

## Introduction

Antimicrobial resistance (AMR) is a major humanitarian and global threat.<sup>1</sup> Antimicrobials deliver extensive value in reducing global burden of infection<sup>2</sup> and in enabling healthcare.<sup>3</sup> As the centenary of Fleming's discovery approaches,<sup>4</sup> we must focus holistically to learn from history. We therefore approached this with a narrative exploration of beta-lactam development and policy through the lens of resistance evolution. The study of resistance evolution focuses on proximate causes under controlled conditions. Conversely, the association between resistance evolution and policy is poorly understood.

A focus on beta-lactam antibiotics was taken, given their clear development timeline and continuous molecular refinement to meet arising clinical and microbiological needs.

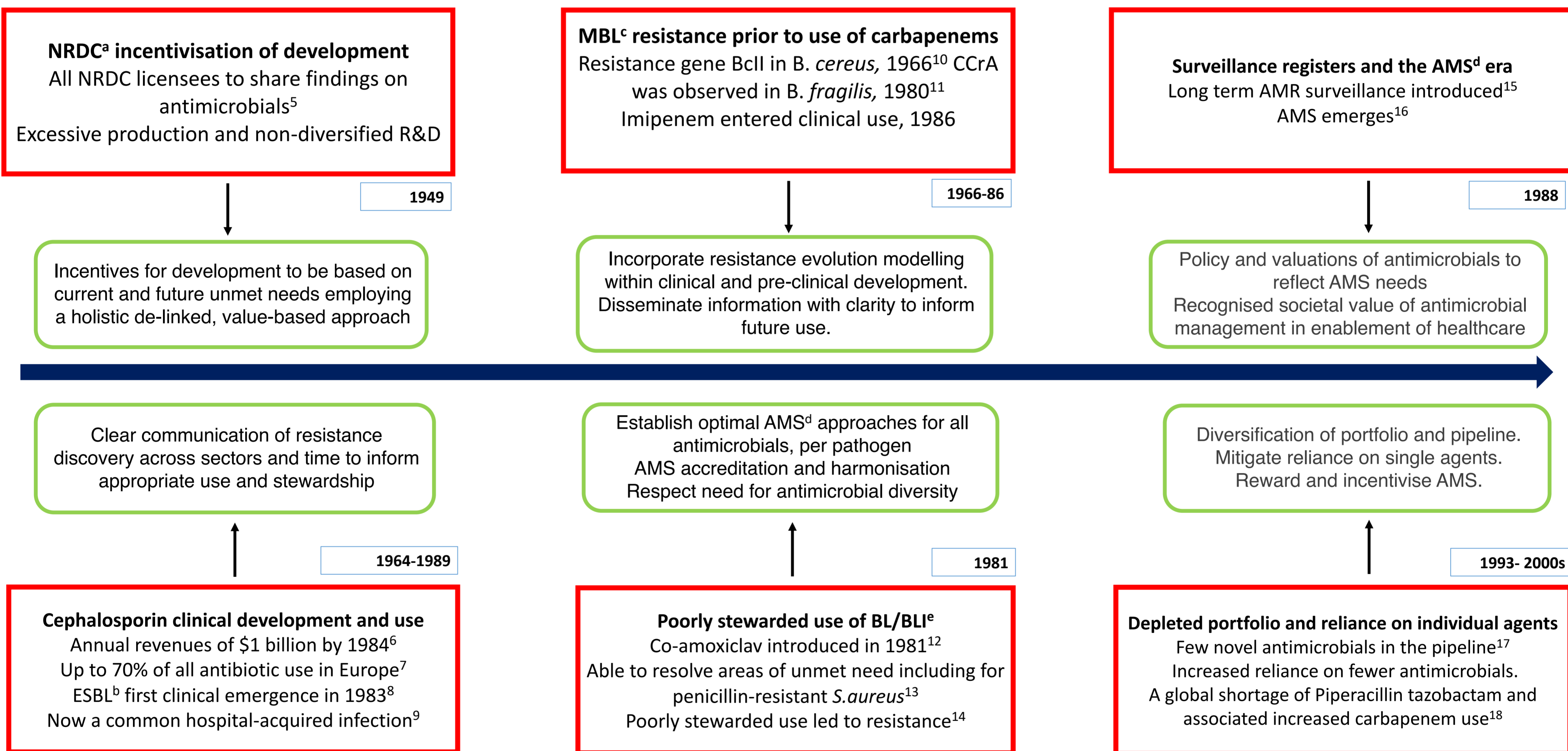
## Objectives

- Undertake an ontological appraisal of beta-lactam development, clinical use and associated resistance;
- Illustrate key timelines in resistance evolution with case study examples;
- Provide a historical basis for future projected recommendations that can mitigate resistance evolution.

## Methods

- A reference timeline of beta-lactam development, initial clinical use and first encounter of resistance was constructed through extensive literature and repository searches. This was illustrated through the use of Miroboard™ to aid structure and understanding;
- Key events within this timeline were explored in depth with case study examples; the influence of each was explored in terms of subsequent resistance evolution. The timeline was reviewed to the present day, with the below timeline iterating the most relevant case studies.

## Findings



## Discussion

- Key events in the resistance evolution timeline have been used to illustrate key learning points from the past
- Knowledge and solutions now exist but global policy lags behind in implementation of an AMS focussed agenda
- There is a strong case for evolutionary microbiology theory to be integrated with policy, industrial decision-making and forecasting for appropriate use and future development
- An AMS focus across all organisational levels and relevant stakeholders is necessary to mitigate the grave threat of AMR.

### References

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### Footnotes

- National Research and Development Corporation
- Extended Spectrum Beta-lactamases
- Metallo Beta-lactamases
- Antimicrobial Stewardship
- Beta-lactam/Beta-lactamase inhibitor combination

### Key

Key events

Recommendations based on lessons learnt