PharmacoEconomics (2023) 41:253–273
https://doi.org/10.1007/s40273-022-01224-9

SYSTEMATIC REVIEW

Impact of Influenza and Influenza-Like Illness on Work Productivity Outcomes: A Systematic Literature Review

Marie-Hélène Blanchet Zumofen[1] · Jeff Frimpter[2] · Svenn Alexander Hansen[1]

Accepted: 10 November 2022 / Published online: 14 December 2022

Abstract

Background Influenza is a persistent public health problem with a significant burden on patients, employers, and society. A systematic review by Keech and Beardsworth (2008) characterized the burden of influenza/influenza-like illness (ILI) on absenteeism. We conducted a systematic literature review evaluating the impact of influenza/ILI on work productivity among adults as an update to the work of Keech and Beardsworth.

Methods This systematic review identified studies evaluating the impact of influenza/ILI on absenteeism, presenteeism, or related work productivity measures for employees and employed caregivers based on laboratory confirmation, physician diagnosis, and/or self-reported illness. Eligible studies were in English, French, or German published from 7 March 2007 through 15 February 2022, in PubMed, Embase, or BIOSIS. Two reviewers completed screening and full-text review, with conflicts resolved by a third advisor. Summary data were extracted by two analysts; all records were quality checked by one analyst. Work productivity outcomes were summarized qualitatively, and risk of bias was not evaluated.

Results A total of 14,387 records were retrieved; 12,245 titles/abstracts were screened and 145 full-text publications were reviewed, of which 63 were included in the qualitative assessment. Studies of self-reported ILI were most frequent (49%), followed by laboratory-confirmed cases (37%) and physician diagnoses (11%). Overall, approximately 20–75% of employees missed work due to illness across study settings and populations. Mean time out of work among ill employees varied widely across study designs and populations, ranging from < 1 to > 10 days, and was often reported to be approximately 2–3 days. Considerable heterogeneity was observed across study designs, populations, and outcomes. Most employees (≈ 60–80%) reported working while experiencing influenza/ILI symptoms. Reporting of costs was sparse and heterogeneous; one study reported annual costs of influenza-related absences equating to $42,851 per 100,000 employee health plan members. Results were partitioned based on the following categories. Among otherwise healthy adults, 1–74% of workers missed ≥1 workday due to influenza/ILI, for a mean [standard deviation (SD)] of 0.5 (1.44) to 5.3 (4.50) days, and 42–89% reported working while ill, for a mean (SD) of 0.3 (0.63) to 4.4 (3.73) days. Among working caregivers, 50–75% missed work to care for children/household members with influenza/ILI, for 1–2 days on average. Similarly, the mean absenteeism among healthcare workers ranged from 0.5 to 3.2 days. Across studies evaluating vaccination status, generally smaller proportions of vaccinated employees missed time from work due to influenza/ILI.

Conclusions This systematic review summarized the productivity burden of influenza/ILI on the worldwide working-age population. Despite notable heterogeneity in study designs, influenza/ILI case definitions, and productivity outcome measures, this review highlighted the substantial productivity burden that influenza/ILI may have on employees, employers, and society, consistent with the findings of Keech and Beardsworth (2008).

Plain Language Summary

The flu (‘influenza’) has an effect on patients, their families, employers, and society. A review of medical studies from 1995 to 2007 reported how having the flu or a flu-like illness causes people to miss work. We updated that paper using the same approach, and found 63 new studies from 2007 to February 2022. Overall, up to 75% of employees missed work when they

✉ Marie-Hélène Blanchet Zumofen
marie-helene.blanchetzumofen@roche.com

Extended author information available on the last page of the article

had the flu or a flu-like illness. Their average time out of work was usually 2–3 days each time they were sick. Most employees who had the flu or flu-like illness also said that they continued to work while they were sick (60–80%). Most employed adults who were caregivers for someone else with the flu said that they missed work to care for someone else for an average of 1–2 days. Overall, people who were vaccinated against the flu missed less time from work compared with their peers who were not vaccinated. This review of published medical studies showed that the flu and flu-like illness has a meaningful impact on people's ability to work, which also impacts their employers and society.

Key Points for Decision Makers

This systematic review identified 63 studies on the impact of influenza/influenza-like illness (ILI) on work productivity worldwide; despite heterogeneity in study designs and outcome measures, there is a consistent productivity burden of influenza/ILI on employees, employers, and societies worldwide.

Overall, 20–75% of employees miss work due to influenza/ILI, for a mean of approximately 2–3 days, and most employees (≈ 60–80%) report working while experiencing influenza/ILI symptoms; generally, fewer vaccinated employees miss time from work due to influenza/ILI compared with unvaccinated peers.

Approximately 50–75% of employed caregivers miss work to care for household members with influenza/ILI, for approximately 1–2 days on average.

1 Introduction

Influenza is a persistent public health problem responsible for millions of hospitalizations and up to 650,000 respiratory-related deaths annually worldwide, with a substantial direct and indirect cost burden on patients, their families, and society [1, 2]. The influenza virus causes acute respiratory infection (ARI) characterized primarily by fever, cough, sore throat, runny nose, fatigue, and muscle ache [3, 4]. Influenza subtypes are classified by the surface glycoproteins hemagglutinin and neuraminidase (e.g., H1N1) [5], which continuously evolve (antigenic drift) to evade immune response [5, 6]. Less frequently, antigenic shifts can occur via reassortment, resulting in new subtypes (with new hemagglutinin, neuraminidase, or both) that can cause widespread pandemics [5, 6]. Annual influenza outbreaks are most robust in colder weather months, leading to seasonal epidemics with an estimated excess mortality rate of 0.1–6.4 per 100,000 people <65 years of age worldwide [6]. Older age groups are more susceptible to clinical complications and mortality upon influenza infection, with excess mortality estimates of 2.9–44.0 and 17.9–223.5 per 100,000 people aged 65–74 years and ≥75 years, respectively [6].

Although the highest rates of influenza-related deaths are among people >75 years of age, the most influenza-related respiratory deaths are among working-age adults (<65 years), estimated to be approximately 175,000 annually from 1999 to 2015 [6]. However, most otherwise healthy (OWH) adults survive influenza infection. In the United States (US), annual influenza cases ranged from 9 to 41 million over the 2010–2020 decade overall, and annual influenza-related hospitalizations ranged from 140,000 to 710,000 overall [1]. Symptom onset typically follows a 1- to 2-day incubation period, and symptoms can last up to 1 week [3], although fatigue may persist after other symptoms have resolved [4]. Infected persons are encouraged to remain at home until resolution of symptoms and to avoid transmission to others [4]. This can translate to a substantial burden on the quality of life and performance of regular activities for all infected persons, with broader implications for the working-age population in particular, their employers, and society [7]. Laboratory testing confirms the presence of true influenza, while suspected influenza cases based on clinical presentation or self-reported illness are considered 'influenza-like illness' (ILI). While some of these cases will not be true influenza, people nonetheless experience similar clinical symptoms that can impact their lives and productivity. Therefore, understanding the impact of physician-diagnosed ILI based on clinical presentation alone or self-reported ILI such as in survey studies is meaningful when considering the burden of influenza/ILI on patients' lives.

Keech and Beardsworth conducted a systematic literature review to characterize the work productivity burden of influenza or ILI on OWH adults [8]. The authors showed a substantial burden of influenza/ILI on workplace absenteeism across studies spanning approximately 12 years. Since then, novel influenza strains have arisen, including the 2009 H1N1 pandemic, and attention to work productivity outcomes and associated costs has increased dramatically in population health research. We conducted a systematic literature review of studies evaluating the impact of influenza/ILI on work productivity among adults as an update to the work of Keech and Beardsworth. Our review used a nearly identical methodology as that used by Keech and Beardsworth, adding the impact of influenza/ILI on presenteeism (working while ill). Since the concept of presenteeism was not identified in the 2008 review, and has received increasingly more attention in population health research since that time, we sought to understand how the impact of influenza/ILI on productivity for those working while ill (known as 'presenteeism') in addition to absenteeism has been studied. Similarly, the potential impact of influenza/ILI on caregivers was considered in the 2008 review but did not retrieve many results from the literature. This review searched explicitly for the work productivity burden of caring for someone with influenza/ILI.

2 Methods

2.1 Search Strategy and Selection Criteria

This systematic literature review identified studies evaluating the impact of laboratory-confirmed influenza or physician-/self-reported ILI on work productivity outcomes in employed adults (full-time, part-time, or unspecified) whether the adults were ill or were caregivers of ill household members. Search terms were based on those used in the original Keech and Beardsworth review, as this work was undertaken as an update to that review, with the addition of the presenteeism concept. The search strategy was left intentionally broad to maximize the chances of identifying relevant studies. Influenza/ILI could be defined as 'influenza' or 'ILI' based on laboratory confirmation (influenza), physician diagnosis (ILI), or self-reported (ILI) by the infected person or a household member. Classifications were based on the use of this specific terminology in the study with or without a clearly defined set of symptoms reported by the study investigators (e.g., ILI may have been defined as presence of fever and cough). Eligible studies had to be published in English, French, or German between 7 March 2007 (1 day after the Keech and Beardsworth cut-off date of 6 March 2007) through 15 February 2022. Participants could have received any or no intervention. Any study design was eligible; non-peer-reviewed sources and non-research publications were excluded, such as editorials, narrative reviews, and letters to the editor that did not report original research findings. A summary of study eligibility criteria according to the 'PICO' framework (Population, Interventions, Comparators, Outcomes) is provided in Online Resource Table A1. This work followed the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; prisma-statement.org).

Eligible influenza/ILI-related productivity outcomes had to be measured or reported absenteeism (defined as lost productivity from missing work due to illness or for an ill household member on an otherwise expected workday), presenteeism (defined as reduced productivity due to attending work while ill), or related relevant measures such as the amount of time lost from work due to influenza/ILI or caregiving requirements. Surveys regarding the attitudes, opinions, or hypothetical behavior of a working adult were excluded, such as self-reported willingness to attend in-person work during a hypothetical future pandemic. Database analyses that did not link specific person or household influenza/ILI cases directly with the same person or household productivity outcomes were also excluded (such as national seasonal influenza caseload analyzed alongside employer-level work attendance). Modeled outcomes using inputs derived from the literature were also excluded.

Study publications were retrieved from PubMed (pubmed.ncbi.nlm.nih.gov), Embase (https://www.embase.com), and BIOSIS (https://www.ebsco.com). Search terms are provided in Online Resource Table A2 and were supplemented by hand search of reference lists from included publications. Two reviewers completed title and abstract screening and full-text review, with any conflicts resolved by a third advisor.

2.2 Data Extraction and Analysis

Summary data were extracted into a prespecified data extraction table by two analysts, and all records were quality checked by one analyst. Study characteristics included citation, objective, design, period, brief description, inclusion and exclusion criteria, sample size and description, and subgroups. Population characteristics included case description (influenza, ILI, influenza/ILI), diagnosis type (laboratory confirmed, physician diagnosis, self-reported), influenza/ILI cases (adults, children, adults and/or children; although work productivity outcomes were extracted for employed adults only), age, sex, country, clinical status (OWH or comorbidity sample), employment status (any, full-time, part-time, other), vaccination status or administration, and antiviral medication history or administration. We did not prospectively differentiate types of caregiving, such as for a child, parent, or partner. All productivity outcomes were limited to working adults (aged ≥18 years) whether the worker had influenza/ILI or the worker was caring for someone else with influenza/ILI. Studies could have reported adult work productivity outcomes for more than one cohort of interest: the worker being ill (adult case is the adult worker), the worker as a caregiver (household case cared for by an adult worker), or both (i.e., one cohort of adults missing work due to their own illness and another cohort of adults missing work to care for an ill household member).

Absenteeism and presenteeism data were extracted at the study cohort level as reported by the study authors. At a minimum, studies had to report the number of employed adults missing work due to their own illness or as a caregiver (absenteeism) or working while ill (presenteeism) for at least

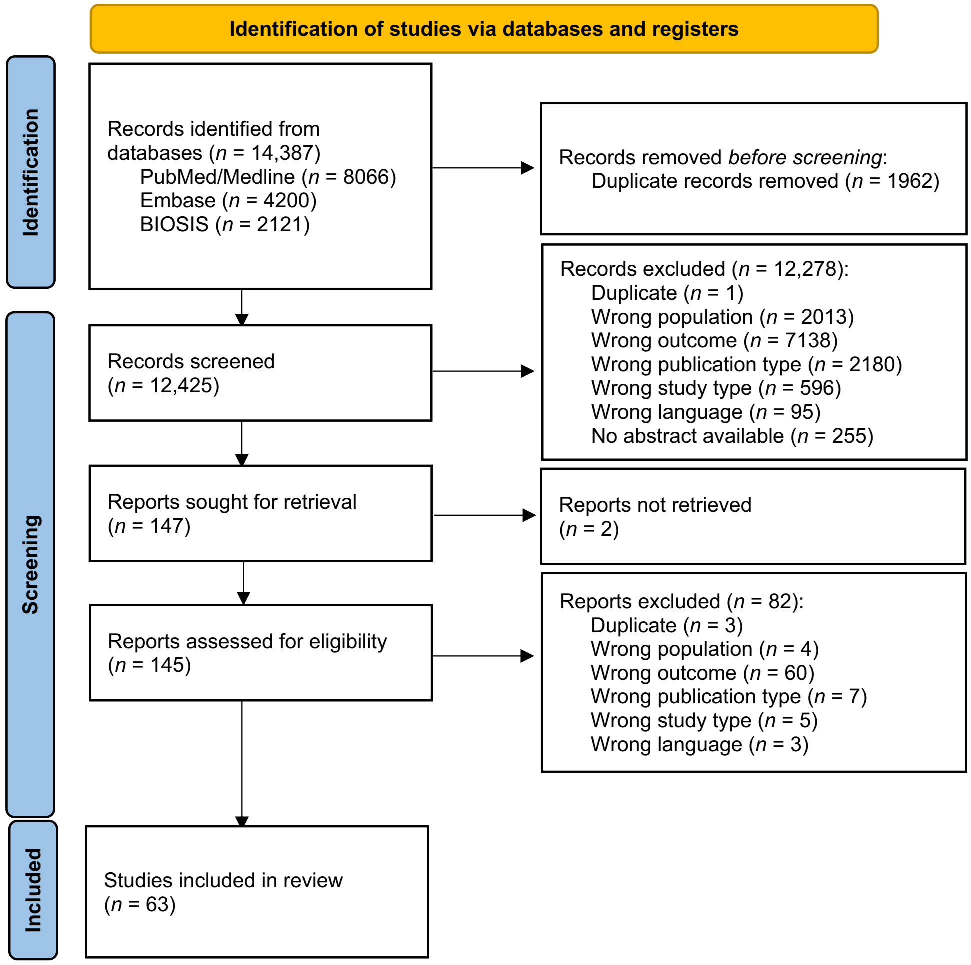

Fig. 1 PRISMA diagram. *PRISMA* Preferred Reporting Items for Systematic reviews and Meta-Analyses

one cohort of interest. Proportions were calculated when a clear numerator and denominator for number of persons was reported. When available, the mean (standard deviation [SD] [9]) and/or median (range or interquartile range [IQR]) time lost from work or time working while ill was also extracted. Time missed from work reported in hours were converted to days, assuming an 8-hour workday (number of missed work hours/8 hours per workday). Direct or indirect costs associated with work productivity losses were also recorded when available. Direct costs were defined as all-cause or influenza/ILI-related healthcare costs such as those associated with provider visits, medications, emergency department (ED) visits, hospital admissions, or similar expenditures reported by the study investigators. Indirect costs were defined as calculations of the monetary impact of absenteeism or presenteeism, or similar financial impact reported by the investigators. Total costs represent the combination of direct and indirect costs.

As in the Keech and Beardsworth review, influenza/ILI-related work productivity outcomes were described qualitatively by type of diagnosis: laboratory confirmation (with or without physician diagnosis), physician diagnosis (without laboratory confirmation), or self-reported (without physician diagnosis or laboratory confirmation). Database studies identifying influenza cases according to International Classification of Diseases codes (ICD-9 or ICD-10) were considered to be physician diagnoses without laboratory confirmation. Risk of bias was not evaluated, as qualitative reporting of descriptive work productivity outcomes was planned; no quantitative analysis was conducted. Descriptive statistics were used to summarize publication, study, and population attributes. All screening and summary statistics were performed using Microsoft® Excel, version 16.61 (https://www.microsoft.com).

3 Results

A total of 14,387 records were retrieved, of which 12,425 (85%) title and abstract records were screened after removal of 1962 duplicates (Fig. 1). One hundred forty-five (1%) full-text publications were assessed, of which 63 (43%) met the eligibility criteria and were included in the qualitative assessment. Key attributes of included studies are illustrated in Fig. 2. One-third of the included studies (21/63; 33%) were published in the period from 2010 to 2012, following the 2009 H1N1 pandemic. Overall, half (48%) of studies reported cases and outcomes in North America (n = 30), 30% in Europe (n = 19), 24% in the Asia/Pacific region (n = 15), one in South America, and one in Africa (one study reported findings across several continents). Self-reported influenza/ILI was most prevalent (49%), followed by laboratory-confirmed cases (37%) and physician diagnoses (without laboratory confirmation, 11%) [Fig. 2]. Two studies (3%) did not report diagnosis type as one of these categories: Colamesta et al. [10] assumed the difference in outcomes between healthy and ill groups to be attributable to influenza (no specified diagnosis or self-reported illness/symptoms), and diagnosis type was not reported by Costantino et al. [11]. Cases were most often reported as ILI (44%), followed by influenza (32%) and influenza/ILI (24%).

A total of 125 study cohorts were identified across the 63 included studies. The results of this review are organized by five prominent themes that emerged from the study cohorts. We have summarized them in the following sections: (3.1) OWH adults with lost productivity due to their own illness (34 study cohorts); (3.2) working adults with lost productivity as caregivers (31 study cohorts); (3.3) healthcare workers (HCWs) with lost productivity due to their own illness or as caregivers (11 total HCW study cohorts); and work productivity related to (3.4) influenza vaccination status or receipt of antiviral treatment (24 study cohorts) and (3.5) the 2009 H1N1 pandemic (25 study cohorts) (Fig. 2). Results for cohorts with overlapping themes (e.g., HCWs as caregivers) are described in the text according to the authors' judgment. Each theme was further organized by type of diagnosis: laboratory-confirmed influenza, physician-reported ILI, or self-reported ILI.

3.1 Otherwise Healthy (OWH) Adults with Influenza/Influenza-Like Illness (ILI)

A total of 18 studies (with 34 cohorts) reported work productivity outcomes among OWH adults with laboratory-confirmed influenza (11%, n = 2/18), physician-reported ILI (17%, n = 3/18), or self-reported ILI (72%, n = 13/18). Primary findings related to OWH adults who were HCWs, experienced work productivity losses as caregivers, or reported outcomes related to the 2009 H1N1 pandemic or vaccination status/antiviral treatment are summarized in separate dedicated sections of this paper. Study characteristics and outcomes are summarized in Online Resource A3. Study cohorts reporting duration of absenteeism or presenteeism are summarized in Fig. 3. Across study cohorts, the proportions of workers who reported absenteeism due to influenza/ILI among all employees ranged from 1.2% (n = 2304/195,366) [12] to 74% (n = 1068/1485) [13], with a mean (SD) duration of absenteeism for those missing work due to influenza/ILI ranging from 0.5 (1.44) days [14] to 5.3 (4.50) days [15] (Fig. 3a). Proportions of ill workers reporting presenteeism ranged from 42% (n = 56/133) [16] to 89% (n = 978/1104 employee months) [17], with a mean (SD) duration of presenteeism ranging from 0.3 (0.63) days [18] to 4.4 (3.73) days [19] (Fig. 3b).

3.1.1 OWH Adults with Laboratory-Confirmed Influenza

Two studies included cohorts reporting work productivity outcomes for OWH adults with laboratory-confirmed influenza. Petrie et al. evaluated absenteeism reported by adults with a medically attended ARI at ambulatory and urgent care facilities in five network centers in the US, stratifying results by those with positive or negative influenza test results, and by vaccination status (see Sect. 3.4 for summary of findings by vaccination status) [20]. Individuals with confirmed positive influenza missed a median of 2.6 days and those with negative results (non-cases) missed a median of 1.9 days, with an adjusted mean difference of 45.2% (95% confidence interval [CI] 26.7–66.5 hours; $p < 0.001$) [20]. In a younger population, Mullins et al. evaluated absenteeism among adults reporting to a university health center with influenza/ILI symptoms, of whom 63% (n = 38/60) had a positive polymerase chain reaction (PCR) test, viral culture, or both (22/60 [37%] had negative test result/viral culture) [21]. Among the 51/60 employed participants, those with positive (71%, n = 36/51) and negative (29%, n = 15/51) PCR tests reported comparable mean days of missed work (1.9 and 1.8, respectively; $p = 0.85$) (Fig. 3a). Severity and duration of influenza/ILI symptoms as well as work absenteeism did not appear to differ between those with positive and negative PCR/viral culture, with the exception of irritability, which was more prevalent among those with a positive influenza result. The small sample size and limited influenza outbreaks (2–3 weeks each year) were noted by the authors and may have influenced the findings. No studies of OWH adults with laboratory-confirmed influenza reported presenteeism outcomes.

3.1.2 OWH Adults with Physician-Reported ILI

Three studies reported work productivity outcomes in OWH employed adults with physician-reported ILI. All three studies analyzed the IBM® MarketScan® databases of commercially insured adults <65 years of age in the US with available data on work absenteeism and claims for short- and long-term disability (worker's compensation claims paid by the employer) in the MarketScan® Health and Productivity Management (HPM) database [12, 14, 22]. Tsai et al. analyzed insurance claims related to physician-diagnosed ILI cases (ICD-9 codes 480–487) that occurred in 1.7% and

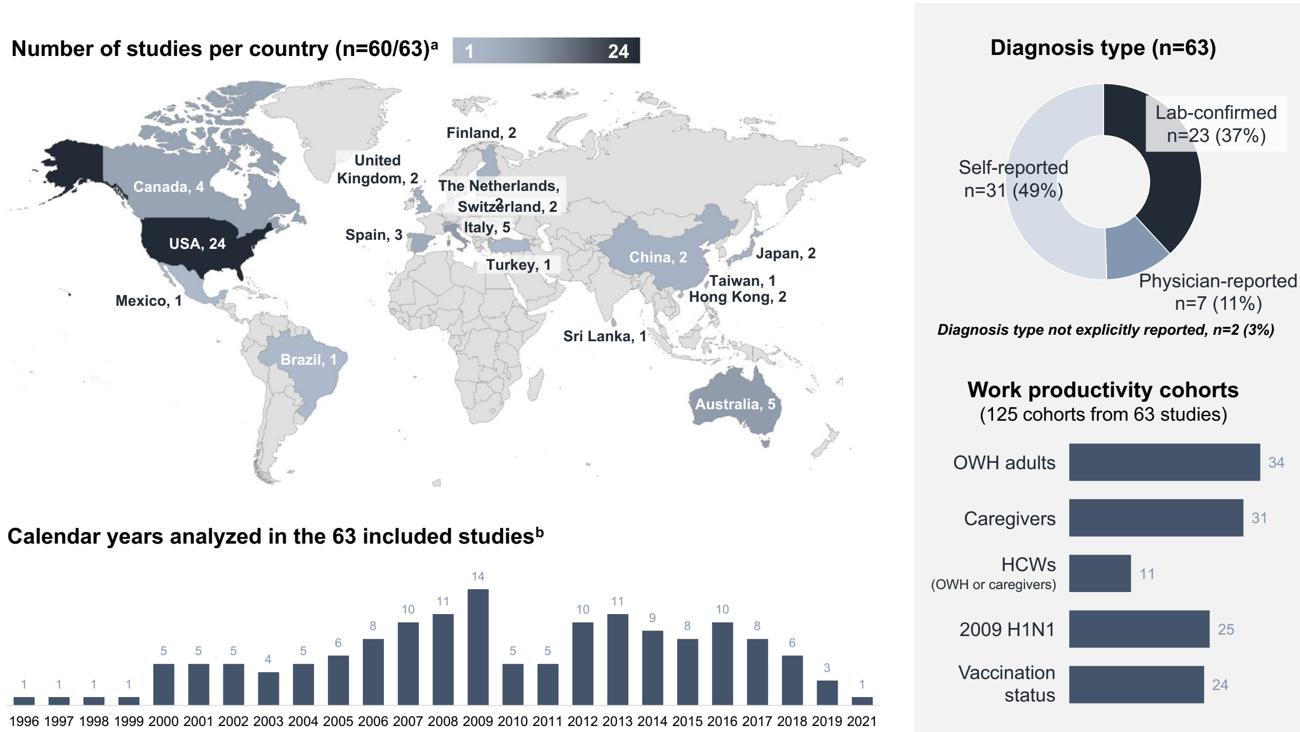

Fig. 2 Key attributes of the included studies (N = 63). [a]Three studies did not report country-level work productivity data: Ambrose and Antonova conducted a post hoc analysis of multinational clinical trials [57]; Li et al. conducted a post hoc analysis of a multinational clinical trial in Europe [63]; and Tartari et al. conducted a cross-sectional survey with geography reported by continent [44]. [b]Outcomes were often reported for >1 calendar year. *HCW* healthcare worker, *OWH* otherwise healthy

1.2% of continuously enrolled beneficiaries in 2007–2008 (n = 3163/186,056) and 2008–2009 (n = 2344/195,366), respectively [12]. Overall, the equivalent of approximately 3 workdays were lost per ILI episode, ranging from 2.95 days in 2007–2008 to 2.99 days in 2008–2009. The mean length of stay for ILI-related hospitalizations ranged from 4.4 to 4.9 full days, resulting in approximately 6 days of missed work [47.0 work-loss hours (5.9 days) and 46.1 work-loss hours (5.8 days)]. Multivariate logistic regression showed significantly more work hours lost per ILI episode among older employees, those who were not in metropolitan statistical areas, and those in the oil and gas extraction or mining industries. No differences were observed based on sex, salaried versus hourly workers, or type of health insurance plan.

Karve et al. analyzed influenza-related productivity losses from the employer perspective over four influenza seasons (2005–2006 through 2008–2009) in the IBM® MarketScan®/HPM databases [22]. Among employees with work absence benefits, 30% (n = 265/881 in 2005–2006) to 37% (n = 1482/4012 in 2008–2009) had ≥ 1 day of influenza-related workplace absence. This increase was likely related to the increasing incidence of influenza cases over the study period, which the authors attributed to several factors, including mismatch vaccine strains in the 2007–2008 season, vaccination rates, and onset of the 2009 H1N1 pandemic. The mean number of influenza-related workplace absence days ranged from 0.8 (2006–2007) to 0.9 (2005–2006). The mean influenza-related direct costs ranged from $254 (2005–2006) to $363 (2008–2009) per case (based on records of inpatient, outpatient, office and ED visits, medications, and ancillary care within 21 days of the influenza diagnosis date). Mean indirect costs per influenza-related workplace absence ranged from $226.34 (2006–2007) to $279.50 (2005–2006). Among employees with short-term disability benefits, 0.5% (n = 20/4488 in 2005–2006) to 1.7% (n = 238/14,393 in 2008–2009) had ≥1 influenza-related short-term disability day. The mean number of influenza-related short-term disability days ranged from 0.1 (2006–2007) to 0.2 (2007–2008), with associated mean total costs to the employer ranging from $2.93 (2007–2008) to $6.69 (2008–2009) per influenza case.

Karve et al. also analyzed productivity outcomes for influenza seasons with matched and mismatched circulating and vaccine influenza B lineages using the IBM® MarketScan®/HPM databases from 2000 to 2009, but did not directly connect vaccination status with illness and outcomes [14]. Overall, 30% of patients with absence/disability benefits who had an influenza episode missed ≥ 1 workday, which was higher

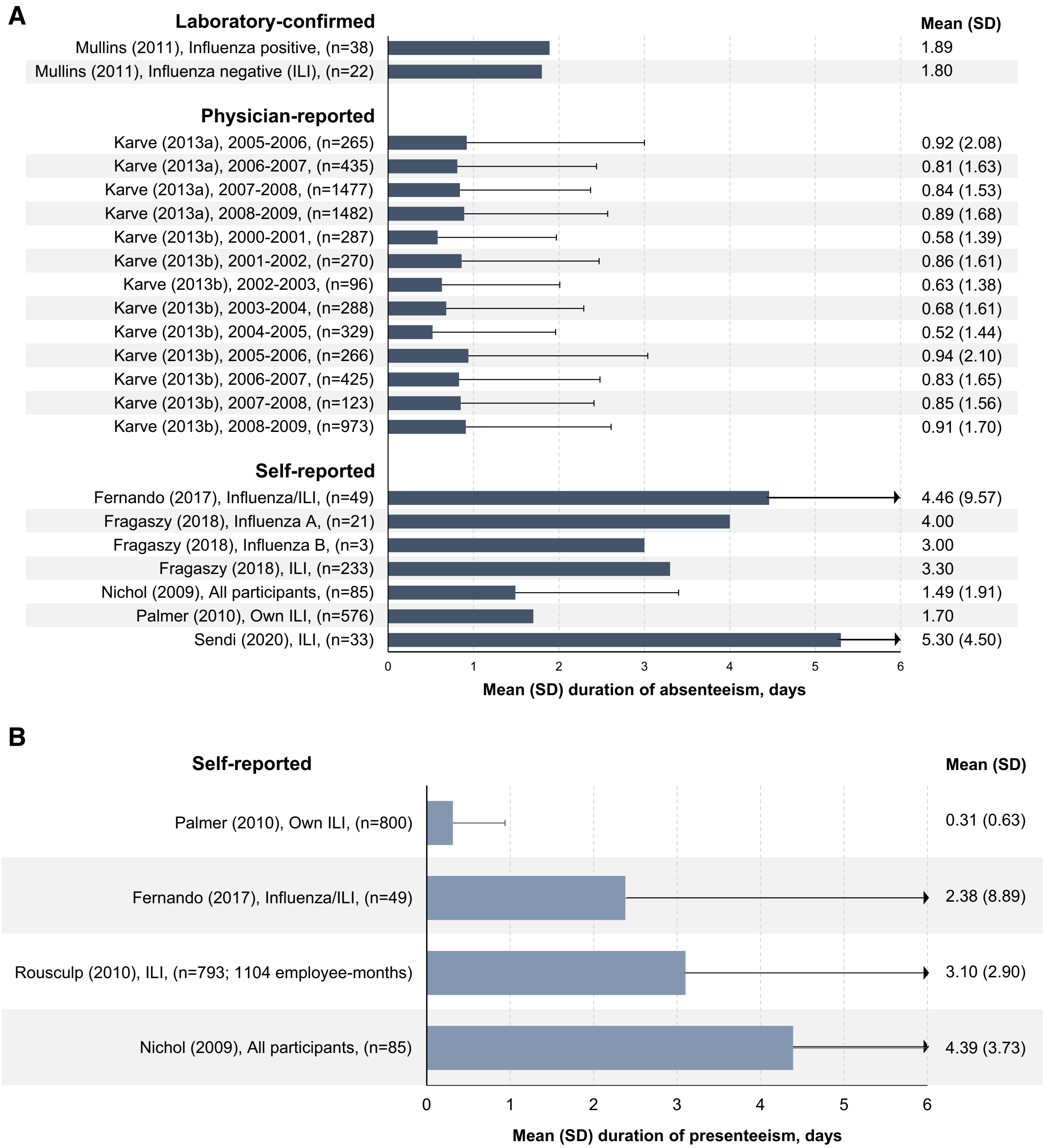

Fig. 3 Mean duration of **a** absenteeism and **b** presenteeism among OWH adults. **a** Study cohorts reporting mean duration of absenteeism for OWH adults with influenza/ILI. Figure comprises study cohorts reporting mean duration of absenteeism per person; some studies did not report standard deviations. Fragaszy et al. conducted a survey study, but participants were requested to submit nasal swabs on Day 2 of their illness, which were then classified as influenza A or B, or ILI in the case of negative tests [7]. The studies by de Perio et al. [26], Johnson et al. [23], Petrie et al. [20], and Rousculp et al. [17] only reported median duration of absenteeism and were therefore not included in the figure. **b** Study cohorts reporting mean duration of presenteeism for OWH adults with influenza/ILI. Figure comprises study cohorts reporting mean duration of presenteeism per person. *OWH* otherwise healthy, *ILI* influenza-like illness, *SD* standard deviation

in mismatched seasons (33% vs. 26% in matched seasons). Employees with influenza-related absences had a mean of 6 hours of missed work, which was also greater during mismatched than matched seasons (6.8 vs. 5.1 h). The mean indirect costs associated with an influenza-related absence was $209.66 overall ($237.31 in mismatched vs. $175.10 in matched seasons), equating to $42,851 per 100,000 employee plan members ($51,483/100,000 in mismatched seasons vs. $31,454/100,000 in matched seasons). No studies of OWH adults with physician-reported ILI reported presenteeism outcomes.

3.1.3 OWH Adults with Self-Reported ILI

Thirteen studies included cohorts reporting work productivity outcomes related to self-reported ILI among OWH adults. Among 150 employees of a small rehabilitation center, Sendi et al. reported that 33 employees (22%, n = 33/150) missed work due to ILI, for a mean (SD) of 5.3 (4.5) days [15]. Absenteeism was compared between 1 month of an outbreak (63%, n = 25/40 employees with ILI) and the rest of the influenza season (33%, n = 8/40). The overall total of 175 missed workdays equated to a loss of CHF87,000 (€81,308). A similar estimate was reported by Johnson et al. in which 24% of adults (n = 76/315) reported missing ≥ 1 day of work due to their own ILI during a school closure period in Yancey County, NC, USA [23]. At the upper range of self-reported absenteeism, in a survey of employees from several professions in Sedgwick County, KS, USA, Ablah et al. reported 84% of responders (n = 1207/1442) "would leave work with a fever/flu-like illness" but only 74% (n = 1068/1450) "have left work with an ILI", suggesting a potential disparity between intentions and behavior [13]. Ablah et al. also found 61% (n = 906/1474) of working adults reporting that they had worked with an ILI [13]. A similarly high proportion of absenteeism was reported among 72% (n = 576/800) of adults with self-reported ILI from three large national US employers, by Palmer et al. [18]. Working adults participating in the Palmer et al. analysis of the CHIEF study also reported a mean (SD) of 0.3 (0.63) days of presenteeism during their own ILI [18].

Fernando et al. reported a mean (SD) of 2.4 (8.89) days among 49 employees with ILI at a Sri Lankan company (49/150 survey responders from 700 employees) who indicated performing at a lower level than usual while present at work due to ILI [24]. When accounting for overall work productivity loss due to influenza (absenteeism plus presenteeism), Fernando et al. reported a mean (SD) of 7.0 (13.55) days lost due to influenza [24]. The authors projected 1605.5 workdays lost due to influenza across all 700 employees, which, in a 264-day work-year, would equate to a total cost of $5133 to the employer (based on a blended salary assumption of $811/year for skilled operative employees in Sri Lanka) [24]. Nichol et al. reported an estimated mean (SD) of 1.5 (1.91) workdays lost and 4.4 (3.73) days of ILI-related presenteeism in a study of 497 working adults aged 50–64 years regardless of vaccination status [19], with results by vaccination status summarized separately in Sect. 3.4. Overall, those reporting presenteeism rated their level of work effectiveness to be 70–75% of normal for the days they worked while ill [19]. Fragaszy et al. analyzed work productivity loss among adults in an English community with self-reported ILI (42%, n = 2013/4818 reported illnesses) or PCR-confirmed influenza A (6%, n = 177/3161 illnesses tested for influenza A or B) or influenza B (1%, n = 45/3161 illnesses tested for influenza A or B) [7]. Approximately one-quarter (26%, n = 303/1169) of adults (aged 16–64 years) with self-reported ILI took time off work for their illness for a mean of 3.3 days, compared with 31% (n = 31/99) and 20% (n = 3/15) of those with confirmed influenza A or B, respectively, who reported missing a mean of 3.8 and 3.0 days.

Interestingly, a study by Lee et al. suggested that employee-reported productivity is better and indirect costs are lower with more space and ventilation in the physical office environment. In a survey of 2175 employees of a large employer in Hong Kong, Lee et al. evaluated the impact of ILI episodes on productivity by a measure of employee-reported 'equivalent days of perfect health' lost (EDPH) due to ILI, adjusted for severity, where mild symptoms were attributed 0.75 EDPH, moderate symptoms 0.5 EDPH, and severe symptoms 0.25 EDPH [25]. The mean EDPH loss accounting for self-reported ILI severity was then compared across groups based on the nature of the physical work environment. Overall, the mean EDPH loss per person with an ILI episode per year was 10.7 days, equating to a loss of $833 per person per year. Employees working in a 'confined work area' had a mean of 13.28 EDPH lost ($1206), those in a 'typical office environment' had a mean 9.58 EDPH lost ($697), and those in a 'well-ventilated area' had a mean 7.35 EDPH lost ($296).

Among 133 school nurses in Missouri, USA, who completed an optional survey, Rebmann et al. found that 42% (n = 56/133) claimed to have worked while ill with ILI symptoms at least once in the previous 3 years [16]. The most common reasons for presenteeism provided by the school nurses were related to being cleared for work by their primary care provider (84%, n = 112/133) and believing their illness was mild (74%, n = 99/133). de Perio et al. surveyed 841 school employees in an Ohio, USA, school district of whom 412/841 (49%) completed the survey and 120/412 (29%) reported ILI symptoms during the study period [26]. Respondents reported a median of 1 day (range 0–7) of absenteeism due to ILI and 77% (n = 92/120) reported working while ill with ILI, most often citing a professional

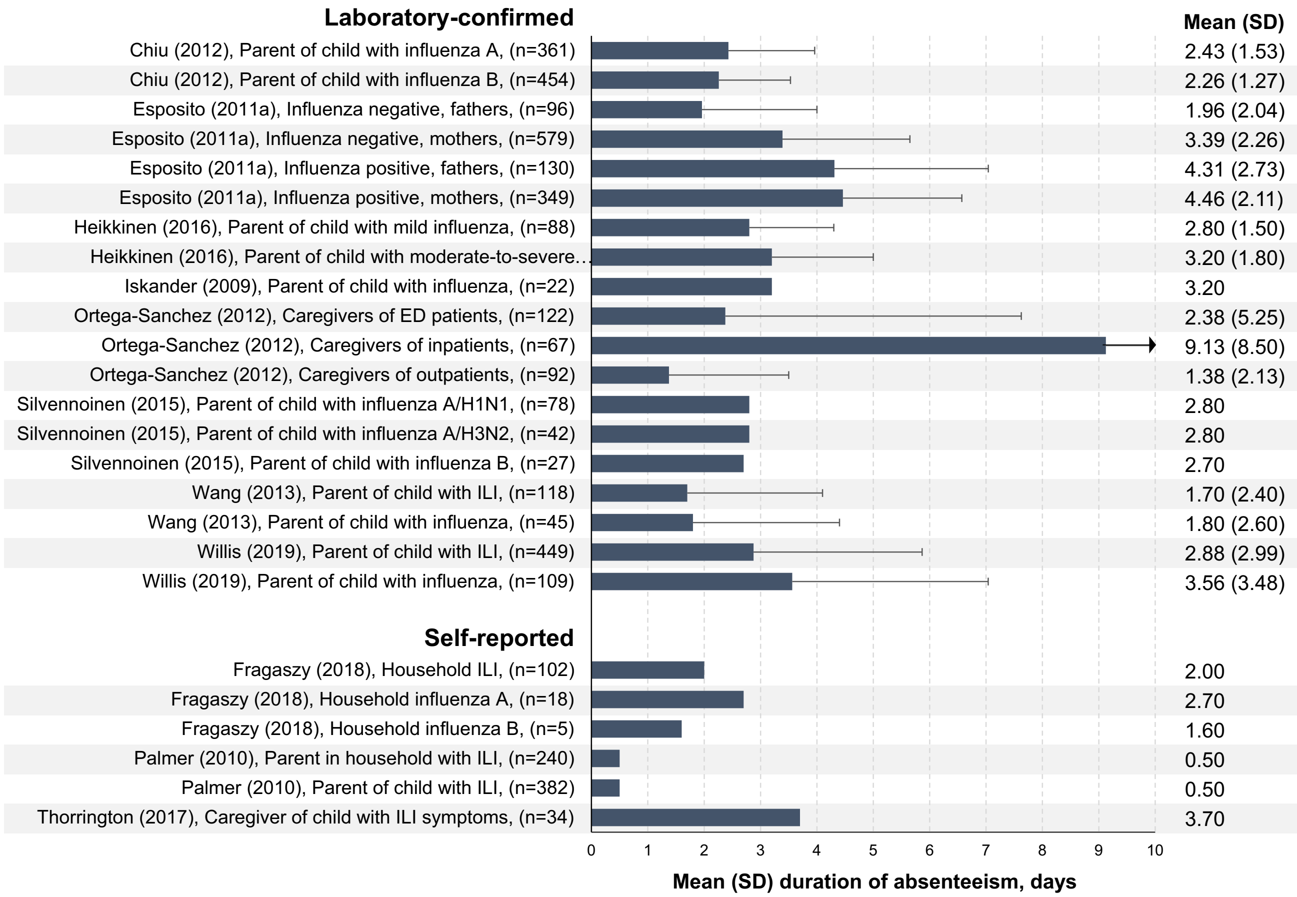

Fig. 4 Study cohorts reporting mean duration of absenteeism for caregivers. Figure comprises study cohorts reporting mean duration of absenteeism per person; some studies did not report SDs. The studies by Iskander et al. [36], Mughini-Gras et al. [41], Tsuzuki et al. [31], and Wang et al. [39] only reported median duration of absenteeism and were therefore not included in the figure. *ED* emergency department, *ILI* influenza-like illness, *SD* standard deviation

obligation to the students (28%, n = 25/90) or not knowing they were ill or contagious (23%, n = 21/90).

Dalton et al. analyzed self-reported ILI over the 2011–2014 influenza seasons from Australia's *Flutracking* surveillance system, reporting peak self-reported absenteeism rates of 2.5% in 2014 and 1.6% in 2013 [27]. In a survey of 122 registered veterinarians in New South Wales, Australia, Pasfield et al. reported that 66% (n = 81/122) indicated working with ILI symptoms at some point during the previous 24 months [28]. It should be noted that the Pasfield et al. study period of 31 March 2021 through 30 June 2021 was during the coronavirus disease 2019 (COVID-19) pandemic, which may have influenced the results.

Rousculp et al. surveyed 793 employees of three large US employers who had 1104 employee-months of ILI symptoms [17]. A total of 978/1104 employee-months (89%) were attributed to attending work while having ILI symptoms, resulting in a mean (SD) of 3.1 (2.9) days (median 2.0 days). A large proportion of self-reported working sick-time was during the most severe ILI symptoms (72%, 794/1104 employee-months). In an analysis of employer policies, only the ability to work from home was found to be a significant negative predictor of employees with ILI attending work while their ILI symptoms were most severe (57% probability, p = 0.006) and of the number of days employees attended work while their ILI symptoms were most severe (p = 0.026).

3.2 Caregivers

A total of 17 studies (with 31 study cohorts) reported work productivity outcomes for caregivers of household members with influenza/ILI and are summarized in this section (HCWs as caregivers are summarized in the HCWs section). Most studies reported laboratory-confirmed cases (65%, n = 11/17) followed by self-reported ILI (35%, n = 6/17), and none were related to physician-reported ILI. Study characteristics and work productivity findings are summarized in Online Resource A4, and those reporting mean duration of absenteeism are summarized in Fig. 4. Across study cohorts, the mean absenteeism for employed adults caring for a household member with influenza/ILI ranged from 0.5 days for ILI-related household illness [18] to 9.1 (8.50) days for caregivers of a household member hospitalized for influenza/ILI ($n = 67$) [29].

3.2.1 Caregivers of Household Members with Laboratory-Confirmed Influenza

Across studies reporting laboratory-confirmed influenza/ILI, the mean duration of absenteeism for caregivers ranged from 1.4 days [29] to 9.1 days [29]. The highest estimate of absenteeism across studies was for mothers of children hospitalized for influenza/ILI in a US study, which reported that 75% ($n = 50/67$) of mothers reported time off work, with a mean (SD) of 9.1 missed days for their children hospitalized with influenza/ILI [29]. Of the laboratory-confirmed cases, caregiver outcomes were often analyzed based on positive or negative test results for children presenting with ILI symptoms, type of confirmed influenza, and/or type of healthcare encounter, presumably as a proxy for severity (outpatient visit vs. hospital admission). Heikkinen et al. directly analyzed parental absenteeism among those whose children had mild or moderate-to-severe influenza, reporting ≥1 day of work was missed by 49% of parents whose children had mild influenza (mean 2.8 days) and 58% of parents of children with moderate-to-severe influenza (mean 3.2 days) [30]. A large survey in Japan by Tsuzuki et al. analyzed household ILI episodes associated with a median of 2 (IQR 1–5) missed workdays overall [31]. Participants indicating that their physician had provided a diagnosis of influenza (based on laboratory results) also reported a median of 5 days missed from work per episode, compared with 2 days for those with non-influenza respiratory virus.

Wang et al. compared absenteeism for parents of 1537 children <5 years of age visiting the ED for ILI symptoms who then had positive (24%, $n = 365/1537$) or negative (76%, $n = 1172/1537$) influenza test results, reporting mean (SD) days missed from work of 1.8 and 1.7, respectively [32]. Similarly, in Turkey, Aykaç et al. analyzed absenteeism among parents of children hospitalized with ILI symptoms for ≥24 hours by influenza test result for each parent [33]. One-third (33%, $n = 5/15$) of employed fathers of influenza-positive children took leave from work for the child's illness (all mothers of influenza-positive children were not employed). For parents of children with negative influenza results, all employed mothers (100%, $n = 117/117$) and 34% ($n = 39/117$) of employed fathers took leave from work. Willis et al. compared absenteeism between parents of 1191 children <5 years of age in Australia presenting to the ED or hospitalized for acute respiratory symptoms, and compared confirmed influenza cases with non-cases [34]. Generally similar proportions of parents reported work absenteeism across groups [cases, 53% ($n = 109/204$); non-cases, 55% ($n = 449/813$); other respiratory virus-positive, 58% ($n = 329/571$)], but the mean duration of work missed was numerically greater for parents of confirmed influenza cases (3.6 days) compared with non-cases (2.9 days) and other respiratory virus-positive children (2.8 days).

Esposito et al. separately analyzed absenteeism for mothers and fathers of children < 14 years of age presenting with ILI symptoms in Italy who were then determined to be confirmed influenza ($n = 2143$) or non-influenza ($n = 4845$) cases [35]. For confirmed influenza cases, 16% ($n = 349/2143$) of mothers and 6% ($n = 130/2143$) of fathers 'remained absent from work', both of which were statistically significant when compared with mothers (12%, $n = 579/4845$; $p < 0.001$) and fathers (2%, $n = 96/4845$; $p < 0.05$) of non-cases. Parents of children with confirmed influenza also missed significantly more mean days from work than parents of non-cases, both for mothers (4.5 vs. 3.4 days; $p < 0.05$) and fathers (4.3 vs. 2.0 days; $p < 0.01$). Iskander et al. interviewed parents of 260 children in Australia who had been hospitalized for ≥1 week with influenza/ILI, where 71% ($n = 184/260$) of the children had ≥1 parent who needed time off from work to look after their sick child (mean 3.2 days; median 2 days) [36].

Chiu et al. analyzed parental absenteeism for children < 18 years of age hospitalized for asthma exacerbation (with or without fever) or febrile ARI, of whom 10% ($n = 102/1031$) had influenza A and 4% ($n = 45/1031$) had influenza B [37]. One-third of parents of children with influenza A (35%, $n = 34/102$) missed ≥ 1 day of work (mean 2.4 days) to care for their child, and 44% ($n = 20/45$) of parents of children with influenza B missed ≥ 1 day of work (mean 2.3 days). Silvennoinen et al. analyzed parental absenteeism among children with influenza A/H1N1, influenza A/H3N2, or influenza B in Finland, reporting 47% ($n = 78/165$; mean 2.8 days), 53% ($n = 42/80$; mean 2.8 days), and 50% ($n = 27/54$; mean 2.7 days), respectively, requiring at least one parent to take ≥ 1 day off of work due to the child's illness [38].

Ortega-Sanchez et al. analyzed parental absenteeism for children visiting an outpatient clinic or the ED, or who were admitted to the hospital for an ARI in New York, USA [29]. Caregivers reporting time off work ranged from 42% ($n = 39/92$) for children attending an outpatient clinic to 75% ($n = 50/67$) of children admitted to the hospital, with mean workdays missed ranging from 1.4 days for outpatient clinic visits to 9.1 days for hospital admissions. Wang et al. analyzed parental absenteeism for 2171 children <5 years of age with PCR-confirmed influenza with outpatient visits or inpatient admissions at a large children's hospital in Suzhou, China [39]. Parents of children with outpatient visits missed a median of 0 days (range 0–2) compared with a median of 7 days (range 6–9) for parents of hospitalized children.

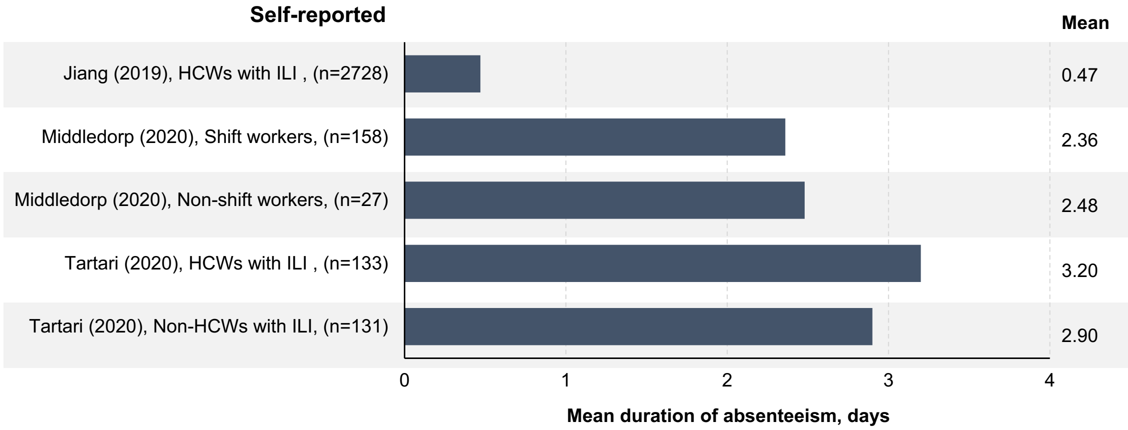

Fig. 5 Study cohorts reporting mean duration of absenteeism for HCWs. Figure comprises study cohorts reporting mean duration of absenteeism per person (studies did not report standard deviations). The studies by Chiu et al. [48] and Laris Gonzalez et al. [46] only reported median duration of absenteeism and were therefore not included in the figure. *HCWs* healthcare workers, *ILI* influenza-like illness

3.2.2 Caregivers of Household Members with Self-Reported ILI

Across six study cohorts reporting the mean (SD) duration of absenteeism for caregivers of household members with self-reported ILI, values ranged from 0.5 days [18] to 3.7 days [40]. Presenteeism was only reported in the Palmer et al. analysis of the CHIEF study, which showed a mean (SD) of 0.2 days (1.3 hours) of presenteeism with any household ILI or when a child in the household had ILI (1.4 hours) [18].

Johnson et al. reported that 47% (n = 36/76) of employed adults who missed ≥1 workday due to illness was for their own illness, and 24% (n = 18/76) missed work to take care of a family member's illness during a 2-week school closure in Yancey County, NC, USA [23]. Thorrington et al. surveyed caregivers of primary school-age children in England, of whom 39% (n = 34/87) had children with ILI symptoms during an influenza outbreak period and missed a mean of 3.7 days from work [40]. Mughini-Gras et al. conducted a large survey of 8768 parent–child pairs in The Netherlands (children had to be >4 years of age) and reported that 22% (n = 282/1307) of sick parents missed work due to their own illness and 16% (n = 309 parents of 1893 sick children) due to their child's illness, for a median of 2 and 1 days, respectively [41].

In the large Flu Watch household survey in England, Fragaszy et al. reported outcomes from illness diaries for households recruited through primary care practices. Respondents were asked to submit nasal swabs on day 2 of reported illness related to 'cough, cold, sore throat or flu-like illness' [7]. A total of 6% (n = 23/361) of working adults missed work to care for a household member with ILI (mean 1.2 days), and of those who submitted nasal swabs, 13% (n = 3/24) missed work for influenza A (mean 2.3 days) and 0 (of 2) missed work for influenza B [7]. In another population-level analysis, Li et al. analyzed the burden of ILI across 12,850 US households with school-aged children [63]. A total of 14% of surveyed households reported ≥ 1 case of ILI in the past year, of which 31% sought medical care [42]. Employed members of households with ILI lost 1.1 more workdays than those in households that did not report any ILI in the past year, which was similar when compared among a subset of households with medical insurance (0.9 more workdays lost).

3.3 Healthcare Workers (HCWs) with Influenza/ILI

A total of nine studies (with 11 cohorts) reporting work productivity outcomes among HCWs are summarized in this section (exclusive of other categories, summarized in separate dedicated sections). There were three laboratory-confirmed influenza studies and six self-reported ILI studies; none were related to physician-reported ILI. Study characteristics and work productivity findings are summarized in Online Resource A5. Study cohorts reporting mean duration of absenteeism due to influenza/ILI are summarized in Fig. 5. Across study cohorts, the mean absenteeism for HCWs, all from self-reported ILI studies, ranged from 0.5 days [43] to 3.2 days [44].

3.3.1 HCWs with Laboratory-Confirmed Influenza

Three studies reported work productivity outcomes among HCWs with laboratory-confirmed influenza, all suggesting that a substantial proportion of HCWs (> 60%) missed work due to influenza/ILI. Kuster et al. evaluated absenteeism and presenteeism among 152 HCWs at a tertiary care hospital in Switzerland across the 2015–2016 and 2016–2017 influenza seasons [45]. HCWs missed a total of 121 working days, of which 100 (83%) were attributable to influenza in 36 participants (n = 36/45 missed work due to any illness). The authors reported no difference in work productivity outcomes between influenza seasons or based on demographic characteristics or profession. Laris Gonzalez et al. evaluated PCR-confirmed influenza or unconfirmed influenza/ILI among HCWs in a pediatric referral hospital in Mexico, reporting that 78% of surveyed HCWs (n = 62/79) missed ≥1 day of work (median 2 days) [46]. In a smaller study, Wilson et al. reported that 64% (n = 9/14) of surveyed HCWs remained at work while ill during an influenza A/H3N2 outbreak in an inpatient oncology unit [47].

3.3.2 HCWs with Self-Reported ILI

Six studies reported work productivity for HCWs with self-reported ILI. Chiu et al. surveyed 1913 HCWs in the US, where 41% (n = 183/414) of those with a self-reported ILI indicated that they had worked during an ILI episode [48]. Tartari et al. [44] reported that 64% (n = 185/289) of HCWs returned to work while symptomatic, compared with 62% of non-HCWs (n = 178/289) [44]. Hoang Johnson et al. surveyed HCWs in a US tertiary care system regarding occurrence of ILI and work productivity during the 2017–2018 influenza season, where only 57% (n = 759/1334) reported staying home when they had ILI symptoms [49]. When asked about perceived barriers to remaining home while ill, those who worked with ILI symptoms more often reported a perceived lack of support from their management to stay home, felt responsibility to patients and coworkers, said they felt well enough to work, or did not have or want to use time off compared with those who did not work with ILI symptoms. Turnberg et al. analyzed surveys of 627 HCWs in five US medical centers, only 30% (n = 185/627) of whom reported always taking sick leave when they have flu-like symptoms, and fewer than half (43%, n = 271/627) reported that their employer encourages them to take sick leave when they have flu-like symptoms [50].

Jiang et al. analyzed surveillance data from 2093 Canadian HCWs collected over the 2010–2011 to 2013–2014 influenza seasons, of whom 95% (n = 980/1036) of those with ILI symptoms reported working ≥1 day and 52% (n = 539/1036) worked every day when they had ILI symptoms [43]. These equated to a mean of 1.9 days working with ILI and 0.5 missed days due to ILI. Middeldorp et al. analyzed data from the prospective Klokwerk+ cohort study of 531 HCWs in The Netherlands (450 shift workers, 81 non-shift workers) who completed questionnaires after ILI episodes [51]. Absenteeism of ≥ 1 day was reported for similar proportions of ILI episodes among shift workers and non-shift workers, at 13% (n = 201/1527 ILI episodes) and 14% (n = 31/221 ILI episodes), respectively. Absenteeism due to ILI was associated with a mean of 2.4 and 2.5 missed days from work, respectively.

3.4 Vaccination Status or Antiviral Treatment

A total of 11 studies (with 24 cohorts) reported work productivity outcomes according to vaccination status or for antiviral treatment (three laboratory-confirmed, one physician-reported, five self-reported, and two unspecified). Study characteristics and work productivity findings are summarized in Online Resource A6. All studies reporting work productivity outcomes by vaccination status or receipt of antiviral treatment are summarized in this section, whether for caregivers, HCWs, or otherwise. Across study cohorts, generally fewer vaccinated employees as well as employees treated with antivirals missed time from work due to influenza/ILI, although findings related to duration of absenteeism varied across settings and influenza seasons (Fig. 6).

3.4.1 Vaccination Status Reported with Laboratory-Confirmed Influenza

Among studies of laboratory-confirmed influenza, Van Wormer et al. retrospectively analyzed data from four seasonal influenza vaccination studies of 470 adults in the US with ARI including cough (study participants had ≤ 7 days of illness) [52]. A regression model showed that adults with ARI and a positive influenza PCR test result lost 69% of expected work hours from their work week due to illness (absenteeism plus presenteeism) from ARI symptom onset to survey follow-up (7–17 days). Those with H1N1 who were not vaccinated lost 74% of expected work hours (the most of any group), and those with ARI and a negative influenza test result lost 58% of expected work hours (the least of any group). The authors observed that any type of influenza was associated with greater productivity loss than non-influenza ARI. Morales-Suárez-Varela et al. evaluated the impact of influenza on unvaccinated women during the 2009 H1N1 epidemic in Spain, reporting lower work absenteeism-related indirect costs per patient for pregnant women (€63.83) than for non-pregnant women (€104.59) between November 2009 and February 2010 [53].

Ambrose and Antonova analyzed data from three previously published studies evaluating the efficacy and safety of live attenuated influenza vaccines (LAIV) in European and Israeli children [54–56]. Only one of these studies, by Vesikari et al., reported productivity outcomes for working adults [56, 57]. In study years 1 and 2, 55% (n = 6/11) and 29% (n = 6/21) of parents of children in the LAIV group missed workdays, respectively, compared with 51% (n = 28/55) and 44% (n = 54/123) of parents of children in the placebo group. The mean number of missed days was 1.8 and 2.8

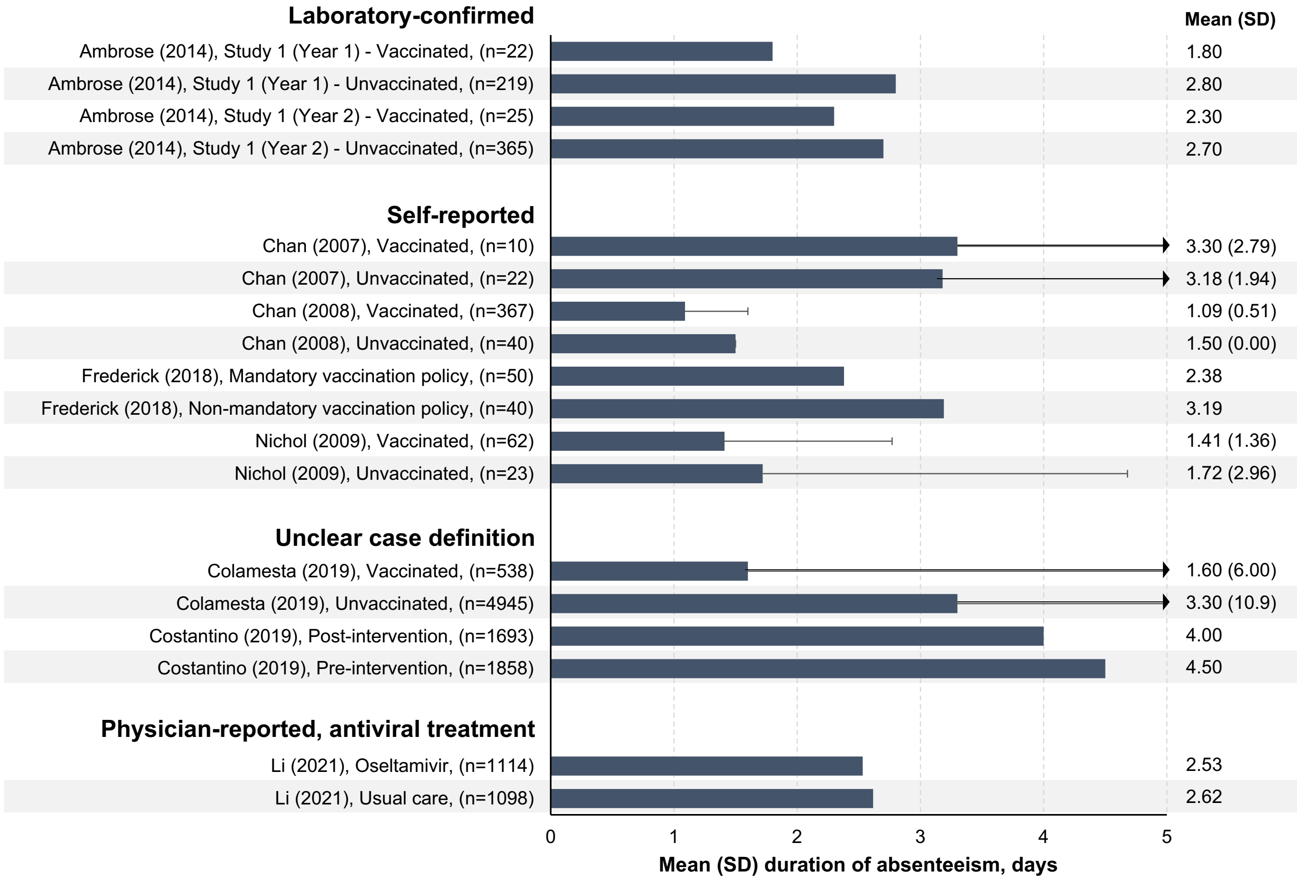

Fig. 6 Study cohorts reporting mean duration of absenteeism by vaccination status or antiviral treatment. Figure comprises study cohorts reporting mean duration of absenteeism per person; some studies did not report SDs. The studies by Petrie et al. [20] and Li et al. [63] only reported median duration of absenteeism and were therefore not included in the figure. *SD* standard deviation

days in the LAIV and placebo groups in Year 1, respectively, and 2.3 and 2.7 days for the LAIV and placebo groups in Year 2, respectively. Surprisingly, the Petrie et al. study in the US showed vaccinated workers with a positive influenza test result to have missed a median of 3.0 days (95%, n = 221/233) compared with a median of 2.5 days among unvaccinated peers (94%, n = 335/355); however, this difference was not statistically significant (p = 0.80) [20].

3.4.2 Vaccination Status Reported with Self-Reported ILI

Among studies with self-reported ILI cases, Chan reported significantly fewer vaccinated (30%, n = 10/33) than unvaccinated (55%, n = 22/40) employees in Hong Kong taking sick leave due to ILI (p = 0.034), but with similar durations of missed time from work (mean 3.3 vs. 3.2 days; p = 0.88) [58]. In another study in Taiwan by Chan et al, a larger sample of employees also showed a smaller proportion of vaccinated employees (4%, n = 15/367) requiring sick leave due to ILI than unvaccinated employees (8%, n = 3/40), with numerically fewer mean days lost per vaccinated employee with ILI compared with unvaccinated employees (1.1 vs. 1.5) [59]. Nichol et al. also reported numerically fewer days lost from work for vaccinated HCWs with self-reported ILI, where vaccinated employees missed a mean (SD) of 1.4 (1.36) days and unvaccinated counterparts missed 1.7 (2.96) days (p = 0.17) [19]. Vaccinated employees also had fewer mean (SD) days working while ill (presenteeism) compared with unvaccinated employees (3.9 [3.22] vs. 5.6 [4.70], respectively; p = 0.002).

Frederick et al. compared work productivity between employees at facilities with mandatory vaccination requirements (3 facilities, 2304 participants), where 92–97% of participants were vaccinated, and non-mandatory vaccination policies (4 facilities, 1759 participants), where only 60–68% of participants were vaccinated [60]. Over three influenza seasons (2012–2013 to 2014–2015), a lower proportion of participants at the mandatory vaccination sites missed ≥1 workday due to viral respiratory illness (20%, mean of 50.0 participants over 3 years) compared with those at sites with non-mandatory vaccination policies (28%, mean of 40.4 participants over 3 years), among whom a mean of 2.4

and 3.2 workdays were missed due to influenza/ILI, respectively. Murti et al. analyzed payroll and self-reported sick leave data for 107,258 HCWs across seven health centers in British Columbia, Canada, to evaluate a ‘vaccination or mask’ policy from 2012 to 2017, which required anyone (including HCWs or visitors) entering a patient care area to wear a mask if they had not received an influenza vaccine for that season [61]. Generally, lower rates of absenteeism were observed for vaccinated than unvaccinated HCWs. Zaffina et al. compared absenteeism rates among HCWs in a pediatric hospital in Italy, showing a lower average sickness absenteeism rate for vaccinated vs. unvaccinated HCWs (1.6 vs. 2.0) [62].

3.4.3 Vaccination Status with Unclear Case Definition

Two studies did not have clearly discernible diagnosis or self-reported ILI cases, but appeared otherwise relevant to this review. Colamesta et al. compared absenteeism among hospital staff with and without a record of vaccination during the 2017–2018 influenza season in Rome, assuming any difference in work absences due to sickness were attributable to influenza [10]. The mean (SD) number of missed workdays due to sick leave was 1.6 (6.0) for the vaccinated group and 3.3 (10.9) for the unvaccinated group. Neither identification of influenza/ILI cases nor exploration of other factors that may have been different between the groups other than the employer having a record of influenza vaccination were reported. Costantino et al. evaluated the impact of an influenza vaccination awareness campaign among patient-facing clinical staff at a hospital in Palermo, Italy, from 2013 to 2019 [11]. Absenteeism during annual influenza seasons was calculated as workdays missed overall and workdays missed due to acute sickness, but no influenza/ILI case identification method was reported. A 25% increase in vaccination adherence was observed from the 2014–2015 season during the vaccination campaign (pre-intervention) to the 2018–2019 post-intervention influenza season. From the pre-intervention period (2009–2010 to 2014–2015) to the post-intervention period (2015–2016 to 2018–2019), an 8.8% decrease in HCWs missing work during the influenza season was reported, along with a 12.9% reduction in working days lost during influenza seasons overall and 11.1% reduction in mean working days lost due to acute sickness.

3.4.4 Antiviral Treatment

In an evaluation of antiviral treatment-related outcomes, Li et al. conducted a post hoc analysis of the ALIC4E clinical trial to evaluate direct and indirect costs between patients with ILI who received usual care or usual care plus oseltamivir across 15 European countries (2015–2018) [63]. Approximately half of the usual care group (55%, n = 712/1289) and half of the usual care plus oseltamivir group (54%, n = 704/1306) reported ≥1 instance of missed work for a mean of 20.9 hours (median 8.5) and 20.3 hours (median 8.0), respectively, equating to 2.6 and 2.5 missed workdays. Approximately 7% (n = 95/1289) and 10% (n = 130/1306) of each group, respectively, reported any activity loss (not restricted to paid work) as a caregiver for a dependent. From a societal perspective, the authors calculated the mean indirect costs from productivity losses to be €369.00 per patient receiving oseltamivir (median €157.58) compared with €382.39 per patient receiving usual care alone (median €162.84). Ultimately, improved productivity contributed to lower average total costs per ILI patient in the usual care plus oseltamivir group compared with the usual care group without antivirals [63].

3.5 The 2009 H1N1 Pandemic

A total of 11 studies (with 25 cohorts) reported work productivity outcomes related to influenza/ILI during the 2009 H1N1 pandemic period (four laboratory-confirmed influenza, three physician-reported ILI, four self-reported ILI). Study characteristics and work productivity findings are summarized in Online Resource A7. Across study cohorts, employed adults with absenteeism due to their own influenza/ILI or as a caregiver to an ill household member during the 2009 H1N1 pandemic missed a mean of 2.4 days of work (OWH adults) [64] to 30.5 days of work (adults hospitalized for influenza/ILI) [65]. Several studies evaluated absenteeism during the pandemic compared with seasonal influenza periods of prior years, as well as outcomes among HCWs providing care during the H1N1 pandemic (Fig. 7).

3.5.1 The 2009 H1N1 Pandemic Based on Laboratory-Confirmed Influenza

Four studies reported work productivity outcomes related to laboratory-confirmed influenza during the 2009 H1N1 pandemic. Esposito et al. analyzed absenteeism for mothers and fathers of 1001 children <15 years of age between seasonal and pandemic influenza periods, showing generally comparable mean absenteeism between the 2008–2009 seasonal influenza and 2009–2010 H1N1 pandemic influenza periods (mothers, 5.9 days each; fathers, 3.4 and 3.3 days, respectively), which were both higher than the 2007–2008 seasonal influenza estimates (mothers, 3.9 days; fathers, 1.2 days) [66].

Three of the laboratory-confirmed influenza studies assessed the impact of the H1N1 pandemic on employees of healthcare organizations. Murray et al. studied the impact of the 2009 H1N1 pandemic on employees of a tertiary care hospital and two community hospitals in Vancouver, reporting 8101 sick days due to influenza during

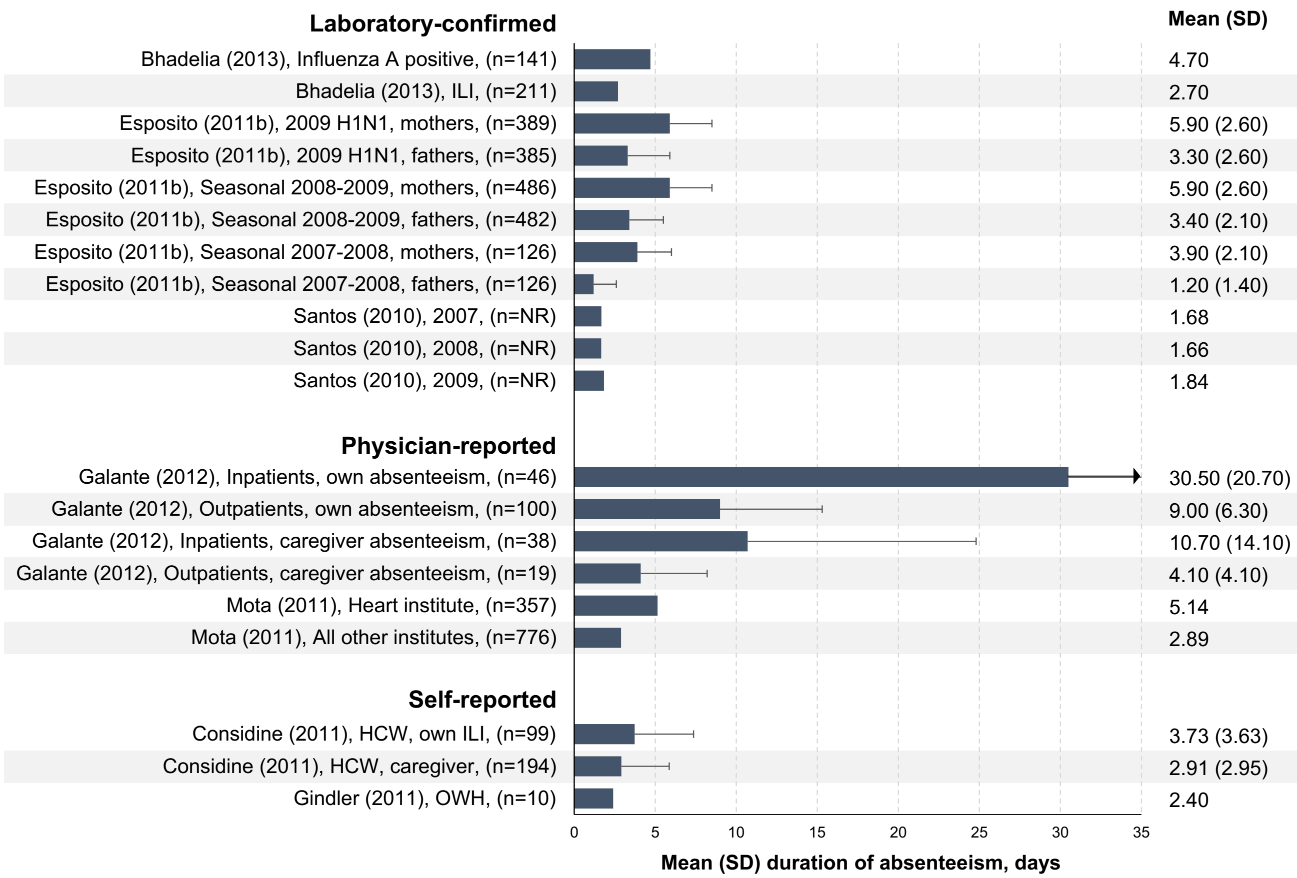

Fig. 7 Study cohorts reporting mean duration of absenteeism during the 2009 H1N1 pandemic. Figure comprises study cohorts reporting mean duration of absenteeism per person; some studies did not report SDs. *HCW* healthcare worker, *ILI* influenza-like illness, *OWH* otherwise healthy, *SD* standard deviation

the 24-week pandemic [67]. This represented a 3.6-fold increase in sick days at the peak of the pandemic (compared with the week with the fewest reported sick days). Similarly, Santos et al. compared absenteeism among employees of New York-Presbyterian Health System during the 2009 H1N1 pandemic compared with the same periods in 2007 and 2008 [68]. The mean number of sick hours across all types of employees in five hospitals were significantly greater in 2009 compared with 2007 [14.7 vs. 13.4 mean sick hours, respectively (+9.7%); $p < 0.001$] and 2008 [14.7 vs. 13.3 (+10.5%); $p < 0.001$]. The greatest differences between 2008 and 2009 were observed for social workers and counselors (+27.8%: $p = 0.04$), nurses and clinical technicians (+12.4%; $p < 0.01$), and administrative and support staff (+11.1%; $p < 0.01$). Across departments, the greatest increase in mean work hours missed by staff were in the Pediatrics (+41.2%; $p < 0.01$) and Pediatric Emergency (+81.4%; $p = 0.01$) departments. Bhadelia and colleagues also studied the impact of the H1N1 pandemic on approximately 13,000 employees of the Columbia University Medical Center in New York City from 31 March 2009, through 28 February 2010 [69]. Of 393 HCWs presenting with ILI, 352 (90%, $n = 352/292$) were tested, and 40% ($n = 141/352$) were positive. Nearly all (93%, $n = 327/352$) missed ≥ 1 day of work due to influenza or ILI (1095 days total) [69]. Most clinical staff reported working with ILI symptoms (overall, 65%; physicians, 67%; nurses, 63%) for a mean of 2 days.

3.5.2 The 2009 H1N1 Pandemic Based on Physician-Reported ILI

Three physician-reported ILI studies analyzed the work productivity impact of the 2009 H1N1 pandemic. Mota et al. evaluated the impact of the 2009 H1N1 pandemic on HCWs in one Brazilian hospital compared with the 2008–2009 pre-pandemic period [70]. Overall, hospital HCWs had 884 ILI-related work absences during the 2009 season compared with 96 during the 2008 season ($p < 0.001$). The effect of sick leave policies was also compared, where a 7-day sick leave policy in one department equated to total costs of $1127 per work absence (for a total of $190,602 from 169 staff members with ILI-related work absences). All other hospital institutes, which had a '2-day leave plus reassessment' policy, equated to $609 per work absence (for a total of $252,761 from 415 staff members with ILI-related work absences).

Galante et al. reported work productivity associated with H1N1 infection among adults and/or children who were inpatients or outpatients with influenza A/H1N1 across 24 hospitals in Spain [65]. Overall, 94% of employed patients (n = 146/155) reported being absent from work due to influenza, and 22% of inpatients (n = 37/172) and 9% of outpatients (n = 19/224) had a caregiver who missed work due to influenza. The mean number of lost working days was 30.5 for inpatient cases and 9.0 for outpatient cases. Tora-Rocamora et al. evaluated the impact of the 2009 H1N1 pandemic in the Spanish region of Catalonia, analyzing influenza/ILI cases among the working population from endemic and epidemic periods from January 2007 through March 2010 using an endemic-epidemic index to compare observed vs. expected caseloads [71]. Of 3.7 million sickness absences in the region for the entire study period (39 months), 4% (157,447/3.7 million) were attributable to influenza and 22% (811,940/3.1 million) to influenza/ILI. There were 5844 more influenza-related work absences during the observed (epidemic) than expected (endemic) periods of peak influenza activity. Data were otherwise reported on a weekly basis and have not been summarized further in this review due to space limitations. Overall, the authors observed a doubling of influenza burden in the epidemic period and a longer duration of sickness absences that differentially impacted business sectors across Catalonia.

3.5.3 The 2009 H1N1 Pandemic Based on Self-Reported ILI

Four studies analyzed the work productivity impact of the 2009 H1N1 pandemic related to self-reported ILI. Gindler et al. reported a mean of 2.4 workdays lost among members of the US Centers for Disease Control and Prevention Emergency Operations Center 2009 H1N1 response team [64]. Among HCWs, Mitchell et al. reported that 72% (n = 170/236) of HCWs missed work for their own illness and 4% (n = 37/986) missed work related to caregiving from September through December of the 2009 H1N1 pandemic in Canada [72]. Considine et al. surveyed members of three emergency nursing and medicine colleges in Australia, 36% of whom (n = 177/486) reported becoming ill with ILI during the pandemic period and approximately half of those with ILI (57%, n = 99/175) missed ≥ 1 workday for a mean (SD) of 3.7 (3.63) days [73]. Of those who reported being a caregiver for someone else with ILI, 18% (n = 34/194) missed ≥ 1 day of work for a mean (SD) of 2.9 (2.95) days.

Rebmann et al. conducted a survey of 471 human resources professionals across 33 US states from June to August 2011; participants were asked to report the frequency with which they reported to work while ill during the 2009 H1N1 pandemic [74]. Most of the respondents reported not going to work while having symptoms of infection during the pandemic (85%, n = 401/471). Of the 70 participants (15%, n = 70/471) who did report working with symptoms, the most common reasons were related to the belief that the H1N1 influenza was a mild disease (67%, n = 47/70), fear of falling behind at work (67%, n = 47/70), not having coverage by a coworker (46%, n = 32/70), and feeling pressured by colleagues or a supervisor to work (36%, n = 25/70).

4 Discussion

This systematic literature review has qualitatively characterized the substantial work productivity burden of influenza/ILI on the worldwide working-age population as an update to the work of Keech and Beardsworth [8]. Overall, our findings were consistent with those summarized by Keech and Beardsworth, with both reviews showing a clear, comprehensive burden of influenza on the global workforce despite substantial heterogeneity in study designs, populations, and outcomes. From 1995 to March 2007, Keech and Beardsworth identified 28 unique publications of human studies related to influenza/ILI and work productivity [8]. From March 2007 to February 2022, we identified 63 (+ 125%) relevant unique studies. Despite notable heterogeneity in study designs and settings, influenza/ILI case definitions, and work productivity outcome measures, this large systematic review has highlighted the well-documented worldwide productivity burden of influenza/ILI on employees, employers, and society. Prominent influenza outbreaks and increased attention to indirect costs and work productivity in the medical literature at large have likely contributed to the relative increase in research on this topic since the review by Keech and Beardsworth. This review identified similar proportions of studies reporting laboratory-confirmed cases (37%) as Keech and Beardsworth (36%), physician-diagnosed cases (11% and 14%, respectively), and self-reported cases (49% and 50%, respectively). Of interest, we noted a large proportion of excluded studies were surveys of employees, particularly HCWs, regarding their attitudes and opinions about working while ill or during a pandemic and about getting vaccinated.

Across studies in this review, the proportion of adults missing ≥ 1 workday due to their own illness varied widely based on study settings and subgroups. Up to 75% of employees missed work due to illness across study settings and populations. Overall, the average time out of work was often reported to be approximately 2–3 days. The majority of employees with influenza/ILI reported working while experiencing symptoms. When asked, employees who reported working while ill rated their work performance during that time as notably less productive or efficient compared with normal healthy working days. In the caregiver setting, 50–75% of employed caregivers missed work to care for their dependents for approximately 1–2 days on average, reaching as many as 9 days off work for hospitalized children. Across studies evaluating vaccination status, generally smaller proportions of vaccinated employees missed time from work due to influenza/ILI, and estimates of the duration of missed work time varied based on study settings.

There were several noteworthy findings from this review. First, an influenza epidemic or pandemic creates a clear spike in work productivity loss across countries and industries, well beyond the substantial productivity burden from seasonal influenza/ILI. Studies of the 2009 H1N1 pandemic showed a 3.6-fold increase in influenza-related sick days over a 24-week period [67] and an increase of up to 81% [69] in missed work time based on profession and specialty for hospital-based HCWs. Studies of endemic vs. epidemic outbreaks on work productivity and subsequent costs would be of interest for future work. The majority of infected employees reported going to work despite experiencing influenza/ILI symptoms, including HCWs. Overall, work productivity burden appeared greatest when the employee was sick as opposed to being a caregiver, although similarly high proportions of employees missed ≥1 workday when they were sick as when a household member was sick. As such, employed adults missed slightly less time from work overall when in a caregiving role, the reasons for which were not investigated but may have been related to shared caregiving responsibilities and/or flexibility in the work environment. Interestingly, employed mothers of sick children appeared to bear a greater productivity burden than fathers. Finally, on the whole, fewer vaccinated employees missed workdays than unvaccinated employees, with differences ranging widely across studies. Although duration of absenteeism appeared only slightly more favorable for the vaccinated, fewer employees missing work could still have a meaningful impact on productivity costs borne by employers and society. This review only included one study evaluating the impact of antiviral treatment on work productivity, where numerically less work productivity loss translated to numerically lower total costs when oseltamivir was added to usual care, although the differences were not statistically significant [63]. The impact of antiviral treatment on reducing healthcare resource utilization and costs was not part of the scope of our review. As oseltamivir and newer treatments such as baloxavir marboxil have shown effectiveness in reducing influenza symptoms and viral load [75], the potential implications for work productivity would be of interest for future research.

It is worth noting that the generally widespread behavioral changes borne by the COVID-19 pandemic, including increased public hygiene and other contagion mitigation strategies, are likely to impact influenza- and work productivity-related findings. For example, prolonged suppression of seasonal influenza virus circulation may reduce population immunity and increase the severity of future influenza virus epidemics [76]. However, increased mask use and hand hygiene in combination with greater adherence to public health measures (i.e., self-isolation when experiencing flu-like symptoms) may reduce viral transmission and the overall societal impact of influenza. Future work may focus on HCW intentions and behaviors related to absenteeism, presenteeism, and vaccination during a pandemic, which may further inform virus transmission research and capacity preparedness efforts. Furthermore, potential changes to the work environment such as increased working from home and less business travel may also impact both absenteeism and presenteeism in ways that should be accounted for in future work. One publication in this review had a study period that would have been influenced by the COVID-19 pandemic (Pasfield et al; study period, 31 March 2021–30 June 2021) [28]. Therefore, the intersection of the COVID-19 impact on work productivity outcomes with influenza/ILI is more likely to impact future work in this area.

The inherent strengths and limitations of this work should be considered in the interpretation of our findings. We used a relatively broad search strategy to identify as many potentially relevant publications as possible to be more closely adjudicated for their relevance in title/abstract and full-text screening. Search terms were based on those used for the original Keech and Beardsworth review, with the addition of the presenteeism concept. While we used three prominent sources of peer-reviewed scientific literature, it is possible that relevant studies could have been published in other sources, such as in non-indexed journals or in scientific meeting abstracts. This review included work productivity outcomes related to unconfirmed illness (ILI) that may have been a manifestation of other viruses or health conditions; therefore, the self-reported and ILI-related findings should be interpreted with some degree of caution. Studies reporting laboratory-confirmed influenza are likely to offer the most robust information when purely influenza-specific outcomes are of interest.

While this report was intended to illustrate the available information on work productivity related to influenza/ILI, results should nonetheless be interpreted in the context of case and outcome definitions, particularly from studies that did not report laboratory-confirmed illness. It should also be noted that sampling and reporting biases were likely to impact case identification and subsequent outcomes across studies. Moreover, absenteeism and presenteeism could have been reported from the same patient for the same illness episode. It would be of interest if future work could differentiate work productivity outcomes by the severity of different influenza strains, which was not possible in this review.

Costs associated with presenteeism would also be of interest but were not reported.

The substantial heterogeneity of study designs, populations, case definitions, and outcomes should also be noted, which limited the calculation of high-level summary statistics and broad generalizability. Future work on subtopics in this area, such as the impact of influenza on HCW productivity, may find opportunities to reduce heterogeneity and perform deeper analysis and quantitative assessment, including analysis of costs of lost work productivity in different employment settings and industries. Since our objective was to provide an updated view of available information on influenza/ILI-related work productivity outcomes in the literature, and to summarize identified studies qualitatively, we did not perform a risk-of-bias assessment. Future work with more focused objectives intended to derive specific, quantitative estimates should interpret their findings through the lens of potential study biases. Attitudes and opinions about working with influenza/ILI symptoms, working during a pandemic, and/or being vaccinated were not in the scope of this review. However, future work may further investigate the influence of these factors on absenteeism (and subsequent implications on the workforce and economy) and on presenteeism (and subsequent implications for viral transmission). Finally, this review did not aim to analyze employer policies and benefits regarding missed work time due to illness, which may be important to understanding the reasons for some of these findings, particularly for presenteeism, and to addressing disparities related to the nature of employment and health.

5 Conclusions

Influenza and ILI have a meaningful impact on the ability of working adults to continue working in a safe, productive manner in the context of their own illness or that of a household member or dependent. Across countries, industries, and professions, influenza/ILI causes notable proportions of the workforce to miss planned work time, which has received greater attention in the medical literature over the past 15 years. Perhaps more detrimental to the person and to society, most employees still go to work with influenza/ILI symptoms. This systematic literature review has aimed to characterize the work productivity burden of influenza/ILI to support more effective and equitable health management strategies for working adults and their families worldwide.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40273-022-01224-9.

Acknowledgments Support for third-party writing assistance for this manuscript, furnished by Health Interactions, Inc., was provided by F. Hoffmann-La Roche Ltd. The authors wish to thank Charli Dominguez, PhD, and Hossein Heidari Torkabadi, PharmD, PhD, of Health Interactions, Inc. for assistance with record screening and data extraction. The authors also thank Anna Steenrod for her guidance, and Hassan Zaraket and Kunal Samanta for their thorough review of the paper, all from F. Hoffmann-La Roche Ltd.

Declarations

Funding This study was funded by F. Hoffmann-La Roche Ltd.

Conflicts of interest Marie-Hélène Blanchet Zumofen and Svenn Alexander Hansen are employees and shareholders of F. Hoffmann-La Roche Ltd. Jeff Frimpter has no conflicts of interest to declare.

Availability of data and material The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions Conceptualization: M-HBZ, SH. Literature search: JF. Data analysis: All authors. Manuscript draft and critical revision: All authors.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Codeavailability Not applicable.

References

1. Centers for Disease Control and Prevention. Disease burden of flu. https://www.cdc.gov/flu/about/burden/index.html. Accessed 19 May 2022.
2. World Health Organization. Global influenza programme. Burden of disease. https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/burden-of-disease. Accessed 2 June 2022.
3. Gaitonde DY, Moore FC, Morgan MK. Influenza: diagnosis and treatment. Am Fam Phys. 2019;100:751–8.
4. Krammer F, Smith GJD, Fouchier RAM, et al. Influenza. Nat Rev Dis Primers. 2018;4:3.
5. Taubenberger JK, Morens DM. Influenza: The once and future pandemic. Public Health Rep. 2010;125(Suppl 3):16–26.
6. Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2018;391:1285–300.

7. Fragaszy EB, Warren-Gash C, White PJ, et al. Effects of seasonal and pandemic influenza on health-related quality of life, work and school absence in England: results from the flu watch cohort study. Influenza Other Respir Viruses. 2018;12:171–82.
8. Keech M, Beardsworth P. The impact of influenza on working days lost: a review of the literature. Pharmacoeconomics. 2008;26:911–24.
9. Chouaid C, Danson S, Andreas S, et al. Adjuvant treatment patterns and outcomes in patients with stage IB-IIIA non-small cell lung cancer in France, Germany, and the United Kingdom based on the LuCaBIS burden of illness study. Lung Cancer. 2018;124:310–6.
10. Colamesta V, Tamburrano A, Barbara A, et al. Cost-consequence analysis of influenza vaccination among the staff of a large teaching hospital in Rome, Italy: a pilot study. PLoS ONE. 2019;14: e0225326.
11. Costantino C, Casuccio A, Caracci F, et al. Impact of communicative and informative strategies on influenza vaccination adherence and absenteeism from work of health care professionals working at the University Hospital of Palermo, Italy: a quasi-experimental field trial on twelve influenza seasons. Vaccines (Basel). 2019;8:5.
12. Tsai Y, Zhou F, Kim IK. The burden of influenza-like illness in the US workforce. Occup Med (Lond). 2014;64:341–7.
13. Ablah E, Konda K, Tinius A, et al. Influenza vaccine coverage and presenteeism in Sedgwick County, Kansas. Am J Infect Control. 2008;36:588–91.
14. Karve S, Meier G, Davis KL, Misurski DA, Wang CC. Influenza-related health care utilization and productivity losses during seasons with and without a match between the seasonal and vaccine virus B lineage. Vaccine. 2013;31:3370–88.
15. Sendi P, Drager S, Batzer B, et al. The financial burden of an influenza outbreak in a small rehabilitation centre. Influenza Other Respir Viruses. 2020;14:72–6.
16. Rebmann T, Turner JA, Kunerth AK. Presenteeism attitudes and behavior among Missouri kindergarten to twelfth grade (K-12) school nurses. J Sch Nurs. 2016;32:407–15.
17. Rousculp MD, Johnston SS, Palmer LA, et al. Attending work while sick: implication of flexible sick leave policies. J Occup Environ Med. 2010;52:1009–13.
18. Palmer LA, Rousculp MD, Johnston SS, Mahadevia PJ, Nichol KL. Effect of influenza-like illness and other wintertime respiratory illnesses on worker productivity: the child and household influenza-illness and employee function (CHIEF) study. Vaccine. 2010;28:5049–56.
19. Nichol KL, D'Heilly SJ, GreenbergEhlinger MEE. Burden of influenza-like illness and effectiveness of influenza vaccination among working adults aged 50–64 years. Clin Infect Dis. 2009;48:292–8.
20. Petrie JG, Cheng C, Malosh RE, et al. Illness severity and work productivity loss among working adults with medically attended acute respiratory illnesses: US influenza vaccine effectiveness network 2012–2013. Clin Infect Dis. 2016;62:448–55.
21. Mullins J, Cook R, Rinaldo C, et al. Influenza-like illness among university students: symptom severity and duration due to influenza virus infection compared to other etiologies. J Am Coll Health. 2011;59:246–51.
22. Karve S, Misurski DA, MeierDavis GKL. Employer-incurred health care costs and productivity losses associated with influenza. Hum Vaccin Immunother. 2013;9:841–57.
23. Johnson AJ, Moore ZS, Edelson PJ, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. Emerg Infect Dis. 2008;14:1024–30.
24. Fernando M, Caputi P, Ashbury F. Impact on employee productivity from presenteeism and absenteeism: evidence from a multinational firm in Sri Lanka. J Occup Environ Med. 2017;59:691–6.
25. Lee KK, Li SC, Kwong KS, et al. A study of the health and economic effects of influenza-like illness on the working population under different working environments of a large corporation in Hong Kong. J Med Econ. 2008;11:639–50.
26. de Perio MA, Wiegand DM, Brueck SE. Influenza-like illness and presenteeism among school employees. Am J Infect Control. 2014;42:450–2.
27. Dalton CB, Carlson SJ, McCallum L, et al. Flutracking weekly online community survey of influenza-like illness: 2013 and 2014. Commun Dis Intell Q Rep. 2015;39:E361–8.
28. Pasfield K, Gottlieb T, Tartari E, WardQuain MPA. Sickness presenteeism associated with influenza-like illness in veterinarians working in New South Wales: results of a state-wide survey. Aust Vet J. 2022;100:243–53.
29. Ortega-Sanchez IR, Molinari NA, Fairbrother G, et al. Indirect, out-of-pocket and medical costs from influenza-related illness in young children. Vaccine. 2012;30:4175–81.
30. Heikkinen T, Silvennoinen H, HeinonenVuorinen ST. Clinical and socioeconomic impact of moderate-to-severe versus mild influenza in children. Eur J Clin Microbiol Infect Dis. 2016;35:1107–13.
31. Tsuzuki S, Yoshihara K. The characteristics of influenza-like illness management in Japan. BMC Public Health. 2020;20:568.
32. Wang D, Zhang T, Wu J. Socio-economic burden of influenza among children younger than 5 years in the outpatient setting in Suzhou, China. PLoS ONE. 2013;8: e69035.
33. Aykac K, Basaranoglu ST, Gözmen O, Yetimakman AF, Teksam O, Kara A. The comfort burden of seasonal influenza and influenza-like disease in hospitalized children: 2015-2016 season. J Pediatr Inf. 2017;11:e100–e105.
34. Willis GA, Preen DB, Richmond PC, et al. The impact of influenza infection on young children, their family and the health care system. Influenza Other Respir Viruses. 2019;13:18–27.
35. Esposito S, Cantarutti L, Molteni CG, et al. Clinical manifestations and socio-economic impact of influenza among healthy children in the community. J Infect. 2011;62:379–87.
36. Iskander M, Kesson A, Dwyer D, et al. The burden of influenza in children under 5 years admitted to the Children's Hospital at Westmead in the winter of 2006. J Paediatr Child Health. 2009;45:698–703.
37. Chiu SS, Chan KH, So LY, et al. The population based socioeconomic burden of pediatric influenza-associated hospitalization in Hong Kong. Vaccine. 2012;30:1895–900.
38. Silvennoinen H, Huusko T, VuorinenHeikkinen TT. Comparative burden of influenza A/H1N1, A/H3N2 and B infections in children treated as outpatients. Pediatr Infect Dis J. 2015;34:1081–5.
39. Wang Y, Chen L, Cheng F, et al. Economic burden of influenza illness among children under 5 years in Suzhou, China: report from the cost surveys during 2011/12 to 2016/17 influenza seasons. Vaccine. 2021;39:1303–9.
40. Thorrington D, Balasegaram S, Cleary P, Hay C, Eames K. Social and economic impacts of school influenza outbreaks in England: survey of caregivers. J Sch Health. 2017;87:209–16.
41. Mughini-Gras L, Pijnacker R, Enserink R, et al. Influenza-like Illness in Households with Children of Preschool Age. Pediatr Infect Dis J. 2016;35:242–8.
42. Li S, Leader S. Economic burden and absenteeism from influenza-like illness in healthy households with children (5–17 years) in the US. Respir Med. 2007;101:1244–50.
43. Jiang L, McGeer A, McNeil S, et al. Which healthcare workers work with acute respiratory illness? Evidence from Canadian acute-care hospitals during 4 influenza seasons: 2010–2011 to 2013–2014. Infect Control Hosp Epidemiol. 2019;40:889–96.
44. Tartari E, Saris K, Kenters N, et al. Not sick enough to worry? "Influenza-like" symptoms and work-related behavior among

healthcare workers and other professionals: Results of a global survey. PLoS ONE. 2020;15: e0232168.
45. Kuster SP, Boni J, Kouyos RD, et al. Absenteeism and presenteeism in healthcare workers due to respiratory illness. Infect Control Hosp Epidemiol. 2021;42:268–73.
46. Laris Gonzalez A, Villa Guillen M, Lopez Martinez B, et al. Influenza-like illness in healthcare personnel at a paediatric referral hospital: clinical picture and impact of the disease. Influenza Other Respir Viruses. 2018;12:475–81.
47. Wilson KE, Wood SM, Schaecher KE, et al. Nosocomial outbreak of influenza A H3N2 in an inpatient oncology unit related to health care workers presenting to work while ill. Am J Infect Control. 2019;47:683–7.
48. Chiu S, Black CL, Yue X, et al. Working with influenza-like illness: presenteeism among US health care personnel during the 2014–2015 influenza season. Am J Infect Control. 2017;45:1254–8.
49. Hoang Johnson D, Osman F, Bean J, et al. Barriers and facilitators to influenza-like illness absenteeism among healthcare workers in a tertiary-care healthcare system, 2017–2018 influenza season. Infect Control Hosp Epidemiol. 2021;42:1198–205.
50. Turnberg W, Daniell W, Duchin J. Influenza vaccination and sick leave practices and perceptions reported by health care workers in ambulatory care settings. Am J Infect Control. 2010;38:486–8.
51. Middeldorp M, Loef B, van der Beek AJ, van Baarle D, Proper KI. Sickness absenteeism, work performance, and healthcare use due to respiratory infections for shift and non-shift workers. Chronobiol Int. 2020;37:1325–34.
52. Van Wormer JJ, King JP, Gajewski A, McLean HQ, Belongia EA. Influenza and workplace productivity loss in working adults. J Occup Environ Med. 2017;59:1135–9.
53. Morales-Suárez-Varela M, Llopis-Gonzalez A, Gonzalez-Candela F, et al. Economic evaluation of health services costs during pandemic influenza A (H1N1) Pdm09 infection in pregnant and non-pregnant women in Spain. Iran J Public Health. 2016;45:423–34.
54. Ashkenazi S, Vertruyen A, Aristegui J, et al. Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections. Pediatr Infect Dis J. 2006;25:870–9.
55. Fleming DM, Crovari P, Wahn U, et al. Comparison of the efficacy and safety of live attenuated cold-adapted influenza vaccine, trivalent, with trivalent inactivated influenza virus vaccine in children and adolescents with asthma. Pediatr Infect Dis J. 2006;25:860–9.
56. Vesikari T, Fleming DM, Aristegui JF, et al. Safety, efficacy, and effectiveness of cold-adapted influenza vaccine-trivalent against community-acquired, culture-confirmed influenza in young children attending day care. Pediatrics. 2006;118:2298–312.
57. Ambrose CS, Antonova EN. The healthcare and societal burden associated with influenza in vaccinated and unvaccinated European and Israeli children. Eur J Clin Microbiol Infect Dis. 2014;33:569–75.
58. Chan SS. Does vaccinating ED health care workers against influenza reduce sickness absenteeism? Am J Emerg Med. 2007;25:808-11.
59. Chan AL, Shie HJ, Lee YJ, Lin SJ. The evaluation of free influenza vaccination in health care workers in a medical center in Taiwan. Pharm World Sci. 2008;30:39–43.
60. Frederick J, Brown AC, Cummings DA, et al. Protecting healthcare personnel in outpatient settings: The influence of mandatory versus nonmandatory influenza vaccination policies on workplace absenteeism during multiple respiratory virus seasons. Infect Control Hosp Epidemiol. 2018;39:452–61.
61. Murti M, Otterstatter M, Orth A, et al. Measuring the impact of influenza vaccination on healthcare worker absenteeism in the context of a province-wide mandatory vaccinate-or-mask policy. Vaccine. 2019;37:4001–7.
62. Zaffina S, Gilardi F, Rizzo C, et al. Seasonal influenza vaccination and absenteeism in health-care workers in two subsequent influenza seasons (2016/17 and 2017/18) in an Italian pediatric hospital. Expert Rev Vaccines. 2019;18:411–8.
63. Li X, Bilcke J, van der Velden AW, et al. Direct and indirect costs of influenza-like illness treated with and without Oseltamivir in 15 European countries: a descriptive analysis alongside the randomised controlled ALIC(4)E trial. Clin Drug Investig. 2021;41:685–99.
64. Gindler J, Grohskopf LA, Biggerstaff M, Finelli L. A model survey for assessing 2009 pandemic influenza A (H1N1) virus disease burden in the workplace. Clin Infect Dis. 2011;52(Suppl 1):S173–6.
65. Galante M, Garin O, Sicuri E, et al. Health services utilization, work absenteeism and costs of pandemic influenza A (H1N1) 2009 in Spain: a multicenter-longitudinal study. PLoS ONE. 2012;7: e31696.
66. Esposito S, Molteni CG, Daleno C, et al. Impact of pandemic A/H1N1/2009 influenza on children and their families: comparison with seasonal A/H1N1 and A/H3N2 influenza viruses. J Infect. 2011;63:300–7.
67. Murray M, Grant J, Bryce E, ChiltonForrester PL. Facial protective equipment, personnel, and pandemics: impact of the pandemic (H1N1) 2009 virus on personnel and use of facial protective equipment. Infect Control Hosp Epidemiol. 2010;31:1011–6.
68. Santos CD, Bristow RB, Vorenkamp JV. Which health care workers were most affected during the spring 2009 H1N1 pandemic? Disaster Med Public Health Prep. 2010;4:47–54.
69. Bhadelia N, Sonti R, McCarthy JW, et al. Impact of the 2009 influenza A (H1N1) pandemic on healthcare workers at a tertiary care center in New York City. Infect Control Hosp Epidemiol. 2013;34:825–31.
70. Mota NV, Lobo RD, Toscano CM, et al. Cost-effectiveness of sick leave policies for health care workers with influenza-like illness, Brazil, 2009. Emerg Infect Dis. 2011;17:1421–9.
71. Tora-Rocamora I, Delclos GL, Martinez JM, et al. Occupational health impact of the 2009 H1N1 flu pandemic: surveillance of sickness absence. Occup Environ Med. 2012;69:205–10.
72. Mitchell R, Ogunremi T, Astrakianakis G, et al. Impact of the 2009 influenza A (H1N1) pandemic on Canadian health care workers: a survey on vaccination, illness, absenteeism, and personal protective equipment. Am J Infect Control. 2012;40:611–6.
73. Considine J, Shaban RZ, Patrick J, et al. Pandemic (H1N1) 2009 Influenza in Australia: Absenteeism and redeployment of emergency medicine and nursing staff. Emerg Med Australas. 2011;23:615–23.
74. Rebmann T, Wang J, Swick Z, Reddick D, Minden-Birkenmaier C. Health care versus non-health care businesses' experiences during the 2009 H1N1 pandemic: financial impact, vaccination policies, and control measures implemented. Am J Infect Control. 2013;41:e49-54.
75. Hayden FG, Sugaya N, Hirotsu N, et al. Baloxavir Marboxil for uncomplicated influenza in adults and adolescents. N Engl J Med. 2018;379:913–23.
76. Dhanasekaran V, Sullivan S, Edwards KM, et al. Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination. Nat Commun. 2022;13:1721.

Authors and Affiliations

Marie-Hélène Blanchet Zumofen[1] · Jeff Frimpter[2] · Svenn Alexander Hansen[1]

[1] F. Hoffmann-La Roche Ltd, Grenzacherstrasse 124, 4070 Basel, Switzerland

[2] Health Interactions, Inc, San Francisco, CA, USA