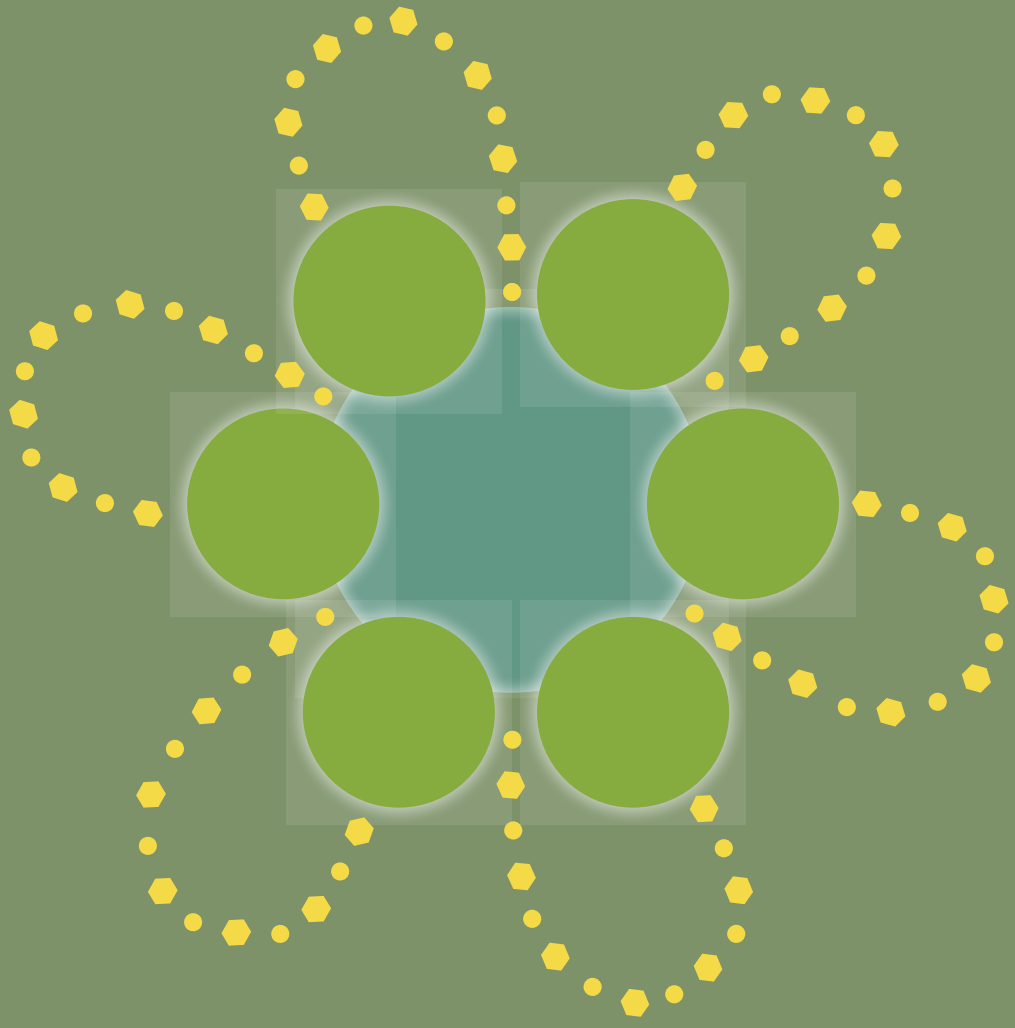
Regional collaboration in Infection Prevention and Control, Antibiotic Resistance, and COVID-19

in Nursing Homes



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Regional collaboration in Infection Prevention and Control, Antibiotic Resistance, and COVID-19 in Nursing homes

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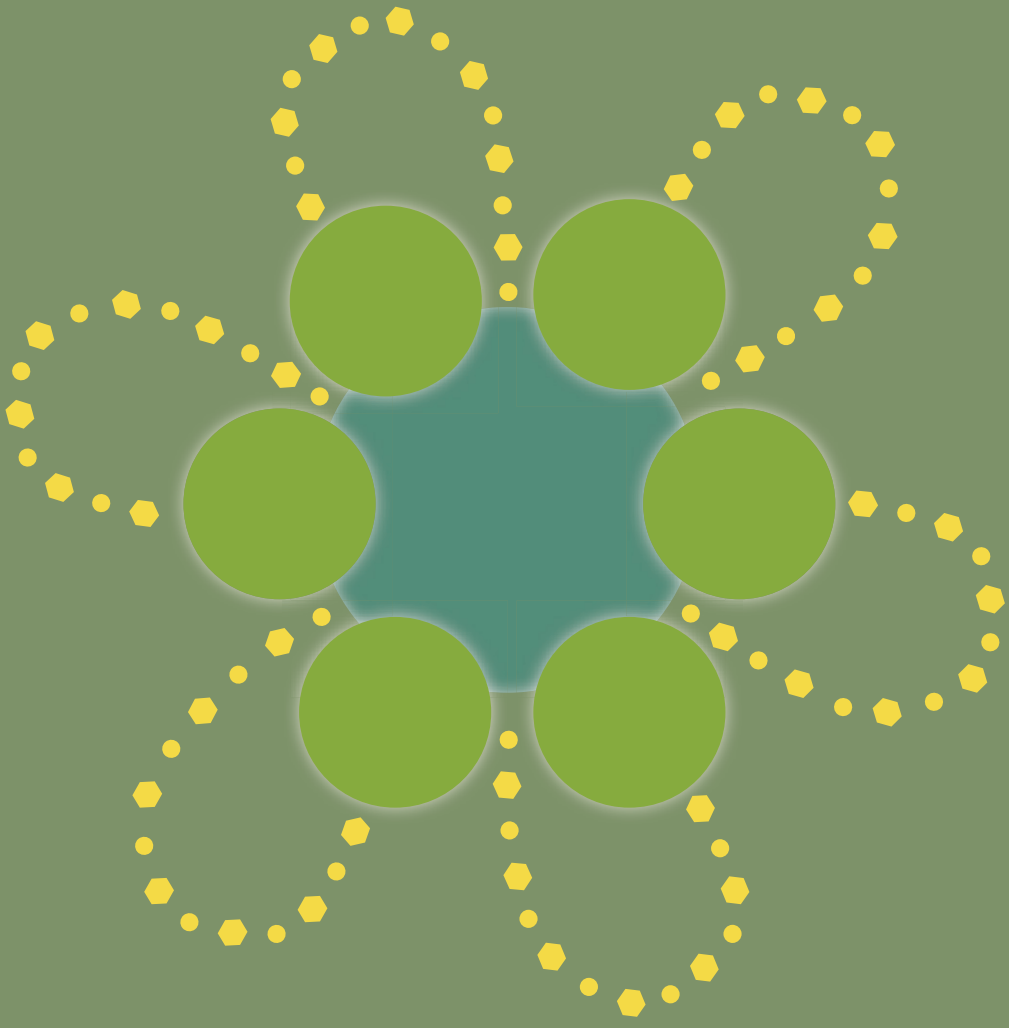

CHAPTER 1

General introduction

Healthcare-associated infections

Healthcare-associated infections (HAIs) are defined as "infections occurring in a patient during the process of care in a hospital or other health care facility which was not present of incubating at the time of admission".[1] In nursing homes, HAIs pose a serious problem and are associated with excessive comorbidity and mortality.[2,3] The most common HAIs occurred are respiratory tract infections (RTI), urinary tract infections (UTI), and skin and soft tissue infections (SSTI). Bacteremia in nursing homes typically arises as a consequence of a localized site of infection linked to one of these infections. Gastrointestinal infections (GI) are often recognized and documented in outbreak situations.[3]

Nationally and internationally, the imperative is clear: the care of elderly should be secure and contribute to a dignified final phase of life.[5] The title "Home in the Nursing Home" (in Dutch: "Thuis in het verpleeghuis") from the Dutch program on the quality of nursing home care[6], underscores the essence of the nursing home setting. A nursing home serves as a home for many residents, where they share their daily lives with other residents. Concurrently, the setting accommodates residents with fragile health conditions, encompassing chronic illnesses, cognitive disorders, and functional disabilities, thereby increasing their susceptibility to infectious diseases.[7] The heightened level of care required by residents in nursing homes, close contact with their carers and other residents, and spending considerable amounts of time in enclosed spaces contributes to an elevated risk and transmission of HAIs.[8]

Consequently, the scope of infection prevention and control (IPC) should extend beyond mere risk reduction but should encompass the establishment of an environment reminiscent of a home, where residents can maintain their dignity and autonomy. Simultaneously, it is paramount to acknowledge that residents share living spaces based on availability and professional assessments, rather than personal choice. Balancing the medical perspective with the aspects of quality of life, as well as individual and collective interests presents an added complexity. Understanding of this dynamic is essential for the development and implementation of IPC measures, aiming to reduce infection risks and transmission of antibiotic resistance bacteria while preserving the quality of life of residents. Hence, practices on IPC and combating antibiotic resistance from hospitals to nursing homes is not a straightforward copy-and-paste process.

Definition of a nursing home

Notable discrepancies exist across countries worldwide of what constitutes a nursing home. For instance, there are facilities that provide medical care and 24-hour assistance with activities of daily living (ADL) to elderly persons who are physically and/or cognitively impaired and reside permanently in these facilities. Other facilities provide medical care and therapy to elderly persons for a period of rehabilitation, with the goal of facilitating their return to their homes or another facility. These disparities extend to the type of care, duration of stay, funding sources (publicly or private), and the presence of skilled personnel in these facilities. A definition for nursing homes was formulated based on international consensus, and it reads as follows: "A nursing home is a facility with a domestic-styled environment that provides 24-hour functional support and care for persons who require assistance with ADL and who often have complex health needs and increased vulnerability. Residents within a nursing home may stay relatively brief for respite purposes, short term (rehabilitative), or long term, and may also receive palliative/hospice and end-of-life care".[9] In the Netherlands, care for the elderly in nursing homes is publicly funded under the Long-term care act (in Dutch: Wet Langdurige Zorg, Wlz). Furthermore, the medical care is delivered by a multidisciplinary team led by an elderly physician, a separate medical specialty. This thesis also incorporates the term Long-Term Care Facilities (LTCFs). When referencing other studies, an LTCF could encompasses a broader spectrum of care facilities providing services to elderly persons. In the context of our research, the LTCFs conforms to the nursing home definition.

Regulations on IPC in Dutch nursing homes

In the Netherlands, the Inspectorate of Health and Youth (Dutch acronym is IGJ) regulates compliance with statutory standards, which are founded on legislative requirements, as well as field- and professional standards established by healthcare professional association related to infection prevention and antibiotic policies in nursing homes.[10] The assessment framework addresses the practical implementation of infection prevention guidelines in the workplace, as well as the managerial responsibilities of administrators and the medical responsibilities of elderly care physicians. The Public Health Act, establishing the statutory foundation of public healthcare, the response to infectious disease crises, and the isolation of individuals or transportation modes that may pose international health risks. Article 26 of this statute outlines the formal procedure for reporting infectious diseases [Public Health Act].

Since 2021, the guidelines on infection prevention, previously established by the Working Party on Infection Prevention (WIP), are being revised by the Partnership for Infection Prevention Guidelines (in Dutch: Samenwerkingsverband Richtlijnen Infectiepreventie, SRI[11]).

Regional network collaboration: our approach

In 2007, the regional IPC network (Dutch acronym is REZON) was established in the South-East region of the Netherlands. Currently, seven organizations operate across 45 locations accommodating a total of more than 2,700 elderly persons with a "Wlz" indication. Additionally, these organizations offer other various forms of care, including home care services to elderly residing in their own homes, and persons experiences deafness and blindness. This initiative emerged from the existing collaboration among elderly care physicians, who had recognized the need for regional effort on IPC policies. REZON is a subregional network within one of the ten regional antibiotic resistance care networks created by the Ministry of Health, Welfare, and Sport (Dutch acronym is VWS) focus on antibiotic resistance (Dutch acronym is ABR) in 2016.[12] Managed by an infection control practitioner who is contractually affiliated with the hospital's regional laboratory, annual prevalence studies on HAIs and antibiotic use are conducted. Collaborative IPC protocols are developed, which are based on national guidelines and are subsequently integrated into the quality management systems of participating institutions. Linked-nurses (in Dutch: Hygiëne Kwaliteit Medewerkers (HKM'ers) or hygiëne aandachtsvelders) are trained in IPC. Best practices are shared among professionals of the participating organizations. Furthermore, various locations have contributed to one or more of the studies included in this thesis.

IPC program

In 1997, the first guideline on infection prevention and control was presented by the Society for Healthcare Epidemiology of America (SHEA)/Association for Professionals in Infection Control and Epidemiology (APIC) and updated in 2008. The structure and components of an infection control program described in the guideline include the following: Infection control committee (ICC), infection control professional, surveillance, outbreak control, the facility (preconditions), isolation and precautions, asepsis and hand hygiene, resident care, resident health program, employee health program,

education, policies and procedures, miscellaneous aspect, antibiotic stewardship, and regulations.[13]

Data on some of these elements have been gathered since 2010 as part of the triennial prevalence survey of HAIs in European long-term care facilities. Results from the third-point prevalence study of HAIs in European long-term care facilities (LTCFs) demonstrated that only just over a third of the homes have an ICC. Furthermore, over two-thirds of the facilities did have at least one person with IPC training available to them, and the majority had access to an external team for providing and supporting IPC. A written hand hygiene protocol was present in almost all facilities.[14]

As part of the Interreg IVa-funded Dutch-German cross-border project EurSafety Health-NET, an infection prevention and control quality improvement program for nursing homes was developed.[15] A multi-step plan was developed to improve infection control practices in nursing homes on both sides of the border. Once the board of directors provided their commitment, facilities received certification when they met at least five of the predetermined criteria and have up to three years to realize the remaining criteria, before advancing to the next step. The criteria included in the first certificate, determined in close collaboration with frontline staff, were the presence of a ICC, at least a one-yearly prevalence study on HAIs, a signed agreement with the GGD regarding notifications under Article 26 of the Public Health Act (in Dutch: Wet Publieke Gezondheid), guideline for MRSA, general hygiene, including hand hygiene, urinary tract infection guideline, influenza guideline, norovirus guideline, linked-IPC nurses/carers and/or presence of an infection control practitioner, and incidence study on urinary tract infections. This program was further developed and disseminated as part of the follow-up project EurHealth-1Health. However, in our regional network, the program was confined to nursing homes within our network, while in Germany, the program was adopted by the German Public Health Services and widely implemented.

Nevertheless, this program was used in a project to establish IPC standards and assessment criteria in nursing homes in the Netherlands, funded by the Ministry of VWS in 2017. This project also drew insights from a survey involving professionals engaged in IPC in nursing homes, such as elderly care physicians, nurses/carers, infection control practitioners and infectious disease physicians of the Public Health Service (Dutch acronym is GGD) and the Infection Risk Scan.[16] The contents of this report are outlined below.

In the context of fostering learning and development as criterion for ensuring quality of care[17], a distinction was made between enforcement standards and standards that institutions strive for. The latter was chosen to offer flexibility for adaptation to the various contexts in which nursing homes care is provided. First, it was considered important for a facility to conduct prevalence studies periodically in order to determine the facility's risk profile based on care-profile considered as an enforcement standard. In the Netherlands, the care profile determines the provision of care and the corresponding financial compensation, which is assessed and determined by the Healthcare Needs Assessment Center (in Dutch: Centrum Indicatiestelling Zorg, CIZ). To establish a comprehensive risk profile, facilities should strive to include the following additional data in their periodic prevalence studies: the degree of dependency on assistance for activities of daily living, the percentage of residents with healthcare-associated decubitus of grade 2 or higher, and the prevalence of urinary catheters, HAIs, antibiotic consumption, and ESBL-E carriage. Subsequently, eight themes were selected and further elaborated upon, as shown in Table 1.

Table 1. Themes on IPC standards and assessment criteria in nursing homes (funded by Ministry of Health of Health, Welfare, and Sport. Based on the infection prevention and control quality improvement program for nursing homes (funded by EurSafety Health-NET), insights from a survey involving professionals engaged in IPC in nursing homes, and the Infection Risk Scan[16]

Theme 1. Structure IPC and antibiotic policy		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Multi-year policy plan on IPC	The document can be provided and has been approved by the board of directors	E
Multi-year policy plan on antimicrobial stewardship (AMS)	The document can be provided and has been approved by the board of directors	S
Commitment of the board of directors to joining the regional network	A signed agreement of the board of directors can be provided	S
Active ICC	Regulations of the ICC can be provided Agenda and minutes of the last three meetings can be provided It can be demonstrated that the ICC convenes at least three times per year Nursing home location is either self-represented or represented through a designated liaison in the ICC There is an active internal communication structure from and to the ICC. Provide at least one example, such as announcements/messages on intranet, internal notices (e.g., bulletin board), letters/email correspondence It can be demonstrated that the ICC includes at least one elderly care physician and in infection control professional, and a professional (mandated) link to the management team	E
Feedback on the findings from (compliance) measurements is provided in the ICC	The minutes of the ICC regarding this feedback can be provided	E
Feedback on the findings from (compliance) measurements is provided to the involved healthcare workers	It can be demonstrated that feedback is provided	E
There is a contract with an infection control practitioner for ongoing tasks	The contract can be provided to illustrate continuous tasks, which included participation in the ICC, rather than solely incident-related engagements	E

Continuation Table 1. Themes on IPC standards and assessment criteria

Theme 1. Structure IPC and antibiotic policy		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
There is an IPC network for and by local healthcare workers (link-nurses). If it is organized differently, a procedure is described to clearly outline how protocols are implemented	The document outlining IPC for and by healthcare workers (link-nurses) can be provided. When interviewing one of these healthcare workers, it is indicated that they are given dedicated time for this purpose. If it is organized differently, at least two healthcare workers are asked about how protocol implementation occur	S
There is an educational training offering related to IPC and AMS for healthcare workers directly involved in care for residents (e.g., classroom-based, e-learning, symposium)	At least 75% of the healthcare workers in direct care for residents have utilized one of the provided forms of education at least once every four years.	S
IPC is integrated into orientation program for new healthcare workers in direct care for residents, with an explicit emphasis on hand hygiene, the use of personal protective equipment (PPE), and procedures for reporting infections by healthcare workers.	The program can be provided	E
Exist a formal agreement with the Public Health Service that outlines the reporting requirements in accordance with Article 26 of the Public Health Act.	The written agreement is available for presentation and remains valid within the last four years	E
Resident satisfaction regarding IPC is assessed (at least once every four years). For residents with decision-making capacity or their representatives in cases of incapacity	The findings from the assessment can be provided	S
A prevalence study or an incidence study of one HAI is conducted at least once every two years	The findings from the surveillance can be provided	E
Surveillance is conducted on highly-resistant microorganisms from clinical cultures	The findings from the surveillance can be provided. Additionally, documentation of activities undertaken in response to unexpected findings are also accessible	S
The organization has an internal or external wound consultant	A document can be provided to demonstrate this	S
The organization has an internal or external continence consultant	A document can be provided to demonstrate this	S

Continuation Table 1. Themes on IPC standards and assessment criteria

Theme 1. Structure IPC and antibiotic policy		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Theme 2. Hand hygiene		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Hand rub is available "at point at care", which is where three elements converge: the resident, the healthcare worker, and the location where resident's care or treatment occurs	Verify the presence of hand rub (in dispensers/bottle/portable bottles) within the reach of residents' care occurs	E
Hand rub complies with the EN 1500 standard	Verify a minimum of three hand rub bottles	E
Periodic (at least two times per year) hand hygiene compliance measurements are conducted. These data can be direct observations or through automatic registration (e.g., consumption, hand hygiene events by electronic monitoring)	The findings from the compliance measurements can be provided Feedback on the findings from (compliance) measurements is provided to all who are involved	S
Theme 3. Personal hygiene healthcare workers		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Compliance measurements regarding prerequisites for adequate hand hygiene and healthcare workers' attire, as outlined in the local protocol derived from national guidelines, are carried out	The findings from the compliance measurements can be provided Feedback on the findings from the compliance measurements is provided to all who are involved	E
	The compliance rate regarding prerequisites for adequate hand hygiene and healthcare workers' attire is 90% or higher	S

Continuation Table 1. Themes on IPC standards and assessment criteria

Theme 4. Use of transurethral catheters		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
At least once every four years, prevalence is measured to assess correct/incorrect use of transurethral catheters	The findings from the prevalence measurements can be provided. The assessment employs a standardized flowchart (conform PREZIES[18])	E
	The prevalence of correct transurethral catheter use is 85% or higher (requiring a minimum of seven residents with a transurethral catheter to achieve this rate)	S
Theme 5. Cleaning		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Random objective measurements, such as adenosine triphosphate (ATP) are conducted at least once every two years to assess environmental contamination with predefined cleanliness cutoff points in the organization	The findings from the measurements conducted in the living areas where residents reside can be provided A minimum of ten predetermined surfaces are checked for environmental contamination in four categories: non-resident-related surfaces, resident-related surfaces, sanitary surfaces, and department-related surfaces	E

Continuation Table 1. Themes on IPC standards and assessment criteria

Theme 6. Audit		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
An audit system for IPC is in place	A document can be provided to demonstrate that an annual audit plan and evaluation of results are carried out, including an improvement plan for aspects requiring enhancement A basic audit checklist is available, covering the following components: PPE, prerequisites for disposal of urine and feces, availability of hand rub, hand hygiene, including prerequisites, healthcare workers' attire, separation of clean and soiled waste and linen streams, storage of sterile materials. Additionally, facility-specific protocols derived from national guidelines for waste, standard precautions (hand hygiene, personal hygiene healthcare worker, PPE, cleaning and disinfection, and accidental blood exposure) HRMO, methicillin-resistant *Staphylococcus aureus* (MRSA), continence/catheters, influenza, legionella, resident personal care, isolation, norovirus, storage, bedpans and urinals, outbreak management, scabies, laundry, and wound care	E
Theme 6. Audit		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
An outbreak of norovirus is under control within ten days (i.e., no further spread occurs). This is applicable only if the organization has experienced an outbreak in the past year	Documents can be provided to demonstrate that an outbreak of norovirus was under control within the time frame form day 0 to 10. Day 0 is the day when the first resident developed symptoms indicative of norovirus. Day 10 is the day when the last resident and/or healthcare workers developed symptoms	S

Continuation Table 1. Themes on IPC standards and assessment criteria

Theme 7. Transmission of HRMO		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
The risk assessment for HRMO, including MRSA upon the admission of residents is documented in the electronic health record (Dutch acronym: is EPD)	Examine ten resident records In at least 90% of admissions, a risk assessment for HRMO, including MRSA, is conducted in advance (or promptly in the case of crisis admissions)	E
The organization has established that an outbreak of HRMO, including MRSA is reported at the healthcare institutions and antimicrobial resistance alert committee (Dutch acronym is SO-ZI/AMR)	The document containing this information can be provided	E
Theme 8. Antibiotics		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
Antibiotic formularies are up-to-date, having been revised within the past two years. The formularies comprise information pertaining to urinary tract infections, respiratory tract infections, and skin and soft tissue infections	The documents can be provided	E
An up-to-date antibiotic policy is in place, not exceeding four years in age	The policy includes at least: the responsible committee for antibiotic policy development and evaluation of formularies: by whom, frequency, method of feedback to elderly care physicians other activities undertaken to monitor antibiotic usage and prescribing behavior, including feedback to elderly care physicians	S
Theme 8. Antibiotics		
Standard	*Assessment criteria*	*Enforcement (E) Strive (S)*
An Antibiotic Team (A-team) is set up	The A-team comprises of professionals with relevant expertise (i.e., expertise in the field of microbiological diagnostic, antibiotics, and antibiotic resistance) The composition of the A-team can be verified through minutes of A-team meetings The A-team convenes at least twice a year to discuss prescribing behavior and maintains regular contact via phone or email	S

Continuation Table 1. Themes on IPC standards and assessment criteria

The total quantity of prescribed antibiotics is monitored	Documentation of the monitoring can be provided	S
For residents who do not respond to initial antibiotic treatment, active microbiological diagnostics are performed before starting a new treatment, as described in the formularies	The formularies regarding this issue can be provided	S
At least once a year a point prevalence study is conducted to assess antibiotic prescription behavior	The document containing the results of these measurements can be provided The prevalence of correct use of antibiotics is 86% or higher. For assessment, a standardized flowchart and local protocol is available and used	S

The standards and assessment criteria have been used as input in discussions in various committees concerning the development of standards. For example, it was used in meetings of the ABR networks, with the aim of defining tasks related to audit implementation and education.[19]

Basic components of infection prevention and control

Surveillance

Originally, surveillance denoted the precise observation of an individual to detect the initial signs of an infectious disease without restricting their freedom of movement. In the 1950s, the Centers for Disease Control and Prevention (CDC) began using the term to refer to the tracking of infectious diseases and reporting back to healthcare workers due to their potential causal role. Subsequently, the Study of the Efficacy of Nosocomial Infection Control (SENIC) demonstrated that surveillance reduced the incidence of hospital-acquired infections in hospitals.[20] Additionally, a description of surveillance methods in hospital setting was described.[21] Surveillance evolved, following the iterative steps of the plan-do-study-act (PDSA) cycle. Presently, the characteristics activities of surveillance encompass method development, data collection and recording, data processing, analysis and interpretation, and feedback to all relevant professionals, following the implementation of intervention measures as needed. Over time, the term nosocomial infection is changed to healthcare-associated infection to emphasize both hospital and nonhospital settings.

Prior to conducting surveillance, it is essential to define the objective to determine whether a prevalence or incidence study is appropriate. The prevalence of HAIs represents the number of infections present within a population at a specific time (point prevalence) or over a defined period (period prevalence). Conducting standardized prevalence studies at the organization level yields valuable information with relatively minimal effort. By periodically repeating prevalence studies, trends in infection rates, issues, and risk factors can be observed. It is crucial to conduct prevalence studies during the same time of the year when comparing prevalence data from consecutive years. The occurrence of HAIs is subject to seasonal influences. The incidence of HAIs pertains to the number of new cases of infections occurring within a population over a defined time frame. Incidence studies offer valuable insights into the causal sub-factors of HAIs and can evaluate the effectiveness of improvement efforts. Incidence studies are preferable, but these are very labor intensive.

The definitions of infections for application in long-term care facilities were first published in 1991 and subsequently updated in 2012.[22,23] The first prevalence studies conducted in the USA demonstrated percentages exceeding 10%.[7] The European Centre for Disease Prevention and Control (ECDC) has been conducting pan-European comprehensive prevalence studies on HAIs and antibiotic use in LTCFs since 2010. The prevalence of HAIs has ranged from 2.5% to 3.8% since 2010.[24-26] In 2009, the Dutch National Institute for Public Health and the Environment (Dutch acronym is RIVM) started a national sentinel surveillance network, known by the Dutch acronym SNIV (formerly referred to with the Dutch acronym PREZIES) to gain insights into the prevalence of infections in LTCFs, where prevalence rates for HAIs vary between 2.3% and 5.1%.[27]

In contrast to Dutch hospitals, where the surveillance of HAIs is included in the set of quality indicators, this is not the case for nursing homes.[28]

Hand hygiene

Hand hygiene have always been of utmost importance to prevent transmission of microorganisms and therefore in preventing HAIs in healthcare. As early as 1847, Semmelweis, a Hungarian obstetrician working at the Vienna General hospital is considered as the father of hand hygiene. He found a link between puerperal fever and physicians and medical students who moved back and forth between the dissection room and the maternity ward. By implementing a hand disinfection procedure with a sodium hypochlorite solution, he successfully put an end to the extensive maternal mortality at the institution where he was employed.

Nevertheless, he encountered substantial opposition and resistance, and his recognition came much later.

The 1980s marked a pivotal era in the development of hand hygiene principles in healthcare. During this period, the initial national hand hygiene guideline was introduced[29], with subsequent years witnessing the release of further guidelines in various countries. In 2002, the Healthcare Infection Control Practices Advisory Committee (HICPAC) endorsed the use of alcohol-based hand rubbing as the standard method for hand hygiene in healthcare settings, designating conventional handwashing for specific circumstances.[30] This guidance of care for hand hygiene practices in healthcare settings, whereas handwashing is reserved for particular situations only. This aligns with the recommendations on hand hygiene in LTCFs[13] and currently recommended in practice.

In 2009, the WHO released the guidelines on hand hygiene in health-care, which included including "The five moments for hand hygiene"[31], with a derivative version tailored for non-hospital settings in 2012.[32] The five moments for hand hygiene are presented in Figure 1.

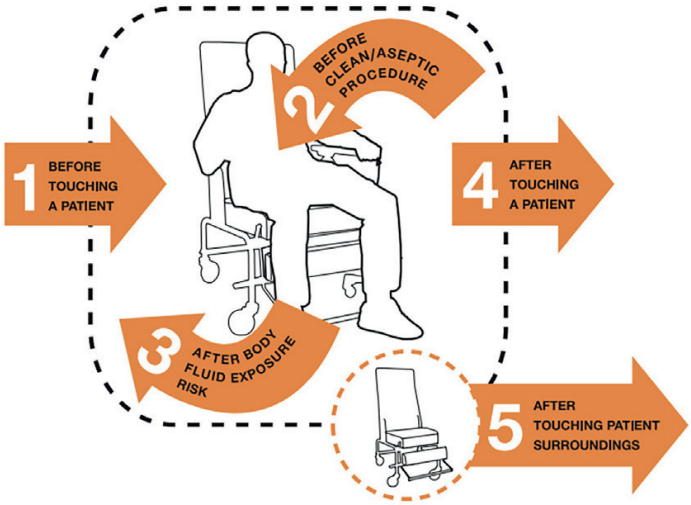

Figure 1. The five moments of hand hygiene (WHO)

The WHO also states that hand hygiene improvement strategies should be multimodal and focus on five elements:

1) System change, including availability of alcohol-based hand rub at the point of patient care and/or access to a safe, continuous water supply and soap and towels;
2) Training and education of healthcare-professionals;
3) Monitoring of hand hygiene practices and performance feedback;
4) Reminders and communication;
5) Institutional safety climate.

Hand hygiene, though seemingly simply, adherence to guidelines has encountered persistent challenges in achieving compliance in healthcare settings. The reported hand hygiene compliance rate in hospital settings averages at 40%, and in nursing homes, it is even lower, with rates ranging from 11% - 27%.[33-39]

Direct observation is the gold standard to monitor compliance, however this method is time-consuming, necessitating skilled and validated observers, susceptible to various forms of bias, including observer, selection bias, and observation bias (Hawthorne-effect). Alternative methods to monitor hand hygiene compliance encompass the monitoring of ABHR and soap consumption, as well as employing electronic hand hygiene monitoring systems.[31] A review of electronic hand hygiene monitoring systems demonstrated various different systems, which were categorized into four groups.[40] The first is an application-assisted direct observation system that aids trained auditors in monitoring hand hygiene compliance using smartphones or tablets, making it possible to monitor the five moments of hand hygiene. Another system involves systems where observations are facilitated by cameras, which can be reviewed by either human auditors or algorithms or analysis. This system also offers the potential to monitor the five moments, depending on where the cameras are placed. Another category involves systems that incorporate sensors, which can be classified into three types: electronic dispensers, electronic dispensers assisted by other sensors (e.g., motion sensors) and inertial measurement units with or without microphone. Electronic dispenser-based systems employ sensors to trigger the electronic dispenser counter, allowing for the quantification of hand hygiene events (i.e., the frequency of dispenser usage) rather than tracking moments of hand hygiene. For this reason, motion sensors can be added to measure room entry or exit. The IMU is an electronic sensor that measures specific force, angular rate, and orientation of the human body, either with or without the inclusion of microphones to distinguish hand hygiene events

form other daily activities. Finally, there are real-time locating systems capable of identifying and tracking objects. It is worthwhile to gain experience with such systems in nursing homes.

Nurses' attire

The introduction of a policy in 2008, where many nursing homes mandated their healthcare workers to wear personal attire, has prompted extensive discussions. From IPC perspective, this was far from ideal. Some studies have shown contamination of clothing worn by healthcare workers in both nursing homes and hospitals.[41-45] However, it remains unclear what the exact contribution is to the development of HAIs or colonization with HRMOs. Considering the frequent (and intensive) physical interactions between nurses and residents, the potential for transmission of microorganisms from healthcare workers' attire to residents and vice versa is conceivable.

The national guideline regarding healthcare workers' attire recommend wearing attire that adheres to the following specifications: leaves the forearms uncovered, is smooth and non-linting, must not hang loosely, preferably has a light color, is machine washable at a minimum temperature of 60^{0}C or at a temperature between 40^{0}C and 60^{0}C and can be dried in a tumble dryer (minimum setting cupboard dry) and/or ironed (minimum setting 150^{0}C). Additionally, it is recommended to change attire before the commencement of each shift and immediately in the presence of visible contamination.[46]

Based on practical experience, we are aware that there is considerable dissatisfaction among carers and nurses regarding the discontinuation of professional attire. Not all healthcare institutions adopted this change, but for those that did, this topic was consistently addressed during IPC training. Wearing personal attire is perceived as unhygienic for both themselves and residents, they are no longer distinguishable from other visitors by residents, and the requirement for carers and nurses to purchase and launder their own clothing, frequently incurring the related costs themselves. Furthermore, this policy on healthcare workers' attire poses a complex challenge in guaranteeing the process.

Guidelines for addressing antibiotic resistance

Antibiotic resistance and antibiotic use

The 1929 publication by the English scientist Fleming, delineating the discovery of penicillin and its subsequent therapeutic application in 1941 by Flory and Chain, marked the onset of the antibiotic era.[47] However, within a mere year of the widespread use of penicillin, the occurrence of resistant Staphylococcus aureus isolates became apparent. Despite the subsequent development of more (classes) antibiotics, the persistent reliance has led to the antibiotic paradox – the intended benefits of antibiotics are counteracted by the emergence of antibiotic resistance.[48]

In 2001, the WHO released a set of recommendations for action to slow the emergence and reduced the spread of antimicrobial resistant microorganisms to all stakeholders.[49] A decade later, the WHO emphasizes on World Health Day the urgency of taking action against antibiotic resistance with the pronunciation, "In the absence of urgent corrective and protective actions, the world is heading towards a post-antibiotic era, in which many common infections will no longer have a cure, and once again, kill unabated".[50] On this day the WHO introduced a policy package to combat antimicrobial resistance.[51] In response to this, a global action plan on antimicrobial resistance was initiated[52], followed by the establishment of a priority research agenda aimed at collect new data to effectively address the challenges posed by antimicrobial resistance.[53] A recent report on antimicrobial resistance in the EU/EEA demonstrated a decline in antibiotic use of 23% between 2011 and 2020. Although the relative use of broad-spectrum antibiotics has raised, and an increase in resistance to critically important antibiotics used to treat common HAIs is observed.[54]

The Dutch Working Party on Antibiotic Policy [Dutch acronym is SWAB], in collaboration with the Centre for Infectious disease control (Dutch acronym is CIb) of the RIVM annually reports data from ongoing surveillance on antibiotic use and resistance in the Netherlands, including data from LTCFs.[55]

In LTCFs, a considerable amount of antibiotics is prescribed[56], with almost a quarter or more of these prescriptions classified as inappropriate.[57-61] Nursing homes are known by restrictive culture sampling in cases of (suspected) infections. Recent data on causative microorganisms of HAIs in European LTCFs showed that, during the point prevalence survey, three-quarters of microbiological data were not available.[26] Although, in the Netherlands, there appears to be a trend indicating an increased frequency of microbiological testing.[62] While there is a scarcity of studies

on the prevalence of HRMO in nursing homes, existing research demonstrated that residents could harbor HRMO, potentially acting as prolonged carriers, and thereby posing a risk of outbreaks.[56,63-67] Moreover, and crucial, in cases of severe infections caused by highly-resistant microorganisms (HRMO) unresponsive to oral antibiotics, residents and/or their representatives must make decisions for hospitalization. The burden of illness, duration of illness, and any associated isolation measures, have the potential to detrimentally affect residents' quality of life.[68]

In the Netherlands, the SWAB has emphasized the pivotal role of an integrated IPC framework alongside an antibiotic policy in healthcare institutions to effectively address antibiotic resistance to achieve three objectives mitigate antibiotic resistance through appropriate antibiotic use, identifying drug-resistant bacteria, and prevention transmission by IPC measures.[69] They assertion that achieving appropriate antibiotic use it is deemed necessary to introduce an AMS program in addition to education and guidelines. Antimicrobial stewardship is defined as: an ongoing effort by a health care institution to optimize antimicrobial use among hospitalized patients in order to improve patient outcomes, ensure cost effective therapy and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance)".[70] It was acknowledged that an exploration is essential to illuminate the strategies for executing a program in nursing homes. The implementation of an AMS program has been compulsory for Dutch hospitals since 2015.[71] In 2018, the Dutch professional association of elderly care physicians (Dutch acronym is Verenso) asserted that it is the responsibility of the elderly care physician group to initiate an AMS program.[72]

Guideline on the prevention of transmission of HRMO

The guideline for preventing the transmission of HRMO in hospitals is not directly applicable to nursing homes[73] and need to be tailored accordingly. While many standard and isolation precautions apply during care moments and take place in residents' room, including toileting, residents with HRMO should have unrestricted movement, including the ability to visit communal areas and participate in social activities. This flexibility is crucial given the typically prolonged duration of HRMO carriage and the residential context. It is imperative for a facility to establish protocols outlining measures that could be undertaken to reduce the risk of transmission as much as possible.

Practice guide on AMS in nursing homes

The practice guide for implementing an AMS program in hospitals[71] is also not suitable for a copy-and-paste approach to nursing homes. The integration

of electronic medical records, prescription systems, and laboratory systems may not function optimally or is lacking. A regular collaboration with a medical microbiologist is not a standard practice or may vary in intensity. The implementation of surveillance on antibiotic use is not standard practice. Despite the recognized need for implementation of an AMS program by the professional association of elderly care physicians, time and budget constraints may vary or hinder the implementation of such a program. Essential elements of an AMS program, as outlined by the Centers for Disease Control and Prevention (CDC) in 2015 – the basis upon which various guidelines for the implementation of an AMS program are developed - include "leadership commitment, accountability, drug expertise, action, tracking, reporting, and education".[74-77]

COVID-19 testing healthcare workers in elderly care

From the beginning of 2020 until May 2022, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), responsible for the COVID-19 disease, exerted its global impact. Elderly persons, especially those residing in nursing homes, encounter elevated mortality rates due to heightened vulnerability and the unique characteristics of nursing homes themselves.[78,79] Given the close and intensive care contact, along with frequent social contact between healthcare workers and residents, healthcare workers became a substantial source of contagion.

Testing is crucial for diagnosing and containing the spread of the coronavirus. In the Netherlands, testing policy is guided by advice from the Outbreak Management Team (OMT), which provides expert advice on infectious disease control.[80] The OMT plays a pivotal role in shaping the country's testing strategy, contributing to the development of case definition in line with the WHO's definition of COVID-19. This ensures a standardized approach to identifying and categorizing persons for testing based on specific criteria. The initial lack of comprehensive understanding regarding the coronavirus, its varied clinical presentations, and the emergence of new variants posed a unique challenge in formulation a case definition.[81]

The OMT also plays a crucial role in mapping and enhancing testing capacity. COVID-19 testing capacity relies on essential resources, including materials to perform the test, as well as materials to analyses, and human personnel for testing, transportation, analysis, and result communication. Adhering to guidelines ensures efficient resource use. The gold standard for testing on SARS-CoV-2 is reverse transcription-quantitative polymerase chain reaction (RT-qPCR). RT-PCR involves

amplifying and analyzing the viral RNA present in a sample. The cycle threshold (Ct) in RT-qPCR is inversely proportional to the viral load, meaning a lower Ct value corresponds to a higher viral load, and vice versa. RT-qPCR tests are highly sensitive and can detect the virus even in individuals with low viral loads. This test requires specialized laboratory equipment and may take longer to deliver results. Given the escalating demand for testing and the resulting challenges in timely scheduling, conducting, and promptly reporting results, the need for alternatives became more pronounced. The ministry of VWS and RIVM selected five Ag-RDTs for clinical validation based on the technical validation and potential availability.[82] Antigen tests detect specific proteins of the virus and are often referred to as rapid tests because they can provide results relatively quickly, typically within 15 – 30 minutes. While convenient for quick screenings, antigen tests may be less sensitive than PCR tests, especially in individuals with lower viral loads.[83]

Aim of this thesis

The overall aim of this thesis is to provide a comprehensive framework that includes various basic components of infection prevention and control, along with guidelines aimed at addressing antibiotic resistance, in the home-like environment of nursing homes. Additionally, the aim of thesis is to elucidate COVID-19 testing strategies among healthcare workers working in elderly care, with collaborative efforts at the regional level during the first and second waves of the COVID-19 pandemic.

Thesis outline

Part 1 Basic components of infection prevention and control

In **Part 1,** various basic components of infection prevention and control in nursing homes are described. **Chapter 2** presents the first series point-prevalence studies on healthcare-associated infections and antimicrobial use in Dutch nursing homes from 2007 to 2009. **Chapter 3** describes the follow-up study from the annual prevalence studies on HAIs as outlines in Chapter 2 up to 2017. **Chapter 4** evaluated the impact of interventions and nudges on hand hygiene events (HHEs) within a rehabilitation unit at a nursing home using an electronic hand hygiene monitoring system. **Chapter 5** describes both residents' preferences regarding nurses' attire and nurses' perceptions of these preferences.

Part 2 Guidelines for addressing antibiotic resistance

In **Part 2,** guidelines aimed at addressing antibiotic resistance in nursing homes are presented. **Chapter 6** delineates the guideline for the prevention of highly-resistant microorganisms (HRMO). **Chapter 7** illustrates a practice guide for implementing an antimicrobial stewardship (AMS) program in nursing homes.

Part 3 COVID-19 testing healthcare workers

In **Part 3,** COVID-19 testing strategies among healthcare workers, with collaborative efforts at the regional level during the first and second waves of the COVID-19 pandemic are shown. **Chapter 8** describes the importance of testing healthcare workers for COVID-19, even when presenting with non-respiratory mild symptoms during the first wave of the COVID-19 pandemic. **Chapter 9** reports on the prospective diagnostic evaluation of the Abbott Panbio™ COVID-19 antigen detection rapid diagnostic test (Ag-RDT) among healthcare workers working in elderly care who met clinical criteria for COVID-19 during the second wave of the COVID-19 pandemic.

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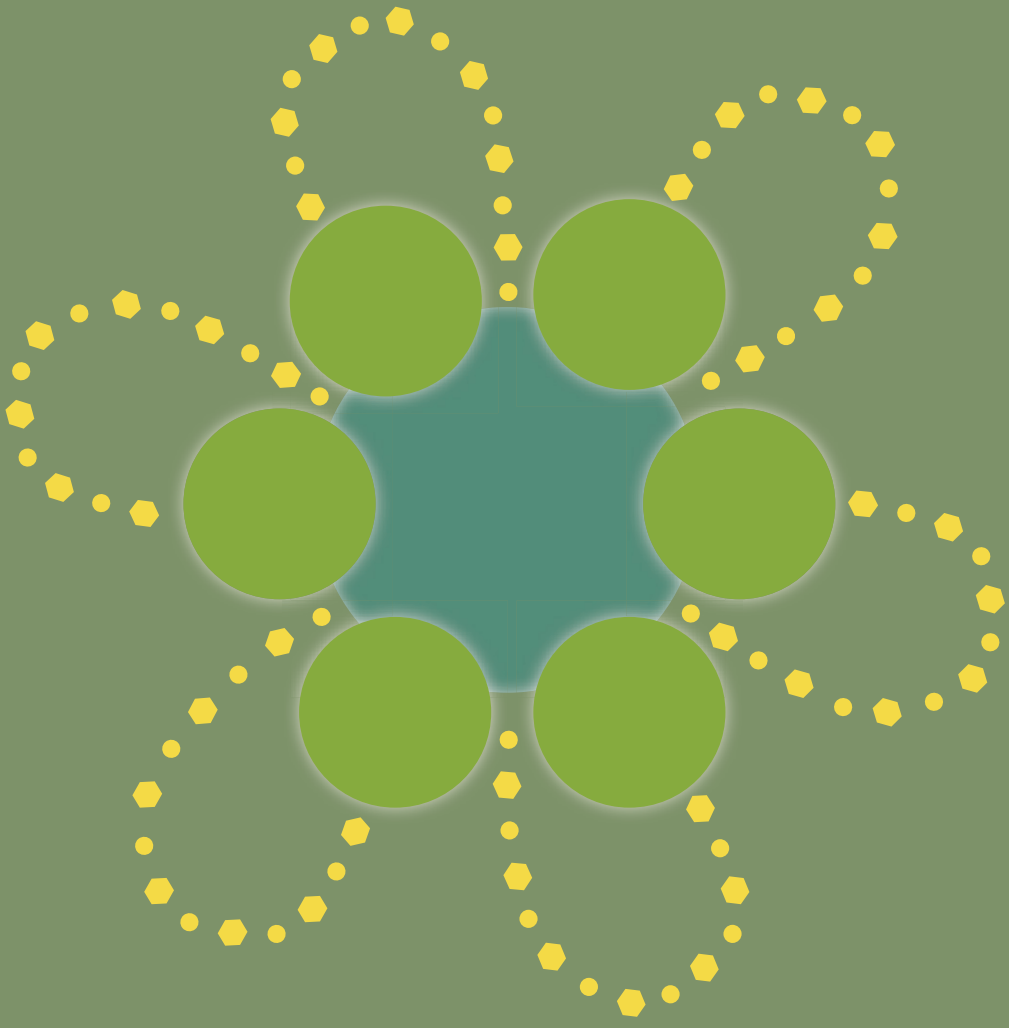
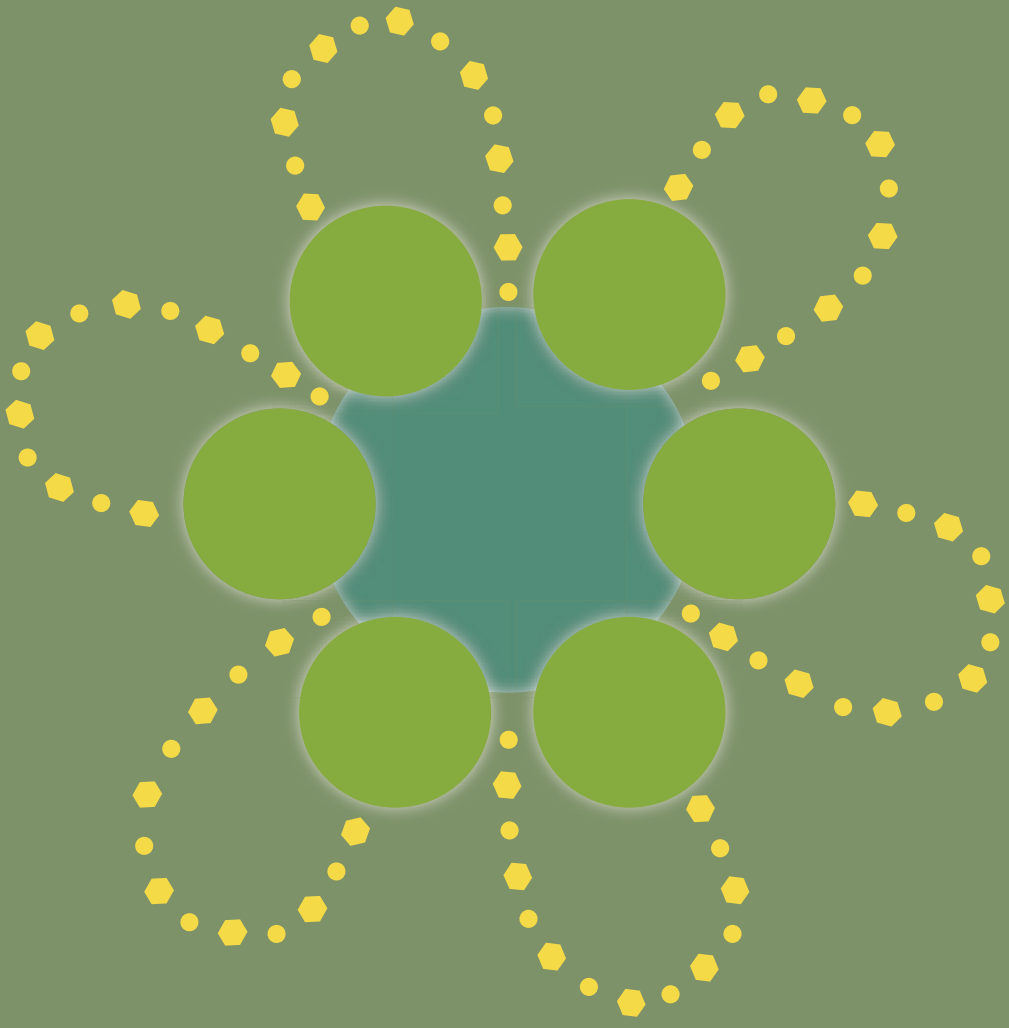


PART 1
BASIC COMPONENTS OF INFECTION PREVENTION AND CONTROL



CHAPTER 2

Three-year prevalence of healthcare-associated infections in Dutch nursing homes

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On behalf of the members of the Regional Nursing home Infection Control Network (REZON)

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Summary

From November 2007 for a period of three years (2007-2009), we conducted an annual one-day prevalence study of healthcare-associated infections (HAIs) among nursing home residents in the Nijmegen region of the Netherlands. In the absence of national HAIs definitions applicable to the nursing home setting, we used modified definitions based on US Centers for Disease Control and Prevention criteria for bloodstream infection, lower respiratory tract infection, bacterial conjunctivitis, and gastroenteritis. For the surveillance of urinary tract infections (UTI), criteria established by the Dutch Association of Elderly Care Physicians were used. Resident characteristics were recorded, and data collection was performed by the attending elderly care physicians. For the three-year period, 1275, 1323, and 1772 nursing home residents were included, resulting in a prevalence of HAIs of 6.7%, 7.6% and 7.6%, in 2007, 2008, and 2009, respectively. The demographics with respect to age (mean 81 years) and sex (31% men, 69% women) were almost identical in all three years. UTI was the most prevalent HAI with 3.5%, 4.2%, and 4.1% respectively. Most HAIs occurred among residents of rehabilitation units. The prevalence of HAIs varied by nursing home (range: 0.0-32.4%). We present the results of the first prevalence study of HAIs in Dutch nursing homes. Point-prevalence studies of HAIs, as part of a quality improvement cycle, are an important cornerstone of infection control programs in nursing homes, allowing us to further increase patient safety efforts in this setting.

Introduction

In 1997 the Society for Healthcare Epidemiology of America (SHEA) and the Association for Professionals in Infection Control and Epidemiology (APIC) provided a rational structure and process for infection control programs in long-term-care facilities.[1] One of their recommendations was the implementation of an active surveillance program based on the experience derived from acute care hospitals. Although the surveillance of HAIs in hospitalised patients in The Netherlands is well established and guided by a national reference centre, these efforts have not been extended to the long-term care facility (LTCF) setting, such as nursing homes. The Dutch Health Care Inspectorate, inspectie voor de Gezondheidszorg (Den Haag), reported in 2005 that 88% of the nursing homes in The Netherlands undertook active surveillance for pressure sores with or without including the use of antibiotics and/or indwelling urethral catheters. However, HAI surveillance was not mentioned.[2]

Healthcare-associated infections (HAIs) in nursing homes are a serious problem and are associated with excessive comorbidity and mortality. Among residents of Norwegian nursing homes the acquisition of an infection was associated with a reduction of their overall physical wellbeing, hospital admission, and death.[3] A study among dementia patients admitted to Dutch nursing homes demonstrated that these patients, compared to those from general practice, were frequently diagnosed with urinary tract infection (UTI), pneumonia, and conjunctivitis.[4] In 2005, Dutch medical professionals, healthcare providers, and client organizations for elderly care published a strategic document describing the prevention and treatment of infections as one of the quality indicators.[5]

Surveillance, as part of the PDSA cycle ('plan, do, study, act'), is an important component of quality improvement programmes. Incidence studies are preferable, but these are very labour intensive. Alternatives to incidence studies are prevalence studies, which are less labour intensive and less accurate, but still give valuable information about HAIs. This information can help steer further infection prevention and control measures and efforts. Since 2009, a systematic surveillance has been conducted in nursing homes in The Netherlands by the Centre for Infectious Disease Control (National Institute for Public Health and the Environment).[6]

The objective of this study was to measure the prevalence of HAIs (overall as well as per type of care) and to gain insight into infection prevention and control and antimicrobial use in Dutch nursing homes.

Methods

In 2007, members of the regional nursing home infection control network (REZON) decided to carry out the first one-day prevalence study on HAIs in nursing homes. Since no national definitions for healthcare-associated infections in nursing homes were available, REZON members modified the Centers for Disease Control and Prevention (CDC) criteria for bloodstream infection, lower respiratory tract infection, bacterial conjunctivitis, and gastro-enteritis for use in Dutch nursing homes (Table 1).[7] Modifications were needed because of differences in the diagnostic approach between hospitals and nursing homes. Nursing homes have limited resources for microbiological diagnostics and other support services and consequently have to rely on clinical manifestations. The definition for UTI was in accordance with the corresponding guideline by the Dutch Association of Elderly Care Physicians.[8] According to these definitions a UTI must meet one of the following criteria: (i) no other recognised cause and antibiotics commenced (unless antibiotics are not desirable, e.g., a terminally ill resident) and physician diagnosis of a UTI with signs or symptoms (with or without an indwelling urinary catheter) and positive dipstick for leukocyte esterase and/or nitrate; or (ii) in the absence of signs or symptoms: positive dipstick for leukocyte esterase and/or nitrate or positive urine culture. Decubitus ulcers (bedsores or pressure ulcers as a result of lying down or sitting) were excluded from these studies due to the Dutch national surveillance study of decubitus ulceration in which most of the institutions participate.

All point-prevalence studies used the same diagnostic criteria. In the final year of the study additional elderly care physicians from a neighbouring area decided to participate and they also accepted and used the selected diagnostic criteria.

The attending elderly care physicians were in charge of data collection and resident assessment. Infections were recorded if on the day of registration clinical symptoms were present and/or there was still ongoing treatment for infection. Infections present or in the incubation period (within 48 h) at the time of admission were not recorded as nosocomial. Also infections as a result of complication or extension of an existing infection at the time of admission were excluded. If a resident had multiple infections in different sites, infections were reported as separate events. When an infection was not confirmed by follow-up diagnostics (ordered at the time the patients were evaluated) the diagnosis infection was discarded. The following data were recorded: gender, age, use of medical devices, infections, type of unit (psychogeriatric, somatic or rehabilitation), occurrence of multidrug-resistant

microorganism (MDRO), and antimicrobial drug use. Somatic units in Dutch nursing homes are those for residents with physical disorders.

In 2007 and 2008 the data were recorded by a written survey; in 2009 an online survey was developed and used. All data were collected and analysed in an Excel-database. Infection rates were calculated and expressed as the number of infections per 100 residents.

Results

In 2007, 2008 and 2009 there were respectively 17, 15 and 24 nursing homes participating in the study and the dataset consisted of 1275, 1323 and 1772 residents, respectively. The mean age of the residents was 81 years in 2007 and 2008, and 82 years in 2009. The distribution with regard to sex was similar in all years, 31% men and 69% women of whom the average infection rate was 6.8 vs 6.9%. The overall prevalence of HAIs was 6.7% (95% confidence interval: 5.4–8.2) in 2007, 7.6% (6.3–9.2) in 2008, and 7.6% (6.4–8.9) in 2009.

The most prevalent HAI was UTI with an overall prevalence of 3.8%. The overall prevalence of other HAIs was 1.6% for pneumonia, 0.9% for bronchitis/bronchiolitis, 0.6% for bacterial conjunctivitis, 0.2% for bloodstream infection, and 0,3% for gastro enteritis. For yearly prevalence rates for the different infection sites, see Figure 1.

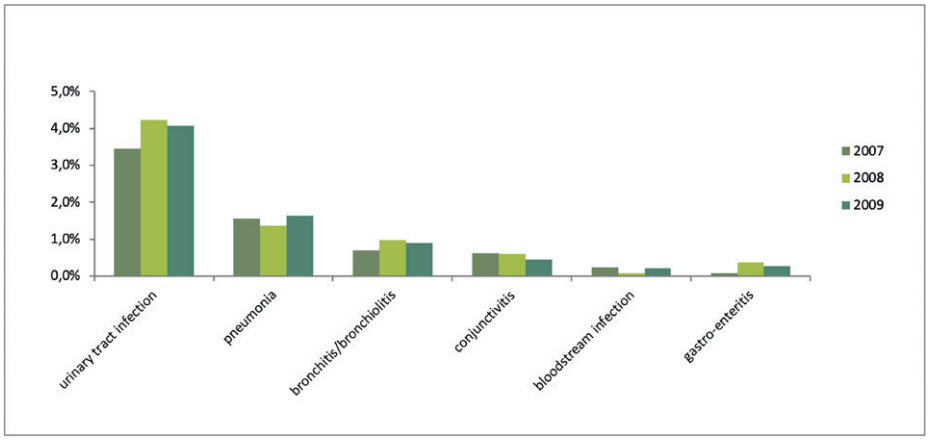

Figure 1. Three-year prevalence of healthcare-associated infections in Dutch nursing homes by different infection sites

Most HAIs occurred among residents of rehabilitation units (mean: 12.1%; range: 10.8-13.3), followed by residents of somatic units (8.0%; 6.4-11.0). Psychogeriatric residents had the lowest overall rates (6.3%; 5.4-7.2), as well as lowest yearly prevalence rates for the different units (Figure 2).

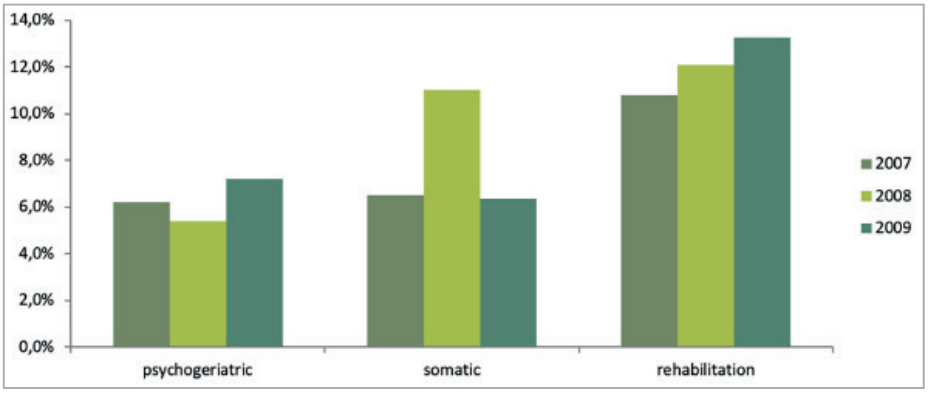

Figure 2. Three-year prevalence of healthcare-associated infection in Dutch nursing homes by units

Considering the distribution of all sites of infections over all study years combined, non-catheter-associated UTI was the most frequently recorded HAI (Table 2). Investigating further the distribution of non-catheter-associated UTI and catheter-associated UTI over all units, non-catheter-associated UTIs occurred in 60.6% of the cases in psychogeriatric, 28.2% in somatic, and 11.3% in rehabilitation units. Catheter-associated UTI occurred in 50.0% of the cases in somatic-, 30.0% rehabilitation, and 20.0% in psychogeriatric units.

Table 1. Definitions healthcare associated infections in nursing homes

Bloodstream infection
The resident must have at least two of the following symptoms (with no other explanation or source for the symptoms): fever (>38°C), hypotension (systolic pressure ≤ 90mm Hg), oliguria (<20ml/hour), positive blood culture(s).
Pneumonia
The resident must have at least one of the following criteria: 1. Rales or dullness to percussion on physical examination of the chest and one of the following: a. New onset of purulent sputum or change in character of sputum; b. Organisms cultured from blood. 2. Chest radiographic examination shows new of progressive infiltrate, consolidation, cavitation or pleural effusion and at least one of the following: a. New onset of purulent sputum or change in character of sputum; b. Organisms cultured from blood; c. Isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy; d. Isolation of virus from or detection of viral antigen in respiratory secretions; e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen; f. Histopathologic evidence of pneumonia.
Other lower respiratory tract infection (bronchitis, tracheobronchitis, bronchiolitis, tracheitis)
The resident must have no clinical or radiographic evidence of pneumonia and at least two of the following signs or symptoms with no other recognized cause: fever (>38°C), cough, new or increased sputum production, rales, wheezing. Preferable are one of the following criteria: positive culture obtained by deep tracheal aspirate/ bronchoscopy or positive antigen test on respiratory secretions. These criteria are optional because of the known difficulty of residents to provide an adequate sputum sample.
Urinary tract infection
Based on the guideline by the Dutch Association of Elderly Care Physicians, a urinary tract infection must meet one of the following criteria: 1. No other recognized cause and start antibiotics (unless antibiotics is not desirable to e.g., a terminal resident) and physician diagnosis of a urinary tract infection by resident with signs or symptoms (with or without an indwelling urinary catheter) and positive dipstick for leukocyte esterase and/or nitrate 2. In the absence of signs or symptoms: positive dipstick for leukocyte esterase and/or nitrate or positive urine culture.
Conjunctivitis
The resident must have at least one of the following criteria: Pain or redness of conjunctiva or around eye Purulent exudates, and preferable pathogens cultured, from the conjunctiva or contiguous tissues, such as eyelid, cornea, meibomian glands or lacrimal glands.

Continuation Table 1. Definitions healthcare associated infections in nursing homes

Gastroenteritis
The resident must have at least one of the following criteria: 1. An acute onset of diarrhea (liquid stools for more than 12 hours) with or without vomiting of fever (>38°C) and no likely noninfectious cause (e.g., diagnostic tests, therapeutic regimen, acute exacerbation of a chronic condition or psychologic stress). 2. At least two of the following signs or symptoms with no other recognized cause: nausea, vomiting, abdominal pain or headache and at least one of the following: a. An enteric pathogen is cultured from stool or rectal swab b. An enteric pathogen is detected by routine or electron microscopy c. An enteric pathogen is detected by antigen or antibody assay on blood or feces d. Evidence of an enteric pathogen is detected by cytopathic changes in tissue culture (toxin assay) e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen.

Table 2. Percentage distribution for all sites of infections in Dutch nursing homes 2007, 2008, and 2009

Type of infection	Psychogeriatric	Somatic	Rehabilitation
Non-catheter-associated urinary tract infection	52.4	40.0	28.6
Pneumonia	21.3	19.0	23.2
Bronchitis/bronchiolitis	11.0	10.0	17.9
Catheter-associated urinary tract infection	3.7	15.0	16.1
Conjunctivitis	5.5	10.0	8.9
Gastroenteritis	2.4	5.0	3.6
Bloodstream infection	3.7	1.0	1.8

The prevalence of HAIs varied by nursing homes (range: 0-32,4%). Using the overall mean prevalence rate of 7.3% for 15 nursing homes that participated in all three prevalence studies, only three nursing homes were outliers with a prevalence rate higher than the mean. The most common medical device was an indwelling urethral catheter (mean: 5.1%; range: 3.8-6.8), followed by supra-pubic catheter (4.5%; 3.8-5.6), percutaneous endoscopic gastrostomy tube (1.8%; 1.6-1.9), tracheostomy (0.06%; 0.0-0.1), and intravascular device (0.05%; 0.0-0.1). On average, antibiotics were used in 6.6% of the residents (range 5.5-7.3). Furthermore, 0.4% (0.2-0.6) of the residents were colonised or infected with MDRO.

Discussion

Point-prevalence, although less accurate than incidence studies, can provide valuable information to guide future infection control interventions with limited use of time and money. They are a perfect start for quality improvement projects in settings where infection control, including surveillance of HAI, in general is less developed than in hospitals. This is the first series of HAI point prevalence studies in Dutch nursing homes, showing an overall mean prevalence of 7.3%. Studies in comparable LTCFs in other countries show prevalence rates between 5.2% and 20.5%, but comparisons are problematic due to the lack of standardised international definitions, different methods of surveillance and heterogeneous resident populations.[9-13] Nevertheless the results from the prevalence study in long-term care facilities for elderly persons in Norway in 2002 and 2003 showed a similar outcome to this Dutch study.[14] The Norwegians reported UTIs as the most frequently occurring HAI and the highest prevalence rate among residents in rehabilitation units. The prevalence of antibiotic use was comparable between Norway and The Netherlands, with means of 5.8% and 6.6%, respectively. This might be lower than in other countries, since both Norway and The Netherlands are well known for their restrictive antibiotic use.[15]

Remarkable in the present study was the distribution of catheter- and non-catheter-associated UTI. Planning infection control interventions for non-catheter-associated UTI is complicated by the fact that the experience from hospitals (mainly catheter-related infections) cannot be used. A focused incidence study is presently ongoing to gain more insight into the source of non-catheter-related UTI in nursing home patients. One possible explanation for the high occurrence of non-catheter-related UTI is fecal incontinence, which could theoretically be influenced by the choice of incontinency materials.

The high variation in the prevalence of HAI over all institutions (range: 0% to 32.4%) was surprising. The low outliers may be explained by the initial participation of two very small, highly specialised nursing homes with only 10-15 clients. These two nursing homes did not participate in the second and third years. The high outliers were among the nursing homes with the highest number of residents, including many in rehabilitation units. Our study did not include a validation of the data through an independent external person, e.g., infection control professional (ICP); such validation is expected to be rather difficult in the nursing home setting, since in the frequent absence of laboratory and diagnostic tests the subjective evaluation of the attending physician is the 'gold standard'. Since all the elderly care physicians

who evaluated their own residents for the purpose of the point prevalence study were part of the group setting up the HAI definitions for nursing homes, we believe that the inter-observer bias, despite the abovementioned problems, is fairly low.

The low prevalence of MDROs (< 0.7% in all three years) is unlikely to reflect the true prevalence in Dutch nursing homes, but is probably due to underreporting as a consequence of limited microbiological diagnostic tests requested by the elderly care physicians. In the last two decades, many reports have documented an increasing prevalence of colonisation with MDRO in residents of long-term care facilities (LTCF).[16-20] While insight into the prevalence of MDROs in LTCFs is an important issue, we can conclude from the present study that, unlike in hospitals, prevalence studies for HAIs will not be able to detect a true rate of MDROs. Therefore, microbiological surveys are needed in addition to HAI prevalence studies.

The increasing emphasis on patient safety warrants the introduction of surveillance as an important cornerstone of infection control programs in LTCFs. Prevalence studies can be seen as a first step to introducing infection prevention and control practices into LTCFs, since they are relatively easy to perform and give an insight into the problem of HAI in this setting. Prevalence results should be used to guide future healthcare improvement projects (e.g., aiming at non-catheter-related UTIs) and should not be seen as the sole method to gather information on the prevalence of MDROs. Investing in microbiological and other diagnostic tests could also improve the insight into HAIs in nursing homes and thereby the means to control them.[21]

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Conflict of interest statement
None declared.

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None.

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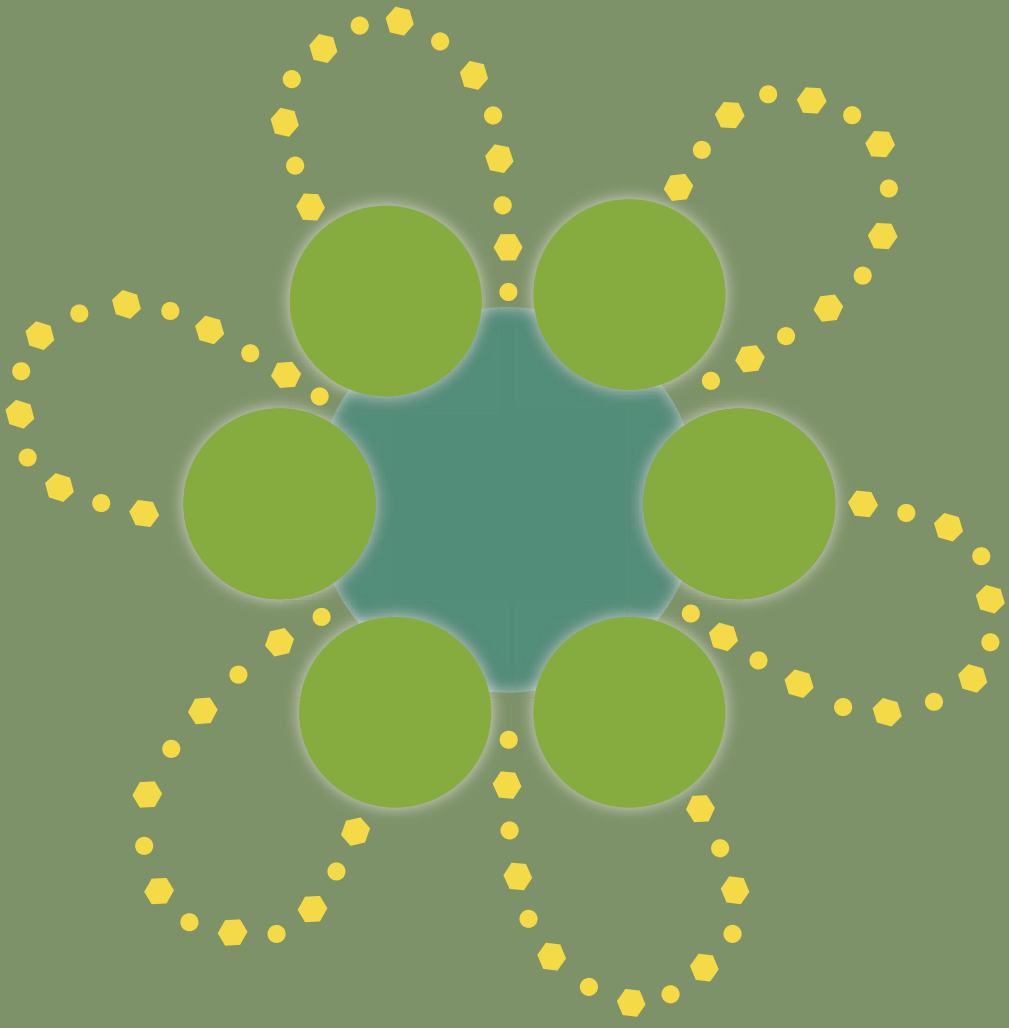

CHAPTER 3

Prevalence of healthcare-associated infections in Dutch nursing homes: follow up 2010 – 2017

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Summary

Following the first point-prevalence study in Dutch nursing homes conducted each November from 2007 to 2009, we conducted a follow-up point-prevalence study of healthcare-associated infections (HCAIs) each November from 2010 to 2017. Similar methods and criteria were used. Resident characteristics were recorded, data collection was performed by the attending elderly care physicians via an online survey, as well as via a specifically designed App from 2012. As of the same year, information on incontinence was added. Between 2010 until 2017 on average 1786 residents per year were included, ranging from 1571 to 2185. HCAI prevalence with respect to age (mean 83 years) and sex (31% men and 69% women) were similar over all the years. The overall mean prevalence rate in the first four years was 6.7% versus 2.2% in the last six years. Urinary tract infection was the most prevalent HCAI with 1.5%. Most HCAIs occurred among residents of rehabilitation units. The prevalence of HCAI varied by nursing home (0.0 – 37.0%). The average use of antibiotics was stable over the years (6.0%) irrespective of HCAI rate. Use of incontinence materials was on average 73.5% with 64.3% of residents being reported as incontinent. Those implementing improvement of infection control and surveillance within a new setting do need to continue for multiple years before seeing the success of their endeavour.

Introduction

Nursing homes are generally characterized by having a vulnerable resident population with chronic illnesses, cognitive disorders, and functional disabilities. The increased level of care needed by the residents and the close proximity of residents to each other, including sharing of sanitary facilities, increase the risk and spread of healthcare-associated infections (HCAIs) [1].

Each November from 2007 until 2009, Eikelenboom-Boskamp *et al.* conducted the first point-prevalence study of HCAIs in Dutch nursing homes, as part of the regional nursing home infection control network (REZON) in the south-east of The Netherlands [2]. They found HCAI prevalences of 6.7%, 7.6%, and 7.6% for 2007, 2008, and 2009, respectively. The most prevalent HCAI was urinary tract infection (UTI), accounting for >50% of all recorded infections.

At that time it was hard to compare results with those from other point-prevalence studies due to the lack of standardized international definitions, different methods of surveillance and heterogeneous resident populations [2, 3]. Between 2009 and 2011 the first European point-prevalence study was performed, called HALT (Healthcare Associated infections in Long-Term care facilities), aiming at establishing an extensive protocol for surveillance of HCAIs, antimicrobial use and resistance [4]. Since 2011, prevalence studies have also been conducted in nursing homes in The Netherlands by the Dutch National Institute for Public Health and the Environment (RIVM) [5]. Additionally, from 2015 the REZON-data were used by the RIVM to generate national reference data.

After the initial HALT study, various European countries have conducted (multiple) HALT studies, aiming to make comparison easier [6]. Additionally, independent HCAI studies in nursing homes have been conducted worldwide [3, 7]. A review study by Nicolle in 2014 showed a variation in prevalence of infection in long-term care facilities of 2.8-14% including five European countries and the USA [8]. The results of these studies indicate that nursing homes still face challenges in controlling HCAIs and that targeting UTIs, especially non-catheter-associated UTIs, is of highest priority [2, 6].

The purpose of this study was to describe and evaluate continued surveillance efforts in infection prevention and antimicrobial use in Dutch nursing homes over a period of 11 years, taking into account case-mix variation.

Methods

The current study was a continuation and expansion of the surveillance activities described previously [2]. Most of the previous locations continued their surveillance activities, while new homes joined the project. All nursing homes in the area were eligible to participate; participation was voluntary. Included were all residents in participating homes who fell under the care of the elderly care physician; therefore, residents predominantly fell within similar care profiles. Over the years of the survey some participating nursing homes closed and new ones opened, hence relocating residents over the different homes, albeit maintaining a fairly consistent population overall.

The same inclusion and exclusion criteria as well as the same definitions for HCAIs as described in the previous study [2] were used, with the exception of the definition for UTI. From 2012 the definition for UTI was applied more strictly in coordination with the Network for Prevention of Nosocomial Infections through Surveillance (PREZIES) of the National Institute of Public Health and the Environment (RIVM). To meet the new criteria for a UTI, the resident had to have signs or symptoms of a UTI and positive dipstick for leucocyte esterase and nitrate or positive urine culture, irrespective of the diagnosis of the elderly care physician. Before 2012 the diagnosis by the elderly care physician was the decisive factor, not whether all criteria were met.

Similar to the previous study the following data were recorded: gender, age, use of medical devices, infections, type of unit (psychogeriatric, somatic or rehabilitation), and antimicrobial drug use. In both studies, all antimicrobials for systemic use (ATC code J01) with use for all routes were recorded and some of the other antimicrobials most frequently reported in nursing homes (antimicrobials for topical use). From 2010, the reason for use (HCAI or not HCAI) was also recorded. From 2012 complete information on incontinence (faecal incontinence, urinary incontinence, and both) was included. In 2010 and 2011 data were recorded via an online survey; from 2012, data were recorded using an App specifically developed for this study [9].

The data were collected annually in November and were analysed in an Excel database. Trend analyses using χ^2-tests (linear by linear association) and two-group comparison for (in)continence and UTI using a Mann-Whitney test were performed using IBM SPSS, version 22 (IBM Corp., Armonk, NY, USA).

Results

Over the study period between 2010 and 2017 the number of participating nursing homes increased from 25 to 44 locations; eight nursing homes participated in every year of the survey. As the number of locations increased, the size of the dataset tended to rise, from a minimum of 1571 to a maximum of 2185 residents. The mean age of the residents increased from 81 years in 2012, to 84 years in 2017. The distribution with regard to sex was similar in all years, around 31% men and 69% women. The overall mean prevalence rate of HCAIs was 3.1%; 3.3% for men and 2.9% for women, respectively. The trend for reduction in overall prevalence of residents with an infection over the years 2007-2017 was statistically significant ($P < 0.001$) (Figure 1). For the initial years (2007-2010) the HCAI prevalence rate remained unchanged ($P = 0.75$), with an average infection prevalence of 6.7%. For the years 2012-2017 the trend result was similar ($P = 0.93$) with an average infection prevalence of 2.2%.

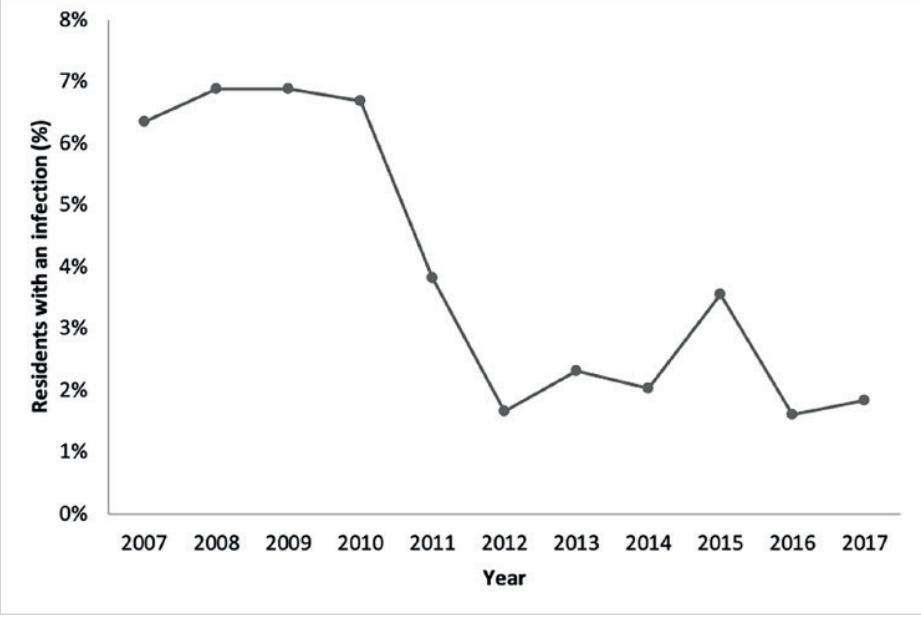

Figure 1. Trend for the percentage of residents with an infection per year

The most prevalent HCAI was UTI with an overall prevalence of 1.5%. For 2010 and 2011 the prevalence of UTI was 3.5% and 2.1%, respectively. For the years 2012 until 2017 the prevalence was 0.7%, 1.2%, 0.8%, 2.6%, 0.6%, and 0.7%, respectively.

The overall prevalence of other HCAIs was 1.0% for pneumonia, 0.2% for bacterial conjunctivitis, 0.1% for bloodstream infection, and 0.2% for gastroenteritis.

Most HCAIs occurred among residents of rehabilitation units (mean: 6.7%; range: 0.7-18.5%), followed by residents of somatic units (3.2%; 1.5-7.0%). Psychogeriatric residents had the lowest overall rates (2.3%; 1.2-4.7%). The prevalence of HCAIs varied by nursing home. The lower limit of the range of HCAIs was 0% every year and the upper limit varied from 8.7% to 37.0%. The number of residents included in each nursing home varied every year, with a mean of 55 residents included at a nursing home (range: 6-268). Over the years 2010-2017 there was a steady increase in the number of residents residing in one-person rooms (from 62.5% to 85%).

Within the Dutch nursing home system, residents are classified by the kind of disorder or disability for which the resident needs care. This care is divided into classes, the so-called 'care profiles'. Over the years the population of residents with the care profile 'protected living with intensive dementia care' made up the majority (49.4%; range: 44.7-53.5%) with an average HCAI prevalence of 2.4% (range: 1.5-5.0%).

The most common medical device was an indwelling urethral catheter (mean: 6.5%; range: 5.2-7.7%), followed by suprapubic catheter (3.9%; 2.9-4.4%), percutaneous endoscopic gastrostomy tube (1.5%; 0.1-2.5%), and intravascular device (0.4%; 0.0-1.3%). The overall prevalence of antibiotic use was 6.0% (range: 5.5-7.0%). On average 2.9% (1.0-3.8%) of the residents were using antibiotics due to an HCAI and 3.1% were using antibiotics for infections not classified as nosocomial. For yearly prevalence rates of antibiotic use by residents due to and not due to an HCAI, see Figure 2.

On average 64.3% of residents were incontinent in any form (faecal, urine, or both). However, the overall percentage of residents using incontinence material was 73.5%. Consequently, 10% of residents wore incontinence material while they were not classified as incontinent. Over the years the percentage of residents who have an UTI and were incontinent was significantly higher than the percentage of residents who had a UTI and were continent (3.7 vs 0.4%; $P = 0.009$).

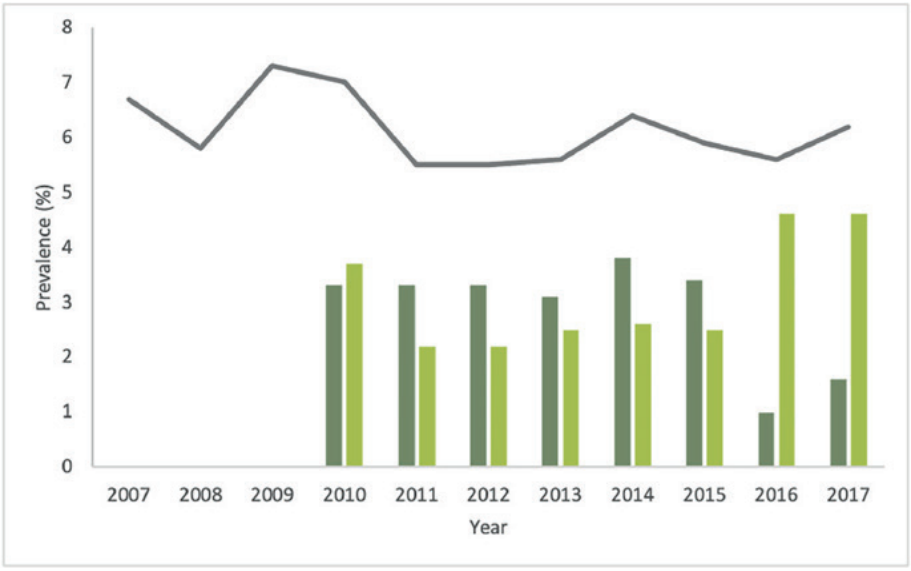

Figure 2. Yearly prevalence rates of antibiotic use due to healthcare-associated infection (HAI; dark green bars) and not due to HAI (light green bars). Grey line: prevalence of antibiotic use in total. For the years 2007-2009 no data were collected on the reason for antibiotic use (HAI or no HAI)

Discussion

Since reporting the first point-prevalence study in Dutch nursing homes, many other reports have followed [2, 4-6]. Improvements have been made over time between the various surveillance systems, by using identical definitions and timing their activities, e.g., measuring in the same season [11].

This study showed an overall mean HCAI prevalence of 3.1% which is lower than the overall mean prevalence of 7.3% published in 2011 [2]. The prevalence of 3.1%, however, is still in the range of HCAI prevalence found by Nicolle in a review of HCAIs in various countries [8]. From 2007 to 2010 the prevalence of HCAIs did not change, but it fell significantly in 2011 and stayed low over the following years. The same effect was observed by Geubbels *et al.* after introduction of surveillance in the Dutch hospital system, but in hospitals the decrease occurred a year earlier [12]. The observed decrease in HCAI might be attributable to an increase in general attention for infection control in the nursing homes, initiated by the feedback of the surveillance results. That the decrease occurred earlier within the hospitals, as compared to the nursing homes, possibly had to do with better established infection control within the hospital setting. Structural improvements to homes over the surveillance period

probably contributed to the improvement observed. Improvements to existing homes, and the opening of new homes, increased the number of residents occupying single-person rooms.

One of the most important conclusions of our study is to motivate those introducing infection control and surveillance into a new setting - to lead them not to expect immediate results, but to continue their efforts for multiple years despite the fact that the improvement is not directly showing in the surveillance results. As seen, changes take time to be implemented and to impact on the infection rate.

The range for maximum HCAI prevalence obtained was 8.7%-37%, thus showing a larger than expected range. Care needs to be taken when interpreting this data, since the number of residents included in each location varied widely. When the prevalence of HCAI is recurrently high, and the percentage of a certain HCAI - e.g., UTI - is disproportionally high, interventions need to be implemented after in-depth analysis of the local situation in co-operation with the local care team (elderly care physician and nurses). Therefore, it is recommended to conduct point-prevalence studies for several continuous years, if possible multiple times a year, in order to obtain more accurate estimates of a possible incidence.

In the present study the average use of antibiotics was 6.0% and was comparable with the 6.6% found in the previous point-prevalence study by Eikelenboom-Boskamp and well within the crude antibiotic prevalence range of 1.0%-12.1% found in the European HALT-2 study [2,6]. However, as a reduction in HCAI was found, we expected to see a decrease in antibiotic use as of 2012. This was not the case. This may in part be explained by the fact that about 50% of all antibiotics were used by residents who were not classified as having a nosocomial infection. This may be partly due to the possibility that, despite the (partial) absence of diagnostic criteria for an infection, antibiotics were still prescribed [13]. Another explanation may be that residents were still receiving suppressive/prophylactic antibiotic treatment for recurrent UTI, despite the recommendation by the Dutch Society of Elderly Care Physicians to limit that practice [9].

Compared to the previous point-prevalence study where the overall prevalence of UTI was 3.8%, this study found an overall UTI prevalence of 1.5%, which is a remarkable reduction measured in the same case-mix population. Based on the results of the previous study, where non-catheter-associated UTI was the most frequently recorded HCAI, attention has been directed to incontinence and the use of incontinence materials, which might explain the drop in UTI rates, as one of the improvements in the nursing

homes was directed at the prevention of prolonged use of incontinence materials [2]. Previously, incontinence material was not changed until maximum level of saturation was reached (complete saturation according to the built-in indicator strip). In addition, the availability of incontinence material per resident may have been insufficient due to financial reasons. While it seems conceivable that prolonged exposure, especially to faeces, should be prevented in order to prevent UTIs, the only study reporting on the frequency of change of incontinence material showed no evidence for an increased risk of developing UTI in relation to use of incontinence material [14].

This study shows a significant difference in the percentage of residents who have a UTI and were incontinent compared to the percentage of residents who have a UTI and were continent. Other studies show that incontinence is a risk factor for bacteriuria [15, 16]. Recently, Dutch care for the elderly has seen a shift in the focus on incontinence toward focusing on maintaining residents' continence for as long as possible. We included measurements of incontinence and use of incontinence materials in our surveillance as of 2012. Thus, we were able to show that about 10% of the nursing home residents using incontinence materials had no established medical need for their use. There is a lack of studies investigating whether wearing incontinence materials can lead to incontinence and therefore promote UTI. However, we assume that a sufficient 'toilet-policy' is preferred over providing incontinence material to residents. The assessment of incontinence and use of incontinence materials seem to be an important step in the management and prevention of UTIs, although more research is necessary.

Last but not least, the adaptation in the definition of a UTI might explain a part of the reduction in UTI found. From 2012 the national definition of UTI was strictly applied, based on diagnostic criteria creating more standardized results. However, these aspects do not explain the major reduction in UTI from 3.8% over the years 2007-2009 to 2.1% in 2011.

Since prevalence studies are easy to perform and may provide valuable information to guide future healthcare improvement projects, increased awareness of the problem of HCAIs and possible risk-factors, such as the use of incontinence materials, is an important motivator to implement improvements and thereby increase client safety. The effect of those improvements may take years to result in decreased HCAI rates. The HCAI point-prevalence studies can furthermore easily be combined with gathering data on antibiotic use, which is needed to establish antimicrobial stewardship in nursing homes.

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Conflict of interest statement
None declared.

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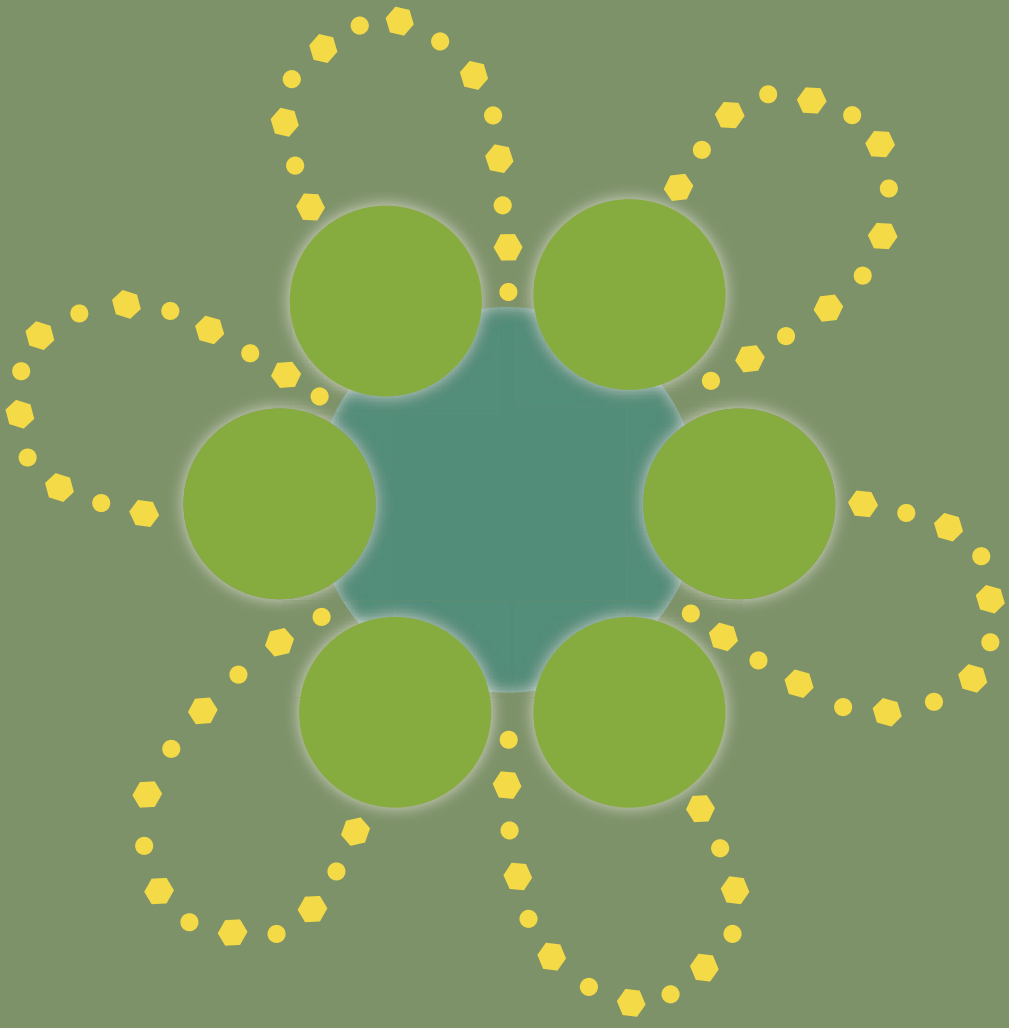

Chapter 4

Effectiveness of various hand hygiene interventions and nudges in nursing homes using an electronic hand hygiene monitoringsystem

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Submitted

Abstract

Objective: To assess the impact of various interventions and nudges on compliance with hand hygiene events (HHEs) in a nursing home, measured by an electronic hand hygiene monitoring system.

Design: A one-group uncontrolled quasi-experimental study.

Setting: Nursing home's rehabilitation unit with 23 beds and one for hemodialysis.

Interventions: The study comprised five intervention phases, preceded by a baseline phase (phase 0). Various interventions and nudges were implemented to assess their impact on hand hygiene events, measured by an electronic hand hygiene monitoring system at a group level throughout a 22-month study period. The interventions and nudges included education, compliance feedback via weekly newsletters - in which during a subsequent phase, the unit's achievement of their self-set goal was assessed - illuminated digital clocks, and a scent system.

Results: The results of the time series analysis indicated that the implementation of the interventions and nudges as a whole, during the intervention period, led to a significantly effect in comparison to the baseline period (429.54, 95%CI: 315.17-543.92, p <0.000). Moreover, the observed effect size was deemed large (d=1.25). Phase 1, involving education, compliance feedback via weekly newsletters, and goal-setting questionnaires, had a significantly positive impact on HHEs (level change 300.19, SE 98.02, t 3.06, sig. 0.003). Including the self-set goal in the weekly newsletter also had a positive, though not statistically significant, effect. Considering only the selected nudges, they appear to have very limited impact, although the HHEs remained above the baseline level.

Conclusions: Our study reveals a positive impact on compliance with HHEs through the implementation of various interventions. Further research is required to investigate the combination of interventions and nudges that could lead to a more effective and sustainable positive impact on HHEs, with a particular focus on nudges, given their budget-friendly nature and ease of implementation.

Introduction

The World Health Organization (WHO) has identified hand hygiene as one of the most important steps in preventing healthcare associated infections (HAIs).[1] Nonetheless, adherence to the WHO 5 moments of hand hygiene is low among healthcare workers in long-term care facilities, with rates ranging from 11% to 27%, as measured by direct observations.[2-8] Efforts to enhance hand hygiene through multimodal interventions resulted in an increase in hand hygiene compliance from 7 to 26% .[4,5,7]

In recent years, another intervention using nudges has gained attention to change behavior of healthcare workers (HCWs). Nudges are intended to influence behavior without the individual being aware that their current behavior is caused by an intervention. One of those interventions classified as nudges is primes. Priming refers to the phenomenon that stimuli have been shown to influence higher-order cognitive and behavioral outcomes without the individual's awareness or appreciation of this influence.[9] This can be a visual, auditory, or olfactory prime. Beyond conscious awareness, the brain registers the stimulus and activates a concept (such as cleanliness) or an emotion. The activation of this concept unconsciously guides the behavior. In a limited number of studies conducted within hospital settings, it has been shown that certain primes, such as flashing lights affixed to the dispenser[10], a clean citrus smell[11], male eyes[11], and posters[12] can effectively serve as interventions to positively influence hand hygiene compliance. To the best of our knowledge, no study has been conducted thus far that has implemented primers in nursing homes.

To assess whether hand hygiene improvement strategies have an effect, direct observation is considered the gold standard.[1] An alternative approach is the use of an electronic hand hygiene monitoring system (EHHMS) that requires less time, does not necessitate trained observers, and reduces observation bias.[13,14] Especially within nursing homes, this could potentially serve as a feasible alternative, given the constraints on financial resources, staffing levels, and the availability of an infection prevention and control professional. The aim of our study was to determine the effect of various interventions and nudges on hand hygiene events within a nursing home using an EHHMS.

Methods

Study design and setting

We performed a one-group quasi-experimental study to evaluate multiple interventions and nudges (henceforth, abbreviated as interventions) aimed at improving to hand hygiene among healthcare workers (HCWs), using hand hygiene events (HHE) measured by an EHHMS as the outcome. This study was conducted in a rehabilitation unit within a nursing home, consisting of 23 beds and one bed for hemodialysis.

Electronic hand hygiene monitoring system

All 59 existing hand rub (43) and soap dispensers (16) were replaced by EHHMS. The EHHMS detected HHEs with each depression of the dispensers, encompassing both hand rub and soap dispensers. If the dispenser was depressed more than once within two seconds, this was counted as one HHE. The EHHMS provided feedback at a group level. Data were transmitted via encrypted WLAN (Wi-Fi) to a centralized monitoring platform. Data were stored in case of a potential Wi-Fi disruption and transmitted when Wi-Fi functionality was restored. Each dispenser was equipped with a built-in system that would notify the supplier of a software failure that could hinder data transfer.

Interventions with timeline

The study commenced with phase 0 to assess the baseline HHEs, followed by an intervention period consisting of phase 1 to 5. In the original plan, the following timeline was set for the implementation of the interventions: a twenty-seven-week baseline period and thirteen weeks for each subsequent intervention. Due to unforeseen circumstances, our project experienced changes that impacted its timeline and progression. As a consequence, some interventions were not implemented separately as initially planned, and their effects could only be evaluated as a bundle instead of separately.

The interventions with the timeline conducted during all phases are listed in Table 1.

Statistical analysis

HHEs data were exported from the EHHMS to Excel. Daily HHEs, adjusted for bed-occupied days, were presented as performance feedback in the weekly newsletter. To assess the unit's goal achievement, adjusted weekly HHEs were divided by the target number, expressed as percentages. The goal was established by aggregating HCWs' survey responses and dividing by the number of respondents.

For subsequent data analysis, the data was imported into IBM SPSS Statistics version 27. Adjusted daily HHEs were described as mean, standard deviation (SD), minimum (min) – maximum (max). Paired sample t-test compared mean adjusted daily HHEs between the baseline period (phase 0) and the intervention period (phase 1 to 5). Effect size measure was performed by using Cohen's d.

The mean adjusted weekly HHEs were graphed, marking different study phases. To estimate intervention effects, we used an autoregressive integrated moving average (ARIMA, p=1,d=0,q=0) model, accounting for autocorrelation. Phases were added as dichotomous variables, indicating intervention inactivation (0) and activation (1). To indicate the change in slope, consecutive numbers were assigned, starting with value 1 at one week after the initiation of the intervention. In this context, we assumed that the interventions conducted in phase 1 had an aftereffect extending through phase 3, because we are of the opinion that education logically has an aftereffect, and the distribution of the weekly newsletter continues in phase 2 and 3. Not accounting for an aftereffect would have resulted in an overestimation of the effect. The observation period, influenza outbreak, and contact tracing prompted by an unexpected MRSA-positive resident were included in the model as covariates for which the same coding was applied. Subsequently, in order to assess the effect of each phase in which the interventions were implemented compared to the baseline (phase 0), phases 1 to 5 were added to the model, as well as the covariates. The level change was incorporated into the model, whereas the slope change was not, as it did not yield a substantial improvement to the model and complicated the interpretation. This was attributed to the fact that the phases during the intervention period had varying durations. Finally, to gain insight into the effect between the separate subsequent phases, one phase was compared to the following phase for level and slope changes. This allowed insight into the trend of HHEs during the study period.

To determine model reasonable model fit, we assessed the parameters, observed-fitted value graphs, and residual plots. Two-sided p-values ≤ 0.05 were considered statistically significant.

Table 1. Interventions conducted during all phases

Phase	Intervention		Duration
Phase 0	Baseline registration	This phase began with measuring the baseline for HHEs. All existing alcohol-based hand rub and soap dispensers were replaced by EHHMS at the same location eight weeks prior (see Phase 3 for dispenser locations). Four weeks after the dispensers were installed, the company resolved a technical issue in ten dispensers. This problem did not recur thereafter. HCWs were informed that the dispensers were replaced but were not made of the dispensers' capability to measure usage. Hand hygiene observations were conducted over a period of five weeks, totaling 25 hours during the morning shift. HCWs were informed that someone would be present to conduct infection prevention observations in general. The objective of these observations was to gain insight into the performance of hand hygiene by HCWs, to be used for teaching purposes planned for phase 2 of the study, focused on the performance of hand hygiene at moment 1, 4, and after glove removal (moment 3).	37 weeks
Phase 1	Start performance feedback in weekly newsletter following preceding education, questionnaire goal setting	This phase commenced with performance feedback through the distribution of a weekly newsletter. The initial newsletter, which included information on HHEs in the past week, was distributed during a team meeting that concurrently included hand hygiene education. The education covered several topics, the importance of hand hygiene, the 5 moments of hand hygiene according to the WHO combined with the findings obtained during the observations in phase 0, the technique of hand hygiene, and the ongoing hand hygiene events measurements results. Following the initial distribution, the newsletter was sent weekly on the same day via email to the unit's mailing list and designated contact persons. These persons were responsible for printing and posting the newsletter on the bulletin board in the team room. Additionally, a questionnaire was distributed with the aim of setting a goal for the number of HHEs the unit aimed to achieve per resident per day. The questionnaires, labeled with room numbers, were distributed to the attending HCWs in a random order. HCWs who were not present received a questionnaire in their mailbox. To assist HCWs in establishing a target for the unit, various questions were posed, addressing how frequently they interact with the resident during the day and the tasks they carry out for the resident. All 23 HCWs received the questionnaire.	12 weeks
Phase 2	Performance feedback in weekly newsletter with goal	This phase commenced by mentioning the extent to which the unit had achieved the goal they had set for themselves in the weekly newsletter, see Figure 1 (for this publication translated to English).	9 weeks

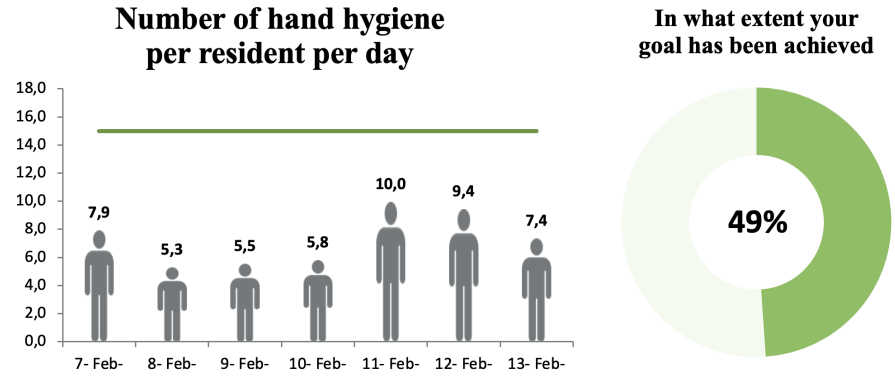
Continuation Table 1. Interventions conducted during all phases

Phase	Intervention		Duration
Phase 3	Performance feedback in weekly newsletter with goal and red illuminated digits on digital clocks	This phase commenced by implementing a nudge: digital clocks with red illuminated digits (referred to as clocks hereafter) were placed on top of each EHHMS (see Figure 2), in addition to the weekly newsletter with goal. At the entrance and exit of the resident's room, the hand rub dispenser was placed on the wall where the door was located, making the clocks not immediately visible upon entry but noticeable upon leaving the room (see Figure 1, option 1), or placed on the side wall upon entering (see Figure 1, option 2). In the bathroom, the hand rub and soap dispensers were positioned on the wall next to the sink, nearly directly across from the toilet, making the clocks immediately visible. In the communal area, the hand rub and soap dispensers were located above the various countertops, making the red illuminated digits immediately visible. On the two medication trolleys, the hand rub dispensers were affixed with a standard, with the red illuminated digits visible from the front of the trolley.	8 weeks
Phase 4	Stop performance feedback in weekly newsletter with goal, only clocks	In this phase, the weekly newsletter with performance feedback and goal was discontinued, while the clocks on the dispensers remained.	19 weeks
Phase 5	Clocks and scent system	This phase commenced by installing a scent system (nudge) in the corridor of the unit with a fragrance chosen and assessed as refreshing by two HCWs. The clocks placed on the top of the dispensers remained.	9 weeks

NEWSLETTER HAND HYGIENE

Dear healthcare workers from team 1 and 2,

Hereby, you receive our thirteenth newsletter in which you can read about how often you have used as a team the hand soap en hand rub dispensers per resident per day. Your goal is fifteen hand hygiene events per resident per day, represented by the grey line.



Hand hygiene is the most crucial measure to prevent infections

Figure 1. Performance feedback in weekly newsletter with goal

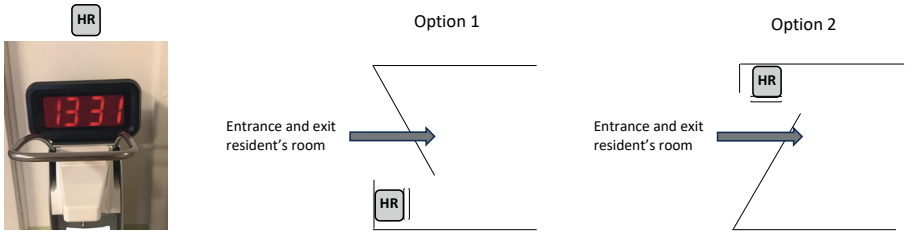


Figure 2. Red illuminated digits on digital clocks placed on the top of each hand rub and soap dispenser HR: Hand rub dispenser

Ethical approval

The institutional research committee was notified about the trial and decided to participate. The study was deemed not subject to the Medical Research Involving Human Subjects Act (WMO) and, as a result, did not undergo a full review by an accredited MREC.

Results

HHEs per resident per day

Overall, the mean HHEs per resident per day during the baseline period were lower compared to the period in which all interventions took place, 8.45 and 13.41, respectively. The mean difference in HHEs per client per day between these two periods was 4.96 (95%CI: 4.27- 5.65), identified as a significant difference ($p < 0.001$). The effect size was deemed large ($d=0.88$). As illustrated in Table 2, the mean HHEs per resident per day showed an increase during phases 1 and 2, followed by a subsequent decline. By the end of the study period, the HHEs were slightly higher compared to the baseline period (phase 0). The ratio between the use of hand rub and the use of soap remained the same before and after the start of the interventions, namely 4:1, respectively.

Goal setting

The questionnaire distributed during phase 1 was completed by 65% (15/23) of the HCWs. The goal for HHEs per resident per day was set at 15 HHEs (range: 5 – 25). However, this goal was not achieved in phases 2 and 3 where the goal was included in the weekly newsletter. The mean percentage of goal achievement during these two phases was 46.44% (SD 8.15, min – max 36 – 68%).

HHEs per week

Figure 3 presents the mean HHEs per week, adjusted for occupied bed days, throughout the study period in which the interventions took place.

Based on the results of the time series analysis (level change -150.22, SE 79.583, t -1.888, sig. 0.08; slope change 50.487, SE 30.570, t 1.651, sig. 0.12), in which we compared the observation period in phase 0 with the period before, we decided not to include the observation period as a covariate in the subsequent analysis.

Table 2. HHEs per resident per day during all phases

Phases‡	Total HHEs per resident per day	
	Mean (SD)	**Min, Max**
Phase 0#	8.45 (2.78)	3.68, 28.96
Before observation only	7.68 (2.09)	3.90, 15.71
Observation only	7.58 (2.67)	3.68, 17.23
After observation only	9.25 (3.05)	4.30, 28.96
Phase 1	12.22 (3.44)	4.89, 24.07
Phase 2^	16.52 (4.93)	8.06, 32.63
Influenza outbreak only	19.59 (5.91)	10.57, 32.63
After influenza outbreak only	14.77 (3.71)	8.06, 24.48
Phase 3&	13.90 (3.98)	6.91, 24.54
Before contact tracing only	12.66 (3.65)	6.91, 19.27
Contact tracing only	15.32 (3.56)	10.97, 22.40
After contract tracing only	15.09 (4.36)	7.55, 24.54
Phase 4	10.75 (3.63)	4.63, 21.38
Phase 5	9.50 (2.57)	4.03, 17.30

‡ Interventions conducted during all phases are listed in Table 1; # Baseline, including observation; ^ Interventions, including influenza outbreak; & Interventions, including contact tracing due to unexpected MRSA-positive resident

Logically, the mean difference in HHEs per week between the baseline period and the intervention period was also identified as significant (429.54, 95%CI: 315.17-543.92, p <0.000), and the effect size was deemed large (d=1.25). However, time series analysis estimated level changes in HHEs per phase, including the covariates influenza and contact tracing MRSA, did only demonstrated a statistically significant immediate effect in phase 1 (level change 300.19, SE 98.02, t 3.06, sig. 0.003), see Table 3. In the phases that followed, the effect of the interventions on HHEs was not statistically significant. At the start of phase 2, there was an increase in HHEs once again, hence; hence it appears that the HHEs in phase 2 were the highest, partly due to the three-week-long influenza outbreak. In contrast, at the beginning of phase 3, a drop in HHEs was observed, while the contact tracing MRSA contributed to an increase in HHEs. Once more, an immediate effect on HHEs was observed at the commencement of phase 4 and 5.

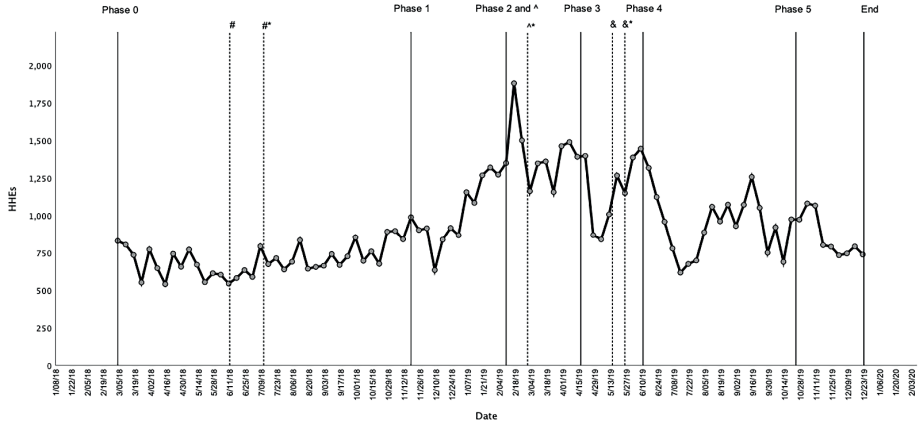


Figure 3. Mean HHEs per week across all phases

Phase 0. Start measurement of hand hygiene events; #) start observations, #*) stop observations; Phase 1. Education, performance feedback in weekly newsletter, and distribution questionnaire goal setting; Phase 2. Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal; ^) start influenza outbreak, ^*) stop influenza outbreak; Phase 3. Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal and red illuminated digits on digital clocks, hereafter referred to as clocks; &) start contact tracing due to unexpected methicillin-resistant *Staphylococcus aureus* resident, &*) stop contact tracing; Phase 4. Discontinuation of performance feedback in weekly newsletter with the extent to which the unit's goal achievement, while maintaining the clocks; Phase 5. Clocks and scent system. The solid vertical lines marked phase 2, also denote the commencement of the influenza outbreak, as it coincided concurrently with the start of phase 2.

Table 4 displays the results of the time series analysis on HHEs level and slope changes of one phase compared to the subsequent phase, including covariates. Although the results did not demonstrate any statistically significant changes in the level or slope of HHEs between one phase and the subsequent phase, these comparisons also reveal that the most pronounced effect seemed to be achieved by conducting a combination of education and performance feedback with the extent to which the unit had achieved the goal (phase 1 and 2). Both level and slope changes were positive. In phase 3, there is an immediate decrease in HHEs compared to phase 2, although the slope, which is relatively flat, exhibits a positive trend. In phase 4, where the weekly newsletter with the goal was discontinued, and only the clocks placed on the dispensers remained, another immediate decrease in HHEs was observed compared to phase 3. Also, in phase 4 the change in slope was negative. In phase 5, during which a scent system was introduced in addition to the clocks, a positive change in HHEs level was observed compared to phase 4, although the slope change was still negative.

Table 3. Autoregressive model estimated level changes in HHEs per phase during intervention period compared to the baseline. Covariates (influenza and contact tracing MRSA) included

	Estimate	SE	t	Sig.
Phases				
Phase 0[0], baseline	749.06	54.30	13.80	0.000
AR	0.57	0.10	5.73	0.000
Level change phase 1[1]	300.19	98.02	3.06	0.003
Level change phase 2[2]	177.617	138.71	1.28	0.20
Level change influenza	195.44	143.29	1.36	0.18
Level change phase 3[3]	-160.67	131.57	-1.22	0.23
Level change contract tracing MRSA	124.76	132.29	0.94	0.35
Level change phase 4[4]	138.85	83.22	1.67	0.10
Level change phase 5[5]	149.51	105.16	1.42	0.16

[0]Start measurement of hand hygiene events; [1] Education, performance feedback in weekly newsletter, and distribution questionnaire goal setting; [2] Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal; [3] Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal and red illuminated digits on digital clocks, hereafter referred to as clocks; [4] Discontinuation of performance feedback in weekly newsletter with the extent to which the unit's goal achievement, while maintaining clocks; [5] Clocks and scent system.

Discussion

Our study, utilizing an EHHMS, has demonstrated that the interventions we implemented had a positive effect on HHEs in nursing homes, indicating an increase hand hygiene compliance. The phase 1 intervention, involving the distribution of a weekly newsletter with HHEs per resident per day and the determination of a self-set HHE goal-rate, significantly contributed to this outcome. Adding the extent to which the unit achieved its self-set goal in the weekly newsletter did not show an additional significant effect in our study. An explanation could be the demotivating factor of not attaining self-set goals, which may require earlier adjustments, aiming to establish more realistically achievable objectives from the beginning. Introducing interim targets could potentially serve as a solution to that problem.

Given the design of our study, in which we combined nudges with established interventions, we were unable to demonstrate whether a positive effect would have also been achieved solely through the deployment of nudges. The clocks (first nudge) were introduced in phase 3, while another intervention continued from phase 2. As a result, the effect may have been influenced even when only this nudge was present in phase 4. In addition, the first nudge remained in place even when the scent system (second nudge) was introduced in phase 5. Although, in general, the selected nudges seem to have had limited effect, although the HHEs level still remained above the baseline level.

Table 4. Autoregressive model on HHEs level and slope changes of one phase compared to the subsequent phases

Phases	Estimate	SE	t	Sig.
Phase 1[1]				
Phase 0[0], baseline	700.14	25.85	27.08	0.000
AR	0.35	0.14	2.47	0.018
Level change phase 1[1]	89.95	79.306	1.13	0.26
Slope change phase 1[1]	41.48	11.596	3.58	0.001
Phase 2[2] (incl. influenza outbreak)				
Phase 1[1]	1028.60	86.20	11.93	0.000
AR	0.339	0.28	1.21	0.24
Level change phase 2[2]	38.07	350.32	.11	0.92
Slope change phase 2[2]	49.56	58.09	.85	0.41
Level change influenza	305.15	392.25	.78	0.45
Slope change influenza	70.98	161.27	.44	0.67
Phase 3[3] (incl. contact tracing MRSA)				
Phase 2[2] C + MRSA	1328.15	114.54	11.60	0.000
AR	0.083	0.46	0.18	0.86
Level change phase 3[3]	-158.44	228.89	-0.69	0.51
Slope change phase 3[3]	0.26	45.74	-0.01	1.00
Level change influenza	162.34	264.81	0.61	0.56
Slope change influenza	82.08	194.36	0.42	0.68
Level change contact tracing MRSA	-135.94	320.10	-0.43	0.68
Slope change contact tracing MRSA	235.02	374.73	.0.63	0.55
Phase 4[4]				
Phase 3[3]	1170.06	141.56	8.27	0.000
AR	0.62	0.16	3.87	0.001
Level change phase 4[4]	-11.069	173.96	-0.06	0.95
Slope change phase 4[4]	-21.09	15.45	-1.37	0.19
Phase 5[5]				
Phase 4[4]	984.18	118.28	8.32	0.000
AR	0.74	0.14	5.23	0.000
Level change phase 5[5]	206.23	160.04	1.29	0.21
Slope change phase 5[5]	-51.59	30.49	-1.69	0.10

[0]Start measurement of hand hygiene events; [1] Education, performance feedback in weekly newsletter, and distribution questionnaire goal setting; [2] Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal; [3] Performance feedback in weekly newsletter with the extent to which the unit had achieved the goal and red illuminated digits on digital clocks, hereafter referred to as clocks; [4] Discontinuation of performance feedback in weekly newsletter with the extent to which the unit's goal achievement, while maintaining the clocks; [5] Clocks and scent system.

The time series analysis conducted to assess the changes in level and slope between one phase and the subsequent phase did not show statistically significant differences. A notable observation during the intervention period was the immediate decrease in HHEs during phase 3, corresponding to the placement of clocks on the dispensers as an additional intervention beyond those implemented in the previous phases. We cannot explain this immediate drop in HHE. It seems that the clocks, which were intended to draw extra attention to the dispensers, had a detrimental effect on dispenser usage, despite the fact that the use of the elbow-operated dispensers was not hindered by the presence of the clocks. An explanation could be that the clocks may have primed HCWs to hasten their activities and skip hand hygiene. Despite the fact that the HHEs remained above the baseline with the implementation of this nudge, as well as the addition of the scent system, the results are disappointing, warranting the examination of other nudges.

A noteworthy finding was the peak in HHEs observed during the influenza outbreak in phase 3. We are familiar with this phenomenon from several studies conducted in hospital settings regarding hand hygiene compliance in relation to outbreaks. Hand hygiene is more frequently applied to isolated patients than to non-isolated patient[16], and hand hygiene, as considered by HCWs, is particularly aimed at protecting themselves from cross-infection.[17,18] This latter result aligns with the findings made by Israel et al. who stated that HCWs are afraid of being infected. They found a marked enhancement in hand hygiene compliance in the COVID-19 area.[19] The negative change in level and slope in phase 4 could possibly be attributed to the discontinuation of performance feedback in the weekly newsletter, including information on the extent to which the goal was achieved.

Our study has several limitations, of which two are the most important ones. Firstly, there was an absence of a control group. The unit consisted of two teams, although we could not allocate these teams into intervention and control groups due to their close collaboration and frequent interchange of HCWs between the teams. Secondly, our study quantified dispenser usage, omitting an exploration of whether hand hygiene adhered to the WHO 5 moments of hand hygiene. Nevertheless, research conducted in hospitals has demonstrated that a comparable EHHMS and HHE's are valid indicators for hand hygiene.[20-22]

Another limitation of our study was that we were unable to separately measure the effect of the different interventions. Furthermore, beyond the dispensers being utilized by HCWs, there were also used by residents and visitors. However, we would not expect a change in use by that group, as the interventions were primarily geared towards HCWs. Finally, the weekly newsletter was sent via email with the request to print and display the newsletters in the team room. We were unsure whether this was consistently followed.

To achieve sustainable enhancement of hand hygiene in nursing homes, continuous effort is required. Therefore, infection prevention and control (IPC) professional or linked nurses could play a role in this. A recent study by Ali-Brandmeyer et al. demonstrated significantly higher hand rub usage in nursing homes with an IPC-linked professional.[23] Moreover, when developing and implementing hand hygiene programs, it is important to consider setting-specific determinants.[8,24]

The findings of our study indicate that the combined interventions and nudges achieved a positive effect on HHEs in nursing homes, although the additional effect of the selected nudges was very minimal. Therefore, the use of an EHHMS to provide feedback at a group level seemed to be a useful and feasible approach. Further research is needed to explore which combination of interventions and nudges could contribute to achieving a more effective and sustainable positive effect on HHEs, taking into account setting-specific determinants. It would be intriguing to investigate, especially, how nudging strategies can anticipate the determinants[8,24] in this setting, given their budget-friendly and ease of implementation. Additional research is also needed to explore the feasibility of implementing EHHMS on a regular basis in nursing homes.

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Conflict of interest statement
AE, KS, and AV report no conflict of interest.

Siegfried Steltenkamp also employed by and member of the Department of New Technologies at Ophardt Hygiene Technik GmbH + Co. KG.

Bert Pol and Daniëlle Broeze report no conflict of interest.

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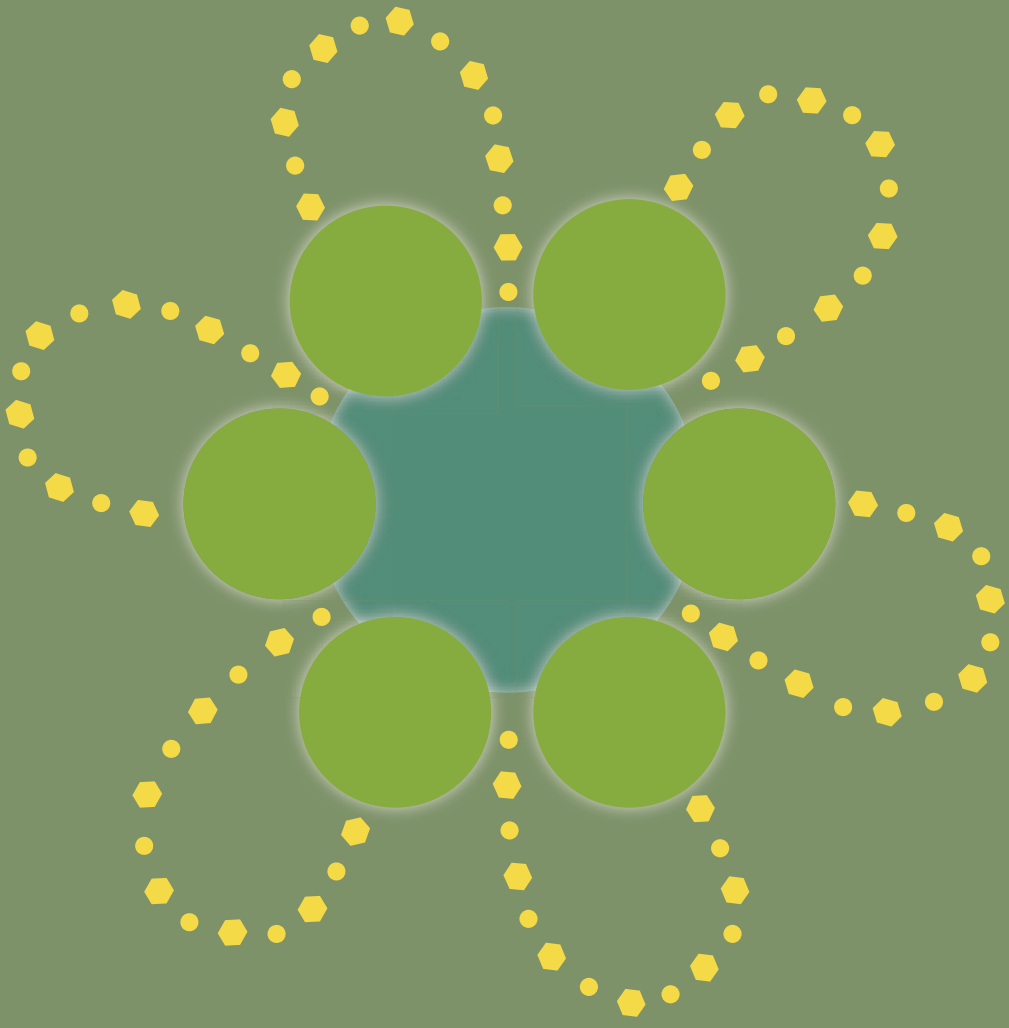

CHAPTER 5

Preferences for healthcare worker attire among nursing home residents and residents' preferences as perceived by workers: A cross-sectional study

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Abstract

Background: In Dutch nursing homes, healthcare workers' attire has been the subject of debate for years. White uniforms and professional white jackets are increasingly being replaced by casual personal attire. Many nursing homes have made this choice because they want to create a homey atmosphere. However, with regard to infection control, casual personal attire is far from ideal. It is unknown what attire is preferred by residents.

Objective: To determine both residents' preferences regarding nurses' attire and nurses' perceptions of these preferences.

Design: Cross-sectional.

Setting: Nursing homes, the Netherlands.

Participants: Residents and nurses.

Methods: Between February and October 2019, a convenience sample of 94 participants were surveyed across 10 Dutch nursing homes among residents with physical impairments and nurses caring for them. A standardized data collection tool included color photographs of a female nurse dressed in: 1) casual attire; 2) professional polo shirt with blue jeans; 3) professional white jacket with blue jeans; and 4) completely white uniform. Six randomly composed photosets of two different types of attire were shown to each participant. Participants had to select one out of two displayed photographs (forced choice method) guided by two propositions regarding 'comfort preference' and 'care preference'. The propositions for residents were: 1) I feel most comfortable with this nurse, and 2) I would prefer to be cared for by this nurse. The propositions for nurses were: 1) I think residents feel most comfortable with this nurse, and 2) I think the residents would prefer to be cared for by this nurse. Some demographic data and personal characteristics of the participants were collected. (Perceived) preferences for nurses' attire were calculated in estimated marginal means (preference per type of attire compared to the other three types of attire) with 95% confidence intervals. Differences were tested with the Chi-squared test.

Results: In total, 92 participants were included in the analysis. Overall, the strongest (perceived) preference was for a professional white jacket with blue jeans, compared to the three alternative types of nurses' attire for both propositions in both groups. Casual attire was the least preferred. Residents of 85 years or older and nurses who had been working for two years or fewer were more likely to choose more formal attire.

Conclusion: Residents preferred more professional attire, which conforms to infection control requirements.

Tweetable abstract: involve nursing home residents in determining nurses' attire, a professional white jacket should be one of the options @AEICP

Keywords: Attire, clothing, elderly care facilities, infection control, nursing homes, nurses, patient preference, resident preference

What is already known

According to the management of many nursing homes, white uniforms and professional white jackets do not suit a homey atmosphere. Therefore, these are increasingly being replaced by casual personal attire. Casual personal nurses' attire is far from ideal with regard to infection control measures.

What this paper adds

Our findings demonstrate that residents in nursing homes generally prefer (or are generally perceived by nurses to prefer) that nurses wear professional white jackets with blue jeans.

Regarding 'care preference' and 'comfort preference', there are differences in (perceived) preferences for attire between residents and nurses; however, casual attire was (perceived to be) the least preferred option in all cases.

Introduction

In Dutch nursing homes, the homey atmosphere is considered to be of great importance. Since 2008, many nursing homes have been eschewing professional attire; i.e., white uniforms and professional white jackets. This attire is perceived by nursing homes as having a 'hospital look' and not suitable in a home-like environment, especially in psychogeriatric care and the care of residents with physical impairments. Instead of professional attire, healthcare workers have increasingly been wearing personal attire or colored polo shirts (Spijkerman, 2008). Additionally, healthcare workers often have to purchase and launder attire by themselves. From an infection control point of view, there are concerns about this change in attire policy. Risk of contamination of nurses' attire is present in settings where nurses are caring for residents who are likely to have urinary or fecal incontinence. Regulators, nursing home administrators, and professional groups in the Netherlands are still discussing potential ramifications of this change in nursing attire policies.

Several researchers have examined the risks of microbial contamination of healthcare workers' attire. Gaspard et al. found high levels of methicillin-resistant *Staphylococcus aureus* contamination on healthcare workers' uniforms in elderly care settings (Gaspard et al., 2009). Heudorf and associates investigated laundry handling in nursing homes and found that used gowns had significantly higher levels of contamination compared to freshly reprocessed ones (Heudorf et al., 2017). Other researchers in hospital settings have shown frequent contamination of attire with potential pathogenic bacteria, including multidrug-resistant organisms (Perry et al., 2001, Wiener-Well et al., 2011, Mitchell et al., 2015). Furthermore, attire can also play a role in transmission of potentially harmful microbes in home and everyday life settings (Bloomfield et al., 2011).

The likelihood that contamination of healthcare workers attire leads to the development of healthcare-associated infections or multidrug-resistant organism colonization is not clear. What we do know is that in elderly care facilities, a high prevalence of multidrug-resistant organisms among residents does occur (Rooney et al., Verhoef et al., 2016, van Dulm et al., 2019). Given that nurses working in nursing homes have frequent (and intensive) physical contact with residents due to the fact that residents are unlikely to be able to perform daily activities, the risk of transmission from healthcare workers' attire to residents and vice versa is plausible.

In 2016, the Dutch Working Party for Infection Control issued requirements regarding healthcare workers' attire, including laundry rules regarding wash temperature and use of tumble drier or iron (Dutch Working Party on Infection Prevention 2017). At that time, it was already common in many facilities for nurses to wear personal attire. Hence, the requirements apply to both professional attire and personal attire.

However, due to the fact that many healthcare workers have to purchase and wash their attire themselves, it seems difficult or even impossible to monitor how healthcare workers launder their attire. Additionally, healthcare workers may not wash it at the proper temperature and dry it according to the laundry rules owing to the type of fabric (Dutch Working Party on Infection Prevention 2017). A German study performed in 44 nursing homes showed that attire washed by nursing staff at their own home had significantly higher contamination rates than attire washed in the certified external laundry or in nursing homes themselves (Heudorf et al., 2017). In addition, non-professional attire frequently does not meet other requirements for professional attire in healthcare, such as the requirement for short sleeves (Dutch Working Party on Infection Prevention 2017).

Since the start of the Coronavirus disease pandemic, the debate regarding nurses' attire has become more relevant. Currently, nursing homes are reconsidering their policies regarding healthcare workers' attire, returning to more professional attire that meets requirements with regard to washing, drying, and sleeve length, for example. However, residents' preferences are unknown. The objective of this study was to determine nursing home residents' preferences regarding nurses' attire and nurses' perceptions of residents' preferences.

Methods

Between February and October 2019, a convenience sample of 94 participants were surveyed across ten nursing homes in the South-East of the Netherlands. Forty-five of the participants were residents with physical impairments. Forty-seven of the participants were nurses of varying educational levels caring for residents with physical impairments. Prior to the study, a standard data collection tool was developed (PsychoPy®) and piloted among two residents and two nurses. Based on the results of the pilot, no changes were made. The data collection tool included color photographs of a female nurse dressed in: 1) a black t-shirt with blue jeans defined as casual attire; 2) a blue polo shirt with blue jeans (shortened to blue polo shirt); 3) a professional white jacket with blue jeans (shortened to professional white jacket); and 4) a completely white uniform, see Fig. 1. For each photo, the same female model was used. She was photographed in the same pose with a friendly expression and with the same solid background. Six randomly composed photosets of two different types of attire (photo: 1-2, 1-3, 1-4, 2-3, 2-4, 3-4) were displayed. The participants had to select (forced choice method) one of the two displayed photos, guided by two propositions. To compensate for left-right preferences, the same combinations were displayed in reverse (photo: 2-1, 3-1, 4-1, 3-2, 4-2, 4-3) within the same session. Hence, each participant was surveyed with 12 photosets per proposition. The two propositions concerned 'comfort preference' and 'care preference' which seem to compete with each other regarding nurses' attire. The propositions for residents were: 1) I feel most comfortable with this nurse (so-called 'comfort preference'), and 2) I would prefer to be cared for by this nurse (so-called 'care preference'). The propositions for nurses were: 1) I think residents feel most comfortable with this nurse (so-called 'comfort preference'), and 2) I think the residents would prefer to be cared for by this nurse (so-called 'care preference').

Figure 1. Photographs of a nurse wearing four types of attire: **1)** casual attire; **2)** blue polo with blue jeans; **3)** professional white nursing jacket with blue jeans; **4)** complete white uniform.

Residents were pre-selected by nurses to be approached for participation based on their cognitive ability (without a known diagnosis of dementia) and ability to understand and speak the Dutch language. Residents who did not meet these inclusion criteria were not approached for participation in the study. Subsequently, residents were approached by the researcher on a one-to-one basis in their rooms and were asked to participate in the study. Nurses were asked to participate when the researcher was visiting the facility. The participants were surveyed directly after they had given consent to participate. The researcher explained to all participants that results would remain anonymous, and results would be reported only by group, as mentioned in the study letter that they received at the same time during the visit. Moreover, the researcher explained to all participants that at any time they could withdraw from the study. In addition, the following demographic data and personal characteristics were collected: residents' sex, age, and whether or not they were incontinent; nurses' sex, age, and number of years they had worked in healthcare.

The results regarding the respondents' preferences collected in PsychoPy® were generated in a conditional logit model and analyzed by mixed-effects logistic regression using Jamovi version 1.6.23. Continuous variables are expressed as mean, median, interquartile range (IQR), or minimum-maximum (min – max] and illustrated with boxplots. Categorical variables are expressed as counts and percentages. The (perceived) preference scores for attire were calculated in estimated marginal means with a 95% confidence interval (CI) and illustrated with figures. These preference scores showed the preference per attire compared to the three alternative options for nurses' attire in this study. To determine whether age of residents and working years of nurses influenced preferences for attire in both propositions, residents were divided into two groups (≤ 84 years and ≥ 85 years) to perform a meaningful analysis. Nurses were classified into three groups based on working years (≤ 2, 3 to 10, and > 10 working years). Difference testing for comparisons of groups was calculated with the Chi-squared test. P-values less than 0.05 were considered statistically significant.

Ethical approval

The study was reviewed (File number CMO: 2018-4932**)** by the ethics committee of the Radboud University Medical Centre, which decided that the study was not subject to the Medical Research Involving Human Subjects Act and did not require full review by an accredited Medical Research Ethics Committee. The 'University Knowledge network for Older adult care Nijmegen', a regional network which

develops, distributes, and implements scientific knowledge, also reviewed the study. All participants provided written informed consent.

Results

The population surveyed consisted of 94 participants. For two participants, their status as either a resident or nurse and their age was missing; they were therefore excluded from further analysis. Of the 92 persons included in the analysis, 45 (48.9%) were residents and 47 (51.1%) were nurses.

The age of 37 residents and 37 nurses was known. The mean age of residents was 81.5 years (median 83.0 years; IQR 13.0 years, min – max: 56-96 years) and the mean age of nurses was 37.6 years (median 37.0 years; IQR 29.0 years; min – max: 17-61 years). Nineteen residents were 84 years or younger and 18 residents were 85 years or older. Among both the residents and the nurses, most of the participants were women; there were 27 (60.0%) and 42 (89.4%) respectively. The number of working years was known for 39 nurses. They had worked in their profession for 8.4 years on average (median 2.5 years; IQR 14 years; min – max: 0 – 43 years). Fourteen nurses had worked 2 years or fewer in healthcare and had a mean age of 27.8 years (median 25.0 years; IQR 8 years; min – max: 17 – 54 years). Ten nurses had worked 3 to 10 years in healthcare and had a mean age of 38.3 years (median 34.0 years; IQR 22 years; min – max: 23.0 – 61.0). Fourteen nurses had worked more than 10 years in healthcare and had a mean age of 49.8 years (median 52.0 years; IQR 6 years; min – max: 37 – 58 years). Incontinence was present in 15 (33.3%) of 22 residents. For eight (17.8%) residents, it was unknown whether they were incontinent or not. The continence status of some of the residents was not known either because the resident did not want to answer this question or because the researcher forgot to report their answer. Due to the limited number residents for whom the continence status was known, we did not analyze the data by this variable to compare the differences in preferences for nurses' attire.

Overall, the estimated marginal mean for professional white jackets was 0.70 (95% CI, 0.66-0.74), which was the highest value for both propositions in both groups, indicating that there was a strong estimated (perceived) preference for this attire compared with the other three types of attire. A blue polo and a completely white uniform nearly shared second place for (perceived) preference, with values of 0.52 (95% CI, 0.48-0.56) and 0.50 (95% CI, 0.46-0.54) respectively. Casual attire had a value of 0.28 (95% CI, 0.25-0.31), the lowest value. This indicates that there was significantly

less (perceived) preference for this attire ($p < 0.001$) compared with the other three types of attire.

Fig. 2. illustrates the estimated (perceived) preferences regarding attire by group and by proposition. Residents slightly preferred a professional white jacket regarding 'care preference' (0.70, 95% CI: 0.61-0.77) compared with 'comfort preference' (0.67, 95% CI: 0.59-0.75). According to nurses, residents preferred this attire even more during care (0.75, 95% CI: 0.67-0.81), although the preference with respect to feeling comfortable is equal to what residents had reported (0.67, 95% CI: 0.59-0.75).

Residents expressed a stronger preference for a completely white uniform regarding 'care-preference' (0.54, 95% CI: 0.46-0.63) compared with 'comfort preference' (0.46, 95% CI: 0.38-0.54). In the perception of nurses, the preference between the two propositions for this attire differed from residents, 0.60 (95% CI, 48.7-64.8) and 0.43 (95% CI, 35.2-51.3) respectively.

Residents preferred a blue polo shirt and casual attire less (0.54, 95% CI: 0.46 – 0.63 and 0.22, 95% CI: 0.16-0.29, respectively) for the 'care preference' than for the 'comfort preference' (0.59, 95% CI: 0.51-0.67 and 0.28, 95% CI: 0.21-036, respectively). The same trend was seen for the nurses (0.46, 95% CI: 0.38-0.54 and 0.22, 95% CI: 0.16-0.30, respectively versus 0.49, 95% CI: 0.41-0.57 and 0.40, 95% CI: 0.33-0.49, respectively).

The preferences for attire among the resident participants differ significantly between residents at the age of 84 years or younger and at the age of 85 years or older (χ^2 12.307, $p = 0.006$). As presented in Fig. 3, residents aged 85 years or older had a stronger preference for a professional white jacket or a completely white uniform (0.75, 95%CI: 0.66-0.82; 0.60, 95% CI 0.50-0.68) with regard to both propositions, rather than a blue polo shirt or casual attire (0.53, 95% CI: 0.43-0.62 and 0.13, 95% CI: 0.08-0.21). In contrast, residents at the age of 84 or younger preferred a professional white jacket or a blue polo shirt rather than a completely white uniform or casual attire (0.67, 95% CI: 0.58-0.75 and 0.60, 95% CI: 0.50-0.68 vs 0.47, 95% CI: 0.38-0.57 and 0.26, 95% CI: 0.19-0.35).

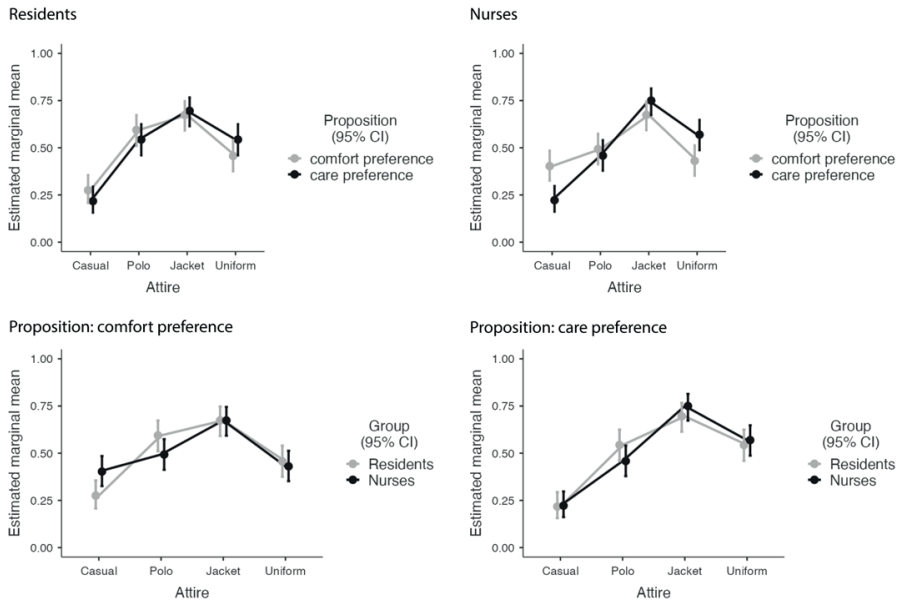

Figure 2. (Perceived) preferences for attire by residents and nurses and by proposition

The perceived preferences for attire among nurse participants in both propositions differed significantly by working years (χ^2 17.101, p = 0.009). As shown in Fig. 3, nurses who had been working two years or fewer were more likely to choose a professional white jacket (0.81, 95% CI: 0.71-0.88) versus a completely white uniform, a blue polo, or casual attire (0.50, 95%CI: 0.40-0.60; 0.40, 95%CI: 0.31-0.51 and 0.28, 95%CI: 0.20-0.39, respectively). For nurses who had been working for 3 to 10 years, the perceived preferences for a professional white jacket and blue polo were closer to each other (0.63, 95%CI: 0.51-0.75 and 0.60, 95%CI: 0.47-0.72, respectively) and equal for a completely white uniform and casual attire (0.38, 95%CI: 0.27-0.51). Among nurses who had worked more than 10 years, the perceived preferences for attire were relatively less divergent (professional white jacket 0.66, 95%CI: 0.55-0.75; blue polo shirt 0.54, 95%CI: 0.44-0.64; completely white uniform 0.50, 95%CI: 0.40-0.61; casual attire 0.30, 95%CI: 0.22-0.41).

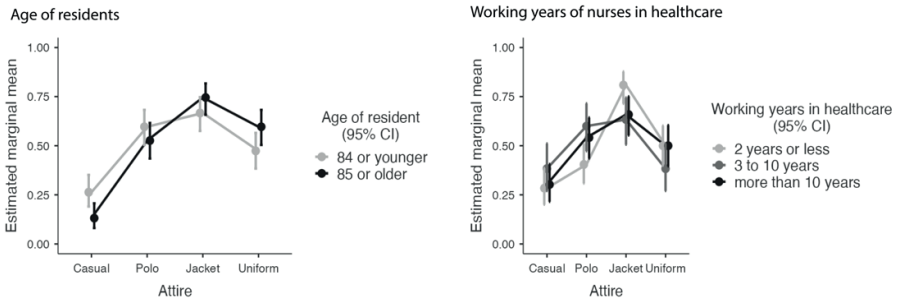

Figure 3. (Perceived) preferences for attire by age of residents and working years of nurses in healthcare

Discussion

We found that a professional white jacket with blue jeans was the option most preferred by residents in nursing homes. Although there are differences in (perceived) preferences for attire regarding 'care preference' and 'comfort preference' between residents and nurses, casual attire was (perceived to be) the least preferred in all cases. It is remarkable that the highest difference in (perceived) preference between both groups was found regarding 'comfort preference'. Nurses thought that residents felt more comfortable with casual attire than the residents actually did (0.40 versus 0.28). It is also notable that nurses working two years or fewer, who were in general younger, were more likely to choose a professional white jacket with blue jeans compared to their colleagues who had been working longer in healthcare. Although we could not find confirmation of this in the literature, we expected that the younger generation would prefer informal attire rather than attire with a more formal look. We do not have an explanation for this result.

Research on preferences regarding healthcare workers' attire is very limited. Previous studies in other healthcare settings have also shown preferences for attire with a professional look. A study on nurse professionalism demonstrated that middle-aged and older patients admitted to an American tertiary healthcare center preferred a white uniform compared with colored or patterned uniforms (Albert et al., 2008). Another study of patients' perceptions of nursing attire in an American hospital setting showed different perceptions among four generations of patients. The oldest generation (58+ years old) perceived a nurse wearing a white uniform as the most professional and approachable, as most wanting to care for patients, and easiest to identify. Younger respondents also perceived a white uniform as the most professional; however, a lavender printed uniform was perceived as most

approachable (Skorupski & RE, 2006). An integrative review demonstrated that attire that is at least standardized in color and style contributes to patient perception of nurses' professionalism and recognition (Hatfield et al., 2013).

To our knowledge, the current study is the first to quantify the (perceived) preferences for nurses' attire in nursing homes with a main emphasis on creating a homey atmosphere. Based on practice in recent years, many executives of nursing homes assume that formal attire is not suitable in a setting with a homey atmosphere. However, it is not so clear what constitutes such an environment. Fleming et al. (2017) showed that the concept of a homey atmosphere is complex, dynamic, and very personal. The only clear common features for a homey atmosphere were found to be certain physical characteristics of the building and residents feeling that they had control over their life and were able to carry out their personal routines and activities. We agree with the authors' conclusion that we should focus on ensuring that residents with complex health issues feel a sense of control within a safe and comfortable environment (Fleming et al., 2017).

This first study on (perceived) preferences for nurses' attire has several limitations. First, we cannot ensure how representative our sample is due to our residents' recruitment method, from which we did not know the total size of eligible residents. Secondly, the choices for healthcare workers' attire were limited to four. We do not know if other colored or patterned attire would have resulted in other (perceived) preferences. In addition, we did not expand the choices for attire with or without name badges to make it easy for residents to identify nurses. However, we know that the wording on name badges is small and unreadable by most residents, so we do not know whether this would have influenced the preferences. Furthermore, name badges are often not worn due to risks attached with moving and handling patients. Thirdly, in our study we used only a female nurse in the photographs. We do not know if preferences would have been the same if a male model had been used. Fourthly, our study was limited to two dimensions: 'comfort preference' and 'care preference'. We do not know the residents' preferences from other dimensions. Fifthly, our study focused on residents with physical impairments. Residents with cognitive impairments, such as dementia, were excluded. However, our study design was not suitable to obtain reliable results within this group of residents. Finally, our data represented only Dutch participants, from whom we did not collect data about country of birth or ethnic background. We do not know whether preferences would be different among residents in facilities in other countries. Despite this limitation, our study has demonstrated that even in the Netherlands, which is generally known for having a quite informal culture, professional attire is preferred.

We have shown that a homey atmosphere in nursing homes does not preclude more formal attire for healthcare workers. Healthcare workers' attire that contributes to a safe environment does not restrict residents' sense of control or limit their daily routines and activities. We recommend including a professional white jacket as one of the options for nurses' attire among residents with physical impairments. Furthermore, it is important that healthcare workers receive sufficient garments from their organization to meet the requirement to always wear clean (properly washed) attire (Dutch Working Party on Infection Prevention 2017). We also recommend involving residents in the development of national guidelines regarding healthcare workers' attire to take into account their preferences. It should be noted that preferences could also change over time or be different among countries.

Further research is needed to better understand residents' preferences for nurses' attire, as well as the attire of other types of staff in nursing homes. Moreover, such research should examine other dimensions of preferences and include residents with cognitive impairments.

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CRediT authorship contribution statement

Andrea Eikelenboom-Boskamp: Conceptualization; Data curation; Formal analysis; Investigation; Methodology, Project administration; Writing - original draft; Writing - review & editing; collecting data, analysis and interpretation of data, writing – original draft, writing – review & editing. Anita Huis: Conceptualization; Data curation; Software; Writing – review & editing. Katja Saris: Conceptualization; Investigation; Writing – review & editing. Tim Stobernack: Writing – review & editing. Monica de Leeuw: Investigation; Writing – review & editing. Marlies Hulscher: Conceptualization; Writing – review & editing. Andreas Voss: Conceptualization; Supervison; Writing – review & editing.

Conflict of interest statement

All authors report no conflict of interest.

Data available statement

The data that support the findings of this study are available on request from the corresponding author, AE-B. The data are not publicly available due to restrictions [e.g. their containing information that could compromise the privacy of research participants].

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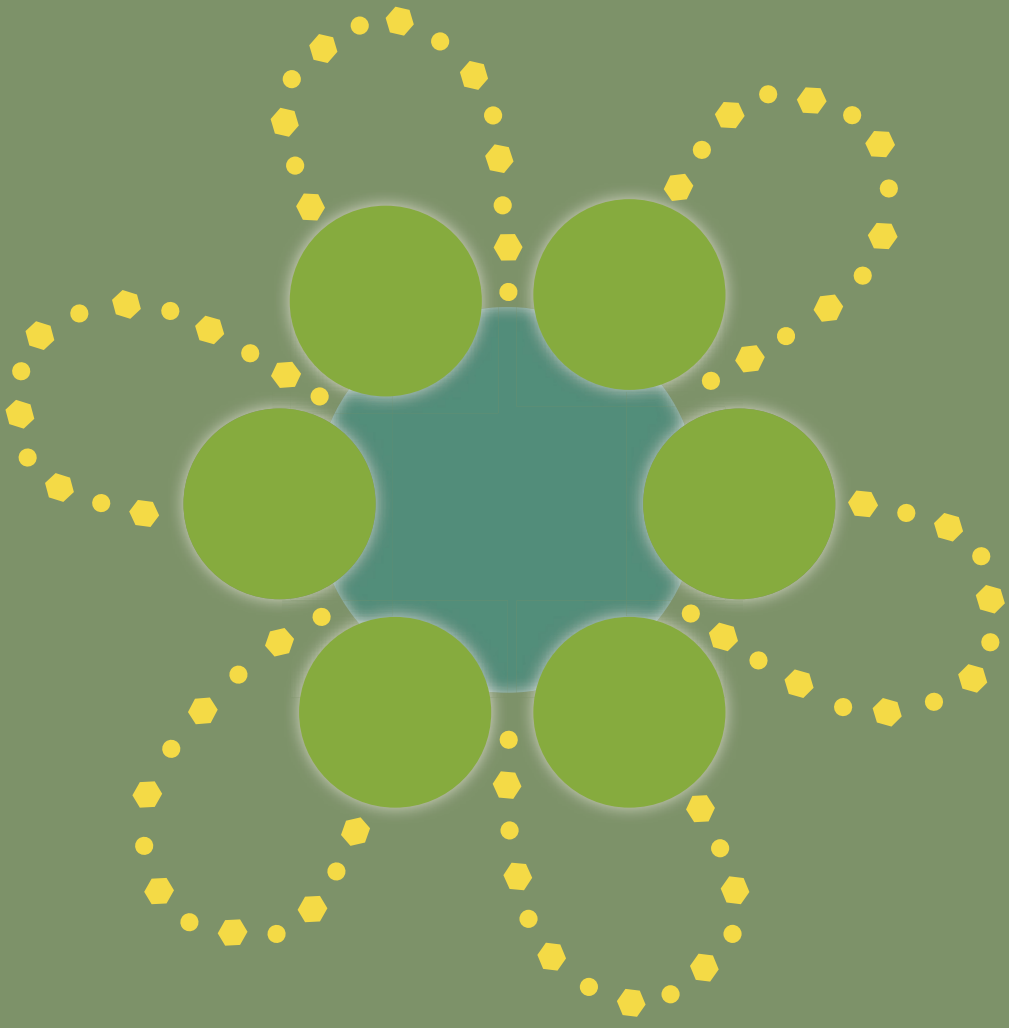
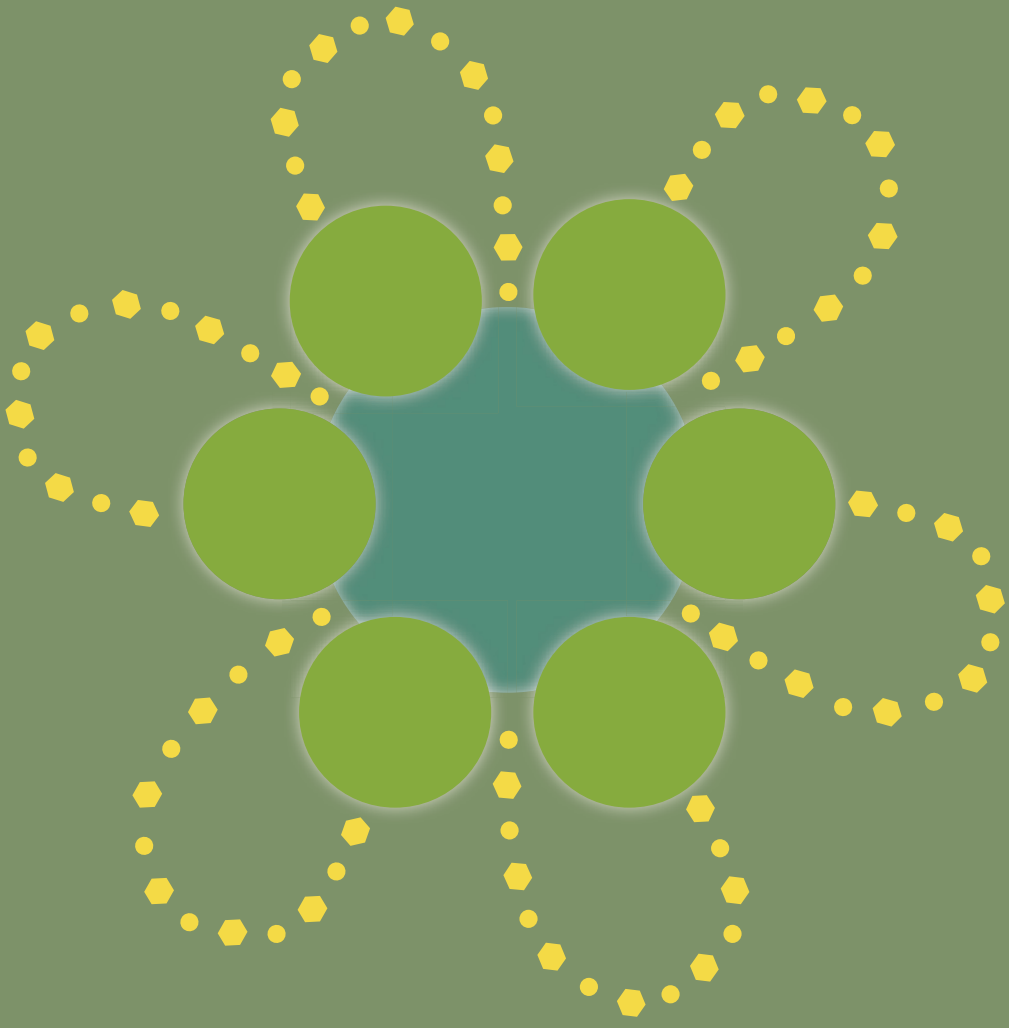


PART 2
GUIDELINES FOR ADDRESSING ANTIBIOTIC RESISTANCE



CHAPTER 6

Dutch guideline for preventing nosocomial transmission of highly-resistant microorganisms (HRMO) in Long-term Care Facilities (LTCFs)

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Abstract

In 2012, the Dutch Working Party for Infection Control (WIP) issued the first Guideline for prevention of transmission of highly-resistant microorganisms (HRMO) in Hospitals. The next step was to focus on long-term care facilities (LTCFs) both for nursing homes as for small-scale living facilities with nursing home care. These facilities providing care for residents with functional disabilities, chronical illnesses and cognitive disorders, such as dementia. The objective was to adapt the Guideline for prevention of transmission of HRMO in hospitals to LTCFs with a strong accent on living conditions and social interactions.

Residents of LTCFs may be carriers of HRMO over a long period of time and most of the residents of the LTCF stay for extended periods of time. To respect individual living circumstances and to prevent unnecessary limitations in the social life of the residents due to the use of isolation measures, the WIP has chosen to describe infection control precautions per individual microorganism instead of a 'one size fits all' method. The term "isolation" was therefore replaced by the term "additional" precautions". This guideline describes the screening policies for residents in LTCFs, definition and detection of HRMO carriage, standard and additional infection control precautions for HRMO positive residents, documentation, and communication of HRMO carriage and discontinuation of additional infection control precautions. It also describes contact tracing of HRMO, environmental control/investigation, surveillance of HRMO and what is important when there is an outbreak.

Keywords: Highly-resistant microorganisms, HRMO, Antibiotic resistance, Antimicrobial resistance, Long-term care facilities, LTCF, Infection control precautions, Guidelines.

Introduction

Antimicrobial resistance (AMR) is a worldwide threat to healthcare as common empiric antibiotics may no longer be effective to treat infections, including those that are life-threatening. Consequently, AMR may result in increased morbidity, mortality and cost of healthcare.

The World Health Organization (WHO) issued the Antimicrobial Resistance, Global Report on surveillance in 2014. This report summarizes all information on AMR and speaks of alarming levels of AMR in many parts of the world [1]. In the Netherlands, AMR has, with a few exceptions, stayed on the same level from 2010-2015 [2]. Still, to control the increase in AMR, antibiotic should be used wisely, and infection control precautions should be installed to prevent transmission of Highly Resistant Microorganisms (HRMO).

In 2012, the – by now former - Dutch Working Party for Infection Control (WIP) issued the first Guideline for prevention of transmission of HRMO in Hospitals [3,4]. This guideline provides definitions for classification of HRMO and recommendations on surveillance, isolation precautions for patients and advice on outbreak management. It is currently implemented in Dutch hospitals. The next step was to focus on long-term care facilities (LTCFs), providing care for residents with functional disabilities, chronical illnesses, and cognitive disorders, such as dementia. In the Netherlands, these residents are in the care of an "elderly care physician", a distinct medical specialization, exclusively working in LTCFs. Within the structure of the WIP, a so-called "Expert group LTCFs" was established, with professionals working (partially) in/for LTCFs. The expert group was tasked with the development of multiple Infection prevention and control guidelines, the first of which was 'the prevention of transmission of HRMO in LTCFs'.

Based on the Guideline for prevention of transmission of HRMO in hospitals, the ultimate goal was to adjust this guideline [5] to the living circumstances in LTCFs. This concerns all forms of nursing home care within institutions such as nursing homes or small-scale living facilities with the exception of geriatric departments of a hospital. These facilities have a strong emphasis on living conditions and social interactions. As residents of LTCFs may be carriers of HRMO over a long period of time [6] and as most of the residents of the LTCF stay for longer periods of time, infection control precautions may have a negative impact on the quality of life [7]. In order to respect individual living circumstances and to prevent unnecessary limitations in social life, the WIP has chosen to describe infection control precautions per

individual microorganism instead of a 'one size fits all' method. In addition, the term "isolation" was replaced by the term "additional precautions".

This guideline focusses on the control of HRMO and not for control of Methicillin-resistant *Staphylococcus aureus* (MRSA) for which a separate guideline is available in the Netherlands.

Screening policies for residents in Long-Term Care Facilities

When a resident is admitted to a LTCF and has stayed in a healthcare facility outside the Netherlands, HRMO screening must be initiated under the following circumstances:

- When the resident was admitted to a foreign health care facility (outside the Netherlands, the Caribbean islands not included) in the 2 months prior to admission to the LTCF and
- When the duration of admission in a foreign health care facility was longer than 24 hours

It is also advised to test a resident for HRMO carriage if the resident is transferred from a ward or small-scale living group within the healthcare facility or another healthcare facility with an ongoing HRMO outbreak within the Netherlands.

Definition and detection of HRMO carriage

The definition of HRMO is determined by the microorganism and the specific antibiotic where the microorganism has shown resistance to. The criteria for HRMO are based on the guideline "Laboratory detection of highly resistant microorganisms (HRMO)" of the Dutch society for Medical Microbiology [8]. This way, the definition of HRMOs is consistent with the established HRMO guideline for hospitals, making adequate information exchange easier [3,4].

Three main groups of HRMO are distinguished: highly resistant Enterobacteriaceae (Table 1); highly resistant Gram-negative nonfermenters (Table 2), and highly resistant Gram-positive bacteria (Table 3).

To detect residents that carry HRMO, specific cultures have to be taken (Table 4).

Table 1. Definition of highly resistant *Enterobacteriaceae*

Gram-negative rods	ESBL	Carbapenemase	Aminoglycosides	Quinolones
Enterobacteriaceae	A	A	B	B

ESBL extended-spectrum beta-lactamase; **A:** presence of ESBL or Carbapenemase is sufficient to define the microorganism as highly resistant; **B:** resistance against both antibacterial agents from the two indicated groups is required to define the microorganism as highly resistant

Table 3. Definition of highly resistant gram-positive bacteria[a]

Gram-positive bacteria	Penicillins	Vancomycin
Streptococcus pneumoniae	A	A
Enterococcus faecium	B	B

[a]MRSA not included; **A:** resistance against an antibacterial agent from the indicated group is sufficient to define the microorganism as highly resistant; **B:** resistance against both antibacterial agents from the two indicated groups is required to define the microorganism as highly resistant

Table 4. Diagnostic screening procedure for residents suspected for HRMO carriage in LTCF

Microorganism/Indication	Standard Cultures[a]	Additional cultures (when indicated)[a,b]
Enterobacteriaceae (ESBL and CPE inclusive)	Rectal swab or stool sample	Wound swab, sputum sample, urine sample
Acinetobacter species	Rectal swab or stool sample and sputum sample or oropharyngeal swab[c]	Wound swab, urine sample
Stenotrophomonas maltophilia	Rectal swab or stool sample and sputum sample or oropharyngeal swab[c]	Wound swab, urine sample
Pseudomonas aeruginosa	Rectal swab, stool sample and sputum sample or oropharyngeal swab[c]	Wound swab, urine sample
Streptococcus pneumoniae	Sputum sample or oropharyngeal swab[c]	-
Enterococcus faecium	Rectal swabs or stool samples	Wound swabs, sputum samples, urine samples
When resident is transferred from health care facility outside the Netherlands	Rectal swab or stool sample and sputum sample or oropharyngeal swab[c]	Wound swab, sputum sample, urine sample

[a]Single swab/sample from the stated site, excepting for Enterococcus faecium. Standard and additional cultures for Enterococcus faecium: five swabs/samples on five consecutive days;

[b]Depending on clinical presentation of the signs and symptoms of resident: ▪ culture of sputum when resident has a persistent cough ▪ culture of wound if present ▪ urine culture when urinary tract catheter is in place

[c]Preferably sputum sample. If sputum sample cannot be obtained, collect oropharyngeal swab

Table 2. Definition of highly resistant gram-negative nonfermenters

Gram-negative nonfermenters	Carbapenemase	Aminoglycosides	Quinolones	Ceftazidime	Piperacillin	Co-trimoxazole
Acinetobacter spp.	A	B	B[a]	n/a	n/a	n/a
Stenotrophomonasmaltophilia	n/a	n/a	n/a	n/a	n/a	A
Pseudomonasaeruginosa	C	C	C	C	C	n/a

[a]only Ciprofloxacin and/or Levofloxacin, due to the intrinsic resistance of Acinetobacter species for norfloxacin; **A:** Carbapenemase or resistance against an antibacterial agent from the indicated group is sufficient to define the microorganism as highly resistant; **B:** resistance against antibacterial agents from at least two indicated groups is required to define the microorganism as highly resistant; **C:** resistance against antibacterial agents from at least three of the indicated groups is required to define the microorganism as highly resistant; n/a: not applicable

Standard and additional infection control precautions for HRMO positive residents

In general, when giving physical care to residents, healthcare workers (HCWs) should always take standard precautions, such as adequate hand hygiene. These are meant to reduce the risk of transmission of pathogens from both known and unknown sources. The standard precautions are the minimal precautions a HCW must take in the care of all residents [9-11].

The additional infection control precautions are described in Table 5a and b. In order to be clear and undisputable, all precautions are listed, including the standard precautions such as hand hygiene.

Documentation and communication of HRMO carriage

The documentation of the HRMO carriage is of utmost importance. Without knowing this, precautions to prevent transmission in the LTCF and other healthcare facilities (HCFs) cannot be taken. Therefore, all HCW involved, including those who are involved outside the LTCF (e.g., treating physicians in a hospital, primary care physicians), should be informed of the HRMO status of the resident. In addition, the HRMO status should be documented in the (E) Health records for (para)medical and nursing staff.

Before transferring a HRMO positive resident to another ward/small-scale living group within the facility, or another facility, or before visiting e.g., an outpatient department, all those providing care should be informed about the HRMO status. When a HRMO positive resident is re-admitted to a LTCF and there have not been 2 sets of negative HRMO cultures according to the rules mentioned in the section "Discontinuation of additional infection control precautions" below, additional precautions should be taken.

The HRMO carriers themselves/or the first contact person and their caregivers should be notified about the HRMO status in order to receive needed information with regard to the consequences as well as being able to apply adequate infection control measures. It is necessary that the physician-in-charge and other HCWs of the LTCF have the opportunity to consult a medical microbiologist and/or an infection control practitioner for advice regarding the prevention of transmission, diagnostics, and treatment for HRMO positive residents.

Table 5. Standard and additional infection control precautions by HRMO positive residents, per HRMO in a non-outbreak setting

HRMO or indication	Hand hygiene[b]	Personal Protective Equipment			Single room/ apartment	Sanitation		Use of shared facilities such as living room
		Gloves[c]	Apron/Single use isolation gown with long sleeves[c]	Mask		Toilet/commode chair	Bathroom	
Enterobacteriaceae (ESBL included, not CPE[a])	Yes	Yes	Apron	No[d]	no	No sharing with other residents	Sharing possible[e]	Yes[f]
CPE[a]	Yes	Yes	Isolation gown	No[d]	Yes[g]	No sharing with other residents	No sharing with other residents	Depending on individual situation[h]
Acinetobacter species	Yes	Yes	Isolation gown	No[d]	Yes[g]	No sharing with other residents	No sharing with other residents	Depending on individual situation[h]
Pseudomonas aeruginosa *Stenotrophomonas maltophilia*	Yes	Yes	Apron	No[d]	no	No sharing with other residents	Sharing possible[i]	Yes[f]
Streptococcus pneumoniae (PRP)	Yes	Yes	Apron	FFP1[j]	Yes[g, k]	Sharing possible	Sharing possible[e]	Yes, under conditions[f, l]
Enterococcus faecium (VRE)	Yes	Yes	Apron	No[d]	Yes, by preference[g]	No sharing with other residents	No sharing with other residents	Yes[f]
Recent admission foreign HCF	Yes	Yes	Isolation gown	None[d, m]	Yes[g]	No sharing with other residents	No sharing with other residents	Depending on individual situation [h, l]

a. CPE: Carbapenem resistant Enterobacteriaceae
b. WHO 5 moments of hand hygiene (part of standard precautions).
c. Wear only when giving physical care to residents and/or contact with material of residents. Do not wear during pure social activities.
d. Use a surgical mask whenever there is a risk of splashing of body fluids (part of standard precautions).
e. When resident shares a bathroom: HRMO positive resident is the last one to use the bathroom, immediate cleaning procedure after use.
f. Give resident instruction on how to perform hand hygiene. If residents have wounds or indwelling catheters, cover these with an appropriate (wound)dressing.
g. If HRMO positive resident shares his room or apartment with another resident (e.g. couples), the other resident is also to be considered as an HRMO positive resident.

h. Consult the medical microbiologist and/or infection control practitioner to determine if visiting shared facilities (e.g. living room) is appropriate (taking into account the risk of transmission to other residents). If using shared facilities is permitted, see footnote f.
i. If resident shares bathroom facilities, ensure that after use immediate cleaning and disinfection takes place (important issue because of long survival duration of these microorganisms).
j. FFP: Filtering facepiece particle; Put FFP1 mask in place before entering resident's room (only in the acute phase of a respiratory infection which means, in the first 48 hours after appropriate antibiotic treatment has started).
k. Single room/apartment is only necessary in the acute phase of a respiratory infection, which means in the first 48 hours after appropriate antibiotic treatment has started.
l. Use of shared facilities not allowed in the acute phase of a respiratory infection, in the first 48 hours after appropriate antibiotic treatment has started.
m. Special note: When a resident is suspected of MRSA carriage (e.g. after recent admission in foreign HCF, use surgical mask as part of the precautions for prevention of MRSA)

Table 5. (continued) Standard and additional infection control precautions by HRMO positive residents, per HRMO in a non-outbreak setting

HRMO or indication	Materials, instruments, devices used for care of HRMO positive resident	Cleaning and disinfection of room/bathroom[n]			Disposal of materials
		Cleaning	Disinfection	Terminal cleaning[o]/ terminal disinfection[p]	Waste or Laundry
Enterobacteriaceae (ESBL included, not CPE[a]	No sharing with other residents[q, r]	Daily	Yes, if used for other residents as well[s]	Terminal cleaning procedure	Disposal in closed, intact bag
CPE[a]	No sharing with other residents[q, r]	Daily[t]	Yes, if used for other residents as wel[s]	Terminal disinfection procedure	Disposal in closed, intact bag
Acinetobacter species	No sharing with other residents[q, r]	Daily[t]	Yes, if used for other residents as well[s]	Terminal disinfection procedure	Disposal in closed, intact bag
Pseudomonas aeruginosa *Stenotrophomonas maltophilia*	No sharing with other residents[q, r]	Daily	Yes, if used for other residents as well[s]	Terminal disinfection procedure, only sanitation room(s)	Disposal in closed, intact bag
Streptococcus pneumonia (PRP)	No sharing with other residents[q, r]	Daily	Yes, if used for other residents as well[s]	Terminal cleaning procedure	Disposal in closed, intact bag
Enterococcus faecium(VRE)	No sharing with other residents[q, r]	Daily	Yes, if used for other residents as well[s]	Terminal disinfection procedure	Disposal in closed, intact bag
Recent admission foreign HCF	No sharing with other residents[q, r]	Daily[t]	Yes, if used for other residents as well[s]	Not applicable	Disposal in closed, intact bag

n. For instructions for cleaning and disinfection of (bath) room: follow national guidelines.

o. Terminal cleaning (or end-cleaning): cleaning of room (all surfaces, touch surfaces, floor, splashing zones of walls) including bathroom and all re-usable materials present in this room. Re-usable materials which cannot be cleaned and non-reusable materials will be discarded of. Terminal cleaning takes place if additional precautions are discontinued or when resident is discharged, transferred or deceased.

p. Terminal disinfection (or end-disinfection): after terminal cleaningo, terminal disinfection of the room is performed (all surfaces, touch surfaces, floor, splashing zone of wall) including bathroom facilities and other re-usable materials present in the room (e.g. curtains, remote control, etc.). A terminal disinfection takes place after the additional precautions of the HRMO positive resident are discontinued, or the resident is discharged, transferred or deceased. Re-usable materials which cannot be disinfected, should be discarded of.

q. A small supply of necessary materials for the immediate care of the resident is allowed in the room/apartment. These materials must not be used for other residents and must be discarded after discharge or discontinuation of additional precautions.

r. If re-usable materials are used, they should be disinfected immediately when taken outside the resident's room/apartment.
s. E.g. resident lifting devices, stethoscope
t. Use cleaning material only for the room and devices of HRMO positive resident. Discard non-reusable cleaning material immediately after use. If the cleaning material is re-usable, remove materials after use in appropriate closed bag

Discontinuation of additional infection control precautions

Based on experience from earlier outbreaks and expert opinion, additional infection control precautions can be discontinued in the following cases:

- Resident, suspected for HRMO carriage:
  - o If the HRMO screening cultures (Table 1) are negative, additional precautions can be discontinued. The resident should be without antibiotic treatment for at least 48 hours before cultures are taken.
- Resident, HRMO positive:
  - o If a resident is carrier of *Enterobacteriaceae*, (Extended-spectrum beta-lactamase (ESBL) included, Carbapenemase-producing Enterobacteriaceae (CPE) excluded), *Acinetobacter* species, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* and *Streptococcus pneumonia* (PRP), then additional precautions can be discontinued if at least 2 sets of HRMO screening cultures (taken at least 24 hours apart) are negative.
  - o If a resident is carrier of CPE or vancomycin-resistant *Enterococcus faecium* (VRE), additional precautions can be discontinued if at least 2 sets of cultures are negative, at least 1 year apart.

Contact tracing of HRMO

Contact tracing is recommended in case of unexpected HRMO positive residents. When a contact of the HRMO positive index appears to be HRMO positive too, it could be due to a single transmission event, or it can be the result of broad transmission within a facility. In order to detect and prevent further transmission, contact tracing is recommended for all HRMO, possibly with an exception for ESBL positive Enterobacteriaceae or for Enterobacteriaceae resistant for Quinolones and Aminoglycosides. These two HRMOs are commonly found in the Dutch population with a prevalence of up to 8 – 10% in patients seeing a general practitioner [12]. The scale of the contact tracing is determined by the elderly care physician in collaboration with the medical microbiologist and/or infection control practitioner. In most cases, all residents who have been in contact with the HRMO positive resident will be cultured for HRMO carriage (see Table 4). Additional precautions can be postponed until the culture results from the first investigation are known. Directly changing precautions have much impact for the residents and HCWs and according to expert opinion is not advisable until transmission actually has been proven. If residents are transferred to another ward or HCF, it is advised to take additional precautions while waiting for culture results. Residents who are already discharged to their home-setting, will initially not be cultured unless in the first investigation HRMO positive residents are detected.

Contact tracing is also recommended if HRMO carriage is confirmed with a HRMO suspected resident and it is known that the additional precautions have not adequately been performed in the time between culturing and results. In that time HRMO transmission could have taken place.

Contact tracing among HCWs is not indicated. HCW, if at all, are only transient carriers of HRMO. In addition - and in contrast to MRSA - possibilities for decolonization treatment of HRMOs is limited and not routinely used.

Environmental control/investigation

Initially, culturing the environment to detect a source of the HRMO is not indicated. If, however, during an outbreak with HRMO transmission persists, environmental culturing may be considered to determine a source of the outbreak.

Surveillance of HRMO

Evaluation of the local and regional epidemiology of HRMO provides knowledge in the, sometimes rapidly changing, evolution in this area. Performing surveillance on a local and regional level, by exchanging on a regular basis HRMO data from routine diagnostics, can be very helpful to determine if there is an indication of an increasing level of HRMO. At present, gathering and combining data to receive insight into the regional epidemiology is a task for the Dutch regional networks, initiated by the ministry of health, to combat AMR. To have unbiased surveillance data (at least once a year) point-prevalence studies among the residents of the LTCF should be performed by trained professionals to determine local levels and possible transmission of HRMO in the facility.

Outbreak

A situation is considered to be an outbreak when 2 or more residents have the same HRMO and the presence of an epidemiological link between them.

During an outbreak, it is important to maintain and highlight the standard precautions and additional precautions specific for that kind of HRMO (as described in Table 5a and b).

It is strongly advisable to install an Outbreak Management Team. This multidisciplinary team consists an elderly care physician, medical microbiologist, infection control practitioner, staff members of the wards involved (both nursing and medical), member of the management team and professional of the Local Health Authority. This team which will take care of the arising issues such as

decisions on additional infection control precautions, adjustment of antibiotic therapy, communication within and outside of the LTCF where the outbreak takes place and alert national authorities of this specific outbreak.

When despite tightening up infection prevention precautions, further transmission takes place, confirmation of clonal relationship between the strains or plasmids by molecular typing needs to be done [13].

Discussion

There are limitations to this guideline for HMRO carriage in long term care settings. First, the absolute risk of transmission of HRMO within the Dutch LTCFs (as defined in the guideline) is not known. However, there is a growing understanding of the potential for transmission of HRMO in the LTCF. In 2016, den Dool et al. used mathematical modelling to estimate the contribution of nursing homes in the dispersal of pathogens over the healthcare network in the Netherlands. They concluded that nursing homes have the potential to drive and sustain epidemics across this network and that infection control efforts and surveillance systems should also be targeted at those LTCFs [14]. Recent research in Dutch LTCFs showed that, although in absolute numbers the percentage of HRMO is low (4.2% *Escherichia coli* ESBL carriage among residents), the large variation of HRMO presence between facilities (1-33%) warrants cautious surveillance [15].

Secondly, it is not known how long a resident remains colonised with HRMO. Research shows that carriage can persist over years, depending on the microorganism [15]. The guidance for the decision to discontinue infection control precautions is therefore based on expert opinion. Although research indicates that there might be predisposing factors for prolonged carriage, more research is needed to determine when to discontinue precautions and consider HRMO carriage as ended in long-term care. Despite the lack of studies that show the effect of monitoring of the HRMO carriage of a resident and its consequences in LTCFs, it is logical to assume that these measures are effective to prevent the transmission of HRMO.

Last but not least, it is not known whether the proposed actions in the LTCF on prevention of transmission of HRMO, are equally effective and achievable for the various groups of residents in such facilities, such as e.g., psychogeriatric residents. However, given the rising evidence for spreading of HRMO within the LTCF settings, this is a first step in developing guidelines for prevention of transmission of HRMO.

Over the course of time, with leaders in both infection control and LTCFs, further guidance should be provided, while the absolute risk of transmission and harm as opposed to the adverse events related to additional precautions, such as reduced psychological wellbeing, resident safety and satisfaction in residential care [7].

List of Abbreviations

AMR: Antimicrobial resistance; CPE: Carbapenemase-producing *Enterobacteriaceae;* ESBL: Extended-spectrum beta-lactamase; HCFs: Healthcare facilities; HCWs: Healthcare workers; HRMO: Highly-resistant microorganisms; LTCFs: Long-term care facilities; MRSA: Methicillin-resistant *Staphylococcus aureus*; PRP: *Streptococcus pneumonia*; VRE: *Enterococcus faecium*; WHO: World Health Organization; WIP: Dutch Working Party for Infection Control

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AE-B, JH and MB contributed to writing the manuscript. KS, EP and AV read, commented and approved the final manuscript.

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Competing interests

The authors declare no conflict of interest.

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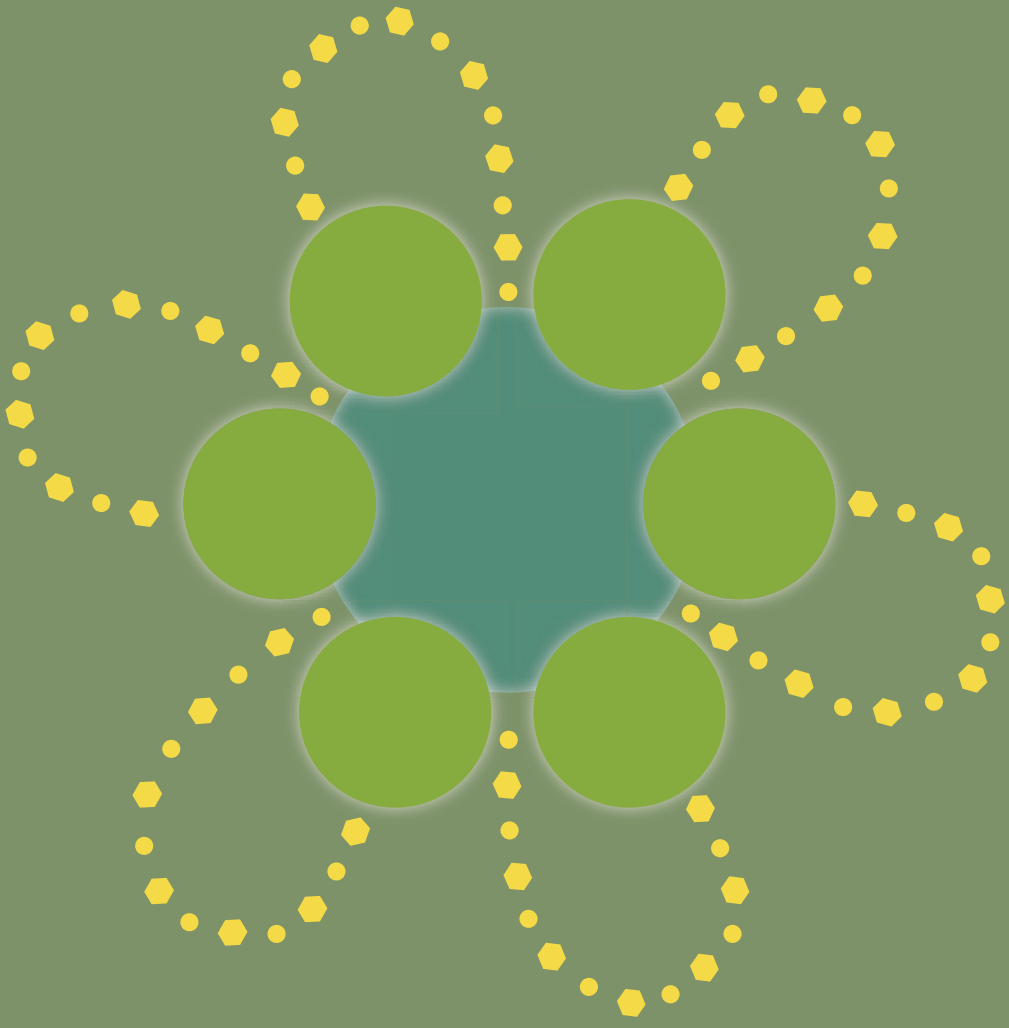

CHAPTER 7

A practice guide on antimicrobial stewardship in nursing homes

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Abstract

A practice guide to help nursing homes set up an antimicrobial stewardship (AMS) program was developed based on experiences gained during a project at one of the largest providers of elderly care in the South-east of the Netherlands. The guideline for the implementation of AMS in Dutch hospitals served as a starting point and were tailored to the unique characteristics of a nursing home setting. This practice guide offers recommendations and practical tools while emphasizing the importance of establishing a multidisciplinary approach to oversee AMS efforts.

The recommendations and practical tools address various elements of AMS, including the basic conditions to initiate an AMS program and a comprehensive approach to embed an AMS program. This approach involves educating nurses and caregivers, informing volunteers and residents/their representatives, and the activities of an antibiotic team (A-team). The practice guide also highlights a feasible work process for the A-team. This process aims to achieve a culture of continuous learning and improvement that can enhance the overall quality of antibiotic prescribing rather than making individual adjustments to client prescriptions. Overall, this practice guide aims to help nursing homes establish an AMS program through collaborative efforts between involved physicians, pharmacists, clinical microbiologists, and infection control practitioners. The involved physician plays a crucial role in instilling a sense of urgency and developing a stepwise strategy.

Keywords: Antimicrobial stewardship, Antibiotic team (A-team), nursing homes, practice guide.

Introduction

Antimicrobial resistance is widely recognized as a crucial concern. Antibiotic use and antimicrobial resistance in long-term care facilities (LTCFs) are substantial due to the significant use of antibiotics [1]. Several studies have demonstrated high rates of inappropriate prescribing of antibiotics, reaching 24% or higher, in LTCFs [2-6]. Notably, in recent years, Dutch LTCFs have shown considerable variability in antibiotic use across facilities [7-11], with a recorded minimum of 2.1 and a maximum of 288.7 defined daily doses (DDD)/1,000 residents per day in 2021 [11].

Since 2015, it has been mandatory for Dutch hospitals to implement an antimicrobial stewardship (AMS) program to enhance the quality of antibiotic use. Consequently, a practice guide was developed to facilitate this process [12]. However, a 'copy & paste' approach to transfer hospital recommendations to nursing homes (NHs) was deemed unsuitable due to substantial differences in organizational structures between these two settings. The connections between electronic medical records (EMRs), prescription systems, and laboratory systems are not always optimal in all NHs, and collaboration with a medical microbiology laboratory consultant is not a standard practice. Moreover, surveillance data on antibiotic use and education on antibiotic-related topics are not regularly available. In addition, the guideline recommends conducting urine cultures in patients displaying signs of tissue invasion, in male patients, in cases of treatment failure, and in instances of recurrent infections (3 to 6 per year) [13]. Based on practical experience, NHs tend to conduct limited culture sampling. Despite the need to improve antibiotic use in NHs, there may be time and budget constraints for applying interventions in this setting.

To investigate the implementation of an AMS program that tailors hospital recommendations to NHs, a project was conducted in one of the largest providers of nursing home care in the South-East region of the Netherlands. The project group comprised the following members: a medical director and an elderly care physician from the provider of nursing home care, a pharmacist responsible for medication supply, a clinical microbiologist from the medical microbiology laboratory providing diagnostics to the organization, an infection control practitioner offering services to the elderly care organization, a representative from a national committee focused on optimizing antibiotic use (Dutch Working Party on Antibiotic Policy (Dutch acronym is SWAB)), representatives from a national institute working on the development and dissemination of information and solutions for medication use, and an administrative support staff member. During the 14-month project, the AMS approach was formulated, and an A-team was established. Antibiotic treatment

protocols for the most common infections in nursing home residents were revised at the regional level, including urinary tract infections (UTIs), lower respiratory tract infections (LRTIs) and skin and soft tissue infections (SSTIs). Scorecards for data collection and assessment were developed to evaluate all antibiotic prescriptions in 4 out of 28 nursing homes. A new rule regarding the use of urine dipstick tests was implemented, and it was required that culture be conducted in accordance with the guideline [13]. A standardized presentation for pharmacotherapy audit meetings (PTAMs) was created to introduce AMS. Additionally, e-learning for nurses and caregivers was developed. A focus group meeting involving residents and their representatives was organized to identify their information needs and preferences on this topic. All aforementioned activities were implemented, evaluated, and adapted as necessary. Finally, physicians were invited to complete a brief questionnaire to evaluate the work of the A-team.

The nursing home facilities met the international definition for nursing homes: 'A nursing home is a facility with a domestic-styled environment that provides 24-hour functional support and care for persons who require assistance with activities of daily living (ADLs) and who often have complex health needs and increased vulnerability. Residents within a nursing home may stay relatively brief for respite purposes, short term (rehabilitative), or long term, and may also receive palliative/hospice and end-of-life care' [14]. Moreover, care in Dutch nursing homes is provided by a multidisciplinary team led by an elderly care physician and is publicly funded.

The lessons learned from this project have been compiled into recommendations, which are presented in the current practice guide to help NHs set up an AMS program.

Conditions for establishing an AMS program

To establish an AMS program, certain basic conditions must be met. The extent to which these conditions are met contributes to the success of the program.

Recommendations

Ensure commitment from the board of directors

One of the crucial conditions is the commitment of the board of directors. This board needs to have a clear vision of the necessity of an AMS program and be willing to allocate the necessary human and financial resources.

Ensure that human and financial resources are sufficient to carry out an AMS program that fits the NH

Another essential condition is ensuring that the human and financial resources required for an AMS program are both adequate and appropriate for the NH. Consequently, assign this specific task to a physician. The baseline situation determines the amount of resources needed, which may vary depending on factors such as existing contracts between cooperating parties and the ability to embed AMS topics into regular processes and meetings. Consider establishing service agreements in which AMS is an integral part of the services for a clinical microbiologist, a pharmacist, and an infection control practitioner who are not employees of the organization. Additionally, having up-to-date treatment protocols and written guidelines for appropriate antibiotic prescribing are needed to easily generate overviews of antibiotic prescriptions. Furthermore, ensuring that physicians mention the indication for the antibiotic prescription in the prescription system will reduce the time investment required for the program. If NHs already have high compliance rates regarding antibiotic prescribing, implementing the program will require less effort. Changes in microbiology culture policies may have financial implications. Finally, purchasing education materials and adapting them may require substantial financial investment and time investment from healthcare workers.

Form a project team to set up and implement an AMS program

To implement an AMS program, it is crucial to form a project team consisting of professionals with relevant expertise. The team should include, at least, a physician who provides medical care to the residents, a pharmacist who supplies the medication to the NH, and a clinical microbiologist of the medical microbiology laboratory that delivers microbiological diagnostic to the NH and has knowledge on local/regional resistance data. To ensure efficient decision-making and create organization-wide conditions for the success of an AMS program, it is recommended to appoint a medical director or member of the management team to the project team. If this is not feasible, one of the project team members should be authorized on behalf of the management team to determine the responsibilities of each member of the project team. It is also advisable to appoint a healthcare professional to the project team who is well-versed in the nursing home organization and has received appropriate training in infection control and antibiotic resistance, such as an infection control practitioner.

Embedding an AMS program within a nursing home

Overall, a comprehensive approach to embedding an AMS program within a NH creates collaboration with and engagement of relevant stakeholders. It incorporates strategies that support the program's sustainability and success.

Recommendations

Align antibiotic and infection control policies and bring both areas of expertise within the responsibility of the same committee

The implementation of an aligned AMS and infection control program and bringing both policy topics under the responsibility of one committee (e.g., infection committee) can help achieve the following objectives: (1) Prevent the development of antibiotic resistance through appropriate use of antibiotics, (2) Detect the presence and transmission of (drug-resistant) bacteria, and (3) Prevent transmission of (drug-resistant) bacteria through hygiene and infection control measures.

Set up an antibiotic team (A-team)

Establishing an A-team comprising a physician, pharmacist, and clinical microbiologist can facilitate the development and revision of antibiotic treatment protocols as well as the monitoring of antibiotic use. It is also advised to examine the feasibility of regional collaborations in certain aspects (e.g., development and revision of antibiotic treatment protocols). It can be highly valuable to add an infection control practitioner to the A-team to coordinate the activities. The A-team's composition allows for a collaborative approach to optimize antibiotic use and promote appropriate prescribing.

Discuss the AMS program with all physicians and make the AMS program a regular topic during meetings (e.g., pharmacotherapy audit meetings (PTAMs))

To obtain physicians' support for the AMS program, they must be involved from the start. Utilizing existing meetings, such as PTAMs or staff meetings, can be an effective way to keep colleagues informed about the program's progress, A-team activities, and antibiotic treatment protocols. The A-team may also use these meetings to discuss issues related to antibiotic choices in treatment protocols, deviations from protocols, or experiences from previous cases, which could result in topics for additional education. Such education can increase physician competence and willingness to adhere to antibiotic treatment protocols.

Offer education on antibiotic use and resistance to nurses and carers

It is recommended to provide education on antibiotic use and antibiotic resistance to nurses and carers for various reasons. These healthcare workers are often the first to recognize signs and symptoms of an infection and serve as the primary contact for residents and their representatives. They play a crucial role in relaying information about residents' conditions to physicians, who do not see residents every day. In addition, they are responsible for carrying out protocols. For example, protocols depicting the use of infection control measures and measures to reduce the risk of a urinary tract infection (UTI) or (aspiration) pneumonia. Often, they also inform residents/their representatives about antibiotic prescriptions. It is important to discuss the feasibility of different modes of education, such as e-learning, which can reach a large target group with relatively little effort, or group discussion training led by an infection control practitioner. Arrangements should also be made regarding whether healthcare workers will receive training during work or during personal time and whether they will have the opportunity to gain accreditation points.

Discuss how volunteers should be informed

In nursing homes, volunteers play an important role in the provision of care, e.g., supporting individual and group activities, assisting caregivers with practical tasks such as serving coffee and tea, aiding in cooking and serving dishes, and offering social and emotional support to residents. This group should be adequately informed about infection control. Specifically, the provision of information on hand hygiene, appropriate measures to take in the event of signs or symptoms of an infection, and food preparation (cooking and serving) should be considered. It is recommended to use reliable, publicly accessible sources of information for the dissemination of general information on infections and antibiotic resistance.

Discuss how to inform residents/their representatives

In addition to the fact that residents and their representatives should always be able to consult nurses, carers, or physicians, it is recommended to offer them information through various media such as paper copies (folders/newsletters), audio recordings, and video presentations so that they can absorb the information at their convenience. It is imperative to contact the residents' council of the nursing home to ascertain their information requirements (for example, information on UTI) and determine the most effective way to convey the information to them. The residents' council should also support the implementation of an AMS program. Similar to volunteers, it is also recommended for this target group to use reliable, publicly accessible sources of information.

A-team activities

It is important to define the activities of an A-team, which is responsible for promoting appropriate antibiotic use.

Recommendations

Define the responsibilities and authority of the A-team

It is important to define the responsibilities and authority of the A-team, which include the following: (1) maintaining treatment protocols up-to-date in accordance with (inter)national guidelines, regional resistance data, and culturing policy, and (2) monitoring compliance with treatment protocols based on predetermined selection criteria. Moreover, the A-team derives its authority from its expertise in the field of antibiotics, making its opinion highly valued. In case of deviations from treatment protocols or the A-team's opinion, prescribing physicians need to state the reason for the deviation in the residents' record. It is also important to emphasize that although the A-team plays a crucial role in antibiotic management, the ultimate responsibility for prescribing antibiotics remains of the individual physician.

Define the working process of the A-team, including selection criteria to identify prescriptions for discussion in the A-team

The working process employed in hospitals will usually not be applicable in NHs. Therefore, it is essential to identify a working process that fits within the NH setting. Based on the project we carried out, we recommend a periodic retrospective review of antibiotic prescriptions for discussion in the A-team. Ideally, in an onsite meeting prior to regularly scheduled plenary meetings (e.g., PTAM). This approach enables A-team members to gain insight into the prescribing behaviour of the preceding months and discuss deviations or issues identified during the plenary meeting. This approach aims to achieve a learning effect for the prescription of antibiotics in the future for all residents. As a consequence, sustainable improvement of the overall quality of antibiotic treatments can be achieved.

To evaluate the activities of the A-team, the following questions could be posed to fellow physicians: (a) How feasible do you consider the treatment protocols to be? (b) If it comes to UTIs, do you think that the nurses adhere to the policy that dipstick tests may only be used after consultation with the physician? (c) What aspects of the A-team's work process are you satisfied with? (d) Are there any bottlenecks or areas for improvement in the work process of the A-team? (e) Do you agree with the policy regarding culturing? (f) Did you change your prescribing behaviour of antibiotics?

To optimize antibiotic prescriptions in NHs, it is recommended to focus on the most common infections, namely, UTIs, lower respiratory tract infections (LRTIs), and skin- and soft-tissue infections (SSTIs). Selection criteria that could be used to identify prescriptions for discussion in the A-team include: (a) prescriptions lacking an indication in the prescription system; (b) prescriptions lacking a (preliminary) stop date in the prescription system; (c) prescriptions with a duration exceeding 7 days; (d) prescriptions for intramuscular or intravenous antibiotics (if applicable); (e) prescriptions for antibiotics other than the first choice based on the applied treatment protocols; (f) prescriptions for combinations of substances, such as amoxicillin + fluoroquinolone; (g) prescriptions for antibiotics regulated for the treatment of particularly resistant microorganisms; and (h) on request of the prescriber.

To determine the time investment required for A-team activities, it is recommended to analyse the volume of prescriptions over a period of one to two months based on the predetermined selection criteria. Priority may be given to one or more of the predetermined selection criteria depending on the results of the analysis. In the prioritization, factors to consider could include (but are not limited to) the severity and frequency of deviations from the treatment protocols, as well as selection criteria where improvement can be achieved quickly and easily.

We advise to oblige physicians to note the indication for an antibiotic in the prescription system. Prescription systems always offer a free text field that can be used, but often it is possible to add a required field for this information. Adding the indication makes it easier to analyse prescription data in relation to infection types and treatment protocols and saves time for the A-team. In addition, complete and correct registration of kidney function, contraindications, over-the-counter (OTC) medication, intolerances, etc. is essential for pharmacists to intervene when necessary.

Define the tasks of all A-team members

To ensure optimal functioning of the A-team, it is recommended to define the tasks of each team member. In addition to the A-team's responsibility for keeping the treatment protocols up-to-date, the following elaboration provides an example of the tasks assigned to each A-team member in monitoring compliance with treatment protocols. The pharmacist generates summaries of antibiotic prescriptions, including the name of the antibiotic, dosage, and duration, based on predetermined criteria. They also review the prescription for potential side effects, toxicity and interactions with other medications used by the resident.

The elderly care physician records relevant data from the resident's medical record on a registration form (see Fig. 1) and requests any missing information from the prescribing physician if necessary. They also provide an assessment regarding the correct or incorrect usage of the antibiotic (see Fig. 2; Table 1). The infection control practitioner collects the registration forms, analyses the data prior to the A-team meeting, and schedules the A-team meetings. Both the elderly care physician and the pharmacist prepare the PTAMs, during which deviations and important issues discussed during the A-team meeting will be addressed. The clinical microbiologist assesses during the A-team meeting whether they agree with the assessment of the antibiotic prescription by the elderly care physician and participates in the PTAM upon request to provide explanations or education on a particular topic.

A summary of the recommendations and their elaboration is included in Table 2.

Name :
Date of birth :
Gender :
Type of care : O psychogeriatric O somatic O rehabilitation
Start date antibiotic :
Name prescribing physician :
Name attending physician :
Weekend : O yes O no
Name antibiotic :
Dose :
Interval/split times : 0 9.00 0 12.00 0 15.00 0 17.00 0 21.00
Administration : O oral O intramuscular O intravenous
Duration :
Indication(code) :

Collect culture : O yes, which site ..... O no
Highly resistant microorganism : O yes O no

Urinary tract infection
According to treatment protocol: O yes O no

Respiratory infection
According to treatment protocol: O yes O no

Superficial skin infection
O Cellulitis O Erythrasma O Impetigo/Impetiginisation
O Folliculitis O Pitted keratolysis

Skin infection deep
O Bite wounds O Furuncle
O Diabetic foot O Furuncle, multiple (furunculosis)
O Ecthyma-ulcus O Furuncle, multiple deep (carbuncle)
O Erysipelas O Hidradenitis suppurativa
O Erythema migrans O Panaritium

Indication code correct: O yes O no

Assessment prescription:
O 1a O 1b O 1c O 2a O 2b O 2 c O 3a O 3b
O 4a O 4b1 O 4b2 O 4 c O 4d1 O 4d2 O 4d3 O 5a O 5b O 5c O 5d

Results of discussion A-team:

Figure 1. Resident registration form

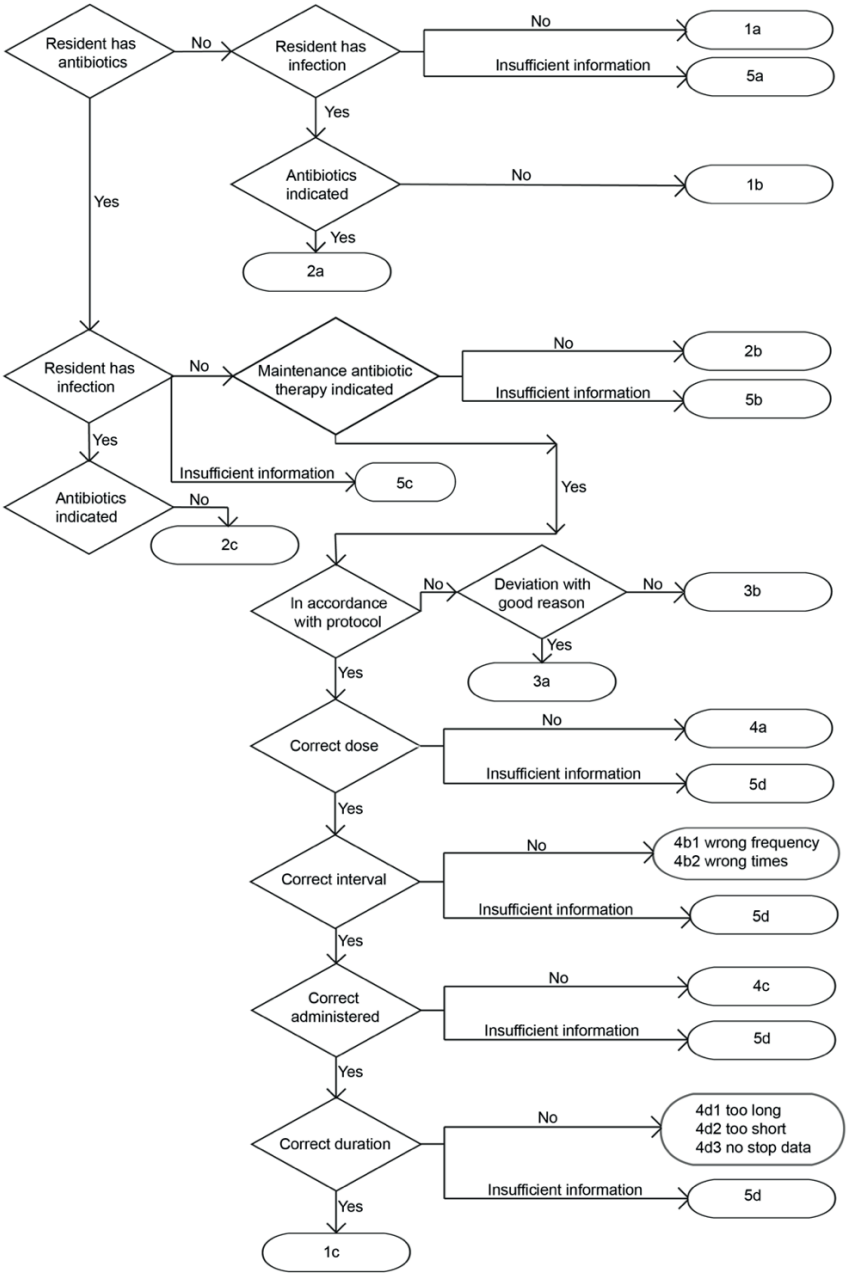

Figure 2. Flowchart of the assessment of antibiotic prescriptions

Table 1. Clarification of the flowchart antibiotic prescriptions assessment*

1	**Correct decision**
1a	No antibiotic(s); no infection; no antibiotic(s) indicated
1b	No antibiotic(s); infection; no antibiotic(s) indicated
1c	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; correct use
2	**Incorrect decision**
2a	No antibiotic(s); infection; antibiotic(s) indicated
2b	Antibiotic(s); no infection; no maintenance therapy indicated; no antibiotic(s) indicated
2c	Antibiotic(s); infection; no antibiotic(s) indicated
3	**Incorrect choice of antibiotic(s)**
3a	Antibiotic(s); infection; antibiotic(s) indicated; not in accordance with treatment protocol; deviation with good reason
3b	Antibiotic(s); infection; antibiotic(s) indicated; not in accordance with treatment protocol; deviation without good reason
4	**Incorrect use**
4a	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong dose
4b1	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong interval: incorrect daily frequency
4b2	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong interval: incorrect times
4c	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong administration form (oral/intramuscular/intravenous)
4d1	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong duration: duration too long
4d2	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong duration: duration too short
4d3	Antibiotic(s); infection; antibiotic(s) indicated; in accordance with treatment protocol; wrong duration: no stop date
5	**Insufficient information**
5a	No antibiotic(s); insufficient information about infection
5b	Antibiotic(s); no infection; insufficient information about maintenance therapy
5c	Antibiotic(s); insufficient information about infection
5d	Antibiotic(s); infection; antibiotic(s) indicated; insufficient information about accuracy of use

**Partly bases on the scoring system for the appropriateness of antimicrobial therapy from Willemsen et al [15] and adapted to the nursing home setting.*

Discussion

In this practice guide, we present a feasible approach for NHs to implement an AMS program. This approach is rooted in the 'Practical Guide Antimicrobial Stewardship in the Netherlands' [12], which is guided towards hospitals and has been tailored to suit the nursing home setting. This was achieved through close collaboration among experts in the fields of elderly care, antibiotic prescribing, antibiotic resistance, and infection control.

This approach can be adapted to local or regional collaborations between NHs, pharmacies, and clinical microbiologists. With the described working process of the A-team, we aim to achieve a learning effect for future antibiotic prescriptions for all residents, thereby enhancing the overall quality of the prescriptions. Moreover, the presence of a peer-review system in which physicians review their colleagues' prescribing behaviour is expected to encourage greater attention to prescribing practices.

The hospital practice guide [12] published in 2015 was based on expert opinion and supporting literature. In 2016, the SWAB guideline committee conducted a literature search with the aim of evaluating the quality of evidence for fourteen antimicrobial stewardship objectives in which the LTCF setting was included. At that time, no supporting evidence for LTCF was found, nor was any contradictory evidence found [16]. Meanwhile, several guidelines have been provided on the implementation of an AMS program in LTCFs [17-19] based on seven core elements published by the Centers for Disease Control and Prevention in 2015 [20]. These seven core elements described are derived from an adaptation of the elements described for hospital antibiotic stewardship and are supported by reviews, intervention studies, regulations, consensus, and surveillance data. No quality assessment of the included studies took place, and the studies were not graded. This also applies to the aforementioned guidance papers [17-19].

In recent years, several systematic reviews have collectively indicated that the implementation of an AMS program has the potential to optimize antimicrobial use in LTCFs [21-24]. The recommendations in our practice guide are corroborated by these studies; however, caution is warranted. The reviewed AMS programs are all unique, lacking standardization in terminology, strategy, evaluation, or reporting. Nevertheless, we were able to compare the strategies in broad terms. Considering the recommendations related to conditions for establishing an AMS program in our practice guide, the recommendation to ensure commitment

from the board of directors is not explicitly described in any of the included studies in these reviews. Although it may be considered implicit, we assert the necessity of explicitly stating this, as outlined in the hospital practice guide [12]. Ensuring that human and financial resources are sufficient to carry out an AMS program tailored to nursing homes is outlined in the review from Wu et al. [21]. Establishing a project team to set up and implement an AMS program is a demonstrated approach across all these reviews [21-24]. However, the elaboration of this recommendation varies across studies. Turning to the recommendations pertaining to embedding an AMS program within a nursing home, aligning antibiotic and infection control policies and bringing both areas of expertise within the responsibility of the same committee, as also described by the SWAB [25], is advocated by the review of Katz [24]. The establishment of an A-team is demonstrated in all these reviews [21-24], albeit the elaborations also vary among the studies. The same applies to the recommendation to discuss the AMS program with all physicians and make it a regular topic during meetings. Offering education on antibiotic use and resistance to nursers and carers is collaborated by Wu et al., Raban et al, and Crespo-Rivas et al [21-23]. None of the reviews included studies on information for volunteers, as we have recommended. We emphasized the importance of this recommendation due to the role volunteers play in the provided care within Dutch nursing homes. Offering information for residents and their representatives is also supported by Wu et al. Raban et al. and Crespo-Rivas et al. [21-23]. Regarding the recommendations related to the A-team activities, recommendations defining the responsibilities and authority of the A-team, the working process of the A-team, and the tasks of all A-team members are corroborated by all reviews; however, here as well, the elaboration also varies in the studies. In addition to referencing the four reviews, it is noteworthy to mention the study by Stone et al. [26], which supports our recommendation to appoint an infection control practitioner in both the project team and A-team. The study revealed a significant positive association between NHs having trained infection control practitioners and performing stewardship activities.

Another crucial aspect to be noted is that in the USA, it became mandatory by law to integrate AMS into infection control programs in NHs in 2016. A survey conducted in NHs showed that the implementation of all seven core elements increased from 43% in 2016 [27] to 71% in 2018 [28]. However, the implementation of an AMS program is still not mandatory in European LTCFs. The results of a survey conducted among LTCFs in Europe [29] regarding the presence of AMS based on ten elements in 2016 and 2017 showed large variation between the participating countries and the ten elements. It is noteworthy that more than half of the LTCFs lacked a therapeutic

formulary and written guidelines for appropriate antimicrobial use, which are the basis for the rational, appropriate, and safe use of antibiotics. As far as we know, recent data on the extent to which stewardship activities have increased in European LTCFs are lacking.

In general, it is crucial to facilitate NHs in implementing an AMS program. NHs should have the flexibility to choose an approach that aligns with their organizational structure. Our current practice guide offers practical tools for establishing an AMS program, which can be considered separate parts of a toolbox. The local context determines the most effective way to utilize the A-team and implement the AMS program's tools. The involved physician should play a significant role in creating a sense of urgency, prioritizing program elements, and proposing a step-by-step approach. In the Netherlands, the Dutch Association of Elderly Care Physicians has endorsed the role of elderly care physicians in infection control and antibiotic resistance in its general guideline [30].

Given the lessons learned from our project, we recommend retrospectively reviewing antibiotic prescriptions by the A-team until EMR, pharmacy, and laboratory systems are appropriately configured to enable automatic feedback upon an antibiotic prescription at the individual level of residents. Subsequently, the results of these reviews should be periodically discussed during regular meetings, such as PTAMs. This approach has two limitations. First, this approach precludes the possibility of individual client adjustments. Second, our focus is limited to residents who receive antibiotics, whereas those who do not receive antibiotics, even when it may be indicated, are excluded. Therefore, we recommend conducting repeated prevalence studies on antibiotic use among all residents.

In conclusion, the development of tailored AMS programs that are feasible in NHs can be facilitated by collaborative efforts between physicians, pharmacists, clinical microbiologists, and infection control practitioners, preferably on a regional level.

Table 2. Summary of recommendations to implement an AMS program

Basic conditions	Recommendations	Elaboration
1. Conditions for establishing an antimicrobial stewardship (AMS) program	1.1 Ensure commitment from the Board of Directors.	• Define the vision on necessity of an AMS program. • Allocate human and financial resources.
	1.2 Ensure human and financial resources are sufficient to carry out an AMS program that fits the nursing home.	• Allocate a physician for this task. • Establish service agreements in which AMS is an integral part of the services for nonemployed professionals.
	1.3 Form a project team to set up and implement an AMS program.	• Establish a project team comprised of members with relevant expertise: a physician, a pharmacist, a medical microbiologist, an infection control practitioner, a member of the management team (MT) or an authorized project team member, on behalf of the MT.
2. Embedding an AMS program within a nursing home	2.1 Align antibiotic- and infection control policies and bring both areas of expertise within the responsibility of the same committee.	• Consolidate AMS and infection control policies under one committee.
	2.2 Set up an Antibiotic team (A-team).	• Establish an A-team comprised of a physician, pharmacist, clinical microbiologist, and preferably also an infection control practitioner.
	2.3 Discuss the AMS program with all physicians and make the AMS program a regular topic during meetings (e.g., pharmacotherapy audit meetings (PTAMs)).	• Involve all physicians from the start and keeping them informed about the process. • Make the AMS program a regular topic in during meetings (e.g., PTAMs).
	2.4 Offer education on antibiotic use and resistance to nurses and carers.	• Determine the mode(s) of education, as well as whether it should be followed during work or personal time, and the possibility to gain accreditation points.
	2.5 Discuss how volunteers should be informed.	• Use reliable, publicly accessible sources of information to disseminate.
	2.6 Discuss how to inform residents/their representatives.	• Inform residents through various media. • Use reliable, publicly accessible sources of information to disseminate.

Continuation Table 2. Summary of recommendations to implement an AMS program

Basic conditions	Recommendations	Elaboration
A-team activities	3.1 Define the responsibilities and authority of the A-team.	• Keep treatment protocols up-to-date. • Monitor compliance. • Emphasize that the opinion of A-team considered as highly valued, although the ultimate responsibility for prescribing antibiotics remains of the individual physician.
	3.2 Define the working process of the A-team, including selection criteria.	• Conduct a periodic retrospective review of the antibiotic prescriptions prior to scheduled plenary meetings (e.g., PTAMs) based on predetermined selection criteria. • Evaluate the activities of the A-team among colleague physicians.
	3.3 Define the tasks of all A-team members.	• Define the tasks of each A-team member.

Authors' contributions

AE-B: Conceptualization, methodology, investigation, data curation, writing – original draft, writing – review & editing, visualization, project administration; MvL: Conceptualization, methodology, investigation, data curation, writing – review & editing; EL-S: Conceptualization, methodology, investigation, writing – review & editing; MN-V: Conceptualization, methodology, resources, writing – review & editing; MV: Conceptualization, methodology, writing – review & editing, supervision, funding acquisition; PG: Conceptualization, methodology, resources, funding acquisition, writing – review & editing: SN: Conceptualization, methodology, writing – review & editing; AV: Conceptualization, methodology, investigation, resources, writing – review & editing, supervision.

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Availability of data and materials
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Declarations

Competing interests
The authors declare no competing interests.

Ethical Approval
Not applicable.

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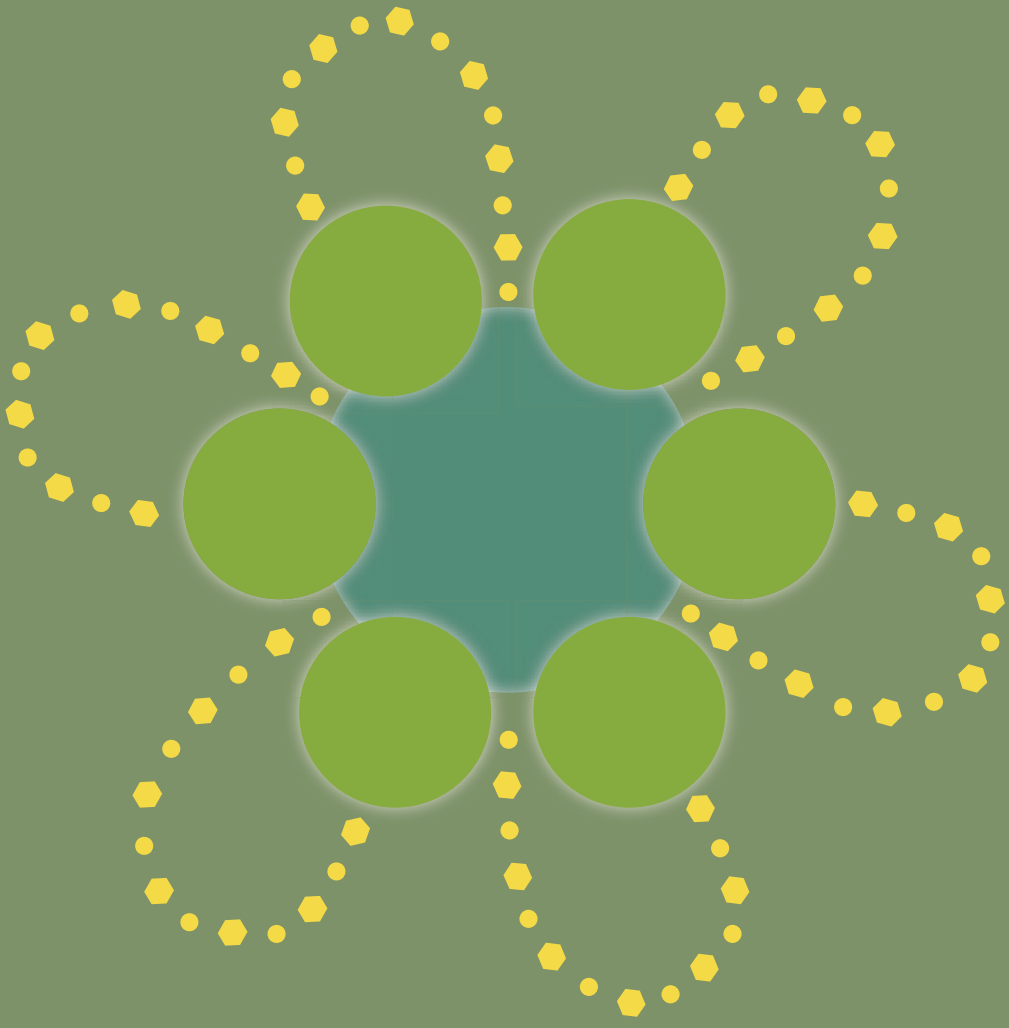
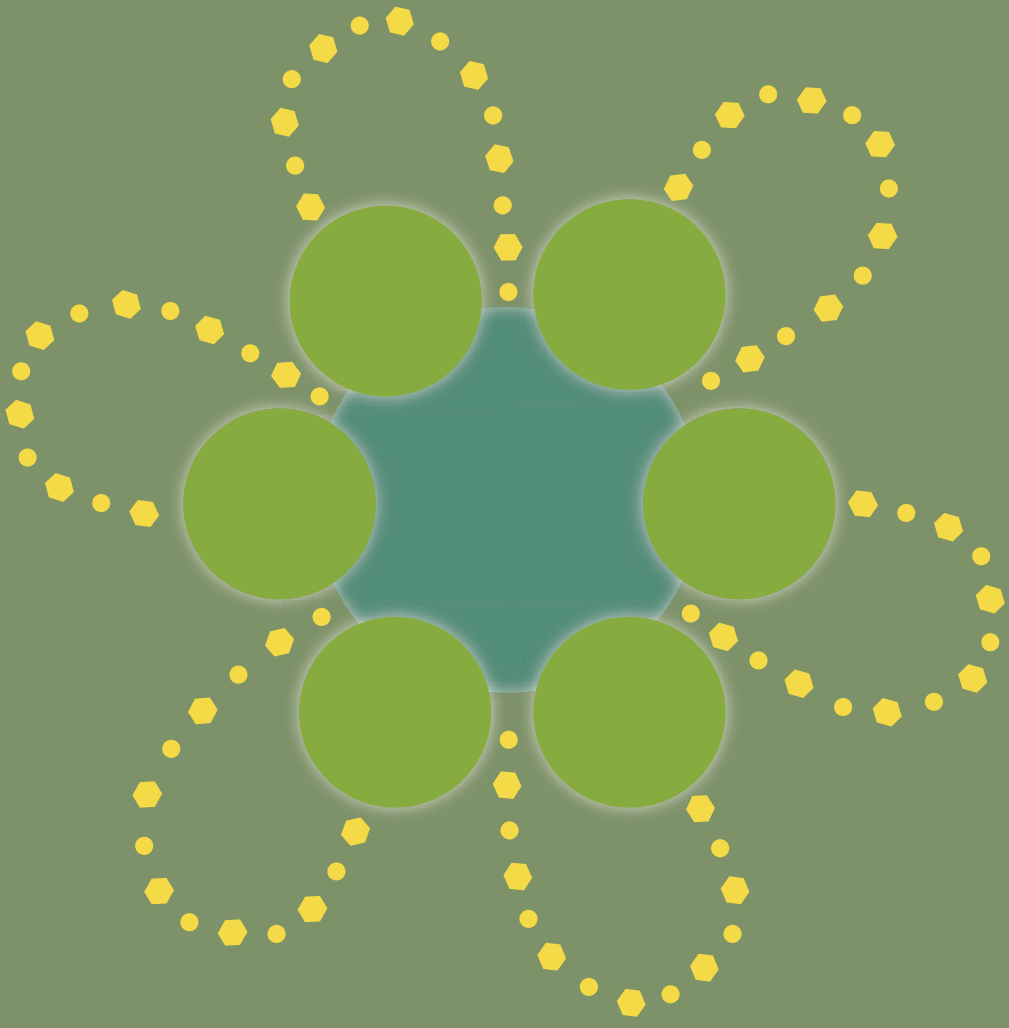


PART 3
COVID-19 TESTING HEALTHCARE WORKERS WORKING IN ELDERLY CARE



CHAPTER 8

Healthcare workers in elderly care: A source of silent SARS-CoV-2 transmission?

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medRχiv, 2020 Sept 09

Abstract

Importance: Healthcare workers (HCWs), including those with mild symptoms, may be an important source of COVID-19 within elderly care.

Objective: To gain insight into the spread of SARS-CoV-2 among HCWs working in elderly care settings.

Design: Cross-sectional study among HCWs working in elderly care in the South-East of the Netherlands, testing for SARS-CoV-2, between March 31 and April 17, 2020.

Setting: HCWs working in geriatric rehabilitation, somatic and psychogeriatric wards or small-scale living groups and district nursing, with a total of 5245 HCWs within 4 organizations.

Participants: 621 HCWs with mild respiratory symptoms.

Main Outcomes: Number of HCWs testing positive for SARS-CoV-2 in pharyngeal swabs, using real-time reverse-transcriptase PCR targeting the SARS-CoV-2 E-gene, N-gene, and RdRP. HCWs filled out a survey to collect information on symptoms and possible sources of infection.

Results: 133/615 (21.6%) HCWs tested positive for SARS-CoV-2, ranging from 15.6 to 44.4% per elderly care organization, and from 0 to 64.3% per separate location of the organizations, respectively. 74.6% of tested HCWs were nursing staff, 1.7% elderly care physicians, 20.3% other HCWs with patient contact and 3.4% HCWs without patient contact. In the univariate analysis, fever, runny or stuffy nose, anosmia, general malaise, myalgia, headache, and ocular pain were associated with SARS-CoV-2 positivity, while gastro-intestinal symptoms and respiratory symptoms, other than runny or stuffy nose were not. Risk factors for SARS-CoV-2 positivity were contact with patients or colleagues with suspected or proven COVID-19. Whole genome sequencing of 22 samples in 2 facilities strongly suggests spread within facilities.

Conclusions and Relevance: We found a high SARS-CoV-2 prevalence among HCWs in nursing homes and district nursing, supporting the hypothesis of undetected spread within elderly care facilities. Structural testing of elderly care HCWs, including track and trace of contacts, should be performed to control this spread, even when only mild symptoms are present.

Introduction

On February 27, 2020, the first COVID-19 patient was detected in the Netherlands.[1] On March 31, there were 12,595 Dutch patients known to be SARS-CoV-2 positive.[2] As of early March, healthcare workers (HCWs) in acute-care settings, including those with mild symptoms, were widely tested, whereas public health services followed different testing strategies for other HCWs. At that time, the public health testing strategy included testing the first two residents with symptoms suggesting COVID-19 within a cohort in an elderly care facility and in case of positive results, precautions for the entire ward were taken. Testing of HCWs was not routinely performed. On March 19, a national policy was launched to ban all visitors to elderly care facilities. Our facilities implemented the ban with exception of end-of life-situations and in case of serious behavioural problems. At about that time all HCWs were asked to wear a medical mask in case of mild symptoms. Also, patients with respiratory symptoms without contact with COVID-positive patients, or travel to endemic region were considered to be at risk of having COVID-19. As of April 6, the national public health strategy was changed, to include testing of HCWs in non-acute settings in case of fever and/or respiratory complaints. Preceding this policy change, we tested HCWs in our regional elderly care facilities and district nursing, to gain insight into the spread of SARS-CoV-2 among HCWs within elderly care, including symptoms and risk factors for acquisition of SARS-CoV-2.

Methods

Study design

A cross-sectional study was performed among HCWs working in elderly care in the South-East of the Netherlands, testing for SARS-CoV-2. In total 621 (11.8%) HCWs were tested spread over four organizations with a total of 5245 HCWs; 536 HCWs working in geriatric rehabilitation, somatic and psychogeriatric wards or small-scale living groups spread over 46 locations, and 85 HCWs working in district nursing in two out of four organizations. Written informed consent was obtained from all HCWs. Analyses were performed on de-identified data.

Study population

HCWs with mild respiratory symptoms (not included in the case definition of COVID-19 at that time) were voluntarily tested between March 31 and April 17, 2020. HCWs were selected based on necessity for continuity of care or concerns with HCW's health status. While the study was primarily intended to only include HCWs with

mild symptoms, not included in the case definition of COVID-19 at that time, nursing homes used the opportunity to finally get their HCWs tested, as the public health services policy at this time only tested the first two cases per unit. Consequently, the included population became a mixture of HCWs with mild to moderate symptoms.

Procedures

Survey

At the moment of testing, HCWs filled out a survey to collect information on symptoms and possible sources of infection. Information was collected on general non-respiratory symptoms (general malaise, anosmia, fever, myalgia, ocular pain, headache, chest pain), respiratory symptoms (runny or stuffy nose, coughing, dyspnoea, sore throat) and gastro-intestinal symptoms (abdominal pain, vomiting, diarrhoea or loose stools), possible sources of infection (attendance to event >50 people, travel abroad, contact with persons suspected or positive for SARS-CoV-2 infection (patients, colleagues, household members or others), and date of start of symptoms.

PCR

Pharyngeal swabs were collected by dedicated personnel, and samples were sent to Wageningen Bioveterinary Research for real-time reverse-transcriptase PCR targeting the SARS-CoV-2 E-gene, N-gene, and RdRP. Extraction was performed on the KingFisher Flex (Thermofisher) with the ID Gene Mag Fast Extraction Kit (ID-Vet Genetics), with an input volume of 145 µl sample and 150 µl lysis buffer, and an output volume of 60 µl. The extraction was internally controlled (duplex PCR) using 5 µl green fluorescent protein (GFP)-RNA. Amplification and detection was performed on the QuantStudio5 (Applied Biosystems) with a cycling profile of 10 min at 52°C, 3 min at 95°C, 45 cycles of 15 sec at 95°C and 30 sec at 58°C. Extracted nucleic acids were amplified using TaqMan Fast Virus 1-step Master Mix (Applied Biosystems), and primer and probe mixture for the E gene as described previously (0.4 uM/primer, 0.2 uM probe).[3] Analyses were performed using QuantStudio5 Design & Analysissoftware v 1.4.3 (threshold 0.1, and visual check of curves). In case of inconclusive PCR results, HCWs were retested.

WGS

Whole genome sequencing (WGS) was performed on a convenience sample of pharyngeal swabs, including samples from known COVID-19 nursing home residents at the corresponding locations. Complete genome sequences were generated by SARS-CoV-2 specific, amplicon-based Nanopore sequencing, as previously described.[4] Sequences were aligned and analysed against the background of a nationally representative set of genomes as described.[4] Analyses were performed using a maximum likelihood tree.

Statistical analysis

Continuous variables are expressed as medians and ranges. Categorical variables are expressed as counts and percentages. No formal sample size calculation was performed. Groups were compared using Pearson's Chi-square test, Fisher's exact test in case of expected counts <5, or Mann-Whitney-U test, and p-values <0.05 were considered statistically significant. Risk ratios were calculated to determine effect size. All analyses were performed with SPSS version 25 (IBM, Armonk, NY, USA).

Results

A total of 621 HCW were tested for SARS-CoV-2, of which six had inconclusive RT-PCR results and were excluded from analyses. Of the 615 remaining HCWs, 133 (21.6%) tested positive (2.5% of all HCWs from the 4 elderly care organizations). The positive HCWs were from all (n=4) elderly care organizations, and from 18 out of 46 (39.1%) locations, respectively. In case of incidental missing values, HCWs were still included, therefore denominators differ throughout the paper. Ten cases with major omissions in the survey were deleted completely from analyses.

Per location, a median of five HCWs were tested, ranging from 1 to 83. The percentage of HCWs infected with SARS-CoV-2 per elderly care organization ranged from 15.6 to 44.4%, and from 0 to 64.3% per separate location of the organizations, respectively. 444 (74.6%) of tested HCWs were nursing staff, 10 (1.7%) elderly care physicians, 121 (20.3%) other HCWs with patient contact (such as nutrition- and living assistants, cleaners) and 20 (3.4%) HCWs without patient contact (Table 1). Median age was 48.7 years, and 6.1% was male. The majority of tested HCWs experienced coughing (67.8%), runny or stuffy nose (66.6%), and general malaise (66.4%).

In univariate analysis, fever, runny or stuffy nose, anosmia, general malaise, myalgia, headache, and ocular pain were associated with SARS-CoV-2 positivity (Table 2, p<0.05). Gastro-intestinal symptoms and respiratory symptoms with the exception of runny or stuffy nose were not associated with a positive SARS-CoV-2 test. SARS-CoV-2 positive HCWs without fever (n=80) presented more often with runny or stuffy nose than HCWs with fever (n=51) (83.8 vs 60.8%). They also report more often working with complaints (75.0 vs 50.0%). SARS-CoV-2 positive HCWs with fever more often presented with general malaise, myalgia, and headache than HCW without fever (96.1 vs 82.5%; 72.5 vs 50%; and 74.5 vs 56.3% respectively, p<0.05).

In our population, attendance to events with more than 50 people, and travel abroad the last 14 days before start of symptoms, were not related to a positive SARS-CoV-2 PCR (Table 3). SARS-CoV-2 positive HCWs more often had contact with any person either proven (63.1 versus 37.7%) or suspected of (71.5 versus 48.1%) COVID-19 than those not infected. HCWs infected with SARS-CoV-2 significantly more often reported contact with patients or colleagues with suspected or proven COVID-19 than those not infected. No difference was seen in contact with proven or suspected household members or other contacts.

Median reported duration of symptoms before testing was 7 days (range 1-44 days) in SARS-CoV-2 positive HCW, and 11 (range 0-53) days in SARS-CoV-2 negative HCWs ($p<0.001$) and is depicted in Figure 1. About 1 out of 10 (11.8%) of the HCWs were no longer able to report the first day of symptoms. One of eight (12.5%) HCWs tested on the first reported day of symptoms, tested positive. For days 2-7, 8-14 and >14, 72/215 (33.5%); 31/141 (22.0%) and 17/169 (10.1%) HCWs tested positive, respectively. In 73 (13.7%) HCWs the reported duration of symptoms was > 21 days, of which seven tested positive. In total 391 (65.6%) HCWs report to have worked while symptomatic, with no difference between HCWs testing positive or negative.

WGS

WGS was performed on 9 samples from one location, and 13 samples from another location. Two patients and seven HCWs from the first location cluster together, and five patients and seven HCWs from the second location cluster together, strongly suggesting spread within the nursing home. Only one patient in the second location had a unique strain, suggesting a separate introduction.

Table 1. Demographics and symptoms of HCWs tested for SARS-CoV-2, by PCR result

	Positive (n=131)		**Negative (n=474)**	
Demographics				
Male	9	6.9%	28[a]	5.9%
Age (years)	48.9	18.5-65.0	48.6[a]	19.4-68.6
Profession[b]				
Medical doctor	0	0.0%	10	2.1%
Nurse	94	72.9%	350	75.1%
Other with patient contact	35	27.1%	86	18.4%
HCW without patient contact	0	0.0%	20	4.3%

Results are given as n (%), or median (range). [a] Missing value for one HCW. [b] Missing values for 2 positive and 8 negative HCWs

Table 2. Symptoms of HCWs testing positive and negative for SARS-CoV-2

	Positive (n=131)		Negative (n=474)		RR (95% CI)	p-value
General non-respiratory symptoms						
General malaise	115	87.8%	287	60.5%	3.6 (2.2-6.0)	<0.001
Anosmia	81[b]	62.3%	126	26.6%	3.2 (2.3-4.3)	<0.001
Fever[a]	51	38.9%	79	16.7%	2.3 (1.7-3.1)	<0.001
Myalgia	77	58.8%	164	34.6%	2.2 (1.6-2.9)	<0.001
Ocular pain	39	29.8%	91	19.2%	1.5 (1.1-2.1)	0.009
Headache	83	63.4%	254	53.6%	1.4 (1.0-1.9)	0.046
Chest pain	39	29.8%	108	22.8%	1.3 (1.0-1.8)	0.099
Respiratory symptoms						
Runny or stuffy nose	98	74.8%	305	64.3%	1.5 (1.0-2.1)	0.025
Coughing	94	71.8%	315[c]	66.7%	1.2 (0.9-1.7)	0.277
Dyspnoea	55	42.0%	195	41.1%	1.0 (0.8-1.4)	0.862
Sore throat	64[a]	49.2%	262[b]	55.4%	0.8 (0.6-1.1)	0.212
Gastro-intestinal symptoms						
Abdominal pain	18	13.7%	49[b]	10.4%	1.3 (0.8-2.0)	0.276
Vomiting	3[b]	2.3%	9[b]	1.9%	1.2 (0.4-3.1)	0.728
Diarrhoea or loose stools	31	23.7%	107	22.6%	1.0 (0.7-1.5)	0.792
Combined symptoms						
Mild respiratory symptoms (runny or stuffy nose and/or coughing and/or sore throat)	122	93.1%	419	88.4%	1.6 (0.9-3.0)	0.119
More severe symptoms (fever and/or dyspnoea and/or myalgia and/or general malaise)	122	93.1%	347	73.2%	3.9 (2.1-7.5)	<0.001

Results are given as n (%), or median (range). [a] Fever is defined as temperature >38^{0}C or >37.5^{0}C with paracetamol. [b] Missing value for one HCW. [c] Missing value for two HCWs

Table 3. Possible sources of infection within 14 days before start of symptoms[a]

	Positive (n=131)		Negative (n=474)		p-value
Attendance to event >50 people	8	6.1%	36[b]	7.6%	0.554
Travel abroad	4	3.1%	19[b]	4.0%	0.607
Contact with person suspected or positive for SARS-CoV-2 infection[c]					
Patient	93	71.5%	187	39.7%	<0.001
Colleague	36	27.7%	76	16.1%	0.003
Household member	6	4.6%	36	7.6%	0.231
Other	12	9.2%	50	10.6%	0.646
No known contact	20	15.4%	192	40.8%	<0.001

[a] Multiple possible sources of infection per HCW are possible. [b] Missing value for two HCWs. [c] Missing values for one positive and three negative HCWs.

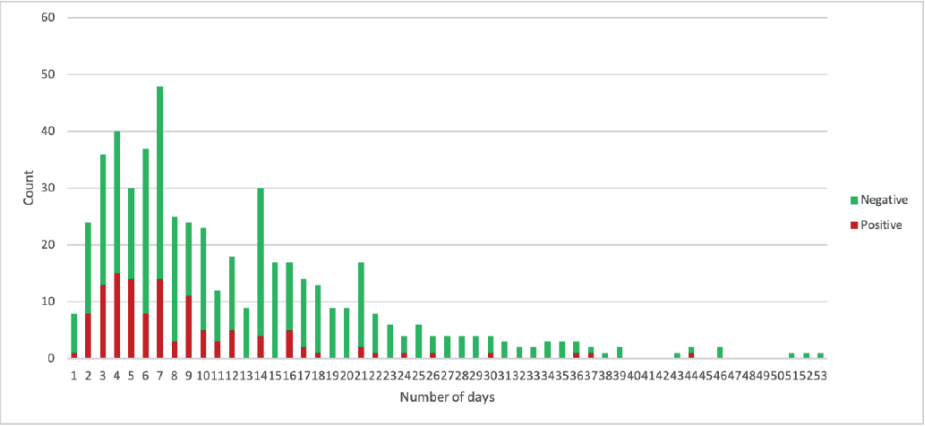

Figure 1. Reported duration of symptoms preceding testing of 533 HCWs in elderly care facilities

Discussion

In a sample of 621 HCWs with mild complaints working in 44 different nursing homes and district nursing, 21.6% tested positive for SARS-CoV-2. This high prevalence supports the hypothesis of undetected spread within elderly care facilities. Using WGS we documented the spread between patients and HCWs within two facilities with positive HCWs and patients.

We found a larger proportion of HCWs positive than the prevalence of 6% of COVID-19 amongst 86 symptomatic hospital HCWs in two Dutch hospitals[5], and 9%

of tested HCW in a university medical centre in our region[6]. There are a few possible explanations for this high prevalence. Our study was performed at a later time, when the prevalence and community spread of COVID-19 was higher in the Netherlands. Hospitals and elderly care facilities differ in the fact that in elderly care facilities there is a strong emphasis on living conditions and social interactions, and until closing of the facilities on March 19, introductions into the facilities could take place not only through HCWs, but also through visitors, and residents visiting places outside the facility, providing opportunity for repeated introduction of SARS-CoV-2 through individuals infected in the community.[5] At the time of our study, nursing home clients with respiratory symptoms were only considered to be at risk of having COVID-19 when they had been in contact with a proven COVID-19-positive patients, or travelled to an endemic region. Mild symptoms such as anosmia or atypical symptoms such as diarrhoea were not recognized as symptoms for COVID-19. In addition, the use of personal protective equipment (PPE) such as masks in the nursing homes, was, at this time, limited to positive or suspected patients and even within that group not always adequate.

The majority of the tested HCWs (66%) report to have worked while symptomatic, which is comparable to 63% recently reported in Dutch hospitals.[5] In addition, only as of mid-March, HCWs had to wear masks at all times in case of mild complaints. The large proportion of HCWs coming to work while symptomatic and the late introduction of masks for HCWs with mild symptoms, certainly contributed to preventable spread of SARS-CoV-2 in this setting.

Contact tracing is an important measure to detect and isolate infection sources and reduce transmission.[7] Within the long-term care setting HCWs are less familiar with the measure, it is more difficult to perform, especially as low-threshold testing of patients was not available on the same scale as in hospitals.

Important risk factors that lead to the introduction of SARS-CoV-2 into the Netherlands, such as travel abroad and attendance of large-scale events (e.g., carnival), had no significant role (or no longer) in transmission of SARS-CoV-2 within our population of HCWs working in elderly care. At the time of our study COVID-19 was already widespread in the community.[4] We did identify contact with patients or colleagues with suspected or proven COVID-19 as a risk factor for SARS-CoV-2 positivity, while no difference was seen in contact with proven or suspected household members or other contacts, suggesting that a significant proportion of infections in HCWs were acquired in the elderly care setting.

We identified fever, runny or stuffy nose, anosmia, general malaise, myalgia, headache and ocular pain to be associated with SARS-CoV-2 positivity, which is largely in line with symptoms identified in a recent Dutch study in hospital-based HCWs.[6] Gastro-intestinal symptoms and respiratory symptoms with the exception of runny or stuffy nose were not associated with a positive SARS-CoV-2 test, and cannot be used in differentiating between a positive and a negative test within HCWs with complaints. Fever was only present in 38.9% of HCWs with COVID-19, so other symptoms should be included to identify HCWs that should be tested. We used the definition of mild respiratory symptoms (runny or stuffy nose and/or coughing and/or sore throat) to identify HCWs that should use a medical mask during patient contact. 93.1% of SARS-CoV-2 positive HCWs met this definition, however, also 88.4% of SARS-CoV-2 negative HCWs, and this definition is therefore not discriminating between SARS-CoV-2 positivity and negativity. We used a definition of more severe symptoms (fever and/or dyspnoea and/or myalgia and/or general malaise) to identify HCWs that were banned from work and should be tested. This latter definition was associated with a risk ratio of a positive test of 3.9 (95% confidence interval 2.1-7.5, $p<0.001$). Seven HCWs report to have had symptoms for an extended period (>21 days) before they tested positive. This can resemble actual long-time positivity; however, initial complaints might have been unrelated to COVID-19, and only mild additional symptoms developed in a later stage.

There are several limitations to this study. First, as HCWs were not familiar with nasopharyngeal swabs, throat swabs were used for testing, which might be less sensitive, and may have let to under detection of SARS-CoV-2.[8,9] Also, as a consequence of the cross-sectional nature of our study, timing of swabs was not optimal, probably leading to under detection of HCWs testing too late in the course of their disease. More studies are needed to determine the prevalence of COVID-19 in this population, possibly based on serological testing.

In this study we showed a large previously undetected pool of COVID-19 within elderly care settings, namely the HCWs. Structural testing of elderly care HCWs, including track and trace of contacts, should take place to control this spread, even when only mild symptoms are present.

Contributors

AV initiated the study. AE-B collected the data. MD analysed the data and wrote the first version of the manuscript. All authors revised the manuscript and approved the final version.

Declaration of interest
We declare no competing interests.

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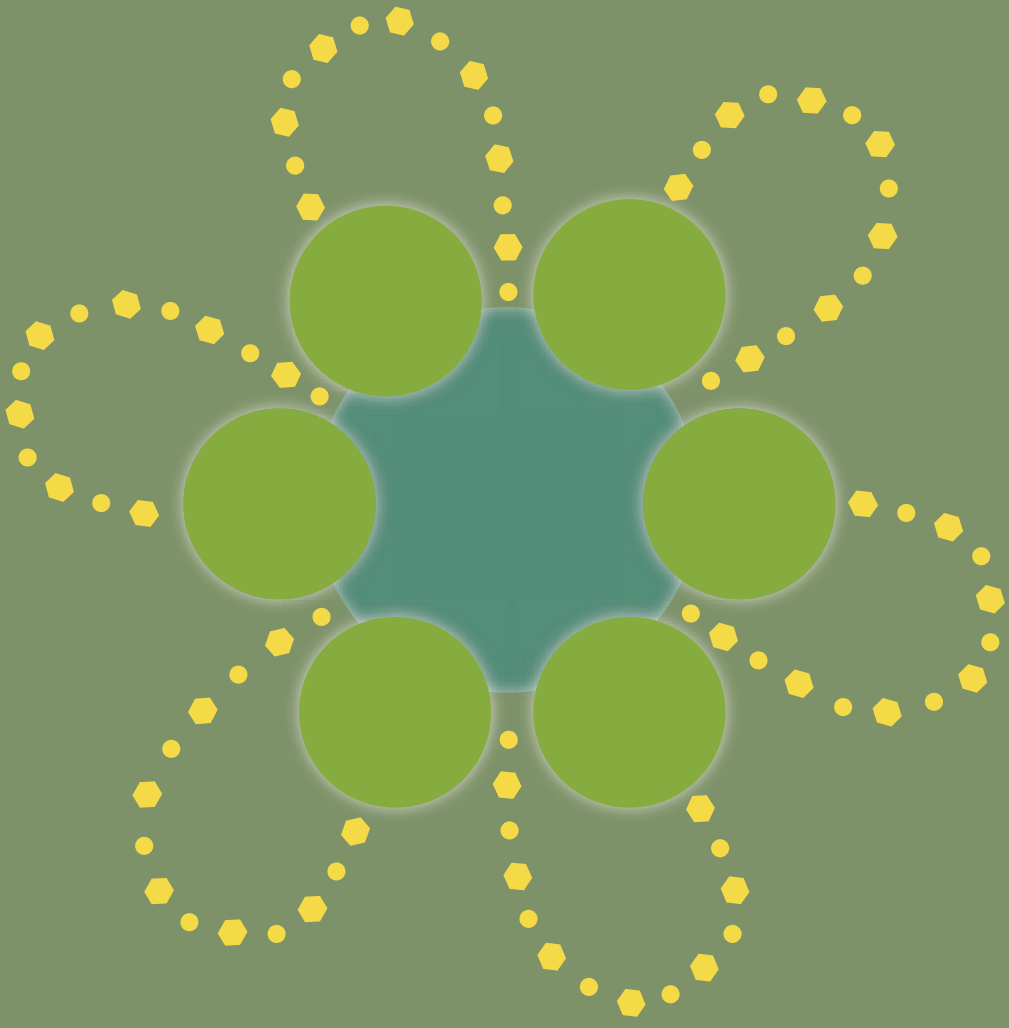

Chapter 9

Evaluation of the Abbott PanbioTM COVID-19 antigen detection rapid diagnostic test among healthcare workers in elderly care

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Abstract

Background: Coronavirus disease 2019 (COVID-19) has been especially dangerous for elderly people. To reduce the risk of transmission from healthcare workers to elderly people, it is of utmost importance to detect possible severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive healthcare workers as early as possible. We aimed to determine whether the Abbott Panbio™ COVID-19 antigen detection rapid diagnostic test (Ag-RDT) could be used as an alternative to reverse transcription-quantitative polymerase chain reaction (RT-qPCR). The second aim was to compare the cycle threshold (Ct) in RT-qPCR with the results of the Ag-RDT.

Methods: A prospective diagnostic evaluation of the Abbott Panbio™ COVID-19 Ag-RDT among healthcare workers across three elderly care facilities as well as home-based elderly care workers who met clinical criteria for COVID-19 during the second wave of the COVID-19 pandemic. Per healthcare worker, the first nasopharyngeal swab was obtained to perform the Ag-RDT and the second swab for RT-qPCR. A Ct-value of < 40 was interpreted as positive, ≥ 40 as negative.

Results: A total of 683 healthcare workers with COVID-19 symptoms were sampled for detection of SARS-CoV-2 by both Ag-RDT and RT-qPCR. Sixty-three healthcare workers (9.2%) tested positive for SARS-CoV-2 by RT-qPCR. The overall sensitivity of Ag-RDT was 81.0% sensitivity (95%CI: 69.6-88.8%) and 100% specificity (95%CI: 99.4-100%). Using a cut-off Ct-value of 32, the sensitivity increased to 92.7% (95% CI: 82.7-97.1%). Negative Ag-RDT results were moderately associated with higher Ct-values ($r = 0.62$) compared to positive Ag-RDT results.

Conclusion: The Panbio™ COVID-19 Ag-RDT can be used to quickly detect positive SARS-CoV-2 healthcare workers. Negative Ag-RDT should be confirmed by RT-qPCR. In case of severe understaffing and with careful consideration, fully vaccinated healthcare workers with Ag-RDT negative results could work with a mask pending PCR results.

Keywords: COVID-19, SARS-CoV-2, Panbio, Rapid antigen test, Elderly care, Healthcare workers.

Introduction

Elderly care facilities are high-risk settings for transmission of COVID-19 to and among residents and healthcare workers. Residents are at a higher risk of developing severe infection due to age and comorbidities. Early detection of SARS-CoV-2 among healthcare workers and vulnerable residents and rapid contact tracing are critical to reduce the risk of SARS-CoV2 transmission and COVID-19-associated morbidity and mortality [1, 2].

Given the epidemiology of the COVID-19 epidemic and changes in guidelines for elderly-care facilities [3], there is a strongly increasing test demand for SARS-CoV-2. Therefore, antigen detection rapid diagnostic tests (Ag-RDTs) with fast results may be an inexpensive, scalable solution. The ministry of Health, Welfare and Sport (VWS) and National Institute for Public Health and the Environment (RIVM) have selected five Ag-RDTs for clinical validation based on the technical validation and potential availability [4]. The Panbio™ COVID-19 Ag rapid test is one of the selected Ag-RDTs and generates a result within 15 minutes. This Ag-RDT was ordered by the elderly care facilities when it became available within the regular ordering system. The manufacturer of the Panbio™ COVID-19 Ag rapid test reported 93.3% sensitivity and 99.4% specificity in specimen post onset symptoms or suspected exposure. The diagnostic performance of this test among healthcare workers is not known.

Our objective was to determine whether the Panbio™ COVID-19 Ag-RDT can be used as an alternative to reverse transcription-quantitative polymerase chain reaction (RT-qPCR) among healthcare workers working in elderly care. Moreover, the cycle threshold (Ct) in RT-qPCR, which is needed to detect virus and inversely proportional to the viral load, was determined.

Methods

Study design and population

Between November 2020 and January 2021, we conducted a prospective diagnostic evaluation of the Panbio™ COVID-19 Ag rapid test determined against RT-qPCR, which is considered as the 'gold standard', among healthcare workers working in elderly care facilities as well as in home-based elderly care who met clinical criteria for COVID-19 [5]. Written information about this study was provided by email to all healthcare workers of the organization and verbal information was given on the spot when healthcare workers came to test. The reasons of healthcare workers who did not want to participate were not registered given the extra workload.

Procedures

Training of personnel

Prior to the start of the study, personnel of the elderly care organization were trained to perform the Ag-RDT in accordance with the manufacturer's protocol.

Nasopharyngeal swabs

Per healthcare worker, two nasopharyngeal swabs were obtained consecutively by dedicated personnel of the organizations themselves wearing personal protective equipment. The first nasopharyngeal swab was taken to perform the Ag-RDT and the second nasopharyngeal swab for RT-qPCR by the laboratory.

Panbio TM COVID-19 Ag rapid test

Panbio™ COVID-19 Ag rapid test device by Abbott (Lake Country, IL, U.S.A) is a membrane-based immunochromatography assay which detects the nucleocapsid protein of SARS-CoV-2 in nasopharyngeal samples. Collected swabs were transferred into dedicated sample collection tubes containing a lysis buffer provided with the test kit. Samples were processed on site, directly after collection. After 15 minutes of assay initiation, tests were interpreted. The test results were documented on the questionnaire as well as the image of the result window on the test device for processing and analysing the data by the researcher. The laboratory analysts involved in doing RT-qPCR were not informed about the result of the Ag-RDTs.

RT-qPCR

Nasopharyngeal swabs were collected using ∑-Transwab® in 1 ml liquid Amies medium and PCR was conducted in a certified clinical laboratory with procedures validated in accordance with the NEN-EN-ISO 15189 standard. Nucleic acid (NA) extraction was performed using MagNA Pure 96 DNA and Viral NA Small Volume Kit and MagNA Pure 96 Instrument (Roche Diagnostics GmbH, Mannheim, Germany) by following the manufacturer's instructions. Before NA extraction, the internal control phocine distemper virus (PhDV) was added to the sample via Xiril robotic workstations (Roche), while another Xiril workstation was used for PCR setup by pipetting 10 µl of NA with 10 µl of master mix containing 5 µl TaqMan® Fast Virus 1 Master Mix (Thermofisher Scientific) and 5 µl of primers and probes, targeting SARS-CoV-2 E-gene and PhDV. Thermal cycling was performed in a LC480-II instrument (Roche) with 1 cycle of reverse transcription at 50°C for 5 min followed by 1 cycle of PCR activation at 95°C for 20 sec, followed by 45 cycles of 95°C for 3 sec and 60°C for 30 sec. Data analysis was performed using Roche FLOW software (Roche) and a Ct-value of < 40 was used to interpret results as positive.

Survey

Healthcare workers were asked to fill out a questionnaire regarding (onset of) symptoms, risk of exposure to SARS-CoV-2 and history of SARS-CoV-2 positivity. Dedicated personnel who performed the Ag-RDT completed the questionnaire with the result of the Ag-RDT.

Scenarios for test results

In addition to current local guidelines for prevention of COVID-19, scenarios were described for testing either positive or negative Ag-RDT (S1 File).

Statistical analysis

Categorical variables were expressed as counts and percentages. Continuous variables were expressed as mean, median, interquartile range (IQR) and/or minimum-maximum (min - max). Difference testing for comparisons of groups was performed with Fisher's exact tests for categorical variables and Mann-Whitney U tests for non-normally distributed continuous variables. Two-sided p-values less than or equal to 0.05 were considered statistically significant for all variables, with the exception of duration of symptoms and Ct-values for which a one-sided test was applied. Risk ratios were calculated to determine effect sizes of symptoms for positive SARS-CoV-2 results by RT-qPCR.

A Ct-value < 32 for E-gene, which is associated with culturable virus in nasopharyngeal specimen and therefore considered as infectious [6], was applied to the analysis mentioned below. Association (*r*) between Ag-RDT results and Ct-values was calculated from the z-score of the Mann-Whitney U test. Association between COVID-19 symptoms and Ct-values was determined using Spearman's Rho (ρ). Sensitivity, specificity and predictive values of the Ag-RDT were calculated with 95% confidence intervals (CI) using the RT-qPCR as the 'gold standard'. The level of agreement between the tests was evaluated using Cohen's kappa score.

Analyses were performed with SPSS statistics 27 (IBM), whereby 95% CI were calculated using OpenEpi version 3.0.3 (http://www.openepi.com/).

Ethical approval

The study was reviewed (File number CMO: 2020-7083) by the ethics committee of the Radboud University Medical Centre, which decided that the study is not subject to the Medical Research Involving Human Subjects Act and did not require full review by an accredited Medical Research Ethics Committee. All participants have provided written informed consent.

Results

Healthcare workers' characteristics

A total of 683 healthcare workers with COVID-19 symptoms were sampled for detection of SARS-CoV-2 by both Ag-RDT and RT-qPCR. Based on RT-qPCR, 63 healthcare workers (9.2%) tested positive for SARS-CoV-2 from 11 November 2020 to 15 January 2021. The mean age of the respondents was 43.2 years (median 46.0; IQR 24.0, min – max: 16-65 years) of which 641 (93.9%) were female. Six (9.5%) of the 63 SARS-CoV-2 positive healthcare workers reported to have tested SARS-CoV-2 positive previously. Results of the samples from these six healthcare workers were included in the diagnostic performance of the Ag-RDT. The reported symptoms were excluded from analyses for the reason that it was unclear whether the reported symptoms were presented at the time of the previous positive test or at the moment of this study.

Compared to negative healthcare workers, SARS-CoV-2 positive healthcare workers reported the following significantly more often: fever, flu-like symptoms (headache, muscle pain and/or fatigue), loss of taste or smell, exposure to SARS-CoV-2 positive household and close contact with SARS-CoV-2 positive person. The mean number of days between symptom(s) onset and tests among SARS-CoV-2 positive and negative healthcare workers by RT-qPCR were 2.0 and 2.2 days, respectively. Median days were equal in both groups, namely 1.0 days. These data are shown in Table 1.

Table 1. Healthcare workers characteristics

	Total N (%)	SARS-CoV-2 positive by RT-qPCR, N (%)	SARS-CoV-2 negative by RT-qPCR[1], N (%)	Risk ratio for cohort positive by RT-qPCR (95%CI)	P value[a]
COVID-19 symptoms	683				
Fever	94 (13.8)	21 (22.3)	73 (77.7)	3.1 (1.9-5.0)	<0.001
Shortness of breath	70 (10.3)	9 (12.9)	61 (87.1)	1.5 (0.8-2.8)	0.276
Respiratory symptoms	530 (77.8)	43 (8.1)	487 (91.9)	0.6 (0.4-1.0)	0.078
Headache, muscle pain, fatigue	376 (55.2)	47 (12.5)	329 (87.5)	2.4 (1.4-4.1)	0.001
Loss of taste or smell	45 (6.6)	11 (24.4)	34 (75.6)	3.0 (1.7-5.3)	0.001
Diarrhea	61 (9,0)	3 (4.9)	58 (95.1)	0.5 (0.2-1.6)	0.351
Hayfever	36 (5.3)	3 (8.3)	33 (91.7)	0.9 (0.3-2.7)	1.000
Unknown	2 (0.3)	0	2 (100)	N/A	N/A
Exposed to SARS-CoV-2 positive person					
Household	27 (4.0)	9 (33.3)	18 (66.7)	4.0 (2.2-7.3)	<0.001
Close contact[b]	132 (19.3)	20 (15.2)	112 (84.8)	1.9 (1.2-3.2)	0.018
Other contact[c]	63 (9.2)	8 (12.7)	55 (87.3)	1.4 (0.7-2.8)	0.359
Other reason for quarantine	48 (7.0)	1 (2.1)	47 (97.9)	0.2 (0.03-1.5)	0.115
Mean days between symptoms onset and both tests [median, SD]	2.2 [1.0 (2.6)]	2.0 [1.0 (2.3)]	2.2 [1.0 (2.6)]	N/A	N/A

[a]Fisher's exact test, two-sided

[b]Close contact: any individual within 1,5m distance of an infected person for at least 15 minutes or high-risk exposure less then 15 minutes

[c]Other contact: any individual at a distance of more than 1,5m of an infected person in the same room for at least 15 minutes

Among SARS-CoV-2 positive healthcare workers, there was a statistically significant association between the presence of fever and Ct values < 32 (p = 0.044); however, the association was considered as weak (ρ = 0.27). For other reported symptoms, no significant differences in Ct-values were identified (shortness of breath, p = 0.320; respiratory symptoms, p = 1.000; headache, muscle pain, fatigue, p = 0.186; loss of taste or smell, p = 1.000; diarrhea, p = 0.339).

Diagnostic performance of the Ag-RDT

As presented in Table 2, 51 healthcare workers tested positive both by RT-qPCR as well as by Ag-RDT. Twelve healthcare workers had negative Ag-RDT results but positive RT-qPCR results, leading to an overall sensitivity of 81.0% (95%CI: 69.6-88.8). When using a cut-off Ct-value of 32 instead of 40, the sensitivity of the Ag-RDT increased to 92.7% (95% CI: 82.7-97.1). False-positive Ag-RDT results were not found, resulting in a specificity of 100% (95%CI: 99.4-100).

Table 2. Diagnostic performance of Panbio™ COVID-19 antigen detection rapid test

	RT-qPCR result			Sensitivity	Specificity	PPV*	NPV‡
	Positive (Ct <32)	***Positive (Ct ≥32)***	***Negative***				
LFA§ result positive	N=51	N=0	0	Overall: 81.0% (95% CI: 69.6-88.8)	Overall: 100% (95% CI: 99.4-100)	Overall: 100 (95%CI: 93.0-100)	Overall: 98.1 (95% CI: 96.7-98.9)
LFA§ result negative	N=4	N=8	N=620	Ct < 32: 92.7% (95% CI: 82.7-97.1)	Ct < 32: (95% CI: 99.4-100)	Ct < 32: 100 (95% CI: 93.0-100)	Ct < 32: 99.4 (95% CI: 98.4-99.8)

*PPV, positive predictive value
‡NPV, negative predictive value
§LFA, lateral flow assay

As illustrated in Fig 1, the median Ct-value was significantly lower among the group of 51 healthcare workers with both positive Ag-RDT and PCR results compared to the group of 12 healthcare workers with negative Ag-RDT and positive PCR results, 20.61 and 32.34 respectively ($p < 0.001$). Negative Ag-RDT results were moderately associated with higher Ct-values ($r = 0.62$) compared to positive Ag-RDT results. The minimum and maximum Ct-value among the group with negative Ag-RDT and positive PCR results were 23.73 and 36.00, respectively. The particular Ct-values from the four healthcare workers with negative Ag-RDT and positive PCR result with Ct-value < 32 were 23.73, 24.11, 27.08 and 30.64. Among healthcare workers with both positive Ag-RDT and PCR results, minimum and maximum values were 15.00 and 29.75, respectively.

The positive predictive value (PPV) and negative predictive value (NPV) in this study cohort with a prevalence of 9.2% were 100% (95%CI: 93.0-100) and 98.1% (95%CI: 96.7-98.9), respectively. Using a cut-off Ct-value of 32, the PPV and NPV were 100% (95%CI: 93.0-100) and 99.4% (95%CI: 98.4-99.8), respectively. The overall NPV for different prevalence are shown in Fig 2. An almost perfect agreement (Cohen's kappa score = 0.885) was found between the two tests ($p < 0.001$), and when working with a cut-off Ct-value of 32 the Cohen's kappa increased to 0.959.

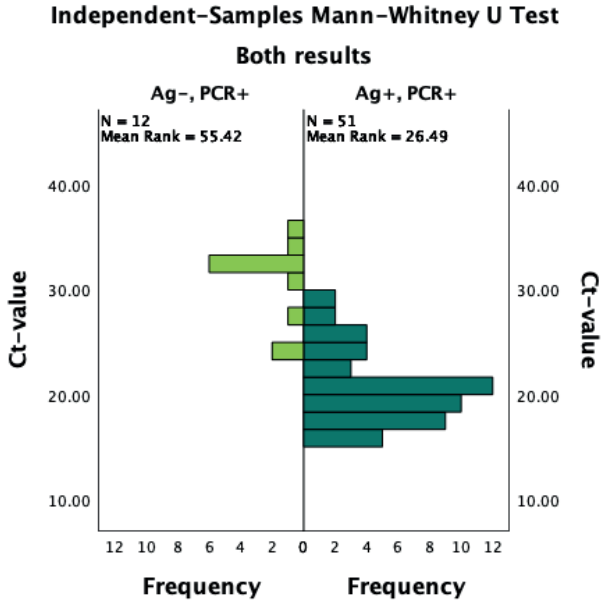

Figure 1. RT-qPCR cycle thresholds (Ct) in specimen of healthcare workers with COVID-19 symptoms testing either negative or positive by Panbio™ COVID-19 antigen detection rapid test

The figure shows the frequency of the median cycle thresholds (Ct) in RT-qPCR in specimen from healthcare workers with COVID-19 symptoms testing either negative or positive by Panbio™ COVID-19 antigen detection rapid test. PCR, RT-qPCR; LFA, lateral flow assay.

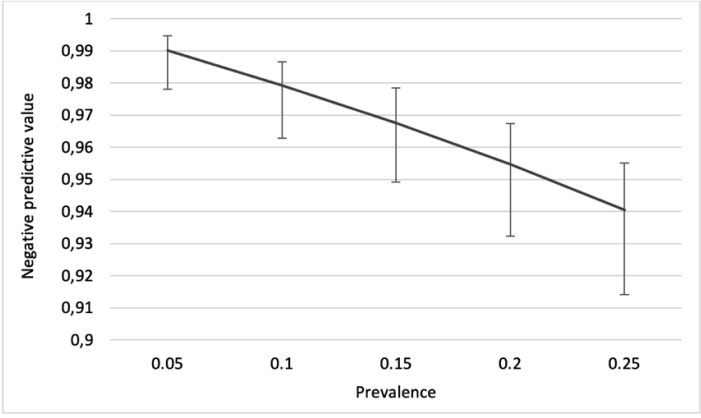

Figure 2. Negative predictive values of Panbio™ COVID-19 antigen detection rapid test for different prevalence of SARS-CoV-2

The figure shows negative predictive values and their 95% confidence intervals of the Panbio™ COVID-19 antigen detection rapid test for different prevalence of SARS-CoV-2 determined against RT-qPCR among healthcare workers working in elderly care facilities as well as in home-based elderly care who met clinical criteria for COVID-19.

Discussion

Our findings have shown that the Panbio™ COVID-19 Ag rapid test can be considered a useful Ag-RDT among healthcare workers. Positive results become quickly available and do not need to be confirmed by RT-qPCR. Contact tracing could be started appropriately and immediately. Negative Ag-RDT results should be confirmed by RT-qPCR even with a reduced prevalence of SARS-CoV-2 in this setting where healthcare workers take care of residents who are at risk of developing severe infection.

In our study, the overall agreement between RT-qPCR and the Ag-RDT was almost perfect ($\kappa = 0.885$) and increased when using a cut-off Ct-value of 32 ($\kappa = 0.959$). Positive Ag-RDT results were found in 81% of positive RT-qPCRs. In 19% of cases, false-negative results were found; however, by considering Ct-values of ≥ 32 as not infectious, false-negative results were decreased to less than 8%.

Several studies have evaluated Panbio Ag-RDT as a useful test in different settings using different cut-off Ct-values as a measure for infectiousness [7-10]. In our laboratory, primer sets targeting SARS-CoV-2 E-gene were used. Hence, we applied a cut-off Ct-value of 32 as measure for infectiousness based on a study from Huang et al. [6] to gain insight into the effect of using this cut-off value to the diagnostic performance of our Ag-RDT and to determine associations with COVID-19 symptoms. Unfortunately, SARS-CoV-2 positive healthcare workers were still prohibited from working because an (inter)national consensus on cut-off Ct-values has not yet been defined. In view of the results of our study, the probability of being infectious when having a negative Ag-RDT result is still low. Therefore, in cases of severe understaffing and pending the PCR results, it may be appropriate to allow fully vaccinated healthcare workers with a negative Ag-RDT, to work as long as they wear a face mask for the entire shift (including during breaks separate from colleagues). Given the vulnerability of the patients in this setting, these policies should be carefully considered. In addition, new SARS-CoV-2 variants may be more contagious than previous variants and vaccination may be less effective against new variants. For example, the delta variant seemed to be more than twice as contagious as previous variants [11], and vaccination was less effective at preventing transmission of the delta variant by vaccinated people than it was with the alpha variant [12]. It is also important to taking into account the time at which patients received a booster vaccination and whether they were experiencing a previous SARS-CoV-2 infection. Altarawneh et al. showed that the strongest protection against symptomatic SARS-CoV-2 infection with the BA.1 or BA. 2 sublineages of the

omicron variant was achieved by experiencing a previous SARS-CoV-2 infection and a recent booster vaccination [13].

An important drawback of this Ag-RDT is that in case of a negative result a second nasopharyngeal swab is needed for RT-qPCR. In our study, all participants provided written consent; however, we do not know if the healthcare workers who did not provide written consent refused to participate in the study because it involved the double-swab method. It does not seem to be deterrent, given the number of participants in the study period. We think that the advantage of obtaining a positive SARS-CoV-2 result rapidly could outweigh the inconvenience and discomfort using a second swab. Despite the user-friendliness of the Ag-RDT, we recommend that this test be performed by trained and dedicated personnel to achieve a high level of accuracy.

An important point to note is that our study was carried out in the common-cold/flu(-like) season, during which many healthcare workers have respiratory symptoms, as well as in a period with a high prevalence of SARS-CoV-2. In such a situation and also in a local outbreak setting, it could be beneficial, in close cooperation with a medical microbiology lab, to establish or maintain a test lane or a local test-team that uses Ag-RDTs. An additional advantage is that results can be easily tracked in order to keep an overview of SARS-CoV-2 infections on an organization-wide level. However, to determine whether this test policy could be beneficial, it is important to take into account the turnaround time for SARS-CoV-2 results by PCR when testing at the Municipal Public Health Services (in Dutch: GGD).

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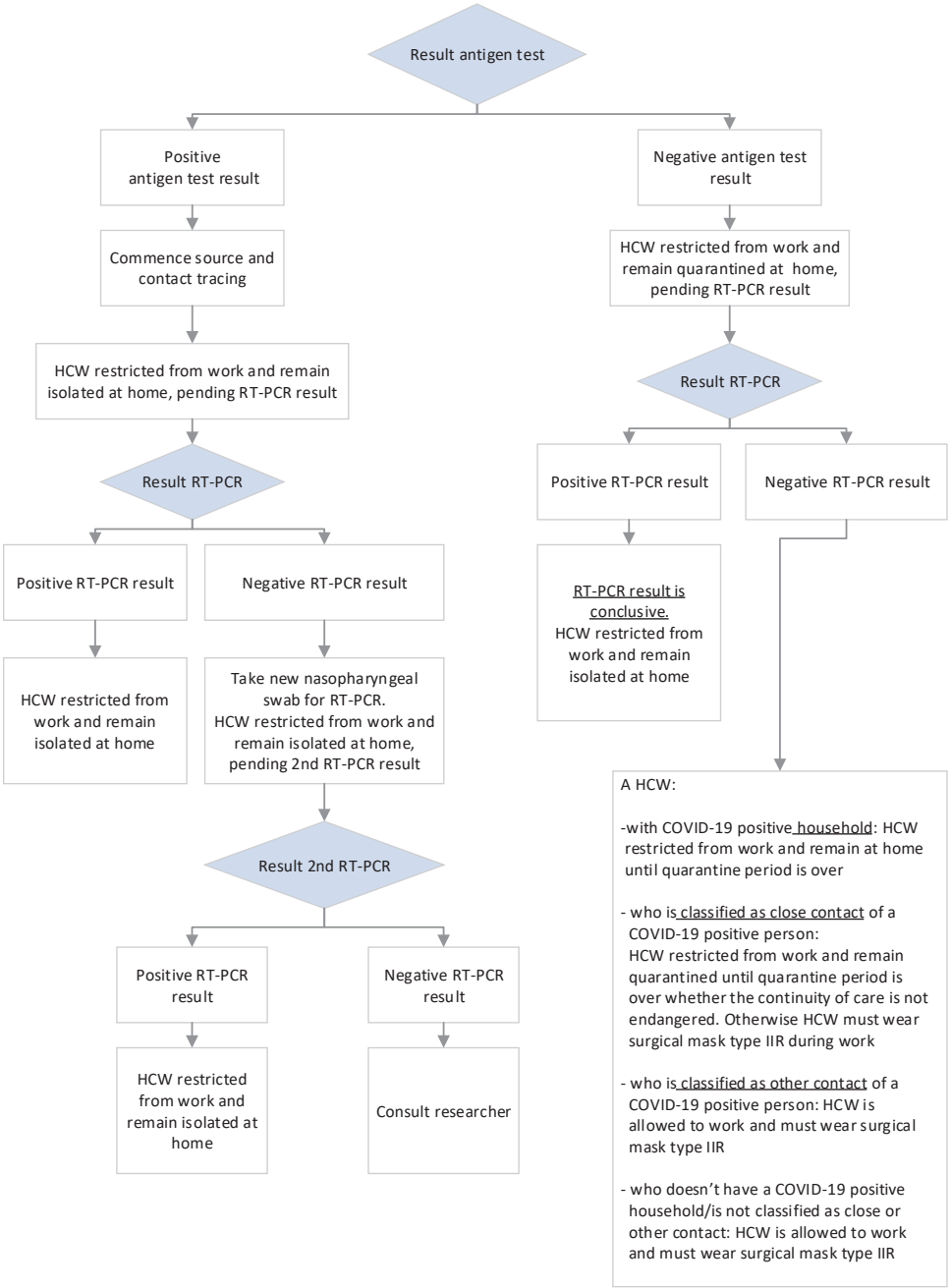
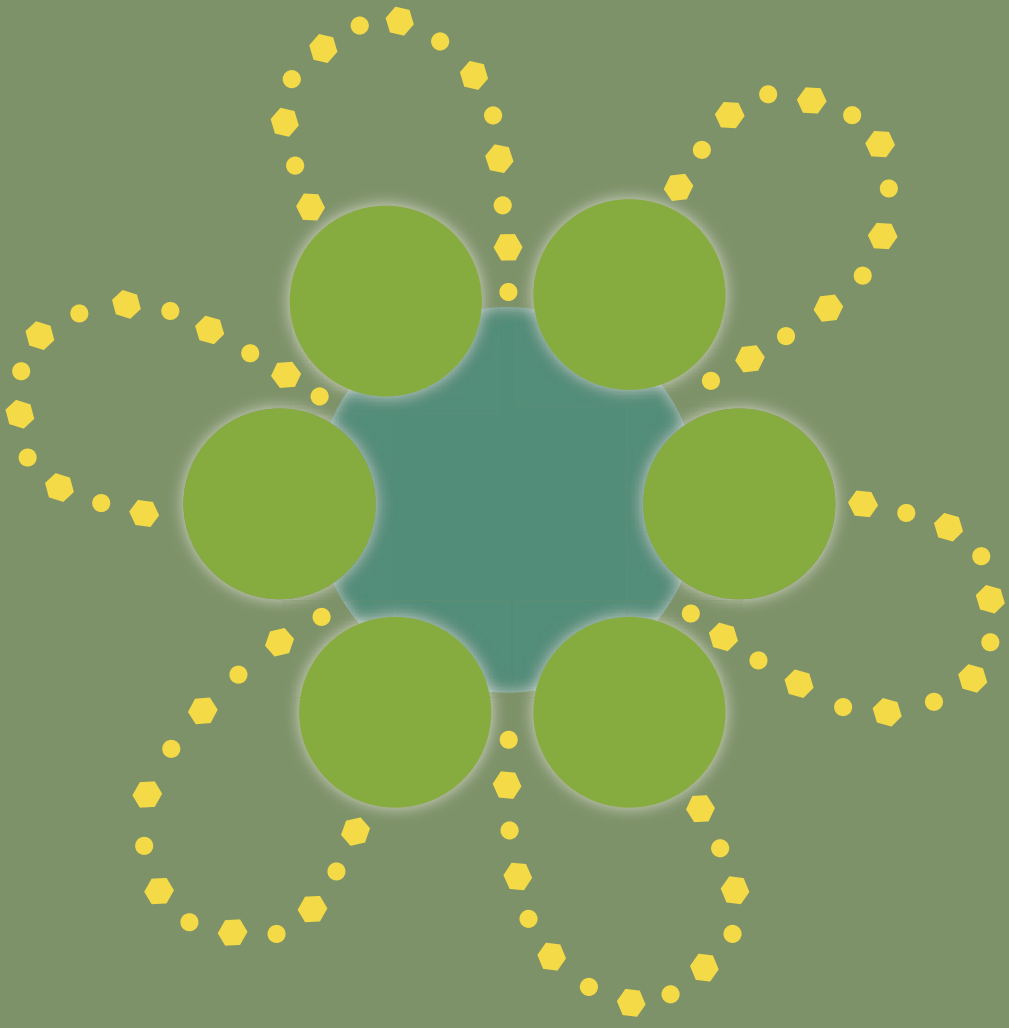
Supplementary file

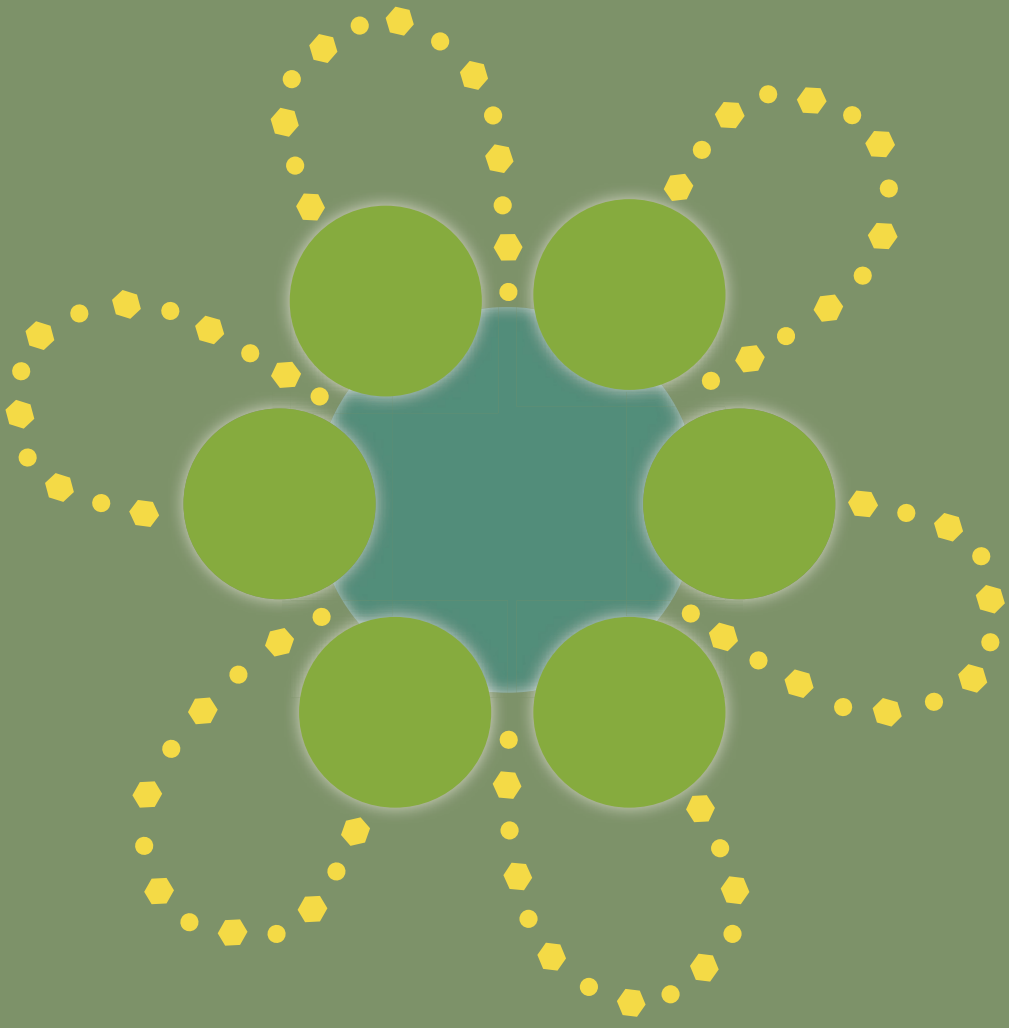


S1 File. Scenarios for antigen detection rapid test and RT-qPCR results

The figure shows scenarios for testing either positive or negative antigen detection rapid test regarding deployment of healthcare workers and retest. HCW, healthcare worker.



SUMMARY, GENERAL DISCUSSION



Chapter 10

Summary, general discussion

Summary

Chapter 1, the general introduction, outlines the context and background of the chapters in this thesis. Various basic components of hygiene and infection prevention, guidelines addressing antibiotic resistance, and testing of healthcare workers on SARS-coV-2 take center stage. All of this occurs within the nursing home setting where elderly reside with vulnerable health conditions, rendering them more susceptible to infectious diseases. The intensive care they require, coupled with close social interactions with healthcare workers and other residents, as well as communal living spaces, heightens the risk of infection spread. These healthcare-associated infections (HAIs) pose a serious problem, often associated with an increased risk of addition health issues and mortality. Adhering to hygienic practices and implementing necessary infection prevention measures reduce the risk of HAIs and the spread of (resistant) microorganisms. During the COVID-19 pandemic, testing healthcare workers proved pivotal in identifying the spread of the SARS-CoV-2 virus, leading to prompt prevention measures. Simultaneously, it is essential to recognize that nursing homes serves as residential environment for vulnerable elderly, with an emphasis on quality of life. Striking a balance between the medical perspective and quality of life makes it challenging to prevent the spread of (resistant) microorganisms to the greatest extent feasible. The fact that residents share their living environment based on availability and professional assessment, requiring the weighing of individual and collective interests, adds an extra layer of complexity. Therefore, the infection prevention policies and approaches to combat antibiotic resistance, as known from hospitals, cannot be directly transposed to the nursing home; however, they must be modified to suit this setting.

Chapter 2 presents the findings of the first prevalence study on HAIs in nursing homes within the South-East region of the Netherlands from 2007 to 2009. International definitions for a bloodstream infection (BSI), lower respiratory tract infection (LRTI), bacterial conjunctivitis, and gastro-enteritis (GI) were modified, due to limited (microbiological) diagnostics in nursing homes. The definition of urinary tract infection (UTIs) was adopted from the professional group of elderly care physicians (Dutch acronym is Verenso). Data collection occurred through a written survey in both 2007 and 2008, shifting to an online survey in 2009. The recorded data included gender, age, use of medical devices, infections, type of unit (psychogeriatric, somatic or rehabilitation), occurrence of highly resistant microorganism (HRMO), and antibiotic use. Prevalence rates for HAIs were 6.7% in 2007 and 7.6% in both 2008 and 2009. Demographics characteristics, with respect to age and sex, were nearly identical across all three years. Indwelling urethral

catheters were the most prevalent medical device; however, the majority of UTIs occurred in psychogeriatric residents without indwelling urethral catheters. The prevalence of HAIs showed a substantial variation, with the majority observed among residents in rehabilitation units. Antibiotics were administered to 6.6% of the residents. Fewer than a half percent of the residents were found to be either colonized or infected with highly resistant microorganisms (HRMO). The increasing emphasis on patient safety warrants the introduction of surveillance as an important cornerstone of infection control programs in LTCFs. Prevalence studies can be seen as a first step to introducing infection prevention and control practices into LTCFs, since they are relatively easy to perform and give an insight into the problem of HAI in this setting.

Chapter 3 describes the follow-up study from the annual prevalence studies on HAIs in the same region as outlined in Chapter 2 up to 2017. Consistent definitions were applied, with the exception of UTI. To meet the updated UTI definition, residents had to show signs or symptoms of a UTI and test positive on a dipstick, regardless of the diagnosis made by the elderly care physician. Nearly identical data were collected, supplemented with information on purpose of antibiotic use (HAI or non-HAI), residents' room types (single-occupancy versus shared multiple-resident rooms), care-profiles since 2010, and incontinence data since 2012. Data collection methods evolved from an online survey in 2010 and 2011 to a dedicated app since 2012. The overall mean prevalence rate in the first four years (2007 to 2010) was 6.7%, contrasting with 2.2% in the following years, indicating a statistically significant downward trend in the overall prevalence of HAIs from 2007 up to 2017. The mean age of the residents showed an upward trend, increasing from 81 in 2012 to 84 years in 2017. The distribution concerning sex remained consistent across all these years, with one-third being male and two-thirds female. Over the years 2010-2017 there was a steady increase in the number of residents residing in one-person rooms. The prevalence of HAIs displayed a notable range among the facilities. UTI emerged as most prevalent. On average, almost two-thirds of the residents experienced some form of incontinence (fecal, urine, or both); however, the percentage of residents using incontinence materials was almost three-quarters. Throughout the years, the prevalence of UTIs among residents with incontinence was significantly higher than among those without incontinence. The overall prevalence of antibiotic use was 6.0%. Nearly half of the residents receiving antibiotics did not have a HAI. The effect of conducting prevalence studies may take several years to result in reduced HAI rates. The HAI point-prevalence studies can easily be combined with gathering data on antibiotic-use, essential for fostering appropriate antibiotic use.

Chapter 4 reports on the impact of various interventions and nudges on hand hygiene events (HHEs) within a rehabilitation unit at a nursing home using an electronic hand hygiene monitoring system (EHHMS) providing feedback at a group level. The study involved five phases during which various interventions and nudges were implemented, preceded by a baseline phase. The selected nudges included the use of red illuminated digits on digital clocks and the implementation of a scent system with a refreshing fragrance. The intervention and nudges implemented in the intervention period resulted in a significantly large effect compared to the baseline period. Phase 1, involving education, compliance feedback via weekly newsletters, and goal-setting questionnaires, had a significant positive impact on HHEs. Including the extent to which the unit had achieved the goal set for themselves in the weekly newsletter also had a positive, but not significant, effect. Considering only the selected nudges, they appear to have very limited impact, although the HHEs remained above the baseline level. Additional research is warranted to explore the optimal combination of interventions and nudges that could contribute to achieving a more effective and sustainable positive effect on HHEs, taking into account nursing homes specific determinants. Moreover, it is needed to investigate the feasibility of implementing EHHMS on a regular basis in nursing homes.

Chapter 5 describes the cross-sectional study in which residents were asked to express their preferences for the attire of the nursing staff. Simultaneously, the nursing staff was queried about the outfits they believed residents would prefer. A data collection tool was employed, featuring color photographs depicting a female nurse dressed in four different outfits, spanning from a formal to an informal appearance. Participants viewed six randomly composed photosets, each containing two attire options. Using a forced choice method, the selected one options based on two propositions The participants had to select (forced choice method) one of the two displayed photos, guided by two propositions, and taking into account left-right preferences. The two propositions concerned 'comfort preference' and 'care preference' which seem to compete with each other regarding nurses' attire. Residents provided feedback on their comfort and care preferences regarding the nurse, while nurses offered their perceptions on resident's comfort and care preferences. The result of this study indicates that residents in nursing homes generally prefer, or are generally perceived by nurses to prefer, nurses wearing professional white jackets with blue jeans. Casual attire was (perceived to be) the least preferred option in all cases. It is noteworthy that the highest difference in (perceived) preference between both groups was found regarding 'comfort preference'. Nurses believed that residents felt more comfortable with casual attire than the residents actually did. This study has shown that a homey

atmosphere in nursing homes does not preclude more formal attire for healthcare workers. It is recommended to involve residents in the decision-making process regarding healthcare workers' attire, including the option of a professional white jacket. Further research is needed to better understand residents' preferences for nurses' attire, as well as the attire of other types of staff in nursing homes. Moreover, such research should examine other dimensions of preferences and include residents with cognitive impairments.

Chapter 6 comprises the tailored guideline designed to prevent transmission of HRMO prevention in long-term care facilities (LTCFs), encompassing both nursing homes and small-scale living facilities. This customized guideline is derived from the HRMO guideline developed for hospitals. The need for adaptation arises from the distinctive context of LTCFs, where care is provided to residents with functional disabilities, chronic illnesses, and cognitive disorders, including dementia. The emphasis is on the specific living conditions and social interactions in this setting. Given the potential for residents to be carriers of HRMO over extended periods and home-like environment, the guideline adopts a nuanced approach. To respect individual living circumstances and mitigate unwarranted restrictions on residents' movement resulting from isolation measures, a microorganism infection control precautions strategy was formulated. This approach led to replacing the term 'isolation' with 'additional precautions'. The guideline describes the screening policies for residents in LTCFs, the definition and detection of HRMO carriage, standard and additional infection control precautions for HRMO positive residents, documentation, and communication of HRMO carriage, and the discontinuation of additional infection control precautions. Additionally, it provides guidance on contact tracing of HRMO, environmental control/investigation, surveillance of HRMO, and essential considerations during outbreaks. However, the effectiveness and feasibility of the proposed actions for preventing HRMO among various groups like psychogeriatric residents remain uncertain. The increasing evidence of HRMO spread in LTCFs underscores the need for further guidance that weighs potential harm against adverse events related to precautions, considering impacts on psychological wellbeing, resident safety, and satisfaction in residential care.

Chapter 7 illustrates a practice guide for implementing an antimicrobial stewardship (AMS) program in nursing homes, drawing by insights from a project conducted at one of the largest elderly care providers in the South-east of the Netherlands. This guide was developed by a multidisciplinary team consisting of a medical director, elderly care physicians, a pharmacist, a clinical microbiologist, and an infection control practitioner. Treatment protocols for UTIs, LRTIs, and skin

infections were collaboratively established at the regional level with multiple elderly care physicians and pharmacists. This guide is based on the Dutch hospital AMS implementation guide and tailored to suit the distinctive characteristics of nursing homes. It provides recommendations and practical tools, emphasizing the importance of a multidisciplinary approach. The guide outlines basic conditions essential for setting up an AMS program, along with strategies to support the feasibility and sustainability of the program, including the activities of an antibiotic team (A-team). These activities encompass a retrospective review of antibiotic prescriptions, their discussion during regular meetings such as pharmacotherapeutic consultations (PTAMs), and the promotion of a culture of continuous learning and improvement aimed at enhancing the overall quality of antibiotic prescriptions, rather than making adjustments to prescriptions on an individual client basis. Subsequently, the guide addresses the crucial aspect of education, underscoring the necessity to provide training for nurses and carers, inform residents or their representatives, and provide information to volunteers. In summary, through collaborative efforts of elderly care physicians, pharmacists, clinical microbiologists, and infection control practitioners, preferably on a regional level, it is feasible to implement an AMS program in nursing homes.

Chapter 8 describes the cross-sectional study conducted among 621 healthcare workers working in elderly care experiencing mild respiratory symptoms of COVID-19 during the first wave of the COVID-19 pandemic. Healthcare workers were tested for severe acute respiratory syndrome)-CoV coronavirus (coronavirus)-2 SARS-CoV-2 using pharyngeal swabs, upon which reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed. A concurrent survey collected information on symptoms and potential sources of infection. The results revealed that just over a fifth of healthcare workers tested positive for SARS-CoV-2. The majority of tested healthcare workers were nursing staff, and fever, runny or stuffy nose, anosmia, general malaise, myalgia, headache, and ocular pain were associated with SARS-CoV-2 positivity. Contact with residents or colleagues with suspected or proven COVID-19 emerged as a risk factor. Whole genome sequencing suggesting the spread of the virus within facilities underscoring the hypothesis of undetected spread within elderly care facilities. The findings emphasize the importance of testing, even in the presence of mild symptoms in healthcare workers working in elderly care. This enables the prompt initiation of contact tracing upon a positive result.

Chapter 9 reports on the prospective diagnostic evaluation of the Abbott Panbio™ COVID-19 antigen detection rapid diagnostic test (Ag-RDT) conducted among 683 healthcare workers, including home-based elderly care workers, in three elderly

care organizations. The study included healthcare workers who met clinical criteria for COVID-19 during the second wave of the COVID-19 pandemic. Each healthcare underwent two nasopharyngeal swabs, one for the Ag-RDT and the other for RT-qPCR. A Ct-value of < 40 was considered positive, while ≥ 40 was considered negative. Results showed that almost a tenth tested positive for SARS-CoV-2 by RT-qPCR. The Ag-RDT demonstrated an overall sensitivity of 81.0% and 100% specificity. When using as Ct-value cutoff of 32, sensitivity increased to 92.7%. Negative Ag-RDT results were moderately associated with higher Ct-values compared to positive results. In conclusion, the Abbott Panbio™ COVID-19 proves effective in quickly identifying positive SARS-CoV-2 cases among healthcare workers. However, negative Ag-RDT results should be confirmed by RT-qPCR. In cases of severe understaffing, and with careful consideration, fully vaccinated healthcare workers with negative Ag-RDT could continue working with a mask pending PCR results. To assess whether this testing policy could be of added value, it is important to take into account the turnaround times of testing by the Municipal Public Health Services (Dutch acronym is GGD).

General discussion

Infection prevention and control in nursing homes

Over a period of more than 25 years, an international guideline was developed on infection prevention and control (IPC) in long-term care facilities.[1,2] In the Netherlands, as indicated in the reports of the Health and Youth Care Inspectorate (previously known as Health Inspectorate) definite improvements has been made within this timeframe in nursing homes, although the progress has been slow.[3-6] Where IPC and antimicrobial stewardship is already an established part of hospital practices, nursing homes, nevertheless still need to address an existing gap in this area. Due to the fundamental differences in the healthcare environment between hospitals and nursing homes, a copy-past approach from the hospital setting to nursing homes is not feasible. This thesis demonstrates that the approach taken in hospitals can provide a foundation for tailoring a strategy that is suited to nursing homes, considering the specific patient population, the nursing home environment, and the constraints of available resources.

Bundling forces through a regional approach

In 2016, the Ministry of Health, Welfare, and Sport (VWS) in the Netherlands initiated the establishment of ten regional networks as part of the program aimed at preventing antibiotic resistance and controlling its spread at the regional.[7] There are two compelling reasons for nursing homes to engage in regional networks, fostering collaborative efforts in IPC and combatting antibiotic resistance. The first reason stems from the pervasive presence of healthcare-associated infections and resistant microorganisms across the entire extra-, semi-, and intramural healthcare network. The mobility of patients within this network contributes to the dissemination of these infections and resistant microorganisms. Several studies endorse a regional approach to IPC and antibiotic resistance, encompassing not only hospitals but also other healthcare facilities, including nursing homes.[8-12] Notably, inter-institutional outbreaks involving multidrug resistant microorganisms have been described.[13,14] The second reason for nursing homes to partake in regional networks is the efficiency attainable through collaborative efforts. Instead of each nursing home independently reinventing the wheel, efforts can be consolidated by, for example, developing shared infection prevention protocols, coordinating training programs, and jointly appointing an infection control practitioner from one of the regional hospitals or the Public Health Service (Dutch acronym is GGD). Our extensive experience within regional collaborative endeavors fully supports these arguments.

Basic components of infection prevention and control

Surveillance

Surveillance essentially serves as a reflection of one's own actions. Regional or national datasets, when collected in a standardized manner, are essential for evaluating the consequences of one's actions, rather than for benchmarking purposes. In nursing homes, data collection for surveillance purposes is predominantly carried out by elderly care physicians. The direct medical involvement instills a high level of confidence in the data. Nevertheless, even with a standardized protocol, trust in others' data is not automatic unless consensus on data validation exists. In our region, no validation of the data occurred. On national level validation has been a mandatory element in participation in the prevalence study since 2014.[15] Nevertheless, caution should be warranted when comparing results between institutions given the wide variety of nursing home types, each serving the needs to different resident profiles and varying in number of residents.

Surveillance of healthcare-associated infections is not included as a quality indicator for Dutch nursing homes[16], in contrast to hospitals where it is incorporated as part of the quality framework and an integral component of IPC. Nursing homes autonomously decide to participate in surveillance activities offered at both regional (in this thesis) and national level.[15] In Chapter 3, we have demonstrated the added value of our continued surveillance efforts, as is also evident in another recent study.[17] This surveillance effect (similar to the "Hawthorne effect"), where a reduction is observed in the occurrence of healthcare-associated infections during ongoing surveillance, is also known from hospital surveillance.[18,19]

Feedback of data to the involved stakeholders is an integral aspect of surveillance. The outcomes of the national prevalence surveillance on HAIs are communicated with all participating institutions at the national level. In addition, it may be valuable to consider reporting data at the regional level. These data can be deliberated within regional networks, facilitating the sharing of best practices among them. Moreover, there could be an added benefit when surveillance results are promptly accessible right upon the surveillance period. Positive experiences with this approach have been demonstrated at the regional level.[20]

To extend and sustain surveillance activities for HAIs in nursing homes, it is imperative to explore the extent to which electronic information systems utilized within these facilities can be adapted for this purpose. Automation of surveillance on HAIs in hospitals has demonstrated a substantial reduction in workload and an enhancement of quality.[21]

Hand hygiene

The importance for adequate hand hygiene have been addressed for many years.[22] However, the compliance rate in all kinds of healthcare settings has always been far from ideal worldwide.[23] For nursing homes alone, the adherence is even lower[24-30] despite extensive multimodal improvement endeavors.[26-28]

System change, as delineated in the WHO's multimodal strategy, is not a concern within Dutch nursing homes. Nevertheless, the remaining four strategies hold significance.[22] In Chapter 4, we have presented some alternatives in strategies in our study. We employed an electronic monitoring system to measure hand hygiene events, rather than observations to assess hand hygiene compliance. Furthermore, we introduced nudges as an alternative to workplace reminders. Despite an increase in hand hygiene events per resident during the study period, the impact was not sustainable. It continues to be an immense challenge to sustainably improve hand hygiene in nursing homes. However, we assert that there is merit in further investigation to explore the use of electronic monitoring systems and the development of easily implementable and cost-efficient nudges as potential interventions within the framework of a multimodal approach. Particularly in a resource-constrained setting, it is crucial to pay attention to setting-specific determinants.[30,31]

The WHO launched a research agenda to improve our understanding of factors influencing hand hygiene behaviour in health care and to strengthen appropriate intervention. This research agenda provides insightful ideas for researchers to direct their projects and funding proposals when conducting investigations on hand hygiene.[23]

Healthcare workers' attire

The decision to shift to personal attire was predominantly determined by management of nursing homes without considering the perspective of IPC. To the best of our knowledge, healthcare workers had minimal to no involvement in this decision, and residents, not in the least. The reason behind this shift was the belief that formal attire is not suitable in a homey environment. Nevertheless, the concept of a homey environment seems to be complex, dynamic, and highly personal. The psychical characteristics of the building, residents' sense of control over their lives, and the ability to maintain their personal routines and activities were the only clear common elements contributing to a homey atmosphere.[32]

In Chapter 5, we found that a professional white jacket was (perceived to be) preferred both regarding 'care preference' and 'comfort-preference'. Interestingly, this study also

revealed that nurses believed that residents felt less comfortable when nurses wore white coats, which did not align with resident' preferences. This indicates that residents have a unique perspective on this topic. The Dutch consortium "BeterOud" underscores the importance of considering the distinct perspectives of elderly on healthcare, which can vary from those of policymakers, researchers, and healthcare professionals.[34]

In general, studies on patient participation and shared decision making in elderly care is widely reported[34-36] and given a high priority.[16,37] However, IPC is to the best of our knowledge hardly integrated into this context. It should be noted that the key question concerns the extent to which residents seek active engagement in shaping IPC policies of nursing homes and, if they do, the strategy by which this engagement should be operationalized. The complexity in this matter stems from the fact that standard precautions, such as the healthcare workers' attire, apply to the resident population as a whole, rather than the individual resident. This area presents field for further research.

Guidelines for addressing antibiotic resistance

Guidelines on the prevention of highly-resistant microorganisms and antimicrobial stewardship

The guidelines presented in Chapter 6 and 7 were originally developed for hospital settings and have been tailored to suit the needs of nursing homes.

The guideline on the prevention of HRMO by IPC measures presented in Chapter 6 was developed by an expert group formed within the broader framework of the Working Party WIP, comprising professionals with working (partially) in/for LTCFs. However, in 2017, the WIP was disbanded, and in 2021 the Partnership for Infection Prevention Guidelines (in Dutch: Samenwerkingsverband Richtlijnen Infectiepreventie, SRI[38]) was launched. The SRI is engaged in developing generic guidelines for specialized medical care, long-term care, and public health.

The development of a generic guideline on the prevention of HRMO has to deal with various challenges, particularly because long-term care, such as nursing homes, is characterized by a home-like environment and provides care over an extended period, which contrasts with the often relatively brief hospital care. Considering that HRMO-carriage varied between HRMOs and can be of a prolonged duration[39-43] which necessitates a patient to stay in their own room in hospital setting, such an approach is not feasible in nursing homes. Tailored approaches may be required, emphasizing the focus on upholding the resident's welfare while minimizing

health-related risks to other residents, consequently, preventing outbreaks. The lack of single-resident rooms can also be a reason to be forced to share a room with a non-HRMO positive resident, even though the risk of transmission to the roommate is increased.[44] Another challenge in controlling HRMO in nursing homes involves the timely identification of HRMO carriers and the early recognition of an HRMO outbreak. Generally, fewer cultures are obtained from residents in nursing homes compared to hospital patients. Performing regular point-prevalence surveys to assess the prevalence of HRMO among residents offers a potential solution for this issue. Once an outbreak of a highly-resistant microorganism emerges in a nursing home, it can be difficult to control, and the measures to be taken have considerable implications for residents, staff, and the affected facility.[45]

Residents or their representatives may encounter confusion when IPC measures vary across different healthcare settings. Therefore, in addition to providing information about the HRMO status and the corresponding IPC measures, it is important to communicate to residents or their representatives about these disparities. Beyond the aforementioned reasons for regional collaboration, the perspective from residents and their representatives also underscores the incentive to endeavor to collaboratively develop protocols derived from the guideline. This will reduce ambiguities among residents and their representatives and is likely to enhance adherence to the measures that apply to them.

It is also imperative to establish clear and standardized transmural agreements regarding patient information exchange concerning HRMO. For this purpose, a national document was developed intended as a foundation for the regional implementation of transmural HRMO information transfer.[46]

In order to achieve the goal of preventing antibiotic resistance through the appropriate use of antibiotics in nursing homes, a practice guide on antimicrobial stewardship, derived from the guide for hospitals[47], is presented in Chapter 7. There are also several international guidelines on the implementation of an AMS program in LTCFs[48-50] based on the seven core elements published by the Centers for Disease Control and Prevention in 2015.[51] However, there is no one-size-fits-all AMS program, the implementation of an AMS program relies on the suitability and feasibility of stewardship activities. This encompasses factors such as the initial prescribing behavior, the existing infrastructure, the ease of data retrieval from resident records and prescribing systems, as well as the availability of human and material resources within the local context. Furthermore, the feasibility to execute select stewardship activities at a regional level is worth considering. This might include activities such

as the provision of educational programs on antibiotics, antibiotic resistance, and IPC measures to all relevant parties. Moreover, the effectiveness of multi-faceted educational programs has demonstrated positive results on appropriateness prescribing.[52-54] It should be noted that the impact supporting the effectiveness of AMS programs in nursing homes on mitigating antibiotic resistance, decreasing mortality, and reducing hospital admissions, has yet not been demonstrated.[55]

Nevertheless, an AMS program demands a considerable amount of time, and has the potential to introduce bias into the findings when manual methods are used. With the introduction of electronic resident records, efforts should be directed towards automated data extraction and processing using algorithms. In the meantime, experience has been acquired in this regard.[56] However, this was restricted to a single electronic health record (in Dutch: elektronisch cliënten dossier, ECD) provider used in nursing homes, even though there a multiple ECD providers in the market, each serving nursing homes. In order to prepare other ECDs for quality registrations, it is imperative to persuade software developers of these ECDs to implement necessary changes. An even more optimal approach would involve government intervention and the enactment of compulsory regulations in this context. In 2019, a project is initiated to ensure continuous and standardized registration for quality purposes.[57]

COVID-19 testing healthcare workers working in elderly care

The COVID-19 crisis has had a significant negative impact on nursing homes. Initially, there was a lack of a comprehensive understanding of the virus's spread and its impact within these facilities. The focus was solely on persons suffered from fever and symptoms typical of a respiratory infection[58], concurrently with a policy of selective and restricted screening. Moreover, at the outset, nursing homes were on the periphery of national and regional crisis management and were significantly acknowledged only at a later stage.

In Chapter 8, we demonstrated that healthcare workers also with non-respiratory mild symptoms were SARS-CoV-2 positive. Our findings were confirmed by a separate study conducted among healthcare workers in a hospital.[59] In the nursing home setting, where there was a scarcity of personal protective equipment and frequent physical interactions stemming from both care-related contact and social contact. This, coupled with the knowledge that adherence to standard precautions, such as hand hygiene is low (Chapter 4), significantly heightened the risk of SARS-CoV-2 transmission to residents. This study was exclusively published on MedRxiv

and faced two rejections by peer-reviewed journals, as it was considered to offer no additional value to existing published research, primarily due to its delayed submission. Consequently, the decision was made not to submit this article for publication in another journal.

In Chapter 9, we presented the results of the validation of one of the antigen detection rapid diagnostics tests designated by the Ministry of Health, Welfare and Sport (Dutch acronym: VWS). This study was conducted during a period when residents and healthcare workers were not yet protected by COVID-19 vaccination, and the turnaround of SARS-CoV-2 culture results were two or more days. The major advantage was that the antigen test provided results within fifteen minutes after sample collection. Immediate measures could be taken and contact tracing could be initiated upon a positive result to reduce further SARS-CoV-2 transmission. However, the dilemma emerged when the antigen test yielded a negative result. Faced with the ongoing challenges of understaffing and the associated risks, we had to decide whether to permit healthcare workers to continue working, under the condition that they were capable of doing so, with the risk that a positive culture result could have significant consequences. Alternatively, we could choose to avoid the risk by mandating that they wait for a negative culture result before being allowed to return to work, considering the vulnerable population they were caring for. In our case, we opted for this latter, but from our practical experiences, we know that other nursing homes, also employing antigen tests, have chosen the former.

Shortly after our study, the vaccination of nursing home residents and healthcare workers commenced, leading to moderate policy. Since March 10th, 2023, the COVID-19 has been considered equivalent to influenza. Nevertheless, it is crucial to remain vigilant when other SARS-CoV-2 variants are circulating, for which vaccination or a prior COVID-19 illness may offer insufficient protection, especially among vulnerable elderly living in close contact with each other in nursing homes.

Nevertheless, the COVID-19 crisis has notably brought IPC to the forefront of the agenda in Dutch nursing homes. This emphasis is considered with respect to proportionality (where there should be a reasonable relationship between the goal and methods used) and subsidiarity (where the least intrusive methods are employed to achieve a specific goal).[60] It is imperative that this discussion extends beyond the boundaries of nursing homes and takes place on a broader scale within the national and regional care system to foster ongoing dialogue about the consequences resulting from the various choices available, for instance, for admissions in hospitals.

The main key messages derived from the COVID-19 crisis are that nursing homes must be integrated into national and regional infectious disease crisis management from the outset, and that nursing homes must embrace IPC as an integral component of quality of care.

Recommendations based on this thesis

1. Seek collaboration at the regional level for a structured approach to IPC.
2. Conduct prevalence studies on HAIs and antibiotic usage at least once every two years, preferably annually.
3. Explore budget-friendly and easily implementable nudging strategies through research as a component of a multimodal approach to improve hand hygiene compliance.
4. Explore the feasibility of implementing electronic hand hygiene monitoring systems for measuring hand hygiene compliance.
5. Incorporate preferences of residents with physical impairments into the selection of nurses' attire, considering a white nursing jacket as an optional choice.
6. Expand the investigation of healthcare workers' attire to also include other healthcare workers beyond the nursing staff, explore various dimensions, and consider residents with cognitive impairments.
7. Develop a tailored HRMO protocol, derived from the national guideline, to strike a balance in reducing infection risks and transmission of HRMO, while concurrently preserving the quality of life for residents.
8. Initiate an AMS program through collaboration among experts in the fields of elderly care, antibiotic prescribing, antibiotic resistance, and infection control, that aligns with the organizational structure, preferably in a regional setting.
9. Establish regional agreements with the medical microbiology laboratory and public health services on diagnostics in infectious disease crisis management.

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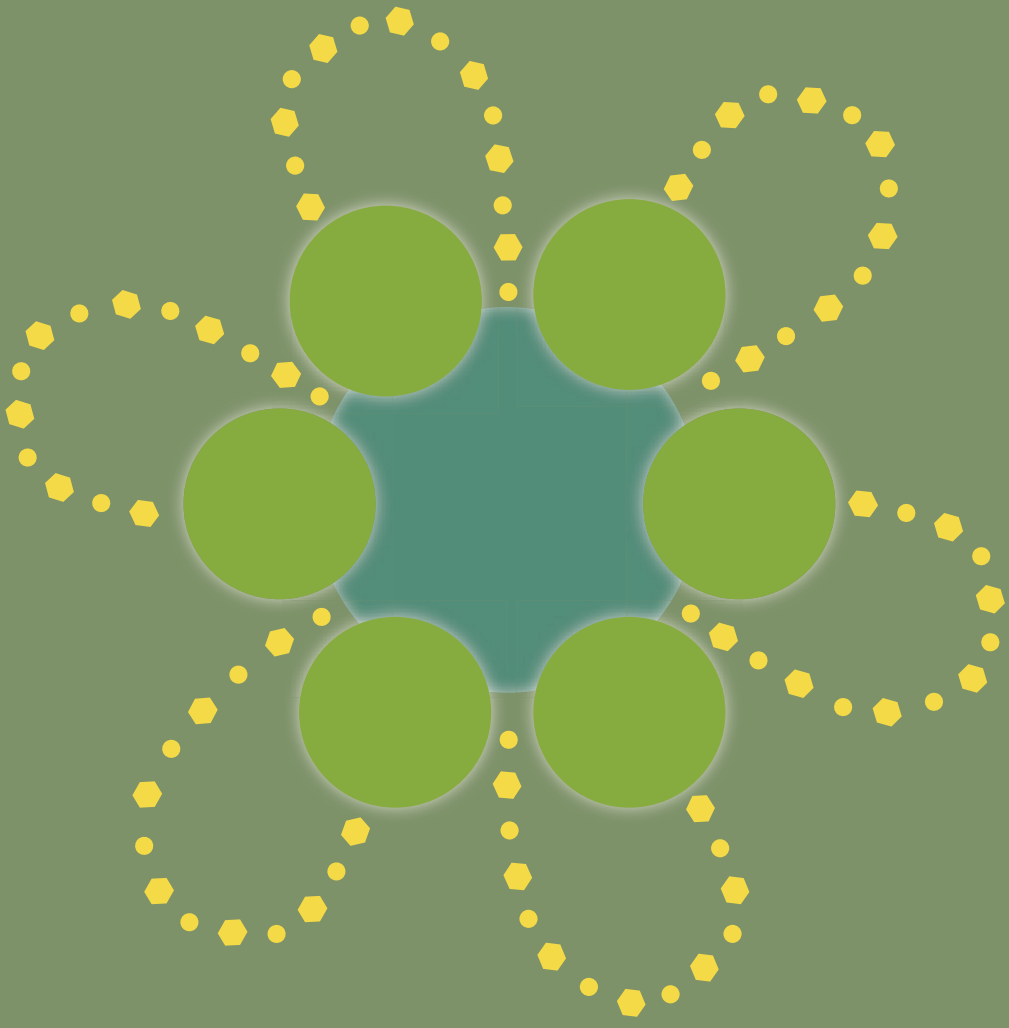

APPENDIX

Nederlandse samenvatting

Hoofdstuk 1, de algemene introductie, schetst de context en de achtergrond van de hoofdstukken in dit proefschrift. Verschillende basiselementen van hygiëne en infectiepreventie, richtlijnen op het gebied van antibioticaresistentie en het testen van zorgmedewerkers op SARS-CoV-2 staan centraal. Dit alles binnen de verpleeghuissetting waar ouderen verblijven met een kwetsbare gezondheid, waardoor ze meer vatbaar zijn voor infectieziekten. De intensieve zorg die ze nodig hebben, tezamen met veelal het nauwe sociale contact met zorgmedewerkers en medebewoners en het met elkaar verblijven in gemeenschappelijke ruimten, verhoogt het risico op verspreiding van infecties. Deze zorggerelateerde infecties vormen een serieus probleem dat gepaard kan gaan met een verhoogd risico op extra gezondheidsproblemen en sterfte. Hygiënisch werken en zonodig nemen van infectiepreventieve maatregelen verminderen het risico op een zorginfectie en verspreiding van resistente micro-organismen. Tijdens de COVID-19 pandemie bleek dat het testen van zorgmedewerkers zicht gaf op verspreiding van het SARS-CoV-2 virus waarop maatregelen genomen konden worden. Tegelijkertijd is het van essentieel belang te realiseren dat een verpleeghuis een woonomgeving biedt voor kwetsbare ouderen, waarbij de nadruk ligt op kwaliteit van leven. Het vinden van een balans tussen het medisch perspectief en kwaliteit van leven maakt het uitdagend om zoveel mogelijk te voorkomen dat micro-organismen zich verspreiden. Het feit dat bewoners hun woonomgeving delen op basis van beschikbaarheid en professionele beoordeling, waarbij individuele en collectieve belangen moeten worden afgewogen, maakt het extra complex. Het infectiepreventiebeleid en de aanpak van antibioticaresistentie, zoals we die kennen vanuit ziekenhuizen, kan daarom niet één-op-één overgenomen worden naar het verpleeghuis.

Hoofdstuk 2 beschrijft de resultaten van de eerste prevalentiestudie naar zorggerelateerde infecties in verpleeghuizen in de regio Zuidoost-Nederland van 2007 tot 2009. Internationale definities voor een bloedbaaninfectie, infectie van de lagere luchtwegen (LLWI), bacteriële conjunctivitis en gastro-enteritis zijn aangepast, omdat in verpleeghuizen maar beperkte (microbiologische) diagnostiek werd gedaan. Voor urineweginfecties (UWI's) werd de definitie gebruikt van de beroepsgroep van specialisten ouderengeneeskunde (Verenso). Specialisten ouderengeneeskunde waren verantwoordelijk voor de gegevensverzameling en deden de beoordeling of er sprake was van een zorggerelateerde infectie. In 2007 en 2008 werden de gegevens verzameld via een schriftelijke enquête en in 2009 via een online enquête. De volgende gegevens werden verzameld: geslacht,

leeftijd, gebruik van medische hulpmiddelen, infecties, type afdeling, voorkomen van bijzonder resistente micro-organismen (BRMO's) en antibioticagebruik. De prevalentie van zorggerelateerde infecties bedroeg 6,7% in 2007 en 7,6% in zowel 2008 als 2009. De leeftijd en het geslacht van de cliënten waren bijna identiek in alle drie jaren. Urinekatheters waren het meest voorkomende medische hulpmiddel; echter de meerderheid van UWI's trad op bij psychogeriatrische cliënten zonder urinekatheter. De prevalentie van zorggerelateerde infecties varieerde aanzienlijk tussen deelnemende verpleeghuizen, met de hoogste prevalentie bij cliënten op revalidatieafdelingen. Gemiddeld kreeg 6,6% van de cliënten antibiotica. Minder dan een half procent van de bewoners was gekoloniseerd of geïnfecteerd met een BRMO. De toenemende nadruk voor patiëntveiligheid maakt het invoeren van surveillance in verpleeghuizen noodzakelijk. Prevalentiestudies zijn een startpunt voor infectiepreventie, omdat ze makkelijk uit te voeren zijn en inzicht geven in het voorkomen van zorggerelateerde infecties.

Hoofdstuk 3 beschrijft de follow-up studie van de jaarlijkse prevalentiestudie naar zorggerelateerde infecties in dezelfde regio zoals beschreven in hoofdstuk 2 tot aan 2017. Dezelfde definities van zorggerelateerde infecties werden gehanteerd, met uitzondering van de definitie van een UWI. Om aan de nieuwe criteria voor een UWI te voldoen, moest de client tekenen of symptomen van een UWI vertonen en positief testen op de dipstick, ongeacht de diagnose van de specialist ouderengeneeskunde. Dezelfde gegevens werden geregistreerd als beschreven in hoofdstuk 2, aangevuld met informatie over de reden van antibioticagebruik (indicatie wel of geen zorggerelateerde infectie), het type kamer van cliënten (een- of meerpersoons), zorgprofielen sinds 2010, en incontinentiegegevens sinds 2012. De gegevensverzameling gebeurde via een online enquête in 2010 en 2011 en vanaf 2012 via een speciaal hiervoor ontwikkelde app. Het gemiddelde prevalentiepercentage in de eerste vier jaar was 6,7%, in tegenstelling tot 2,2% in de jaren daarna, wat wijst op een statistisch significante neerwaartse trend in het voorkomen van zorggerelateerde infecties van 2007 tot en met 2017. De gemiddelde leeftijd van de cliënten vertoonde een stijgende lijn, van 81 jaar in 2012 naar 84 jaar in 2017. De man-vrouw verdeling bleef consistent over alle jaren, met een derde mannelijke en twee derde vrouwelijk cliënten. Tussen 2010 en 2017 steeg het aantal eenpersoonskamers. De prevalentie van zorggerelateerde infecties varieerde aanzienlijk tussen de deelnemende verpleeghuizen. UWI's waren het meest voorkomend. Gemiddeld vertoonde bijna twee derde van de cliënten enige vorm van incontinentie (feces, urine, of beide), echter bijna driekwart van de cliënten gebruikte incontinentiematerialen. Gedurende de jaren was het percentage cliënten met een UWI en incontinentie significant hoger dan het

percentage cliënten met een UWI die niet incontinent waren. De prevalentie van antibioticagebruik was 6,0%. Bijna de helft van de cliënten die antibiotica kregen had geen zorggerelateerde infectie. Het kan enkele jaren duren voordat het uitvoeren van prevalentiestudies leidt tot een afname van zorggerelateerde infecties. Deze studies kunnen vrij eenvoudig worden gecombineerd met het verzamelen van gegevens over antibioticagebruik, wat nodig is om verantwoord antibioticagebruik te bevorderen.

Hoofdstuk 4 rapporteert over de impact van verschillende interventies en nudges op handhygiëne events (HHE's) binnen een revalidatieafdeling van een verpleeghuis. Hierbij is gebruik gemaakt van elektronisch systeem voor het monitoren van handhygiëne (EHHMS), dat op groepsniveau feedback verstrekte. De studie omvatte vijf fasen, waarin verschillende interventies en nudges werden geïmplementeerd, voorafgegaan door een nulmeting. De nudges die werden ingezet waren rood verlichte cijfers op digitale klokjes en de implementatie van een geursysteem met een verfrissende geur. De uitgevoerde interventies en nudges gedurende de interventieperiode leidden tot een significant groot effect in vergelijking met de nulmeting. Fase 1, waarin educatie werd gegeven, compliance feedback via wekelijkse nieuwsbrieven werden verspreid en vragenlijsten werden uitgereikt om zelf een afdelingsdoel te stellen, hadden een significant positieve impact op HHE's. Het opnemen van het eigen gesteld afdelingsdoel in de wekelijkse nieuwsbrief had ook een positief, maar niet significant, effect. Wanneer we alleen kijken naar de nudges dan lijkt hun impact minimaal te zijn geweest, hoewel de HHEs wel hoger bleven dan bij de nulmeting. Verder onderzoek is nodig om te onderzoeken welke combinatie van interventies en nudges bijdragen aan het bereiken van een effectievere en duurzame positieve impact op HHEs, waarbij rekening wordt gehouden met verpleeghuis specifieke determinanten. Bovendien is het nodig om de haalbaarheid te onderzoeken van een brede implementatie van EHHMS in verpleeghuizen.

Hoofdstuk 5 beschrijft de cross-sectionele studie waarin aan cliënten is gevraagd hun voorkeur uit te spreken voor de kleding van de verpleging. Tevens werd aan de verpleging gevraagd welke outfit zij dachten dat cliënten zouden prefereren. Dit gebeurde aan de hand van een gestandaardiseerde vragenlijst. Deze vragenlijst bevatte kleurenfoto's van een vrouwelijk persoon gekleed in vier verschillende outfits, variërend van formeel tot informeel. Deelnemers bekeken zes willekeurig samengestelde fotosets, elk met twee kleding opties. Met behulp van een gedwongen keuzemethode kozen de deelnemers een van de twee weergegeven foto's begeleid door twee stellingen. Om rekening te houden met voorkeuren voor links of rechts, werden dezelfde combinaties tijdens dezelfde sessie in omgekeerde volgorde weergegeven. De twee stellingen die aan cliënten werden voorgelegd

waren: 'Bij deze zorgverlener voel ik mij het meest op mijn gemak' (comfort) en 'Door deze zorgverlener wil ik het liefst verzorgd worden' (zorg). Aan de verpleging werden de volgende stellingen voorgelegd: 'Bij deze zorgverlener voelen bewoners zich m.i. het meest op hun gemak' (comfort) en 'Door deze zorgverlener willen bewoners m.i. het liefst verzorgd worden(zorg)'. Uit deze studie bleek dat cliënten in verpleeghuizen over het algemeen de voorkeur gaven aan een professioneel wit jasje in combinatie met een blauwe jeans, dat zowel werd aangegeven door de cliënten als door de verpleging. De informele outfit was de minst gewenste optie in alle gevallen. Opmerkelijk was dat de verpleging dacht dat cliënten zich meer comfortabel zouden voelen bij informele kleding dan dat cliënten zelf aangaven. Deze studie heeft laten zien dat binnen de huiselijke sfeer in verpleeghuizen, de voorkeur van cliënten met lichamelijke beperkingen uitgaat naar een meer formele kledingstijl. Het is aan te bevelen om cliënten te betrekken bij de keuze van kleding voor de verpleging, waarbij een professionele witte jas als keuzemogelijkheid wordt meegenomen. Verder onderzoek is aan te bevelen om meer inzicht te krijgen in de voorkeuren van cliënten voor de kleding van zowel de verpleging als andere zorgmedewerkers in verpleeghuizen. Hierbij is het van belang om ook andere dimensies mee te nemen en aandacht te hebben voor cliënten met cognitieve beperkingen.

Hoofdstuk 6 omvat de richtlijn met betrekking tot de preventie van transmissie van bijzonder resistente micro-organismen (BRMO's) voor gebruik in verpleeghuizen, wooncentra- en kleinschalig wonen ouderen (VWK). Deze richtlijn is ontwikkeld op basis van de BRMO-richtlijn voor ziekenhuizen, maar is aangepast aan de specifieke kenmerken van de VWK-sector. Hier wordt zorg verleend aan cliënten met functionele beperkingen, chronische ziekten en cognitieve stoornissen, waaronder dementie. De aanpassingen houden rekening met het feit dat cliënten mogelijk langdurig drager kunnen zijn van een BRMO en de setting huiselijk is. Het doel van deze aanpassingen is om de individuele leefomstandigheden van cliënten te respecteren en beperkingen in bewegingsvrijheid zoveel mogelijk te verminderen. De term 'isolatie' is daarom aangepast naar 'aanvullende voorzorgsmaatregelen'. De richtlijn beschrijft het BRMO-screeningsbeleid voor cliënten in de VWK-sector, de definitie en detectie van BRMO-dragerschap, standaard en aanvullende infectiepreventiemaatregelen voor BRMO-positieve cliënten, documentatie en communicatie van BRMO-dragerschap en het stopzetten van aanvullende infectiepreventiemaatregelen. Tevens worden aanbevelingen beschreven met betrekking tot een BRMO-contactonderzoek, onderzoek van de omgeving, surveillance van BRMO en een BRMO-uitbraak. Niettemin blijven de effectiviteit en uitvoerbaarheid van de voorgestelde aanvullende infectiepreventiemaatregelen onduidelijk voor de diverse cliëntengroepen, met name voor psychogeriatrische

cliënten. Het toenemende bewijs van verspreiding van BRMO in VWK onderstreept de noodzaak voor verdere verfijning van de richtlijnen. Hierin dient een zorgvuldige afweging gemaakt te worden tussen risico's verbonden aan BRMO-dragerschap en de mogelijk schadelijke effecten van de maatregelen. Dit omvat aspecten zoals de impact op het psychisch welzijn, de veiligheid en tevredenheid van cliënten.

Hoofdstuk 7 laat zien op welke wijze een 'antimicrobial stewardship' (AMS) programma in verpleeghuizen geïmplementeerd kan worden, gebaseerd op inzichten die zijn verkregen uit een project dat is uitgevoerd bij een van de grootste aanbieders van ouderenzorg in Zuidoost-Nederland. Deze gids is tot stand gekomen door een multidisciplinair team bestaande uit een medisch directeur, specialisten ouderengeneeskunde, apotheker, een medisch microbioloog en deskundige infectiepreventie. De behandelprotocollen voor UWI's, LLWI's en huidinfecties zijn in samenwerking met meerdere specialisten ouderengeneeskunde en apothekers op regionaal niveau opgesteld. Uitgangspunt was de praktijkgids voor de implementatie van AMS in ziekenhuizen, die vervolgens is aangepast aan de specifieke context van verpleeghuizen. De gids biedt aanbevelingen en praktische handvatten voor het opzetten van een AMS-programma in verpleeghuizen met nadruk op het belang van een multidisciplinaire aanpak. De handleiding beschrijft de basisvoorwaarden die essentieel zijn voor het opzetten van een AMS-programma, evenals strategieën om de haalbaarheid en duurzaamheid van het programma te ondersteunen, inclusief de activiteiten van een antibiotica team (A-team). Deze activiteiten omvatten een retrospectieve beoordeling van antibiotica voorschriften, het bespreken ervan tijdens reguliere vergaderingen zoals het farmacotherapeutisch overleg (FTO), en het bevorderen van een cultuur van continu leren en verbeteren die gericht is op het verhogen van de algehele kwaliteit van antibiotica voorschriften, eerder dan op aanpassingen aan voorschriften per individuele cliënt. Daarnaast beschrijft de handleiding het belangrijke aspect van educatie over dit onderwerp, waarbij wordt benadrukt dat het noodzakelijk is om scholing aan te bieden aan verpleegkundigen en verzorgers, cliënten of hun vertegenwoordigers te informeren, en informatie te verstrekken aan vrijwilligers. Samengevat, door gezamenlijke inspanningen van specialisten ouderengeneeskunde, apothekers, medisch microbiologen en deskundigen infectiepreventie, bij voorkeur op regionaal niveau, is het mogelijk om een AMS-programma in verpleeghuizen te implementeren.

Hoofdstuk 8 beschrijft de cross-sectionele studie die is uitgevoerd onder ruim 600 zorgmedewerkers, werkzaam in de ouderenzorg, die milde respiratoire symptomen van COVID-19 ondervonden tijdens de eerste golf van de COVID-19 pandemie.

Zorgmedewerkers werden getest op SARS-CoV-2 met behulp van keelswabs waarop reverse transcription-quantitative polymerase chain reaction (RT-qPCT) werd uitgevoerd. Gelijktijdig werd via een schriftelijke enquête informatie verzameld over de symptomen en mogelijke bronnen van de infectie. De resultaten toonden aan dat iets meer dan een vijfde van de zorgmedewerkers positief testte op het SARS-CoV-2 virus. Het merendeel van de geteste zorgmedewerkers betrof verplegend personeel, en koorts, een loopneus of verstopte neus, anosmie (verlies van rek), algemene malaise, spierpijn, hoofdpijn en oogpijn waren geassocieerd met een positieve SARS-CoV-2 test. Contact met een bewezen COVID-19 positieve of daarvan verdachte medeclient of collega kwam naar voren als risicofactor. Het sequencen van het volledige genoom suggereerde de verspreiding van het virus binnen de huizen, wat de hypothese van onopgemerkte verspreiding binnen de ouderenzorg onderstreepte. De bevindingen benadrukken het cruciale belang van het testen, ook bij milde respiratoire symptomen van zorgmedewerkers werkzaam in de ouderenzorg zodat bij een positieve bevinding een contactonderzoek zo spoedig mogelijk opgestart kan worden.

Hoofdstuk 9 rapporteert over de prospectieve diagnostische evaluatie van de Abbott Panbio TM COVID-19 antigeen detectie sneltest (Ag-RDT) bij meer dan 680 zorgmedewerkers, inclusief wijkverpleging, in drie ouderenzorgorganisaties. De studie omvatte zorgmedewerkers die voldeden aan de klinische criteria voor COVID-19 tijdens de tweede golf van de COVID-19 pandemie. Bij elke zorgmedewerker werden twee gecombineerde keel-/neusuitstrijken afgenomen, een voor de Ag-RDT en de andere voor RT-qPCR. Een Ct-waarde van <40 werd als positief beschouwd, terwijl ≥ 40 als negatief werd beschouwd. De resultaten toonden aan dat bijna een tiende van de zorgmedewerkers positief testte op SARS-CoV-2 via RT-qPCR. De Ag-RDT vertoonde een sensitiviteit van 81,0% en 100% specificiteit. Bij het hanteren van een Ct-grenswaarde van 32, nam de sensitiviteit toe tot 92,7%. Negatieve resultaten van de Ag-RDT waren matig geassocieerd met hogere Ct-waarden in vergelijking met positieve resultaten. Deze sneltest heeft bewezen effectief te zijn in het snel identificeren van SARS-CoV-2 positieve zorgmedewerkers. Negatieve Ag-RDT resultaten moeten echter worden bevestigd door RT-qPCR. In gevallen van ernstig personeelstekort, en met zorgvuldige afweging, zouden volledig gevaccineerde zorgmedewerkers met een negatieve Ag-RDT kunnen blijven werken met een mondneusmasker in afwachting van de PCR-resultaten. Om te bepalen of dit testbeleid van meerwaarde zou kunnen zijn, is het echter belangrijk rekening te houden met de doorlooptijden van het testen door de gemeentelijke gezondheidsdiensten (GGD).

Research Data Management

Ethics and privacy

The research in this dissertation was conducted in accordance with the principles of the Declaration of Helsinki and the guideline of Good Clinical Practice. **Chapter 2 and 3** employed anonymized surveillance data obtained as part of regular care; obtaining consent from residents for these surveys was not deemed necessary by the legal advisors. Participating facilities were assigned a number, and this number was stored in a document separate from the anonymised data. The institutional research committee was notified about the trial in **Chapter 4** and decided to participate. The study was rated as not subject to Medical Research Involving Human Subjects Act (WMO) and thus did not undergo full review by an accredited MREC. The study in **Chapter 5** was reviewed (File number CMO: 2018-4932**)** by the ethics committee of the Radboud University Medical Centre, which decided that the study was not subject to the Medical Research Involving Human Subjects Act and did not require full review by an accredited Medical Research Ethics Committee. The 'University Knowledge network for Older adult care Nijmegen', a regional network which develops, distributes, and implements scientific knowledge, also reviewed the study. Participating facilities in were assigned a number, and this number was stored in a document separate from the anonymised data. All participants provided written informed consent. **Chapter 6** describes a guideline for which no ethical or privacy issues apply. The study in **Chapter 7** was reviewed (File number CMO: 2017-3237) by the ethics committee of the Radboud University Medical Centre, which decided that the study was not subject to the Medical Research Involving Human Subjects Act and did not require full review by an accredited Medical Research Ethics Committee. Data collected for the review antibiotic prescriptions during the project were obtained as part of regular care, for which resident consent is not required. The institutional research committee was notified about the trial in **Chapter 8** and decided to participate. The study was rated as not subject to Medical Research Involving Human Subjects Act (WMO) and thus did not undergo full review by an accredited MREC. All participants have provided written informed consent. The study in **Chapter 9** was reviewed (File number CMO: 2020-7083) by the ethics committee of the Radboud University Medical Centre, which decided that the study is not subject to the Medical Research Involving Human Subjects Act and did not require full review by an accredited Medical Research Ethics Committee. All participants have provided written informed consent. The test results in Chapter 8 and 9 were stored in accordance with hospital policy.

Data collection and storage

The following secure storage options were taken to safeguard the availability, integrity, and confidentiality of the data in the Canisius Wilhelmina Hospital in Nijmegen. Data obtained for **Chapter 2 and 3** were processed anonymously. In Chapter 2, data obtained from written questionnaires were manually processed and entered into an Excel file, and original questionnaires were discarded in accordance with hospital policy. In Chapter 3, data were collected via link a SurveyMonkey link with a protected login in 2010 and 2011, and through a web-based application with protected login from 2012 to 2017. Digital completed questionnaires were deleted after download the anonymous results in an Excel file The Excel files were stored on a computer in the hospital environment in a folder named 'research' of the department of medical microbiology. Data collected for **Chapter 4** does not include personally identifiable information. The Excel file, containing hand hygiene events, was exported from the electronic hand hygiene monitoring system (by protected login) and stored in the aforementioned folder of the department of medical microbiology. Data in **Chapter 5** were collected using a digital program developed specifically for this survey in PsychoPy. After the digital surveys were completed, they were removed following the download of the anonymous results in a .csv file. The .csv file was then uploaded to a Jamovi file and subsequently deleted. The Jamovi file was stored in the aforementioned folder of the department of medical microbiology. The informed consent forms were stored in locked cabinets at the department of medical microbiology. **Chapter 6** describes a guideline for which no data collection and storage apply. The data collected for the review of antibiotic prescriptions during the project in **Chapter 7** were processed anonymously in an Excel file. Original questionnaires were discarded in accordance with hospital policy. The Excel file was stored in the aforementioned folder of the department of medical microbiology. The data from written surveys in **Chapter 8 and 9** were processed anonymously in SPSS database. Original questionnaires were discarded in accordance with hospital policy. The SPSS files were stored in the aforementioned folder of the department of medical microbiology. The informed consent forms were stored in locked cabinets at the department of medical microbiology.

Availability of data

The studies in Chapters 2 and 3 are published closed access, and the studies in Chapter 5, 6, 7, 8, and 9 are published open access. Chapter 5 will be submitted closed access. The data will be archived for 15 years after termination of the study. Reusing the data for future research is only possible after a renewed permission by the participants, as applicable. The anonymous datasets of the published papers included in this thesis are available from the corresponding author upon reasonable request.

List of publications

1. Wulf M, van Nes A, Eikelenboom-Boskamp A, Melchers W, Klaassen C, Voss A. MRSA in Dutch veterinarians and veterinary students associated with livestock contact. Emerg Infect Dis 2006;12:1939-1941.
2. Rau R, Voss A, Eikelenboom-Boskamp A, Inka Daniels-Haardt, Friedrich AW. MRSA – Prävention im Gesundheitswesen und rolle des öffentlichen Gesundheitsdienstes im Kreis Wesel, NRW. In: Prävention und Versorgung. 2012 Georg Thieme Verlag, Seite 125-137, ISBN 978-3-13-169451-5.
3. Eikelenboom-Boskamp A, Voss A. Surveillance in instellingen. Tijdschrift voor Ouderengeneeskunde 2013;01:3-4.
4. De Jong N, Eikelenboom-Boskamp A, Voss A, Hendrix R, van Gemert-Pijnen L. User-centered and persuasive design of a web-based registration and monitoring system for healthcare associated infections in nursing homes. eTELEMED 2014, proceedings of the 16th international conference on eHealth, Telemedicine and Social Medicine, 152-157.
5. Eikelenboom-Boskamp A, Willemsen I, Kluytmans J, Voss A. Afstemming infectiepreventiebeleid en antibioticabeleid: een "conditio sine qua non" in het verpleeghuis. Ned Tijdschr Med Microbiol 2018;26:122-125.
6. Kenters N, Eikelenboom-Boskamp A, Hines J, McGeer A, Huijskens EGW, Voss A. Product dose considerations for real-world hand sanitiser efficacy. Am J Infect Control. 2020 May;48(5):503-506. doi: 10.1016/j.ajic.2019.12.001. Epub 2020 Jan 7. PMID: 31924389.
7. Stobernack T, Van den Berk T, Boom E, Eikelenboom-Boskamp A, Huis A, Van Huizen M, Voss A. Voorkeuren voor werkkleding in de thuiszorg: De mate waarin cliënten en zorgmedewerkers zich op hun gemak voelen bij werkkleding. Verpleegkunde. 2022 Juni;2:7-13. doi:10.24078/vpg.2022.6.128970.

Curriculum vitae

Name:	Andrea Eikelenboom-Boskamp
Date of Birth:	June 8, 1969
Place of Birth:	Terwolde, the Netherlands
2024 –	Network coordinator from the Regional AMR and IPC Health Network Gelderland (Dutch acronym is GAIN), Radboudumc, Nijmegen, the Netherlands
2022 – 2023	Advisor, Knowledge Institute of the Dutch Association of Medical Specialists, Utrecht, the Netherlands
2009 – 2022	Infection control practitioner for elderly care facilities participating in "Regionaal Zorghygiëne Netwerk Nijmegen e.o." (Dutch acronym is REZON), projectmanager and researcher, Nijmegen, the Netherlands Projects: GAIN FTO specialisten ouderengeneeskunde (2021 – 2022), VWS BRMO casemanagement (2018-2020), INTERREG V A-project EurHealth-1Health & Health-i-care (2016 – 2019), ZonMw Antimicrobial Stewardship verpleeghuizen (2016 – 2018), VWS Kwaliteitscriteria Hygiëne Zorginstellingen (2016 – 2017), INTERREG IV A-project EurSafety Health-Net (2009 – 2014), FP7 PILGRIM MRSA ST398 (2009 – 2011)
1997 – 2009	Infection control practitioner, coordinator unit hygiene and infection control, Radboudumc, Nijmegen, the Netherlands
1994 - 1997	Social nurse, GGD Brabant Noord-Oost, Oss, the Netherlands
1997 - 1998	Post-HBO Opleiding Ziekenhuishygiëne STUNA, Breda, the Netherlands
1990 – 1994	HBO Verpleegkunde, Hogeschool IJsselland, Deventer, the Netherlands
Other activities	
2012 - 2016	Member of the expert group long-term care facilities from the Working Party on Infection Prevention (WIP), delegated from the Dutch Society of Infection Prevention in Healthcare (VHIG)
2020 - 2022	Member of the consultation group COVID-19 guideline from the Dutch professional association of elderly care physicians (Verenso), delegated from the Dutch Society of Infection Prevention in Healthcare (VHIG)

PhD portfolio of Geertruida Gijsbertha (Andrea) Eikelenboom-Boskamp

Department:	**Department of Medical Microbiology**
PhD period:	**21/07/2015 – 31/12/2023**
PhD Supervisor:	**Prof. dr. A. Voss**
PhD Co-supervisor:	**Prof. dr. H.F.L. Wertheim**

Training activities	Hours
Courses	
- RU - Beginners' course 'Statistics with JASP' for PhD candidates (2020)	45.00
- RU - Statistiek voor promovendi met SPSS (2021)	60.00
- Radboudumc - Scientific integrity (2023)	20.00
- Workshop GRADE for interventions (2023)	8.00
Seminars	
- BRMO-casemanagement (oral presentation) (2019)	3.00
- Webinar Hoe nu verder na coronavaccinatie in de langdurige zorg (2021)	1.00
- Webinar "Goed gebruik van antibiotica in verpleeghuizen" (oral presentation) (2021)	4.00
- SWAB webinar (2022)	2.00
- SWAB webinar (2023)	2.00
Conferences	
- Vereniging Hygiene en Infectiepreventie in de Gezondheidszorg (2015)	8.00
- Symposium No action today, no cure tomorrow (2015)	3.25
- International Conference on Prevention & Infection Control (2015)	24.00
- Nationaal Congres Antibiotic Stewardship (2016)	8.00
- Congres Vereniging voor Hygiëne en Infectiepreventie in de Gezondheidszorg (2016)	8.00
- Congres Mythen, Missers en Maatwerk Meesterwerk Infectieuze bedreigingen (oral presentation "Als alleen de bacteriën aansterken") (2016)	15.00
- Infectiepreventie in de ouderenzorg (organisation, two oral presentations) (2016)	40.00
- Congres Vereniging voor Hygiëne en Infectiepreventie in de Gezondheidszorg (2017)	8.00
- International Conference on Prevention & Infection Control (two poster presentations (2017)	24.00
- Symposium Infectiepreventie bij medicatietoediening (oral presentation "Opzetten A-team") (2018)	5.00
- Congres Vereniging voor Hygiëne en Infectiepreventie in de Gezondheidszorg (2018)	8.00
- Congres Mythen, Missers en Maatwerk Meesterwerk Infectieuze bedreigingen (2018)	8.00
- Nationale SWAB meeting + SWAB symposium (2019)	8.00
- International Conference on Prevention & Infection Control (2019)	36.00
- Symposium Infectiepreventie is grenzeloos (2019)	4.00
- Congres Mythen, Missers en Maatwerk Meesterwerk Infectieuze bedreigingen (2020)	8.00
- Minisymposium Vereniging voor Hygiëne en Infectiepreventie in de Gezondheidszorg (2021)	4.00
- European Congress of Clinical Microbiology and Infectious Diseases (2021)	24.00
- Congres Mythen, Missers en Maatwerk Meesterwerk Infectieuze bedreigingen (2021)	8.00
- International Conference on Prevention & Infection Control (2021)	24.00
- Symposium Samenwerkingsverband richtlijnen infectiepreventie (2022)	8.00
- European Congress of Clinical Microbiology and Infectious Diseases (2023)	24.00
- Symposium Samenwerkingsverband richtlijnen infectiepreventie (2023)	8.00

Teaching activities	
Lecturing	
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2015)	4.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2015)	8.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus wijkverpleging (2015)	5.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2016)	20.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2016)	10.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus wijkverpleging (2016)	12.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2016)	8.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2017)	16.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2017)	6.00
- Hygiëne Kwaliteitsmedewerkers basiscursus wijkverpleging (2017)	12.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus wijkverpleging (2017)	6.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2017)	12.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2018)	16.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2018)	12.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2019)	12.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus wijkverpleging (2019)	8.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2019)	20.00
- Masterclass in Antimicrobial Stewardship in Long-Term Care Facilities (2019)	7.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus langdurige zorg (2019)	10.00
- E-learning BRMO (2019)	8.00
- E-learning Hygiëne en infectiepreventie en antibioticabeleid voor specialisten ouderengeneeskunde (2019)	80.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2020)	26.00
- Summerschool COVID-19 in verpleeghuizen (2020)	7.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2020)	18.00
- Hygiëne Kwaliteitsmedewerkers vervolgcursus wijkverpleging (2020)	5.00
- Hygiëne Kwaliteitsmedewerkers basiscursus wijkverpleging (2020)	10.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2021)	20.00
- Hygiëne Kwaliteitsmedewerkers basiscursus langdurige zorg (2021)	18.00
- E-learning diagnostiek over luchtweginfecties, urineweginfecties en resistentie t.b.v. specialisten ouderengeneeskunde (2022)	16.00
- Escapespel t.b.v. farmacotherapeutisch overleg specialisten ouderengeneeskunde m.b.t. voorschrijven antibiotica (2022)	40.00
Total	**912.25**

Dankwoord

Graag wil ik eenieder bedanken die op enigerlei wijze heeft bijgedragen aan de totstandkoming van dit proefschrift. Ook wil ik iedereen bedanken die in de afgelopen jaren hebben gezorgd voor afleiding, waarmee zij hebben bijgedragen aan de broodnodige ontspanning.

Het zou te veel worden om iedereen bij naam te noemen, toch wil ik een aantal personen specifiek benoemen.

Mijn promotor, Prof. Dr. Andreas Voss: we kennen elkaar inmiddels al meer dan 25 jaar. Heel veel dank dat je mij dit promotietraject aanbood, het vertrouwen dat je in alle jaren in me hebt gehad en jouw betrokkenheid bij de onderzoeken. Jouw enthousiasme was besmettelijk. Ik heb veel van je geleerd en de samenwerking was fantastisch. Ondanks jouw drukke agenda kon ik altijd bij je terecht, ook als je in het buitenland was en ik soms het tijdsverschil vergeten was. De gezellige etentjes bij jou thuis zal ik ook zeker niet vergeten, waarvoor dank aan Angela. De raclette is inmiddels binnen mijn gezin ook al jaren een traditie tijdens de feestdagen. Ik hoop van harte dat we na het afronden van het PhD-traject contact blijven houden.

Mijn promotor, Prof. dr. Heiman Wertheim: dank voor jouw input tijdens mijn PhD-traject. Vanaf dit jaar gaan we samen verder in de stuurgroep van het Gelders Antimicrobiële resistentie en Infectiepreventie Netwerk (GAIN).

Alle leden van de manuscriptcommissie, Prof. Dr. H. Vermeulen, Prof. Dr. A. Timen en Prof. Dr. J.A.J.W. Kluytmans: graag wil ik u hartelijk danken dat u de tijd en energie heeft genomen om mijn proefschrift kritisch te beoordelen en dat u hierover met mij van gedachten wil wisselen tijdens de verdediging.

Alle andere opponenten: graag wil ik u hartelijk danken dat u de tijd en energie heeft genomen om mijn proefschrift door te nemen en dat u hierover met mij van gedachten wil wisselen tijdens de verdediging.

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Ine Cox-Claessens, destijds medisch directeur van de ZZG Zorggroep: dankzij jou zijn we gestart met het structureel aandacht besteden aan infectiepreventie binnen ouderenzorgorganisaties in onze regio vanuit de afdeling medische microbiologie

van het Canisius Wilhelmina Ziekenhuis (CWZ). Tezamen met Zorgcentra Pantein, Zorggroep Maas en Waal en de Waalboog zijn we van start gegaan en vormden we het Regionaal Zorg Hygiëne Netwerk Nijmegen e.o. (REZON). We zijn onder het motto 'Meten is weten' gestart met de prevalentiemetingen zoals beschreven in hoofdstukken 2 en 3 van dit proefschrift. In de loop van de tijd sloten Kalorama, Luciver, Gasthuis Millingen en Malderburch bij ons netwerk aan. Ik wil het niet alleen laten bij het benoemen van de zorgorganisaties, maar ze heel graag een gezicht geven door het noemen van de namen van iedereen waarmee ik veel heb samengewerkt en/of die deze samenwerking mogelijk hebben gemaakt. Dit zijn: Ellie Boom, Vickey van der Waaij, Miranda Drabbe, Mariëlle van Loosbroek, Raymond Koopmans, Ewoud de Jong, Wim van Boerdonk, Frank de Jongh, Sandra van der Molen, Roel Jutten, Ronald Gort en Marjella Jansen. Natuurlijk wil ik ook Merijntje van Kats en Willem den Hartog bedanken voor de fijne samenwerking bij de start van REZON.

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Mike Verkaaik, Mariëlle van Loosbroek, Evelien Lutke-Schipholt, Marjorie Nelissen-Vrancken, Paul Geels en Stephanie Natsch: we hebben met z'n allen hard gewerkt aan de volgende stap in de aanpak van antibioticaresistentie door het ontwikkelen van de praktijkgids voor Antimicrobial Stewardship (AMS) in verpleeghuizen zoals beschreven in hoofdstuk 7. Hartelijk dank voor de prettige samenwerking.

Helaas kregen we in 2020 maken met de coronapandemie. Wat hebben we binnen ons netwerk ongelooflijk intensief met elkaar samengewerkt. Ik heb het voorrecht gehad om in deze periode met heel veel lieve collega's samen te werken. De waardering en de steun die we elkaar boden gedurende een tijd die veel van ons allen vroeg, zijn onvergetelijk. Drie mensen wil ik in het bijzonder benoemen.
Sandra Egging-Nieuwenhuis: wij hadden in de jaren ervoor al met elkaar samengewerkt maar tijdens de eerste golf van de coronacrisis spraken wij elkaar zeven dagen in de week. Op de verjaardagen van jou of mijn kinderen zongen we eerst het verjaardagslied voordat we de laboratoriumuitslagen en maatregelen met elkaar doornamen. Nadat de nodige ICT-maatregelen getroffen waren was dagelijks contact niet altijd meer nodig, maar nog steeds spraken we elkaar een aantal keren in de week. Dank je wel voor de hele fijne samenwerking.
Eefje Perlot-Nabers: voor de coronacrisis kenden we elkaars namen, maar hadden nog niet direct samengewerkt. Bij de start van de coronacrisis ging onze samenwerking als vanzelf. Bijzonder was het ook om in 2023, terwijl ik een andere baan had, een uitnodiging te ontvangen voor een afsluitend etentje om met het team van de zorggroep de coronaperiode af te sluiten. Hartelijk dank hiervoor.
Wilma Budding, mijn collega bij het CWZ: Wat ontzettend fijn dat jij ons kwam versterken en wij de werkzaamheden in de regio konden verdelen. Ontzettend bedankt voor jouw inzet en samenwerking.

De namen die ik verder nog wil noemen zijn: Annita Opdam, Ate Frans de Bruin, Desiree Lowies, Eesjen Ploeg, Ewoud de Jong, Frank de Jongh, Hanneke van Beusichem, Jessica Bogaerts, Karin van den Heuvel, Linda Everts, Maaike Versteegh, Marcel de Groot, Marieke van Haaren, Mariëlle van Loosbroek, Marina Waaksma, Marionne van Wanroij – van Lenkens, Martijn den Ouden, Miranda Drabbe, Rianne Geurts, Roel Jutten, Ronald Gort, Sandra van der Molen, Tamara Besseling, Theun de Groot en Wil Janssen. Hoofdstukken 8 en 9 zijn mede door hun inzet tot stand gekomen. Daarnaast dank aan iedereen die ik niet bij naam heb genoemd, maar waarmee ik in deze periode heb samengewerkt.

Ook wil ik iedereen bedanken waarmee ik in de afgelopen jaren fijn heb samengewerkt binnen de consortia EurSafety Health-NET, EurHealth-iHealth en

Health-i-care heb samengewerkt. In het bijzonder dank aan Alexander Friedrich, Anja Roters, Corinna Glasner, Annette Dwars, Antje Wunderlich, Inka Daniels-Haardt, Annette Jurke en Nienke Beerlage - de Jong.

Ina Willemsen: dank je wel voor de prettige samenwerking in het project waarin we indicatoren hebben ontwikkeld voor verpleeghuizen.

Voordat ik ga afsluiten, wil ik een aantal personen bedanken die ik nog niet genoemd heb. Mijn enthousiasme voor het vak is mede ontstaan door enthousiaste collega's die ik in de loop der jaren, ook vóór mijn PhD-traject, heb leren kennen.

Clementine Wijkmans: mijn loopbaan begon bij de GGD. Jij ging ermee akkoord dat ik de opleiding ziekenhuishygiëne ging volgen en we hebben op een prettige manier afscheid genomen toen ik de overstap maakte naar het Radboudumc.

Thilly Bensink, mijn medestudent in de opleiding ziekenhuishygiëne die mij attendeerde op de vacature van deskundige infectiepreventie bij het Radboudumc. Dank je wel Thilly.

Al mijn oudcollega's van de afdeling hygiëne en infectiepreventie (HIP) en het medisch microbiologisch laboratorium van het Radboudumc. In het bijzonder Mayke Nillesen: wat hebben wij, tijdens de soms lange werkdagen, fijn samengewerkt en veel lol gehad. Dank je wel dat je mijn paranimf wilt zijn. Esther de Both: dank je wel voor de hele fijne samenwerking en gezelligheid.

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Lieve papa, helaas ben je er niet meer. Wat zou jij trots zijn geweest als je de verdediging had kunnen bijwonen. Je blijft voor altijd in mijn liefdevolle herinnering!

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