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Optimizing epidemic prevention in nursing homes using clinical surveillance of respiratory infections

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SUMMARY

Background: Respiratory tract infections (RTIs) pose a significant risk in nursing homes (NHs), which makes surveillance crucial for timely intervention.
Aim: To monitor the impacts of seasonal RTIs in NHs, which include frequency, the use of rapid diagnostic tests and antibiotics, mortality, and cluster dynamics, with the use of clinical surveillance.
Methods: During the winter periods from 2015 to 2019 (22 weeks), data on general signs (GSs), and respiratory signs (RSs) were collected to define three respiratory clinical sign patterns (CSPs): GS+/RS+, GS−/RS+, and GS+/RS−. Clusters (≥2 cases) were identified and classified into three intensity levels, namely, L1, L2, and L3 (2, 3−5, and ≥6 GS+/RS+/4 days, respectively). CSP frequencies and the 28-day all-cause mortality were calculated.
Findings: In 13 NHs (N = 3,628 resident inclusions, median age: 87.2 years), 1,538 GS+/RS+, 1,482 GS−/RS+, and 233 GS+/RS− cases were observed, with mortality rates of 8.5%, 2.8%, and 6%, respectively. Among the GS+/RS+ cases, 63% received an antimicrobials. GS+/RS+ cluster analysis identified 141 clusters with L1, 100 with L2, and 26 with L3.
A total of 209 rapid diagnostic tests for influenza were carried out, with 72.2% conducted in L2 or L3 clusters. Within clusters, the first case must be identified promptly with rapid outbreak development taking place within the first 2−3 days, and potentially less effective containment efforts following delayed detection.
Conclusion: Clinical surveillance is a comprehensive method that can be utilized for the rapid implementation of preventive measures and appropriate use of antibiotics.

Introduction

Respiratory tract infections (RTIs) are a common cause of outbreaks in nursing homes (NHs) [1]. Until recently, respiratory outbreaks in NHs were mainly associated with influenza virus and respiratory syncytial virus. However, the number of potential pathogens involved is large, yet etiological research is often deficient. Therefore, precisely determining which organisms are prevalent in this setting, which includes bacterial pathogens (such as *Streptococcus pneumoniae*, aerobic Gram-negative bacteria, *Haemophilus influenzae*, *S. aureus*, and atypical bacteria), as well as other viruses beyond those

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identified during outbreak periods, is difficult [2]. Although the epidemic risk in NHs was already known, the COVID-19 pandemic exposed a much greater and more dramatic risk, emphasizing the vulnerability of elderly care facilities [3]. Increased hospitalization rates, severe complications, and higher mortality linked to viral infection clusters are a significant burden in these institutions, which intensifies the need for timely interventions with robust surveillance, rapid diagnosis, and infection control protocols [4].

Considering that NHs have limited human and technical means and the only available data for rapid surveillance are the clinical signs/symptoms, surveillance with a simple methodology is necessary. Frequently, viral respiratory infections share similar clinical signs, namely, cough, fever, sore throat, runny nose, congestion, and fatigue. Additional signs including appetite loss and confusion are particularly common in elderly populations, which further complicate differential diagnosis [5]. Thus, a syndromic approach that considers both the classic clinical signs of respiratory infections as well as other less specific general signs (GSs) must be implemented.

The sign/symptom approach, which employs clinical observations that are available in the institutional electronic health record, could enhance infectious risk management. Signs/symptoms definitions have been already proposed by the US Centers for Disease Control and Prevention (CDC), the European Center for Disease Prevention and Control (ECDC), and recently, Santé Publique France (SPF) [6—8]. SPF specifically proposed the definition of reportable events on the basis of specific signs and symptoms, and an approach that links local clinical surveillance data with the national surveillance methodology must be developed.

Previous studies mainly focused on the impact of isolated outbreaks, whereas this work implemented season-long surveillance, which continuously accounts for both outbreak and non-outbreak cases with the use of real-time clinical data from computerized patient records [9,10]. This study aimed to monitor the impacts of seasonal RTIs in NHs, which include frequency, the use of rapid diagnostic tests and antibiotics, mortality, and cluster dynamics, with the use of a clinical surveillance protocol.

Materials and methods

Design and setting

This retrospective study employed the data collected between 2015 and 2019 from residents of 13 NHs in Southern Alsace, France, comprising a total of 940 beds [9]. Each year, the surveillance for infections or signs/symptoms lasted for 22 weeks, beginning at week 46.

NH resident data

Four seasonal surveillance periods were examined, which encompassed the inclusion of residents and the monitoring of their signs and symptoms over the 22-week investigation period. At the beginning of the surveillance period, the data collected from the individual electronic health record included birth month and year, sex, and arrival date at the NH.

SPF proposed two categories of signs and symptoms to define reportable events, namely, respiratory signs (RSs) and GSs [6]. Given that surveillance is dependent on nurse activities, certain criteria from CDC and ECDC definitions were employed to complement those of SPF, which included symptoms such as malaise, falls, loss of appetite, and new or increased sputum production. Medical information such as abnormal (new or changed) lung examinations were excluded, as well as the CDC and ECDC categorization of respiratory infections into lower, upper, or influenza-like infections.

Clinical signs were recorded daily by nurses in each patient's individual health record as unstructured textual information, which were reviewed weekly by the infection prevention and control team. A software function enabled the simultaneous consultation of all residents' records within a unit. A text mining approach, in combination with professional analysis, was employed [11]. Patient files were systematically scanned using an internet browser for respiratory-associated character strings, numerical values associated with temperature, and entries that indicate antibiotics that are prescribed for respiratory treatments as detailed in Supplementary Table 1. When information on a sign/symptom or antibiotic was identified for a resident, a detailed review of the medical file by the hygiene practitioner was carried out for the relevant period, with the exhaustive collection of information that is related to the identified event. GSs with the following information were recorded: abnormal temperature ($\geq$37.8°C or $\leq$35.0°C), chills, headache, myalgia, and new or increased general status deterioration (e.g., fatigue, fall, malaise, refusal to get up, and unwell feeling). RSs encompassed the nose and throat signs (runny nose, sneezing, or stuffy nose and sore throat, hoarseness, or swallowing difficulty); cough without sputum production (new or increased cough); new or increased sputum production; and new, worsening dyspnea, or increased respiratory rate ($\geq$25 breaths/min), chest pain, or low O_2 saturation ($<$94%). The date of sign/symptom onset was recorded. All-cause mortality was analyzed in respondents who died within 4 weeks after the initial onset of a clinical sign [9]. Moreover, RTI antibiotic prescriptions with medical observations were included.

Virological surveillance

Antigenic rapid tests using the InfluenzaTop® (Alldiag, Strasbourg, France) to identify the influenza virus were available in each NH. Occasionally, samples were sent to laboratories or the national reference center for influenza virus identification via real-time reverse transcription—polymerase chain reaction (RT-PCR) [10]. The date of sample collection and the positive or negative results of the test were recorded.

Data analysis

Clinical sign patterns (CSPs) corresponded to the presence or absence of GS and RS. For the RTI surveillance, CSP by the SPF was defined as the association of at least one new/or increased GS and at least one functional or physical respiratory impact: GS+/RS+ [6]. Two secondary CSPs were examined: GS without RS and no identification of a specific site infection (GS+/RS−) and RS without GS (RS+/GS−). Additionally, the

CSPs were analyzed using the sum of CSPs over 4 moving days in three intensities: L1 = 2 GS+/RS+/4 days, L2 = 3–5 GS+/RS+/4 days, and L3 ≥ 6 GS+/RS+/4 days [6].

Clusters were also defined based on the number of cases over the four-day period. A new cluster began when the number of cases attained two cases or more every 4 days and ended when the number of cases was ≤1 GS+/RS+/4 days. Non-cluster periods were when the number of GS+/RS+/4 days was inferior to 2. Three types of clusters were studied based on the highest intensity observed during the identified period. Exclusive L1 when the cluster was only with a maximum of 2 GS+/RS+/4 days. Clusters with L2 and/or L3 were respectively with a maximum of 3–5 GS+/RS+/4 days or ≥6 GS+/RS+/4 days. Total cluster durations were the difference between the date of the first case (d_0) included in the cluster and the date of the last case (d_{Lcc}) before the following non-outbreak period. Each cluster was characterized by the sequences of L1, L2, and L3, and for each cluster sequence, the respective first day was recorded ($d_{L1,\ L2,\ and\ L3}$). GS+/RS+, GS+/RS−, and GS−/RS+ cases occurring during both cluster and non-cluster periods were recorded to analyze syndrome distribution across the identified time periods. The cluster onset dynamic was analyzed with the duration in days of the first sequence of the clusters with the difference between the respective first days (d_0, $d_{L1,\ L1,\ and\ L3}$) as developed in Supplementary Table 2. Total cluster duration was defined as the time between the first identified day (d_0) and the date of the last recorded case (d_{Lcc}).

Influenza rapid diagnostic tests were analyzed based on positive or negative results and associated clusters. Delays in days were calculated between the first case in each cluster and the date of the first sample collection (positive or negative) within the cluster.

Statistical analysis

Using Chi-square or Fisher's exact test and Kruskal–Wallis test, as applicable, the data were evaluated. The odds ratio (OR) was calculated using the median-unbiased estimation. Differences were considered significant at $P \leq 0.05$. Moreover, using R version 4.3.2 software, statistical descriptive data were analyzed.

Results

CSP analysis

Continuous sign/symptom surveillance (2015–2019) was developed with 3,628 resident inclusions (2,711 (74.7%) women and 917 (25.3%) men), and the median (interquartile range) age was 87.2 (81.9–91.8) years. Through the longitudinal sign/symptom approach, the seasonal epidemic periods could be comprehensively analyzed. During the study period, 1,538 GS+/RS+ CSP were the highest number of cases, followed by 1,482 RS+/GS− and 233 GS−/RS+ cases (Table I). Signs/symptoms according to CSP were examined (Supplementary Tables 2 and 3). Within the same CSP, mortality revealed no significant difference based on the season surveillance: 7.6%–9.8% in GS+/RS+, 1.4%–4.2% in RS+/GS−, and 3.8%–8.8% in GS+/RS−. Mortality in GS+/RS+ was higher than that in GS−/

Table I
Seasonal surveillance of clinical sign patterns

Clinical sign patterns (CSPs) according to seasonal surveillance	Residents with at least one CSP (%)	CSP per 100 residents	All-cause mortality according to CSP (%)	All-cause mortality (%)
- GS+[a]/RS+[b] (N = 1,538)				
2015–2016 (842 residents)	29.5 (248)	37.6 (317)	7.9 (25/317)	8.5% (131/1538)
2016–2017 (927)	40.6 (376)	51.5 (477)	9.8 (47/477)	
2017–2018 (933)	32.7 (305)	42.1 (393)	7.6 (30/393)	
2018–2019 (926)	30.2 (280)	37.9 (351)	8.3 (29/351)	
- RS+/GS−[c] (N = 1,482)				
2015–2016 (842 residents)	32.7 (275)	41.4 (349)	2.9 (10/349)	2.8% (41/1482) p[e] < 0.001
2016–2017 (927)	34.6 (321)	44.2 (410)	2.4 (10/410)	
2017–2018 (933)	28.9 (270)	37.0 (345)	1.4 (5/345)	
2018–2019 (926)	30.8 (285)	40.8 (378)	4.2 (16/378)	
- GS+/RS−[d] (N = 233)				
2015–2016 (842 residents)	2.3 (19)	2.3 (19)	5.3 (1/19)	6.0% (14/233)
2016–2017 (927)	5.3 (49)	5.3 (53)	3.8 (2/53)	NS[f]
2017–2018 (933)	7.7 (72)	7.7 (80)	8.8 (7/80)	
2018–2019 (926)	8.3 (77)	8.3 (81)	4.9 (4/81)	

[a] GS+: at least one new/or increased general sign (abnormal temperature [≥37.8°C or ≤35.0°C], chills, headache, myalgia, and new or increased general status deterioration (e.g., fatigue, fall, malaise, refusal to get up, and unwell feeling).
[b] RS+: at least one functional or physical respiratory sign (nose and throat signs [runny nose, sneezing, or stuffy nose and sore throat; hoarseness; or swallowing difficulty); cough without sputum production (new or increased cough); new or increased sputum production with or without cough; new, worsening dyspnea, or increased respiratory rate (≥25 breaths/min); pleuritic chest pain; and low O_2 saturation (<94%).
[c] GS−: no general sign.
[d] RS−: no respiratory sign.
[e] p: P value for total all-cause mortality comparison with GS+:RS+ reference.
[f] NS, not significant.

Table II
Onset time of the clusters and their durations

Types of clusters / Cluster periods[a]	Median duration (first case—first alert level) (in days)	L1[b] to L2[c] median duration (in days)	L2 or L1 (in absence of L2) to L3[d] median duration (in days)	Total median duration (first case—last case) (in days)
Cluster exclusive L1 (N = 141)	2.0 (1.0—3.0) [e]	-	-	2.0 (1.0—3.0)
Cluster with L2 (N = 100)	1.0 (0.0—2.0) $P < 0.001$	1.0 (0.0—2.0)	-	3.5 (2.0—6.0)
Cluster with L3 (N = 26)	1.0 (0.0—1.0) $P < 0.01$	0.0 (0.0—1.0) $P = 0.01$	2.0 (1.0—3.0)	9.0 (4.2—15.0)

[a] First periods of the cluster.
[b] L1: 2 cases GS+/RS+/4 days.
[c] L2: 3—5 cases GS+/RS+/4 days.
[d] L3: ≥ 6 cases GS+/RS+/4 days.
[e] Interquartile range.

RS+ (8.5% vs. 2.8%) ($P < 0.001$) but was not significantly different from that in GS+/RS− (6.0%) ($P = 0.24$). Additionally, more than 63.0% of GS+/RS+ cases received antibiotics.

Cluster analysis

In this study, 267 clusters (Table II) were identified, with exclusive 141 L1 clusters, 100 L2 clusters, and 26 L3 clusters.

The L1 clusters were punctual situations with a limited duration (2 days). Cluster dynamics were significantly different between the cluster types. For the exclusive L1 clusters, the median duration between the first case and the alert level was 2 days, in comparison to 1 day for the L2 and L3 clusters. When a cluster reached L3, the number of cases also increased more rapidly than in the L2 clusters. The median duration to increase from 2 to 3 or 5 cases every 4 days was 1 day in the L2 clusters, whereas the 0-day median duration observed in the L3 clusters indicated a potential direct jump from 0, 1, or 2 cases to 6 or more cases every 4 days, bypassing the intermediate L1 and/or L2 intensity levels.

Based on the previously identified clusters, the CSP analysis indicated that GS+/RS+ CSP was predominantly found in the exclusive L1 clusters and the L2 and L3 clusters (81.1%, 1247/1538). Additionally, during these cluster periods, 36.2% (538/1482) of GS−/RS+ CSP and 36.1% (84/233) of GS+/RS− CSP were observed.

Antibiotics (N = 970) were more frequently prescribed for GS+/RS+ cases during non-outbreak periods (67.1% [n = 196]), in the exclusive L1 clusters (65.6% [n = 206]) and in the L2 clusters (67.4% [n = 337]), in comparison to the L3 clusters (53.5% [n = 231]; $P < 0.001$).

Virus analysis

Influenza rapid diagnostic tests were mainly conducted during the cluster periods with L3 and L2 (L3: 46.9%, 98/209; L2: 32.1%, 67/209), with 51.0% and 25.4% being positive, respectively. Additionally, 21.5% (93/432) of GS+/RS+ cases in the L3 clusters and 11.6% (58/500) in the L2 clusters were diagnosed with these tests. Moreover, non-outbreak periods and the exclusive L1 clusters were less thoroughly investigated, with only 12.0% (25/209) of the total tests performed during periods without GS+/RS+ clusters (24.0% positive) and 9.1% (19/209) during the L1 clusters (21.1% positive).

Delays (median day) between the first case in each cluster and the date of the first sample collection within the cluster were equal to 0 days in the exclusive L1 clusters, one day for the L2 clusters, and 5 days for the L3 clusters with significant differences ($P = 0.01$).

Antibiotic prescriptions among the 1,538 GS+/RS+ cases were the lowest in case of positive tests (44.2% [34/77]; OR 2.3, 95% confidence interval [CI] [1.5—3.7]), which was followed by negative tests (54.4% [56/103]; OR 1.5, 95% CI [1.03—2.3]), in comparison to cases where no influenza testing was performed (64.8% [880/1358]; $P < 0.001$).

Discussion

Seasonal monitoring of respiratory infections (2015—2019) via syndromic surveillance was tested based on the SPF syndromic definition [6]. This study highlighted the high and complex epidemiological contexts faced by NHs; yearly, 30.0%—40.0% of residents developed a GS+/RS+ CSP with consequent mortality. GS−/RS+ CSP also frequently occurred.

A previous study about outbreak morbidity and all-cause lethality had typically been limited to punctual outbreak analysis rather than continuous, season-long surveillance [9]. Indeed, outbreak inclusion depended on institutional alert to the hygiene team and investigations were carried out with the national recommended definitions for RTI surveillance in geriatric units [12,13]. This limited approach depended on the reports of healthcare professionals, which led to incomplete outbreak data and the absence of non-outbreak case information. In the previous study, 1,823 infected cases were recorded among 5,862 resident inclusions over 11 seasons of surveillance, which corresponded to a ratio of 0.03 cases per resident inclusion per season [9]. Comparatively, in this 2015—2019 study, 1,538 GS+/RS+ cases were reported among 3,628 resident inclusions over four seasons of surveillance, with a significantly higher ratio of 0.11 cases per resident inclusion per season. Moreover, 18.9% of GS+/RS+ cases occurred during non-outbreak periods. Elderly residents frequently display atypical, nonspecific symptoms (including confusion, fatigue, or appetite loss) and may be unable to express what they are feeling, complicating infection classification and potentially underestimating case numbers. Mild or atypical cases may also go unreported despite posing transmission risks. In this 2015—2019 study, 1,482 RS+/GS− and 233 GS−/RS+ cases

were identified, with over 36.2% of RS+/GS− cases observed during clusters in which standard infection classifications might have missed them as potential signals. Text mining enabled continuous, comprehensive surveillance that is independent of healthcare reporting, by considering all observed signs and symptoms as potential epidemiological signals. This method not only enabled the detection of early warning signs within the facility but also empowered healthcare staff, facilitating the faster implementation of hygiene measures that are essential for effective infection control.

The threshold for alert, defined by SPF as 3 cases every 4 days (126 L2 or L3 clusters), was frequently reached, emphasizing the significant burden of these reportable events. Syndromic surveillance may have an essential role in facilitating timely outbreak reporting, especially considering the challenge of limited human resources. It can also serve as a powerful tool for retrospective outbreak analysis, which allows for factual experience feedback that aids in preparing for and anticipating future epidemics. Furthermore, this study confirms the critical importance of the initial days of an outbreak, as case numbers rapidly escalated to L3 intensity (defined as ≥6 GS+/RS+ cases within 4 days) in just 2−3 days from the onset of the first case. Previous studies in French NHs emphasize the need for rapid intervention, finding that interventions within 2 days of the first case significantly reduce outbreak durations and attack rates, whereas delays beyond this period lead to more extensive and prolonged outbreaks [14]. Furthermore, the national reportable event threshold should not be confused with the NH's internal risk management protocols. Preventive measures should ideally be implemented with the first case, not delayed until the outbreak reaches the SPF official reporting level of three cases [6−15]. In this work, different cluster dynamics were observed. A more contagious pathogen, specific circumstances including the absence or limitation of hygiene measures, or events in the NH involving large gatherings could contribute to such distinctive dynamics. These observations emphasized the potential value of dynamic analysis in alert systems to identify contexts with a high risk of extensive and rapid spreading.

Point-of-care (POC) testing could also be essential in rapid outbreak management [16]. However, only 209 POC influenza rapid diagnostic tests were conducted, mainly in L3, highlighting test underuse. Therefore, nurse training or tight follow-up of CSP may increase their early use, and as soon as the first case is diagnosed, new POC tests with better sensitivity could be employed [17,18].

A well-defined protocol for POC (antigenic or nucleic) should be established, and nurses must be trained on the value of these tests, especially in terms of sensitivity and specificity. In cluster management, clinical or syndromic surveillance along with associated preventive measures forms the cornerstone of infection prevention strategies and the RT-PCR is the reference test for etiological diagnosis [19].

Numerous hypotheses can be considered to explain the long median delay (5 days) between the rapid test implementation and the first case in clusters with L3, such as influenza not being initially suspected, the absence of established testing protocols, or reliance on clinical diagnosis for viral infections. Moreover, high vaccination coverage may lead to influenza being wrongly ruled out as a diagnosis; hence, the French High Health Authority issued guidance on the use of oseltamivir in care facilities, recommending its use as a preventive treatment only in the context of a confirmed or potential influenza pandemic, because of its limited medical benefit during seasonal influenza outbreaks [20].

Additionally, our study highlighted the rapid progression of clusters, likely caused by the challenges that residents face in staying in their rooms, the issue of double-occupancy rooms, and inconsistent adherence to hygiene protocols, all of which contribute to this limitation. Therefore, a combination of collective measures, including reinforcing standard hygiene measures with strict hand hygiene, unit compartmentalization when multiple units exist within the facility, and suspension of group activities (e.g., recreation and meals), must be rapidly implemented. Continuous mask wearing by healthcare workers, even without resident presence, use of FFP2 masks for close contact, and routine testing of residents and/or staff were critical. Protocols for ventilating rooms and informing families also could play significant roles in minimizing contamination and controlling the spread of infection [21]. To help curb the spread of infections, adequate ventilation/airflow control, antiviral treatment, and immunization of incompletely immunized patients should also be considered [22,23].

Moreover, antibiotic treatments (63.0%) were frequent in G+/RS+. Although some were bacterial infections or secondary infections of airborne diseases, most of the cases, especially within clusters, were exclusive airborne viral agents. Virus identification via antigenic POC test or even the simple notion of viral airborne clusters within an NH could reduce these unnecessary antibiotics and increase the early use of antiviral treatments [24]. In this study, the cluster context (specifically the L3 clusters) and the use of antigen tests led to a reduction in antibiotic use (44.2% in the case of positive tests compared with an overall rate of 63.0%). Therefore, to reduce inappropriate antibiotic prescriptions, bacterial and viral respiratory infections should be differentiated. Nonetheless, in the NHs, treatment is often empirical, which poses both the risk of withholding necessary antibiotics from vulnerable residents and the high danger of selecting drug-resistant bacteria due to overuse [25,26].

Nevertheless, the CSP approach required continuous surveillance. With careful and daily registration of CSP, using artificial intelligence for automatic alerts could be of great interest [27]. Considering the rapid cluster extension, active surveillance is imperative, and a syndromic with a digital approach could be useful for alert as the first cases appear, although further research is required [28].

The COVID-19 pandemic also highlighted the importance of transmission before the onset of clinical signs due to asymptomatic, presymptomatic, pauci-symptomatic, or atypical cases complicating implementation of prevention. However, real-time clinical surveillance and empowering nurses to perform tests and investigations can help swiftly identify early atypical signs, which allows for the implementation of rapid prevention measures and reduction of the risk of transmission, as previously detailed [29].

This study has limitations. Data collection could have been limited by the amount of work for the nurses to implement the

CSP data, making it less exhaustive, especially during an epidemic. Second, this syndromic approach provided no information regarding potential links between successive clusters; preventive measures were implemented, focusing only on the dynamic of the outbreak onset. Third, the study was realized before the COVID-19 pandemic; although SARS-CoV-2 shares symptoms with other airborne pathogens, COVID-19 has some specific symptomatology, which includes anosmia and ageusia. Alongside etiological research, a more comprehensive surveillance approach, not focusing solely on respiratory symptoms, should be developed.

In conclusion, cluster modeling with CSP is a simple and easy way to monitor RTI occurrence in NHs. In terms of frequency and mortality, GS+/RS+ CSP appears to be an important CSP. With a low cost, quick alarm, and POC test initiation, CSP analysis enables the implementation of preventive and therapeutic measures and can contribute to the appropriate use of antibiotics.

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Author contributions

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Conflict of interest

All authors report no conflicts of interest relevant to this article.

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Ethical aspects and consent

The study protocol was approved by the local ethics committee (Espace Local de Réflexion Ethique, Center Hospitalier de Rouffach; approval number: ERLE-32).

Appendix A. Supplementary data

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