annual savings from phage therapy for infected hip replacements: £32.6 million**

*This is an underestimate because:*

- *It excludes costs of antibiotics, imaging, pre-op outpatient care and post-op care.*
- *It excludes the wider costs to society and the economy.*

- *The success rate of phage therapy is likely greater than 57%, which is based on 28 PJI patients. Systematic reviews of bone and joint infections in general have estimated the efficacy of phage therapy to be 71-93%[10,11]. A systematic review of phage therapy in general, including 2,241 cases,* estimated that 78.8% of patients had clinical improvement[7].

### INFECTED KNEE REPLACEMENTS

According to National Joint Registry data, there were 7,919 knee revision surgeries secondary to infection between 2015 and 2020, an average of 1,584 per year[9].

A 2015 publication noted that infected knee revision patients are in hospital for more than double the length of time of patients without an infection (21.5 days vs. 9.5 days) and that knee revision surgery was estimated to cost £30,011 per patient[12].

The estimated total annual cost of knee revision surgeries is £47.5 million.

The efficacy of phage therapy in prosthetic joint infection has been estimated to be 57%[10].

**Potential annual savings from phage therapy for infected hip replacements: £27.1 million**

*This is an underestimate because:*

- *The cost figures are from 2015.*
- *It excludes the wider costs to society and the economy.*
- *The success rate of phage therapy is likely greater than 57% - see hip infections above.*

### TOTAL ANNUAL SAVINGS – INFECTED HIP AND KNEE REPLACEMENTS

**Potential annual savings from phage therapy for infected hip and knee replacements: £59.7 million**

## SAVINGS SUMMARY

**Phage therapy could save the NHS an estimated £179.7 million/year – just on diabetic foot and hip/knee infection costs.**

This figure itself is an underestimate for the reasons stated above and further underestimates the potential savings associated with phage therapy because it only considers savings to three types of infection - almost all types of bacterial infection could potentially benefit from phage therapy.

Major infection types that could benefit from phage therapy but that are not considered here include:

- Surgical site infections
- Prosthetic or implant-related infections
- Chronic respiratory infections – e.g., in cystic fibrosis, COPD, bronchiectasis
- Infections in immunosuppressed patients – e.g. chemotherapy, transplant
- Urinary tract infections

- Sepsis

Relative to the potential savings, set-up of a GMP-equipped biotherapeutic manufacturing and innovation centre, capable of delivering phage therapy at-scale, to the NHS, is expected to cost £50-75 million.

***The cost of phage therapy relative to antibiotics***

The Office for Health Economics has recently estimated that $4.2 billion is required as an incentive to develop an antibiotic and the AMR Action fund expects to deliver 2-4 novel antibiotics in the next 7 years[13,14].

In contrast, investment of 1-2% of that amount in phage therapy would, in 7 years' time, have delivered an almost infinitely variable and inexhaustible source of onshore antimicrobials for the UK, bringing with it medicines security, rapid response and biodefence capabilities.

The rapid response capability would mean, for example, that phages could be used to quickly address future outbreaks – like the invasive Strep A outbreak last winter in which killed 355 people, including 40 children[15].

## Q3: WHY PHAGES SHOULD BE PRODUCED ACCORDING TO GMP?

The production of pharmaceuticals in accordance with Good Manufacturing Practice (GMP) is important to ensure consistent, high-quality, production that ultimately benefits patients. As an internationally recognised standard, pharmaceuticals produced to GMP are an exportable commercial product.

In terms of phage therapy, the UK has a financial, not a regulatory barrier.

It is possible to produce phages to GMP and, although costly, this will create a commercially attractive and high-quality pharmaceutical product, benefitting both the UK economy and patients.

Current UK medicines regulations stipulate that all phages produced in the UK must be produced in accordance with GMP. This must remain the case to ensure a commercially thriving phage sector and, most importantly, to ensure a high-quality source of phages for use at scale in the NHS. GMP quality also provides sufficient reassurance to pharmacists and other NHS staff charged with overseeing medicines governance.

The requirement for production in accordance with GMP must also remain for named-patient phage used in the UK, otherwise we risk multiple non-GMP sources of varying quality attempting to fulfil this need.

To become a world-leader in the cross-sector phage and microbiome space, the UK Government needs to support on-shore GMP production facilities are available for both commercial and clinical needs.

A Biotherapeutic Manufacturing and Innovation Centre should be established. Analogous to the Vaccine Manufacturing and Innovation Centre, this facility will house GMP phage and microbiome production capabilities, a national phage/microbiome innovation hub and a national specialised clinical phage centre to deliver phage therapy at-scale for the NHS.

## Q4: HOW LONG AND HOW MUCH WILL IT TAKE TO PRODUCE GMP PHAGES?

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| *Time* | Once GMP production is established, it could take around 1 week to produce a phage previously produced to GMP and around 4 weeks to produce a phage not previously produced to GMP. |
| *Costs* | Fixed and variable costs for phage production in a small GMP facility have been estimated to be about £50,000 for a phage previously produced to GMP and about £70,000 for a phage not previously produced to GMP. These costs exclude recouping initial capital investment. |

*These timescales and values have been obtained from non-confidential expert consultancy.*

*April 2023*

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