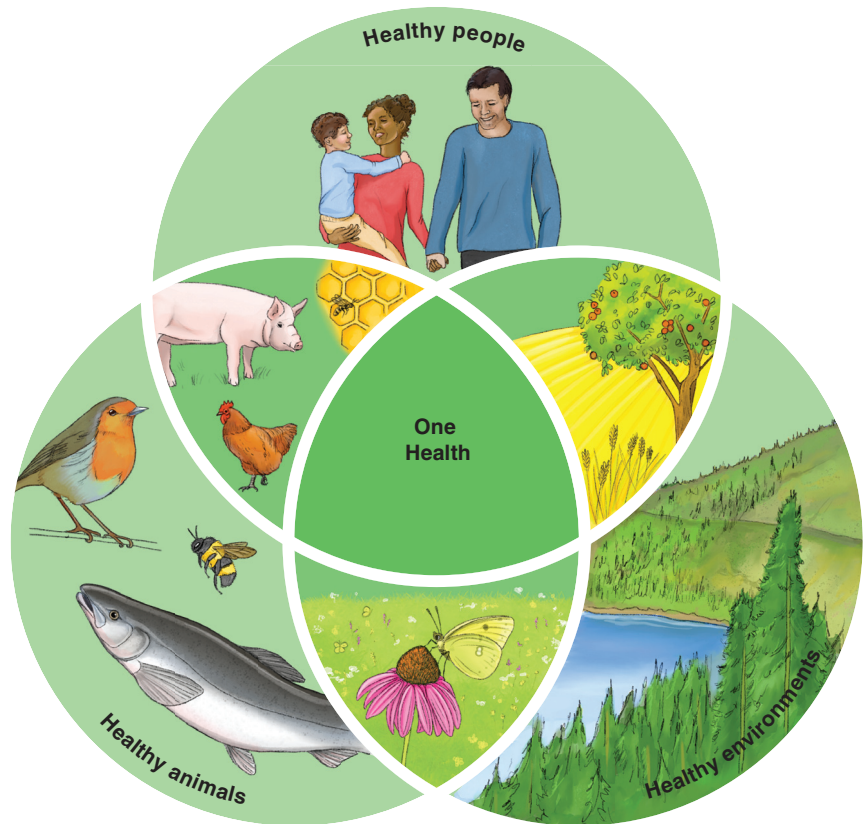


Quick guide  
**One Health**

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**What is One Health?** One Health is an interdisciplinary framework that aims to sustainably advance and safeguard the health of humans, animals, and the environment (Figure 1). At its core, the One Health approach emphasises that the health of people is inextricably linked to that of ecosystems and the species inhabiting them. Through this lens, One Health extends from environmental health to address contemporary health challenges, which is especially relevant given the recent global spread of H5N1 influenza and COVID-19, the rise of antibiotic resistance, and increasing frequency and magnitude of harmful algal blooms. Because One Health inherently brings together all aspects of public health, collaboration among professionals from various domains — including medicine, veterinary science, and environmental science — is essential for effectively managing and preventing health risks. While practical application of the One Health approach is becoming increasingly common, its implementation is not without challenges, requiring effective communication and coordinated policies to bridge disciplinary gaps.

**What progress has been made so far?** Although the term ‘One Health’ is relatively new, its roots extend far back into history. Ancient civilisations already recognised the interconnectedness between human and animal health and the environment, with practices such as animal husbandry, sanitation, and disease control demonstrating this early understanding. In modern times, the foundation of One Health was laid by veterinarian Calvin Schwabe in 1964 when he coined the term ‘One Medicine’, which highlighted the parallels between animal and human medicine and called on veterinarians



**Figure 1. The core of the One Health concept lies in acknowledging the interdependence between human and natural systems.**

This perspective acknowledges the close association between the well-being of humans, animals, and the environment. Illustration by Julie Johnson (Life Science Studios).

and physicians to collaboratively address global health challenges. The concept of One Medicine gained momentum throughout the 20<sup>th</sup> century, particularly with the increasing recognition of zoonotic diseases like rabies, brucellosis, and anthrax — illnesses that can transmit between animals and humans. It became evident that shared environments and physiological similarities between species not only facilitated the spread of these diseases but also fuelled the rise of drug-resistant microbes. This understanding prompted a shift towards viewing public health not solely as a human affair, and instead moving towards a broader, integrated approach aimed at sustainably balancing and optimising the health of all inhabitants of the planet, as well as the ecosystems they inhabit.

Formally coined ‘One Health’ in the early 2000s, the concept gained support from organisations such

as the United Nations Children’s Fund (UNICEF), the World Health Organisation (WHO), the World Organisation for Animal Health (WOAH), and the Food and Agriculture Organisation (FAO), among others. In the 21<sup>st</sup> century, One Health evolved towards a more dynamic approach to health management, recognising the necessity to respond to rapid environmental changes and to increasing human population growth. Consequently, One Health principles build from Environmental Health and are increasingly integrated into policies and health programs around the world, reflecting the ongoing significance of health management at the interface between animal health, human health, and environmental integrity.

**What have been the major recent innovations and breakthroughs?**

In recent years, One Health has seen significant progress through



advancements in research methodologies, technology, and interdisciplinary collaboration to address complex health challenges. Predictive tools and modelling techniques have improved, alongside innovations in surveillance and control strategies, allowing us to better anticipate, detect, and mitigate the spread of zoonotic diseases, such as vector-borne illnesses and emerging infectious diseases like COVID-19. For example, advances in predictive analytics and machine-learning algorithms enable the integration of diverse datasets from human, animal, and environmental sources. This integration allows for better identification of patterns and prediction of disease emergence and spread, facilitating proactive disease prevention and intervention strategies.

The integration of genomic technologies in disease surveillance and control, including high-throughput sequencing techniques, enables rapid identification of emerging infectious diseases and tracking of their transmission dynamics across species boundaries, facilitating an early response to outbreaks. The development of novel therapeutics against zoonotic pathogens, whilst ensuring that unwanted side-effects for non-target species are minimised, has the potential to address the need for effective but environmentally friendly interventions in cross-species pathogen transmission and pollution prevention. Furthermore, biotechnological innovations, such as the use of CRISPR-based gene editing, may offer promising perspectives for targeted manipulation of pathogens and vectors, as well as enhancing host resistance to infectious agents.

Additionally, efforts to better understand and combat antimicrobial resistance, including more responsible use of antibiotics in both human and animal healthcare, as well as attempts to address environmental challenges such as climate change, harmful algal blooms, and pollution through sustainable practices and policies have gained momentum within the One Health framework. Due to the collaborative efforts of researchers, policymakers, practitioners, and community members, and by

integrating insights from fields ranging from epidemiology and public health to veterinary medicine and environmental science, various holistic approaches to health management have been, and are being, developed.

#### **What are the key challenges to the One Health approach?**

Despite its potential, the One Health approach faces significant challenges, particularly amidst the increasing global trade of animals and animal products, increasing human population growth, and rapid human-induced environmental change. One major challenge is the containment or prevention of emerging and/or re-emerging infectious diseases, which pose substantial medical, social, economic, and environmental burdens. Addressing such challenges necessitates interdisciplinary solutions through collaborative efforts among health organisations, policymakers, and community members. Indeed, as per the Manhattan Principle of 2004, no single discipline or sector has sufficient knowledge and resources to prevent the emergence or re-emergence of diseases in today's globalised and interconnected world. Similarly, no nation can single-handedly reverse the global loss of habitat and biodiversity — trends that undermine the health of people, animals, and the environment. A critical challenge is to break down these barriers, translate One Health principles into actionable practices in the real world, and instil sustainable habits in all members of society.

While One Health intersects with various health disciplines and frameworks that have existed for many years or are relatively new to emerge — such as Environmental Health and Planetary Health, respectively — it is essential to recognise both the similarities and differences among these fields. Advancements in the science and the practice of Environmental Health remain crucial for public health around the world, while the emerging field of Planetary Health may offer new perspectives on the interconnectedness of the health of people and the planet, and how to address emerging health challenges effectively.

#### **What are the future directions for One Health?**

At the heart of One Health is the shift from siloed approaches to the adoption of systems-thinking frameworks, which illustrate that complex environment and health systems are products of the interactions among their parts and not simply the sum of these parts, and are thus critical for effectively addressing complex problems in practice. The success of this approach hinges on appropriately training both current and future generations, integrating One Health into public health, global health, and environmental health curricula, alongside providing continuing education at local, national, and international levels. In addition, leveraging established organisations to support One Health-focused working groups and training sessions, facilitated by online learning platforms, can greatly enhance educational reach and networking capabilities. As our understanding of One Health approaches deepens, we must remain flexible and open to refinement in tackling significant challenges such as emerging infectious diseases and widespread environmental contamination. Furthermore, capacity building in low-resource settings is essential to ensure the effective implementation of One Health principles worldwide.

Implementing a systems-thinking approach also requires the further improvement of disease surveillance and control methods. For example, the routine use of wastewater-based epidemiology for pathogen tracking, as successfully demonstrated with SARS-CoV-2 monitoring during the global COVID-19 pandemic, underscores the importance of continuing to integrate complementary and novel approaches.

Finally, a continued push for interdisciplinary collaboration and breaking down disciplinary silos is key for the sustained success of One Health. Creating spaces for these cross-disciplinary interactions and generating successful case studies will further advance One Health-centred actions that inform evidence-based interventions.

**Where can I find out more?**

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**DECLARATION OF INTERESTS**

The authors declare no competing interests.

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**Primer**

**The maternal-to-zygotic transition**

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Rapid cleavage divisions and the transition from maternal to zygotic control of gene expression are the hallmarks of early embryonic development in most species. Early development in insects, fish and amphibians is characterized by several short cell cycles with no gap phases, necessary for the rapid production of cells prior to patterning and morphogenesis. Maternal mRNAs and proteins loaded into the egg during oogenesis are essential to drive these rapid early divisions. Once the function of these maternal inputs is complete, the maternal-to-zygotic transition (MZT) marks the handover of developmental control to the gene products synthesized from the zygotic genome. The MZT requires three major events: the removal of a subset of maternal mRNAs, the initiation of zygotic transcription, and the remodeling of the cell cycle. In each species, the MZT occurs at a highly reproducible time during development due to a series of feedback mechanisms that tightly couple these three processes. Dissecting these feedback mechanisms and their spatiotemporal control will be essential to understanding the control of the MZT. In this primer, we outline the mechanisms that govern the major events of the MZT across species and highlight the role of feedback mechanisms that ensure the MZT is precisely timed and orchestrated.

**The MZT and the NC ratio**

A crucial question in the regulation of the MZT is how it is accurately and reproducibly timed. In most species, the MZT follows a stereotypical number of cleavage divisions. While this number varies between species, its control in each species is extremely accurate, suggesting precise regulation. Classic experiments initially focused on dissecting whether the onset of the MZT is controlled in a time-dependent manner or is dependent on the nuclear-to-cytoplasmic ratio (NC ratio), a quantity that increases

exponentially as nuclei divide in the early embryo. Although the NC ratio seems to be the dominant regulator of MZT timing in *Drosophila* and *Xenopus* embryos, in other organisms, such as mouse and zebrafish, there is evidence that time-dependent processes are more important. In fact, even in *Drosophila* it has been argued that there are two classes of zygotic transcripts: time-dependent and NC ratio-dependent. These observations suggest that all the processes that drive the MZT are tuned to run in a precisely orchestrated temporal pattern even if the mechanisms of their regulation differ in their temporal kinetics and NC ratio dependency.

**The NC ratio, control of the cell cycle and zygotic transcription**

A hallmark phenomenon preceding the MZT is the progression of the embryonic cell cycles, which causes an exponential increase in the NC ratio through rapid rounds of DNA synthesis and mitosis without growth (Figure 1). The mammalian MZT occurs within the first three cell divisions of the embryo, and very little cell-cycle remodeling is observed during this time period. However, in many other species in which the MZT occurs after several rounds of fast cell divisions with no gap phases, the activation of the zygotic genome coincides with a slowing of the cell cycle. It is clear from experiments using *Drosophila* haploid embryos (carrying half the original DNA content) and from mechanical manipulations of nuclear positioning in *Xenopus laevis* that the cell-cycle slowing is dependent upon a sensed ratio of nuclear content to cytoplasm. *Drosophila* embryos, for example, undergo exactly 13 cell cycles before gastrulation, with the 13th cell division lasting about 20 minutes. The 13th cell division in haploid *Drosophila* embryos, however, is faster and these embryos go on to complete a 14th cell cycle prior to major zygotic genome activation.

While it remains an open question exactly how the NC ratio directly impacts the cell cycle and transcription, it is clear in *Drosophila* that the DNA replication checkpoint is a major target of the NC ratio. The lengthening of the cell cycle preceding the MZT requires the activation of this checkpoint, specifically the activation of the

