



Taking flight with Precision Global Health: a scoping review on avian influenza

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Abstract: Avian influenza is an infection of birds caused by the Influenza A virus, which due to crowded conditions and occupational exposure in live poultry markets, has jumped the species barrier to humans. With an estimated case fatality rate of up to 60%, it is vital to map the existing digital technologies that may be utilized to improve disease monitoring and health outcomes for avian influenza. This scoping review aimed to identify which digital technologies may improve disease prevention, detection and control, and could be used as a basis for strengthening health systems. A search was conducted on PubMed and Web of Science for studies that reported the utilization of digital technologies with specific reference to avian influenza. Search dates ranged from 2009 (January) to 2017 (July). Data was extracted into a summative table, citations managed using EndNote software and data synthesized through grouping digital technology domains, using narrative and graphical methods. The scoping review identified 111 relevant studies, and revealed data modelling (n=72) and novel technologies (n=15) referring primarily to diagnostic tools, to be the most utilized technologies in tackling avian influenza. A large portion of the data-modelling domain was compromised of computer-assisted mathematical modelling (n=42) including mathematical modelling (n=8), simulation modelling (n=14) and spatio-temporal modelling (n=20), primarily used to estimate outbreak distribution according to migratory patterns and transmission dynamics. A major challenge reported was poor biosecurity measures of poultry markets. Digital technologies indicated potential in improving disease detection, control and prevention, particularly through the use of data modelling with meteorological data sets. However, it became evident, that to maximize potential of these digital technologies better implementation of biosecurity measures would be necessary in majorly affected regions such as Asia.

Keywords: Avian influenza; highly pathogenic avian influenza (HPAI); Zoonosis; digital technology; mHealth; remote-sensing technologies; modelling; novel technologies; Big Data and disease monitoring

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Introduction

Avian influenza, also known as ‘bird flu’, is caused by one of the major viruses linking animal populations with humans, with an estimated case fatality rate of 60% (1). Avian influenza viruses consist of segmented negative sense; single strand RNA genomes, derived from the Orthomyxoviridae family (2). These viruses can be further sub-categorized into two groups based on the severity of disease they cause, namely highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI) (ibid). Each virus contains one H and one N antigen, and the H5 and H7 strains are known to cause HPAI. It has been hypothesized that HPAI arises from LPAI, due to a faulty polymerase complex resulting in a spontaneous mutation (3). Whilst the latter has been proposed as the most commonly observed pathological pathway, studies have also reported alternative mechanisms, including nucleotide substitutions and recombination with other genes for the emergence of HPAI (ibid).

The natural reservoirs for avian influenza are aquatic birds, which go onto mostly infect domestic poultry and waterfowl, among other bird populations. The virus can be either transmitted through the fecal/oral route, or the respiratory route in land birds (2). Outbreaks of avian influenza are of particular concern in domesticated birds (i.e., poultry) due to the potential to evolve from LPAI to HPAI and death among poultry with HPAI linked to economic losses and trade restrictions (4). In animals, clinical signs for HPAI include sudden onset of high mortalities within flocks associated with edema on the head and face, subcutaneous hemorrhage on the head and wattles and cessation of egg laying (ibid). However, the biggest public health concern is the possibility of the virus to be transmitted to humans. The process in which a disease or infection is transmitted from animal to human, or vice-versa is called zoonosis (1). The first instance of human infection with the avian influenza H5N1 dates back to 1997 in Hong Kong, with 18 identified cases and 6 fatalities, highlighting its pandemic potential (5). Human to human transmission of avian influenza has occurred, with over 200 cases of H7N9 being reported in main land China in 2015 (6). Route of transmission from animal to human is usually via contaminated environments or intermediate hosts, such as pigs, in which exposure may occur through direct contact via slaughtering (6). Conditions for jumping species barriers are ideal in Asia, where poultry, pigs and humans live in crowded conditions, alongside occupational exposure via live poultry markets (3).

In order to mitigate the case of avian influenza, many prevention and control efforts have been put in place, as reducing the risk in animal populations is vital to reduce the risk to humans (1). The so called Tripartite collaboration including WHO, FAO and OIE have set guidelines, and the most common control and prevention measures (7) include: vaccinations of bird populations, legislations such as the OIE Terrestrial Animal Health code (8) and biosecurity measures, which refers to physical and/or procedural measures which may be used to prevent introduction of avian influenza to susceptible poultry (2). The existing prevention and control strategies could be strengthened by the utilization of digital technologies, which may be defined as digital resources which are used to collect novel personal or environmental data (human and animal) from, and by the populations, including but not confined to: mHealth, Big Data and remote-sensing technologies. For instance, spatio-temporal models may be used to more precisely estimate outbreak distributions, remote-sensing technologies for satellite telemetry, and big data analytics to gain insight into human social and behavioural patterns. Digital technologies thus offer great potential in contributing to control and prevention efforts of avian influenza.

Aims and research question

The aim of this scoping review was to identify the existing literature focused on digital technologies and avian influenza, and to further explore their potential in improving disease monitoring. This scoping review aimed to answer the following question:

What digital technologies were utilized to improve and strengthen detection, control and prevention of avian influenza?

Methodology

A scoping review aims to ‘form knowledge synthesis that addresses an exploratory research question aimed at mapping key concepts, types of evidence, and gaps in research related to a defined area or field by systematically searching, selecting and synthesizing existing knowledge’ (9). This review aimed to map the existing digital technologies used to tackle avian influenza.

Search strategy

The search strategy was developed by three authors,

and included a broad range of terms related to digital technologies and avian influenza, which consisted of a combination of free text and MeSH terms (see supplementary appendix). The search terms were used to identify literature that related the use of digital technologies with avian influenza. Disease-related search terms (avian influenza) were identified using MeSH terms from the National Library of Medicine MeSH database, alongside their affiliated catalogued synonyms, whilst digital technology-related search terms were identified through key-terms of a preliminary literature review. Disease-related search terms and digital technology-related search terms were then combined and run in advanced search settings (see *Table S1* in supplementary document). For example, a combination of the following search terms but not confined to: [(Avian Influenza) OR (HPAI) OR (H5N1)] AND [(Technology) OR (Big data) OR (Social media) OR (mHealth)], were used to identify relevant literature. Additionally, reference lists of identified material were searched to identify further material of relevance.

Databases

To ensure a comprehensive review of the literature, two databases, namely PubMed and Web of Science were included in the review. Additional literature was identified from grey literature databases utilizing snowball methodology and hand searching previously identified text.

Study selection, inclusion and exclusion criteria

The review considered any studies that discussed the utilization of digital technologies in improving avian-influenza health related outcomes. The review considered peer-reviewed articles (including original quantitative and qualitative studies), but also editorials, viewpoints and letters indexed in PubMed and Web of Science. Text had to be published in English, Spanish, French or German between 2009 (January) and 2017 (July). There were no restrictions with regard to geographic location, population or study design. The review excluded duplicate studies, publication languages other than those specified above, and literature with a strong veterinarian focus opposed to or not linked to public health, with no explicit focus on digital technologies.

Data collection and extraction

Two reviewers independently assessed inclusion and

exclusion criteria of titles and abstracts for relevance. The lists of selected literature were then compared between the two reviewers, rationale for inclusion or exclusion was argued, and then selected for the compilation of single list from the two lists previously produced by the two reviewers. Additionally, a third reviewer was involved in the selection process, and also double-checked the final list selected for inclusion. Full text articles were obtained and eligible studies were extrapolated into a descriptive summative table focused on: author, publication date, journal, geographic region, geographic origin of author affiliation, digital technology/device, function, study design, data source, target population, health indicator and challenges. Note that digital technology domains were grouped according to those specified below, created by frequency of emergence (see *Table 1*). Citations were managed using EndNote software.

Data synthesis

Data was synthesized using a combination of narrative and graphical methods, for a summative description of findings. Additionally, an author's affiliation network was created to visualize the hubs of digital innovation research in academia. Within the author's affiliation network, the radius of each circle mirrored the number of publications from each country, the edges were colour based depending on what continent they came from, and the links between countries represented the different collaborations between countries (see *Figure 1*). The graph was created by adding an edge between the first author and each of the rest of the authors.

Results

Principal findings

A total of 1,753 titles and abstracts were screened, of which 694 were identified as relevant studies, 191 were excluded as duplicate studies, and 392 did not meet the inclusion criteria. Therefore, a total of 111 studies were selected for inclusion into the review (see *Figure 2*). Studies included in the review uncovered digital technologies or devices used to tackle avian influenza. Five main themes emerged from the 111 studies in the review, including namely: Big Data, mHealth, data modelling, novel technologies and remote-sensing technologies (see *Table 1*). Most of the studies were published in 2016, accounting for 21% of publications. Asia

Table 1 Digital technology domains

| Digital technology domain | Description | References |
|-----------------------------|---|-----------------|
| Big data | A term describing the storage and analysis of large and or complex data sets using a series of techniques including, but not limited to: cloud computing, non-relational databases, natural language processing and machine learning ^[1] | (10-19) |
| mHealth | Medical and public health practices supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices ^[2] | (20-25) |
| Data modelling | Models involve assumption, abstraction and simplification, of complex disease-associated dynamics ^[3] | |
| | Mathematical modelling | (26-33) |
| | Species and ecological spatial distribution modelling | (34-54) |
| | Suitability and niche modeling | (55-63) |
| | Simulation modelling | (64-77) |
| | Spatio-temporal modelling | (78-97) |
| Novel technologies | Case-specific technologies produced or updated, to specifically track and monitor the outbreak, considered “interestingly new or unusual” ^[4] | (98-112) |
| Remote-sensing technologies | Identifying, observing and measuring an object without coming into direct contact with it ^[5] | (57,79,113-118) |

^[1], Stuart J, Barker A. (2013). Undefined by data: A survey of Big Data definitions. Available online: <https://arxiv.org/pdf/1309.5821.pdf>, last accessed 21/08/2017. ^[2], World Health Organisation. (2011). mHealth: new horizons for health through mobile technologies. Available online: http://www.who.int/goe/publications/goe_mhealth_web.pdf, last accessed 21/08/2017. ^[3], Squires H, Tappenden P (2011). Mathematical modelling and its application to social care. National Institute for Health Research: Methods Review. Available online: http://eprints.lse.ac.uk/41192/1/SSCR_Methods_Review_7_web_2.pdf, last accessed 11/06/2018. ^[4], Oxford University Press, 2001. Oxford Dictionaries. Available online: <https://en.oxforddictionaries.com/definition/novel>, last accessed 21/08/2017. ^[5], Graham S. (1999). Remote sensing. Available online: <https://earthobservatory.nasa.gov/Features/RemoteSensing/>, last accessed 21/08/2017.

persistently had the largest amount of publications (57%), whilst there were no publications included in the review from South America.

The existing research output by country was visualized using an author’s affiliation network (see *Figure 1*). The highest level of research output was produced by the USA, who was strongly linked with China and Belgium. Other major contributors were based in Europe, namely Belgium, France, Italy and the UK. Many papers cited the Belgium National Fund for Scientific research and the Biological control and Spatial Ecology Unit at the University of Brussels, alongside the FAO, EMPRES wildlife unit for the animal health service based in Italy, which may explain the large contributions of Belgium and Italy, respectively. Many authors countries within the selected articles were affiliated to institutions based in Asian countries—such as Vietnam, India, Korea, Bangladesh, Japan and Cambodia, which are countries heavily affected by avian influenza.

Data modeling

Data modeling accounted for 65% of studies within the review, ranging from computer-assisted mathematical modeling to spatio-temporal modelling (see *Figures 1,3*). Mathematical modelling including models based on the Monte-Carlo simulation, Bayesian probabilities, and species distribution models, were mostly used to estimate outbreak distributions, predict host-virus interactions, and more accurately study transmission and control dynamics through various scenarios i.e., live poultry market closures. Additionally, models also yielded a more ecological focus, through species niche modelling, and the use of meteorological data sets to predict and map areas with high probabilities of disease occurrence.

Novel technologies

Novel technologies were also included within the review accounting for 13% of findings, through case-specific

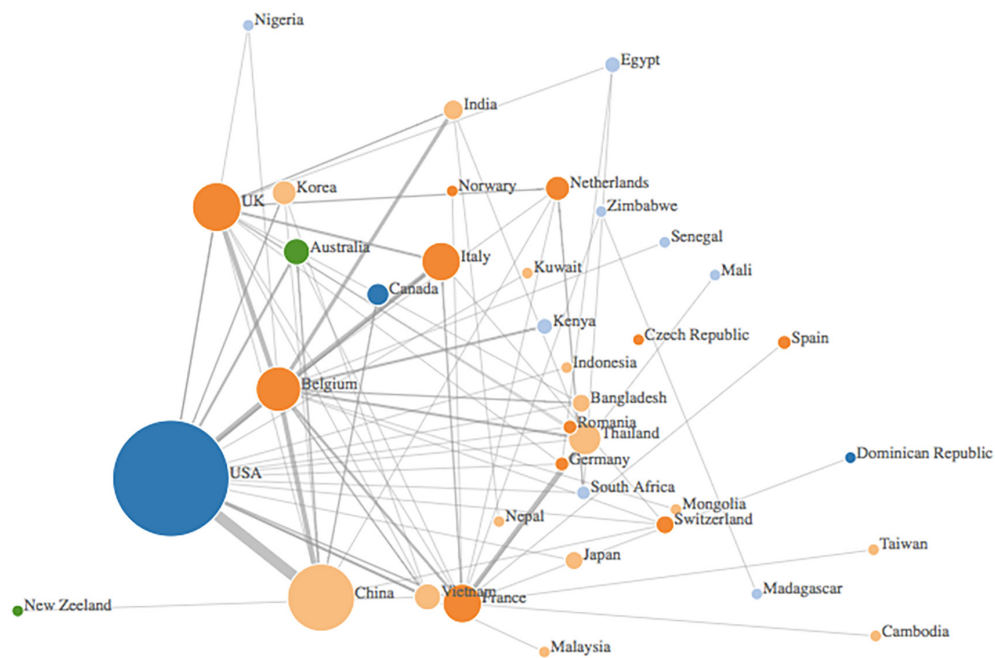


Figure 1 Authors affiliation network of studies included (n=111).

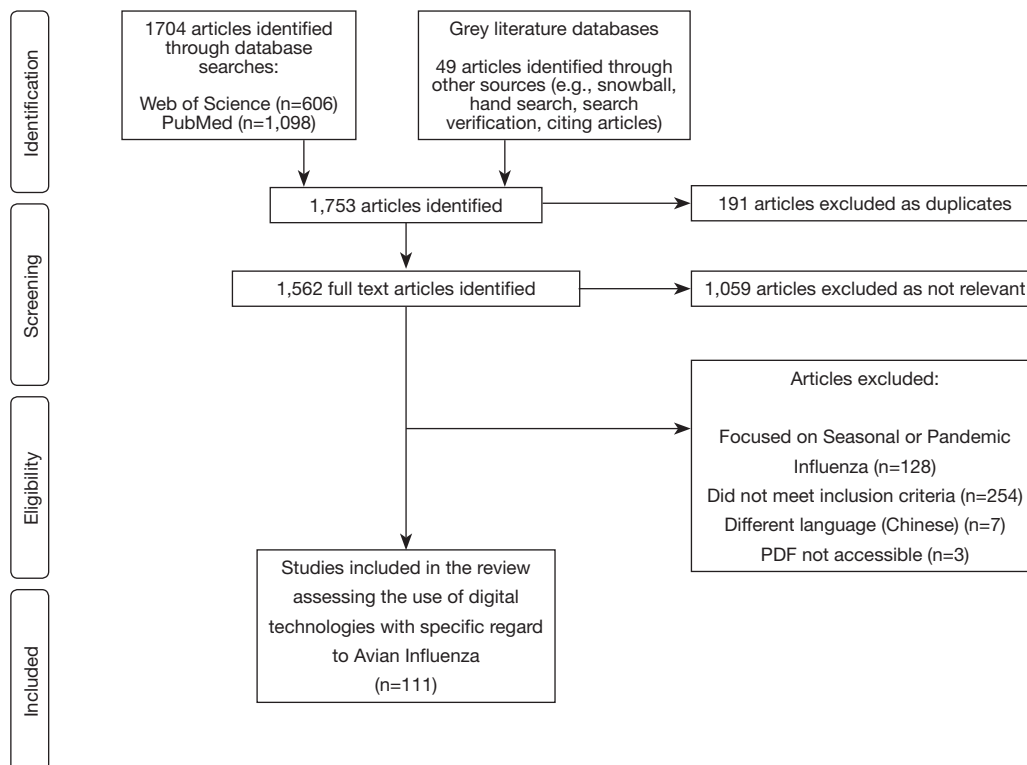


Figure 2 Process of study selection.

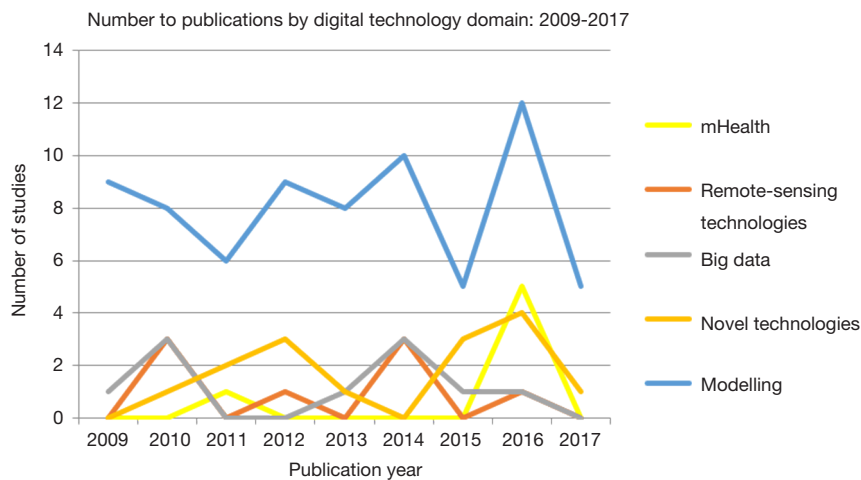


Figure 3 Number of publications by digital technology domain: 2009–2017.

diagnostic devices (67%) nanotechnologies (26%) and wearable's (7%). Novel technologies were mainly utilized for monitoring purposes, with a note-worthy study utilizing nanotechnology for the purpose of treatment.

Big Data

The review identified ten studies (10%) focused on big data, which could be further sub-categorized into social media analytics (40%), web-based surveillance platforms (40%) and online learning resources (20%). Social media platforms were used to capture and inform behavioural changes by measuring user engagement and health communication campaigns. Big data platforms were also utilized for information gathering in the form of web-based surveillance, whilst also supporting online learning.

Remote sensing technologies

A small number of studies explored remote-sensing technologies (7%), under the parameters of satellite telemetry and satellite imagery, capturing how migratory bird populations interacted with their environment, and identifying contaminated bodies of water through earth-satellite observations.

mHealth

A small fraction of research was dedicated to mHealth, constituting 5% of findings within this review. mHealth was mostly used acting as part of a surveillance system, enabled through the SMS or call function for reporting, and GPS technology to track health care workers and cases. However mobile phone devices were also used for diagnostic purposes.

Digital technologies identified within this review were mainly used for surveillance (83%), some dedicated to diagnostics (16%), with low utilization for treatment (1%). Within the surveillance function, data modeling remained dominant, whilst diagnostics were primarily governed by novel technologies and mHealth (see *Table 2*). Although Big Data was only the third largest domain (9%), it showed great potential in combining multiple data sources.

Discussion

The review identified digital technologies used to tackle avian influenza, with data modelling (65%), under the parameters of computer-assisted mathematical modelling, spatio-temporal modelling combined with GPS and GIS function being the most utilized. In the case of avian influenza, digital technologies were especially useful in forecasting potential outbreak hotspots by tracking migratory routes and identifying reservoirs through the use of meteorological data sources (55). Most technologies were utilized for surveillance function, with little use of technologies for diagnostic or treatment purposes. Despite avian influenza mainly affecting countries within Asia, high research output was observed in more northern regions, with the exception of China which demonstrated the second highest research output (see *Figure 1*).

Data modelling was the highest reported utilization of digital technologies within this review (see *Table 1*). Models were able to predict the most significant variables for disease hotspots, with several studies reporting poultry market density and human population density

Table 2 Digital technology domain by function

| Digital technology domain | Surveillance (n=92) | Diagnostics (n=18) | Treatment (n=1) |
|-----------------------------------|---------------------|--------------------|-----------------|
| Big data (n=10) | 9 | 1 | 0 |
| mHealth (n=6) | 3 | 3 | 0 |
| Data modelling (n=72) | 71 | 1 | 0 |
| Novel technologies (n=15) | 1 | 13 | 1 |
| Remote-sensing technologies (n=8) | 8 | 0 | 0 |

to be the most significant predictive variables within said model (28,35,64,80). Spatioal-temporal modelling techniques were also combined with global navigation satellite system functions such as GIS and GPS (24%), enabling the identification of route of transmission, and outbreak hotspots through mapping migratory routes of bird populations (31,71). Many of the studies included in data modelling had a strong ecological focus, modelling migratory patterns linked to outbreak occurrence (28,29,38,40,41,57,64,79,80). However, the One Health approach was also incorporated into models, noted by modelling the species jump and assessing risk of human infection (31,57,67,81).

Novel technologies were mainly utilized for the purposes of diagnostics, including diagnostic devices such as the digital microfluidic device, which had the ability to detect a target molecule within tens of seconds (99), RNAi antiviral vector technology (100) and the portable lateral flow device (104). The wearable sensor node was extremely case-specific, as it allowed for poultry to be continuously monitored, alerting administrators through the internet when an anomalous state of chickens was detected (110). One noteworthy study was categorized under treatment, seemingly through the use of a novel vaccine using a nanotechnology platform on chickens, which indicated success mirrored in an increased IgG response of the vaccinated chickens when compared to the unvaccinated chickens (98).

Big data was primarily composed of social media analytics, which included text mining of platforms such as Twitter, and also country-specific search engines and blogs referring to Baidu Index and Weibo, respectively (11,15). These social platforms aimed at affecting behavioral change through health communication and increasing user engagement. A prominent theme within the review was the use of data collection through web-based forums, showcasing a participatory approach and collaborative spirit. For instance, the online data platforms CaribVnet and

f-FLUA2H both gathered information on avian influenza from both the general population and disease specialists, respectively (12,14). However, a difficulty commonly associated with these forums is the data quality, which may vary by members of the general population. It is important to note that Big Data was also used and generated through online learning tools. For instance, an electronic learning tool specifically tailored for veterinarians focused on avian influenza had a huge success rate, with 90.2% of participants finding online courses useful and convenient, and 97% expected to use the learnt information within their professional lives (18).

Both remote sensing and mHealth represented a small fraction of findings within this review. Remote sensing showcased great potential in capturing migratory patterns and potential hotspots, by utilizing satellite imagery, which identified more contaminated bodies of water which acted as avian influenza reservoirs through earth-satellite observations (113,115,116). Additionally, remote-sensing technologies were able to document poultry market chains through migratory patterns (114). mHealth was mostly utilized for diagnostics purposes, linking mobile phone devices with imaging technologies for a point of use sensing platform (118), but also combining them with fluorescent technologies for a smartphone based fluorescent diagnostic system (21,22).

A major challenge noted in a few of the selected studies (12,79) referenced back to poor biosecurity measures, alongside free-ranging practices which were predominantly highlighted in countries within the Caribbean region and Asia. Within these countries, live poultry markets are a common practice, and as a result guidelines may often not be as closely regulated due to the overarching goal to produce profit. Furthermore, it is also important to consider the economic implications linked to avian influenza, primarily referring to live poultry/bird markets and trade dynamics. As the demand for poultry increases, poultry density and trade activities are also intensified

thus increasing the probability of viral spread (119). Embedded within the economic impacts are the underlying anthropogenic factors linked to the more cultural practices, such as the celebration of Luna New year. A recent study found that poultry meat consumption was increased from 4.3- to 9.6-fold during the Luna New year period, exacerbating the cycle of increased demand, increased poultry density and thus increased risk of viral spread (6).

It is important to note that the review also had its methodological limitations, a major one being that only two databases were searched (PubMed and Web of Science), and therefore not capturing the entire evidence body, and also publication bias. Additionally, throughout the eligibility process a large number of studies were excluded due to the focus on seasonal or pandemic influenza, opposed to avian influenza, which may have been caused by the inclusion of “H2N2” within the search strategy syntax (see *Table S1* in supplementary documents). The search term was included as some articles; specifically review articles, discussed Influenza as a whole (with the inclusion of avian influenza), and despite the majority of results focusing on pandemic influenza, studies regarding avian influenza and zoonosis were also found and selected for inclusion.

Conclusions

Digital technologies show potential to improve detection, control and prevention for avian influenza. The scoping review mapped the existing digital technologies used to combat avian influenza, and uncovered five main digital domains including: mhealth, Big Data, data modelling, remote-sensing and novel technologies. Results indicated data modelling to be the most utilized technology, primarily used for surveillance purposes. The major hubs of digital innovation, in terms of research output included USA, Belgium and China, presumably due to funding, and high disease prevalence, respectively. It is important to note that although the methodological approach for modeling has advanced by combining computer-assisted simulations with meteorological and remotely sensed data sets, more innovative approaches are still required to fulfill the potential of other existing technologies. It also remains vital to find ways of incorporating these technologies to improve both treatment and diagnostic procedures for avian influenza.

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Table S1 Search strategy syntax

| Domain related search terms | Search strategy syntax |
|-----------------------------|--|
| Digital technology | <p>“Digital” OR “Technology” OR “Precision medicine” OR “Biosensor” OR “Sensors” OR “Bio-surveillance” OR “Intelligent surveillance” OR “Participatory surveillance” OR “Genomic epidemiology” OR “Genomic sequencing” OR “Pathogen genomics” OR “Big data” OR “Data storage” OR “Data science” OR “Information processing” OR “Blockchain” OR “Social media” OR “Twitter” OR “Facebook” OR “Instagram” OR “Flicker” OR “YouTube” OR “Wikipedia” OR “Telemedicine” OR “Robotics” OR “Machine learning” OR “Modelling” OR “Mathematical modelling” OR “Spatiotemporal modelling” OR “Mapping” OR “mHealth” OR “Mobilephone” OR “Smartphone” OR “Cellphone” OR “Phone” OR “Cell phone technology” OR “Mobile data” OR “Mobile application” OR “Devices” OR “Connected device” OR “Internet” OR “Web-based” OR “Internet-based” OR “Web-database” OR “Cloud” OR “Cloud-based” OR “eHealth” OR “E-learning” OR “Game-based learning” OR “Augmented reality” OR “Massive Online Open Courses” OR “MOOC” OR “Virtual learning” OR “Virtual reality” OR “Online learning” OR “Gaming technology” OR “Serious game” OR “Crowd sourcing” OR “Citizen Science” OR “Connected device” OR “Remote-sensing technology” OR “Satellite” OR “GPS” OR “Global Positioning System” OR “Geographic Information System” OR “Drones” OR “GIS” OR “Spatial” OR “Participatory” OR “Sensor” OR “App” OR “Artificial intelligence” OR “Tracking” OR “Mapping” OR “Biogeography” OR “Biomarkers” OR “Disease mapping”</p> |
| Avian Influenza | <p>“Influenza in Birds” OR “Influenza, Avian” OR “Fowl Plague” OR “Fowl Plague Virus” OR “Avian Flu” OR “Avian Influenza” OR “Influenza A Virus” OR “Influenza Viruses Type A” OR “Orthomyxovirus Type A” OR “Orthomyxovirus Type A, Avian” OR “Avian Orthomyxovirus Type A” OR “Pestis galli Myxovirus” OR “Myxovirus pestis galli” OR “A (H5N1)” OR “A (H7N9)” OR “A (H9N2)” OR “A (H1N1)” OR “A (H2N2)” OR “Bird Flu”</p> |