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DOKTORI ISKOLA

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Evidence-based hand hygiene:
Volume Optimization for alcohol-based handrubs

PhD thesis

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TABLE OF CONTENTS

LIST OF ABBREVATIONS

AAA	Automated Area Assessment
ABHR	Alcohol-based handrub
CDC	U.S. Centers for Disease Control and Prevention
HAI	Healthcare-Associated Infection / Hospital-Acquired Infection
HCW	Healthcare worker
ISO	International Organization for Standardization
NHS	National Health Service
WHO	World Health Organization

1. INTRODUCTION

1.1. Hand hygiene in healthcare settings

Ignác Semmelweis recognized in 1847 that hands play a key role in the spread of infections. He required healthcare workers (HCWs) in his ward to wash their hands with chlorinated lime, which dramatically reduced infection rates and mortality caused by puerperal fever [1–3]. Almost two centuries later, healthcare-associated infections (HAIs) remain a major concern. In the European Union, 7.1 % of hospital patients get an HAI, risking lives of approximately 4.3 million people each year [4]. At least half of these infections are preventable, and proper hand hygiene remains the most effective, simplest, and most cost-efficient intervention [5, 6].

Hand hygiene remains the most important measure for preventing nosocomial infections. Over the past two decades, performing hand hygiene with alcohol-based handrub (ABHR) has become globally accepted [7, 8]. Hand rubbing offers several advantages over handwashing with soap and water: it acts more rapidly, is more effective, is better tolerated by the skin, and can be performed conveniently at the point of patient care. In 2015, ABHR was included in the World Health Organization's (WHO) Essential Medicines List [9].

1.2. Hand hygiene technique

Hand rubbing is only effective if the entire hand surface is covered with an adequate volume of ABHR. Unfortunately, incomplete hand coverage is common, even among healthcare workers (HCWs). In one study investigating hand hygiene performance among 5200 clinical staff members, only 72 % achieved acceptable hand coverage with ABHR, despite being monitored at the end of a one-week hand hygiene campaign and being notified of the evaluation [10]. Another study examining 1269 HCWs immediately after hand hygiene training, found that only 67 % covered their hands properly [11]. According to another study at 11 National Health Service (NHS) hospitals in United Kingdom, 986 hand hygiene events were recorded and analyzed, and 73 % of HCWs performed acceptable hand hygiene [12]. In a tertiary care hospital, 2297 hand hygiene events were assessed, and appropriate hand coverage was achieved in only 7.9 % of the cases [13].

Over 40 years ago, Taylor demonstrated that thumbs and fingertips are the most frequently missed areas during hand hygiene [14]. Unfortunately, little progress has been made since then; the same areas, especially the thumbs and fingertips on the dorsal side of the hands, remain the most frequently missed areas, as confirmed by more recent studies [12, 15–19]. The central hypothesis of my research was that inadequate hand coverage is primarily caused by the improper volume of ABHR applied.

1.3. Proper ABHR volume

In 2009, the WHO published the *Guidelines on Hand Hygiene in Health Care*, which remains the most widely followed hand hygiene guideline worldwide [20]. The document provides a detailed, step-by-step description on how to perform hand hygiene. Interestingly, however, it does not specify the exact volume of ABHR to be used. Instead, it simply recommends applying 'a palmful of the ABHR product,' noting that the required volume may vary depending on hand size [21]. Similarly, the U.S. Centers for Disease Control and Prevention (CDC) guidelines do not define a specific ABHR quantity, rather state that the entire hand surface should be covered and advise users to 'read the label to learn the correct amount' [22], pushing the responsibility towards the ABHR manufacturer.

To validate the efficacy of an ABHR product, standardized *in vivo* test methods, such as the European Norm EN 1500 (test method for evaluating handrub efficacy) and the North American standard ASTM E1174 are available [23, 24]. These methods typically compare the performance of the test product under test conditions [25]. Both EN 1500 and ASTM E1174 require the application of two consecutive 3 ml doses of handrub. Because these tests were conducted using 3 ml volumes, this is the amount that is commonly labeled on the products and in their user manuals. Some experts also recommend applying 3 ml of ABHR [26]. Meanwhile, a study pointed out that for individuals with larger hands, even an ABHR volume of 3 ml may be insufficient to achieve complete hand coverage [6].

There are major concerns regarding the uniform recommendation of 3 ml. First, this amount often requires more than 30 seconds to dry. Girard et al. tested 26 different handrub formulations using 3 ml volume and found that drying time exceeded 30 seconds

in all cases [27]. Similar findings were reported by another study comparing liquid, gel, and foam formulations, where all formats required more than 30 seconds to dry at 3 ml dose [28]. The application of 3 ml of ABHR was often considered too much, as it did not dry within an acceptable time. In one study, healthcare workers reported that an acceptable volume would be 1.5–2 ml [25]. The International Organization for Standardization (ISO) guideline on hand hygiene states that at least 1.5 ml of ABHR should be used [29]. Another study suggested different volumes based on formats; volume of 1.5–2.25 ml for gel ABHR and 1.5 ml for foams [28].

ABHR products are available in different formats: liquid, gel, and foam. The antibacterial efficacy of these formats appears to be comparable, at least under *in vitro* conditions [30–31]. Gels have higher viscosity, which helps to prevent spillage, although some formulations may leave a sticky feeling on the hands [32]. Gels are usually slightly more expensive than liquids, probably due to the additional ingredients required for gelling [33].

Bacterial reduction also depends on the applied volume of ABHR. One study found that 1.5 ml of ABHR achieved only 2.8 log_{10} reduction, whereas 3 ml resulted in more than 3.9 $\log_{10}$ reduction [25]. Another study similarly demonstrated that increasing the applied volume led to greater bacterial reduction: using 1.1 ml, 2 ml, or 5 ml of the same ABHR resulted in log_{10} reductions of 1.85, 3.35, and 3.58, respectively [34]. Goroncy-Bermes et al. concluded that the volume of 3 ml appears appropriate, as the *log* reduction does not increase significantly beyond that point; however, they also emphasized that individuals with larger hands may require even higher volumes [35]. Bellissimo-Rodrigues et al. reported that bacterial reduction was significantly lower for individuals with large hands compared to those with small hands [36]. These findings further highlight that ABHR volume should be personalized, at least according to hand size.

1.4. Hand hygiene volume used in clinical settings

Individual studies measuring actual ABHR usage in clinical settings have revealed highly variable results. One study reported that the average applied volume was 0.73 ml [37], while another found that an average of 3.4 ml was used per hand hygiene event [38]. Only a few large-scale studies are available in the literature. NHS Scotland published a study

estimating applied volumes based on the total amount of handrub purchased, concluding that healthcare workers used an average of around 1 ml per hand hygiene event [39]. In Germany, an electronic monitoring system (NosoEx) recorded ABHR usages in 17 wards. Based on 931446 hand hygiene events, the average applied volume ranged from 1.32 ml (intensive care unit) to 3.13 ml (neurology), depending on the ward type [40].

The CDC and WHO hand hygiene guidelines recommend that dispensers should dose a sufficient amount of ABHR to cover the entire hand surface and keep the hands wet for at least 15–20 seconds. The Leapfrog 2022 guidance states that each dispenser activation should deliver at least 1.0 ml product [41–43]. This recommendation is reasonable, as a large-scale study analyzing more than 28 million recorded hand hygiene events demonstrated that at 86 % of hand hygiene events only a single dose of ABHR were used, even when one dose was only 0.75 ml [28].

The actual volume that dispensers provide often ranges between 0.6 and 1.3 ml [44]. A study investigating five of the most popular automatic dispensers described that two systems delivered a mean dose below 1.0 ml per activation [42]. Due to market demand, an increasing number of dispensers are being designed to deliver less than 1 ml per dose [19, 21, 43, 45].

Dispensers should ideally be designed to provide the appropriate ABHR volume in a single activation [28]. The aim of this work is to estimate what that optimal ABHR volume should be.

2. RESEARCH OBJECTIVES

Based on the currently available data, it is hypothesized that an optimal, specific relative, personalized amount ABHR exists taking into consideration general efficacy of a product. The present research aimed to estimate this ABHR volume.

My investigation addressed the following topics:

1) **What is the primary factor determining hand hygiene performance?**
   This research question aimed to identify the key determinant of effective hand hygiene, beyond formal compliance with recommended techniques. Understanding the primary driver of hand hygiene performance is essential for optimizing protocols and improving real-world effectiveness.
2) **What practical limitations are associated with the application of larger volumes of handrub in routine clinical practice?**
   While increasing the applied volume of handrub may theoretically improve coverage, it is important to understand the practical constraints that may limit its feasibility in everyday clinical settings. This question addressed the balance between efficacy and usability.
3) **Does the optimal volume of handrub differ between formats (liquid, gel, and foam)?**
   Different ABHR formats have different physical properties, which may influence spreading behavior, drying time, and spillage. This research question explored whether a single optimal volume can be applied universally across formats.
4) **Can a personalized, hand size–dependent handrub volume provide a feasible and effective solution for optimizing hand hygiene performance?**
   This question examined whether personalization could offer a practical and scalable improvement to hand hygiene practice.

3. METHODS

In this dissertation, the research questions were addressed through a series of systematically planned and sequential experimental studies conducted in different healthcare and educational settings. The research questions were examined in various combinations across multiple complementary projects, each focusing on different aspects of hand hygiene performance. The design and settings of these projects are presented and described in detail in the Results section of this dissertation.

3.1. Dosing ABHR

Liquid-format handrubs were dispensed using a Dispensette S Analog-Adjustable bottle-top dispenser (Brand GmbH, Germany). Gel ABHR was dispensed using a Purell ADX-7 dispenser (GOJO Industries Inc., Akron, OH) [2].

Foam-format ABHR dispensers require a special pump design, as air must be added during dispensing to generate the foam. Consequently, only predefined volumes can be applied [43]. Several different foam dispensers were used in our investigations, and the dispensed foam volumes (expressed in liquid-equivalent volume) were monitored during the studies.

First, Cutan Complete Foaming Sanitizer from a plastic bottle was used. This dispenser was selected because a single dose delivered 0.76 ml. During the study, either two doses (1.52 ml) or four doses (3.04 ml) were applied, corresponding closely to the target volumes of 1.5 and 3.0 ml [46].

When different foam ABHRs were compared, three automatic, touch-free dispensers were tested: ES10 (GOJO), Nexa (Ecolab), and Medline (Spectrum) also marketed as Neptune (Ophardt). Automatic, touch-free dispensers were selected because these are increasingly present in clinical settings. Each dispenser was used with its corresponding refill system [47].

3.2. Coverage by handrub

Hand coverage by ABHR during hand hygiene was measured using a fully automated digital hand hygiene technique monitoring device (Semmelweis System, HandInScan

Zrt., Debrecen, HU), which has been shown to outperform any human expert-based evaluation method [19]. The system is based on the well-known fluorescent method: a fluorescent dye is added to the handrub, enabling the device to detect ABHR-covered – and thus disinfected – areas with pixel-level resolution. The system provides immediate, quantitative visual feedback on hand hygiene coverage (Figure 1). The areas identified as correctly disinfected by the Semmelweis software have been shown to correlate closely with microbial culture results, with 95.05 % sensitivity, and 98.01 % specificity [48].

Figure 1. Hand coverage was measured by the Semmelweis System, which automatically analyzes coverage and provides visual feedback: on the user interface provided outcome green indicates handrub-covered areas, while red indicates areas not covered by handrub [2, 33].

3.3. Drying time

Drying time is defined as the duration from applying the handrub until the hands are completely dry. Drying time was measured by a stopwatch. The investigator started the stopwatch when the handrub was dispensed. As soon as participants felt that their hands were dry, they indicated this to the investigator, who then recorded and documented the elapsed time in seconds. Participants were not directly instructed on how to perform hand hygiene right before the experiment. Nevertheless, in general, all institutions participated in the study follow the WHO 6-step hand rubbing protocol in their practice, and participants had previously been trained to comply with this protocol [2, 33].

3.4. Disinfectant spillage

Our spillage measurement technique was continuously improved during the study, and eventually we defined a method that allows precise quantification of spillage.

3.4.1. Spillage determined by asking

After performing hand hygiene, participants were asked whether they noticed any spillage (dripping) of the handrub. It is important that this question was asked before the objective evaluation of coverage with the Semmelweis System. Otherwise, when participants were provided visual feedback, and they missed large areas, the subjects might want to find an excuse, and dripping would be an ideal one. It should also be noted that participants were not informed about the exact volume they received during the measurements.

Investigators reported that, although some participants did not report dripping, spillage was still observed. Dripping may occur without anyone noticing it; therefore, the actual outcomes probably underestimate the real spillage [2].

3.4.2. Semi-quantitative spillage detection

To document disinfectant spillage, a custom experimental setup was designed and used. Participants were required to perform hand rubbing directly above a large sheet of paper (66.329.742 Celeste Chiaro colored paper, A3 size, 80 g/m² grammage, Fabriano, IT) at approximately 20 cm height. As mentioned earlier, the applied handrub contained a fluorescent marker, which stained the paper if dripped. Once the paper dried, it was photographed using a digital camera accessorized with a UV-light. The disinfectant droplets on the paper fluoresced and could therefore be analyzed using appropriate software (segmentation with a custom-written algorithm in Python). Using control measurements as a reference, spillage was evaluated based on the overall intensity and area of the fluorescent patches (Figure 2). The main limitation of this method was that droplet volume and fluorescence intensity were not linearly correlated. In addition, liquid handrubs produced larger stained areas than the same volume of gel handrub [33].

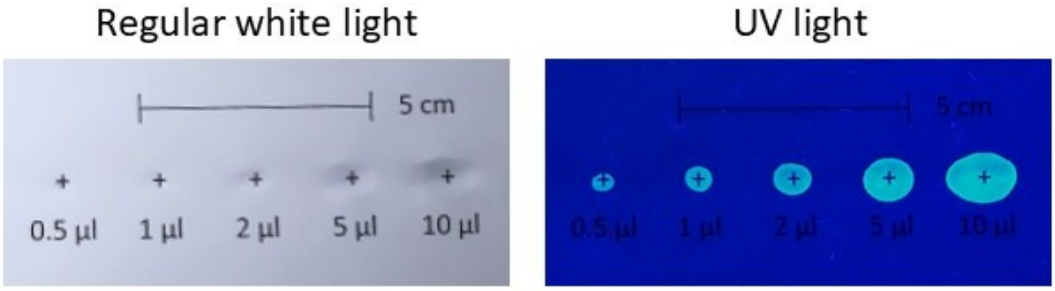

Figure 2. Disinfectant spillage UV photography results: Approximation of dripped volume to intensity [33].

3.4.3. Quantitative spillage detection

Participants were asked to perform hand hygiene 20 cm above an analytical scale (Sartorius Analytic, AC 210 P, Sartorius GmbH, Göttingen, DE) equipped with a wide bowl on top (Figure 3). When handrub spilled, most of the lost volume was collected in the bowl. The researcher recorded the mass of the spilled handrub, which was then converted to volume applying the official density of the product (as specified in the Safety Data Sheet), expressed in g/cm³ [49].

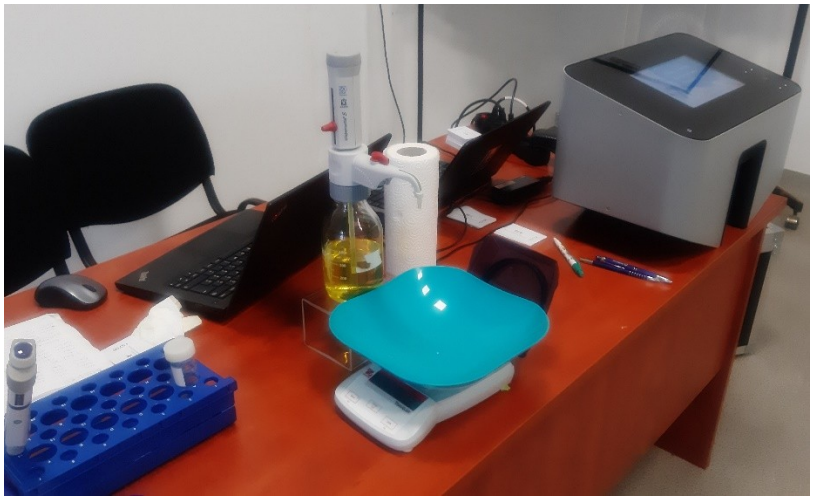

Figure 3. Experimental setup for quantifying handrub spillage [49].

3.5. Hand size determination

Human hand size assessment is a particularly understudied area. The aim was to establish a quick and automated method to measure human hand size. A new method, the Automated Area Assessment (AAA) was developed to determine hand size simultaneously with ABHR coverage measurement. Validation of the method is presented below. All studies presented in my dissertation applied the Automated Area Assessment method [50].

3.5.1. Description of traditional methods and the AAA method

Determining hand size precisely is not a daily clinical demand; however, many studies have focused on hand size. Most of these prior research projects originate from the fields of plastic surgery and burn treatment, where hand size is used to estimate the burned skin

surface. For this reason, measured hand area was often expressed as a percentage of the total body skin area. Hand size determination has not been routinely applied in hand hygiene-related investigations, as traditionally available methods were time-consuming and resource-intensive. Several relevant studies used a very simple approach: measuring the length and width of the hand and multiplying these.

In my investigation, six different methods were compared. Methods #1 and #2 were based on hand outlines (hands were traced with a fine liner pen), while Methods #3 and #4 used digital images of the hands. In Method #5 hands were placed on a flatbed scanner. Methods #1 and #3 applied the above-mentioned "length × width" calculation, whereas Methods #2, #4, and #5 measured the entire hand area. Method #6 was the Automated Area Assessment method that I developed. This method uses the same Semmelweis System applied to measure handrub coverage. The analyzed methods are presented in Figure 4 [50].

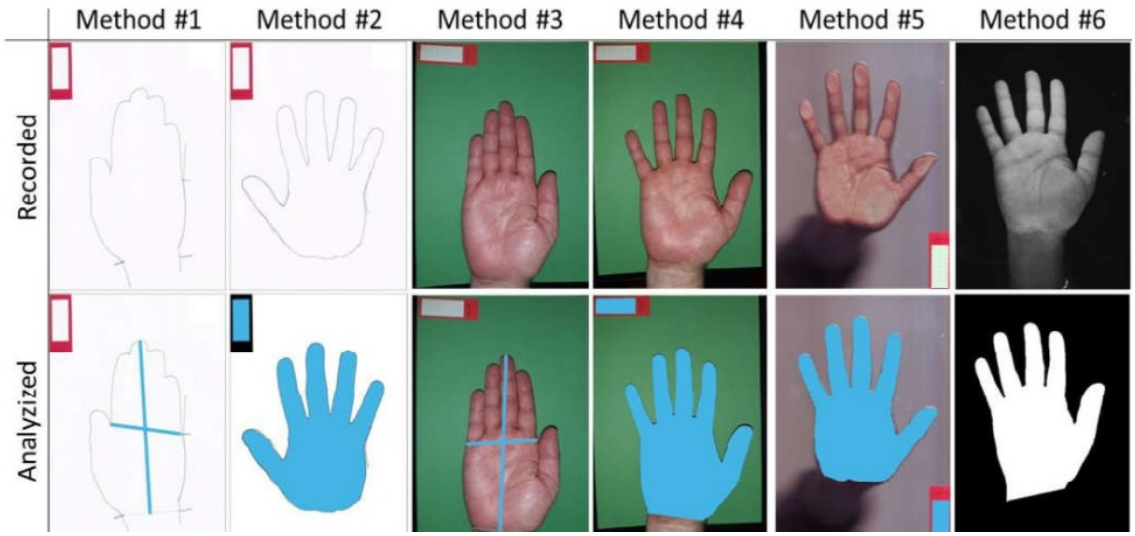

Figure 4. Different methods employed to measure hand size. Image capturing method #1 #5 contained a 10 cm2 (2x5 cm) reference grid mark **[**50].

3.5.2. Comparison of the traditional methods and the AAA method

In the investigation, the hands of 31 healthy adult participants were measured using six different methods. Hand sizes measured by Method #5 and #6 (AAA) were found smaller than those determined by the first four methods. [51]. As a result, the values were smaller but still well correlated with those obtained using traditional methods (Figure 5). Hand size determination can thus be automated using a digital hand hygiene device, making it a feasible, routine measurement in hand hygiene-focused research and trainings [50].

Later on, in my dissertation, hand size always refers to a 3-dimension hand size, not consistent with the values presented in Figure 5.

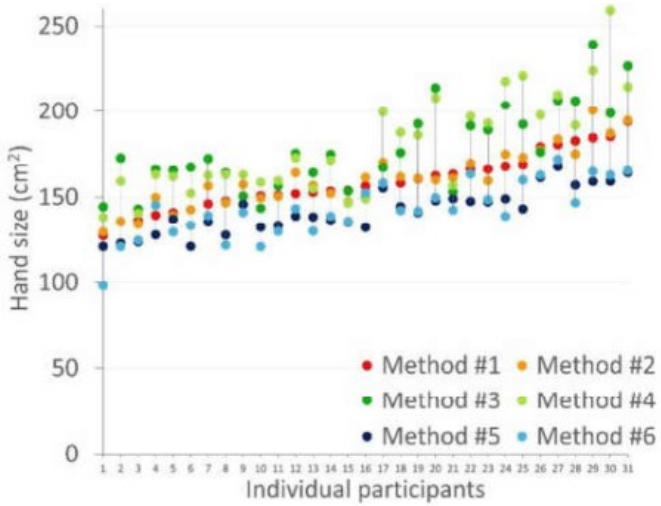

Figure 5. Individual results of hand sizes measured by different methods, ordered by the results of Method #1. Note that hand size here is referred to a 2-dimension projection of the hand. [50].

3.5.3. Calculation of 3-dimesion hand size based on the AAA method

All the above-described methods measured a two-dimensional projection of the hand, which always brings some distortion to the hand size measurements (e.g., excluding the edges of the hand, or determining improper contours between the fingers). Determining the 3D surface of the hand is more challenging. Real hands cannot be measured precisely in 3D because of slight involuntary movements. To address this, we created an artificial silicone hand (Figure 6) by molding, using a volunteer as the hand model. This hand was measured with the AAA method. In parallel, a 3D laser scanner was used to construct a digital model of the hand, from which the true surface area was objectively determined. The artificial hand was created with open fingers so that the entire surface of the fingers could be measured on the 3D model. Based on the ratio of the 2D hand size (measured with the AAA method) and the 3D hand surface, a correction factor was calculated. This correction factor was 1.36, indicating that the true 3D surface of the hand was 1.36 times larger than its two-dimensional projection as determined by the AAA method [50].

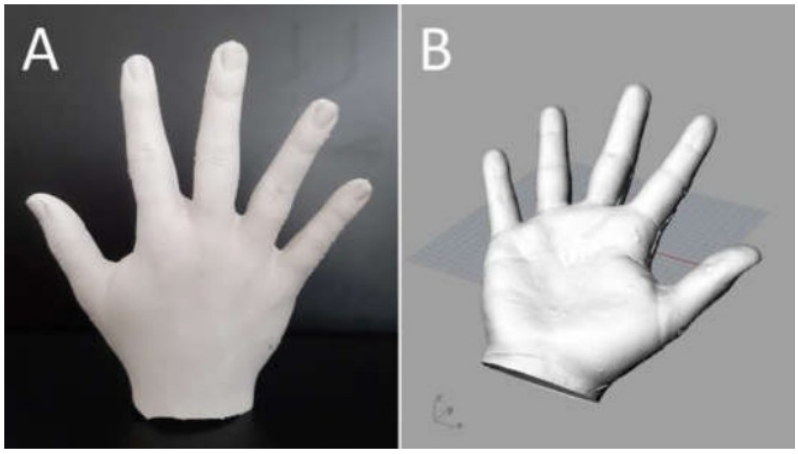

Figure 6. Artificial hand phantom that was fabricated for calibration. A) photo image, and B) 3D scanned and reconstructed digital representation of the hand phantom [50].

3.6. Microbial validation

The gold-standard method for assessing hand hygiene effectiveness is microbiological validation, which directly measures the reduction of viable microorganisms on the hands, the primary objective of hand hygiene. For this reason, the different relative ABHR amounts were also tested using in vitro microbiological validation.

A seven-step, 10-fold dilution series was prepared from a 2.0 McFarland suspension of *Escherichia coli* (ATCC 10536). From each dilution 100 µl was plated onto Eosin Methylene Blue (EMB) agar and spread uniformly to produce a consistent bacterial lawn. From the 1:1000 dilution (10^{-3}) seven additional plates were prepared with lawns formed using 100 µl suspensions. After a 30-minute drying period the plates were treated with varying amounts of handrub (BODE Sterillium). The plates were subsequently incubated at 37 °C for 24 hours and photo documented.

Colony-forming unit (CFU) counts were determined from the recorded images. The initial dilution series served as the basis for calculating the concentration of the original suspension, expressed as CFU/ml [49].

4. RESULTS

4.1. Participants

In my five related publications, the results of 3265 hand hygiene events were summarized. Table 1 provides an overview of the studies this dissertation is built upon, and their key parameters.

Table 1: Key parameters of the involved studies.

Participants	ABHR(s)	Volumes tested	Date	Hand hygiene events	Ref.
Medical students (n=298) Surgical residents (n=57)	Semmelweis Training Rub (liquid)	1, 1.5, 2, 2.5, 3, 3.5, or 4 ml	2018. Oct - 2019. Jun	1622	[2]
Medical students (n=340)	Semmelweis Training Rub (liquid), Semmelweis Training Gel (gel)	1.5 or 3 ml	2019. Nov	641	[33]
Medical students (n= 89)	Semmelweis Training Rub (liquid), Semmelweis Training Gel (gel), Cutan Complete Foaming Sanitizer (foam)	1.5 or 3 ml	2023. Jan – Jun	471	[46]
Medical students (n= 60)	Purell Advanced Hand Sanitizer (foam), Ecolab Quick-Care Foam Hand Sanitizer (foam), Medline Spectrum Hand Sanitizer Foam (foam)	0.68 / 1.36 ml, 0.80 / 1.60 ml, 1.28 / 2.56 ml	2023. Mar - May	183	[47]
Medical students (n= 24), Laboratory staff (n=18)	Semmelweis Rub&Go (liquid)	3 ml, relative volumes	2022. Feb-Aug	348	[49]

4.2. Effect of ABHR volume on coverage

A direct correlation was found between ABHR volume and hand coverage; increasing the handrub volume resulted in smaller uncovered areas. Based on 1622 recorded hand hygiene events, uncovered areas fell below 1 % only when the applied ABHR dose was

3.5 ml or higher (Figure 7). Interestingly, complete (100 %) coverage was not achieved by all participants even with 4 ml dose. It should also be noted that the size of the uncovered areas does not correlate linearly with ABHR volume; as the applied volume decreases below 2 ml, the proportion of the missed surface increases sharply. When only 1 ml of ABHR was used, on average 7.1 % of the hand surface remained uncovered - approximately the size of a finger. Typically missed areas were the fingertips, the thumb and the dorsum of the hand (Figure 8) [2].

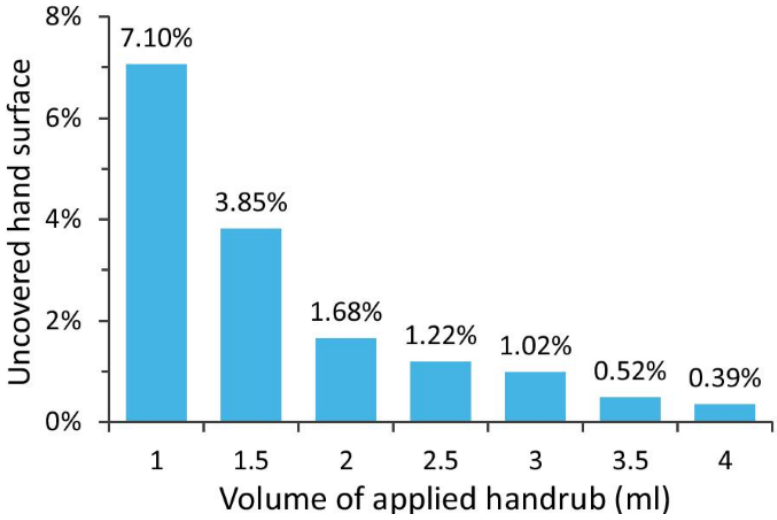

Figure 7. Aggregated hand coverage across all participants (percent of the total hand surface missed during the hand hygiene event) [2].

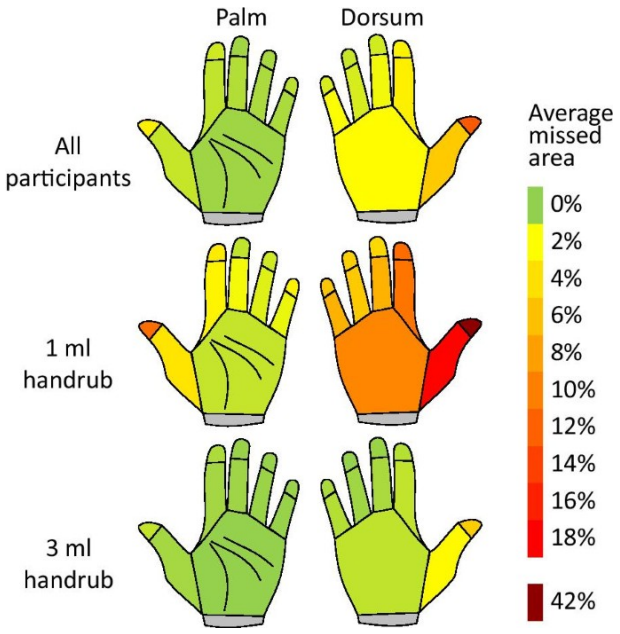

Figure 8. Typically missed areas during the hand hygiene events. (All: n = 1557, 1 ml: n = 153, 3 ml: n = 724) [2]

4.3. Hand size

Digital hand size assessment results from a large-scale study are shown in Figure 9, where the hand size of 355 adult participants was determined using the Automated Area Assessment (AAA) method. The results exhibited a bimodal distribution, with men having larger hands than women. Note that huge differences in hand sizes were observed among participants: the smallest hand surface measured 259.3 cm², while the largest was nearly double, 497.8 cm² [2].

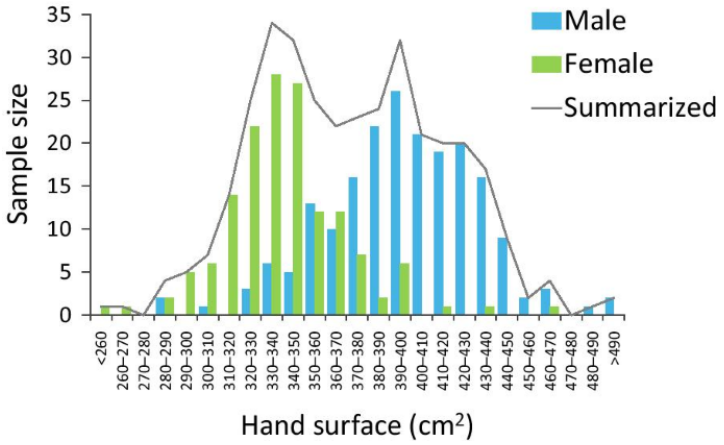

Figure 9. Hand size calculation results, provided by the Semmelweis System's software (Automated Area Assessment method) [2].

4.4. Relative handrub amount

With the advent of automatic hand-size measurement, large datasets on hand dimensions have become available. Building on this, we introduced the innovative concept of the 'relative handrub amount' to objectively account for individual hand size in hand hygiene. [2]. This value is calculated as the applied handrub volume divided by the hand surface area. In the above-mentioned study, the average hand surface area was 372.9 cm², while the median was 370.2 cm². When 3 ml of handrub – the most commonly cited ABHR volume – was applied to a pair of average-sized hands (372.9 cm² each), this corresponded to a specific coverage of 4.02 µl/cm². A relative amount of 4.02 µl/cm² is considered sufficient for an average hand, even in less trained populations, and thus appears to be a valid approximation for individuals with medium-sized hands.

As shown in Figure 10, surgical residents performed considerably better than third-year medical students, indicating that practice also has a substantial effect.

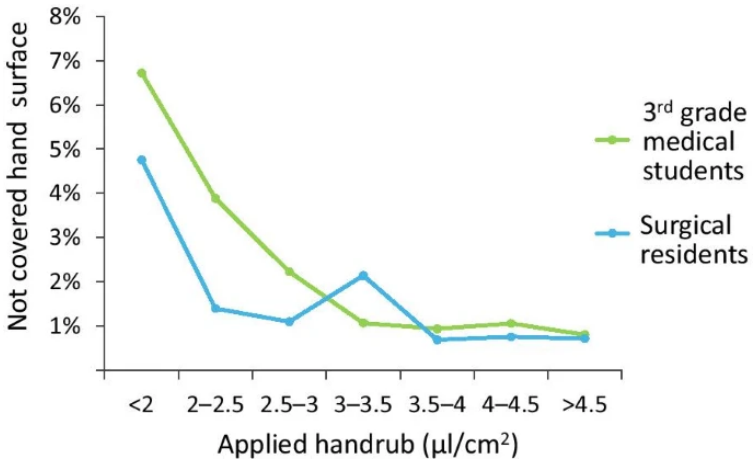

Figure 10. Hand coverage by relative ABHR volume in the case of 3rd grade medical students, who recently learned proper hand disinfection technique, and surgical residents, who have several years of experience. Applying enough ABHR, medical students reached similar results as surgical residents. When suboptimal volumes were used, experience had indeed an impact [2].

4.5. Limiting factor of applying large amount of handrubs

The data indicates that hand coverage improves progressively with increasing volumes of ABHR. Following this logic, one might conclude that the more handrub applied, the better. However, there are practical limitations to applying larger ABHR volumes, which are summarized below.

4.5.1. Drying time

By increasing the disinfectant volume, the application time (drying time) increases as well. At 3 ml volume, a plateau is reached in the mean values (Figure 11). It is important to note that these results concern an ABHR with 70 % ethanol concentration. We may observe slight differences in drying times using different products' formats. Furthermore, the relatively wide variances in drying times indicate that – apart from hand size – other intrinsic and extrinsic factors can potentially influence drying times as well, such as hand dryness or the temperature of the hands and the surrounding environment [2].

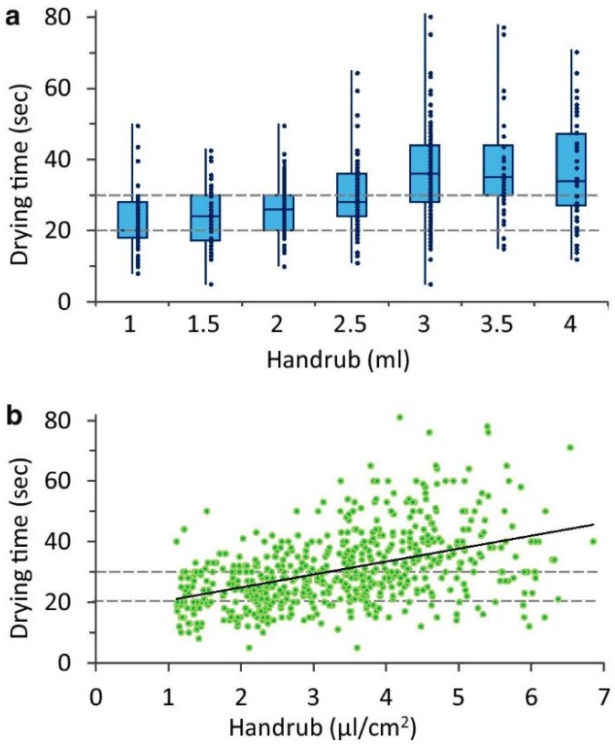

Figure 11. Results of drying time measurements. A) *Drying time* and *ABHR volume* correlation without taking hand size into consideration. B) Drying time and Specific Hand Coverage correlation (hand size taken into consideration). Note: WHO guidelines mention that hand rubbing should take 20–30 s, while the typically prescribed 2.5–3 ml ABHR volume requires longer time to dry [2].

4.5.1.1. Individual differences in coverage and drying times

To better understand individual differences in drying times and coverage, a follow-up study was conducted, in which participants performed hand hygiene with six different relative rub amounts (ranging from 0.6 to 3.6 µl/cm²). Each relative rub amount was tested three times, resulting in a total of 18 measurements per participant. Figure 12 illustrates the remarkable individual variability observed in both drying times and coverage values. The WHO-recommended drying time of 30 seconds was reached at 1.2 µl/cm² by Participant IV, while Participant III required double dose (2.4 µl/cm²) to achieve the same. These individual differences are likely to be related to variations in skin type.

Remarkable differences in coverage were also observed among participants. Some were able to cover their entire hand surface with only 1.2 µl/cm², whereas others required at least 3.6 µl/cm². This variability probably reflects differences in hand hygiene technique. In summary, this high variability in individual performance suggests that the optimal relative amount should not be set below 4 µl/cm² [49].

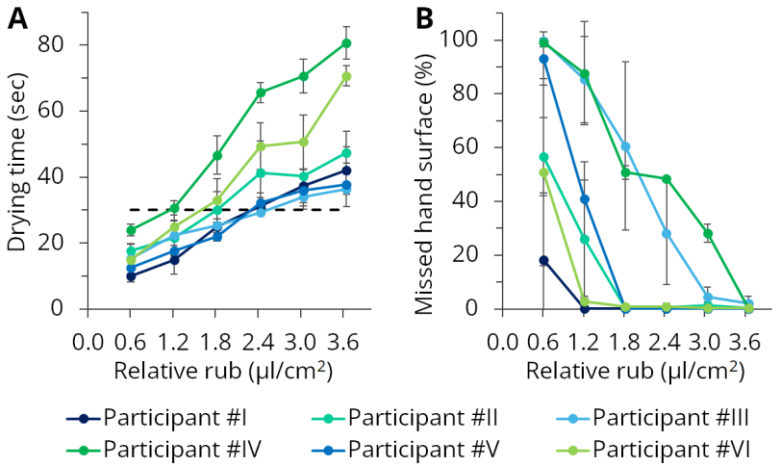

Figure 12. Individual differences in applying ABHR. A small-scale exploratory study showed that A) the drying time increases proportional to the ABHR volume, and B) hand coverage becomes superior at larger quantities of ABHR [49].

4.5.2. Spillage

Increasing the ABHR volume may also increase product loss during hand hygiene, as shown in Figure 13. In that study, dripping was assessed through participants' self-report; however, as described above, dripping may occur without participants noticing it. Therefore, these results likely underestimate the true extent of dripping (or spillage) [2].

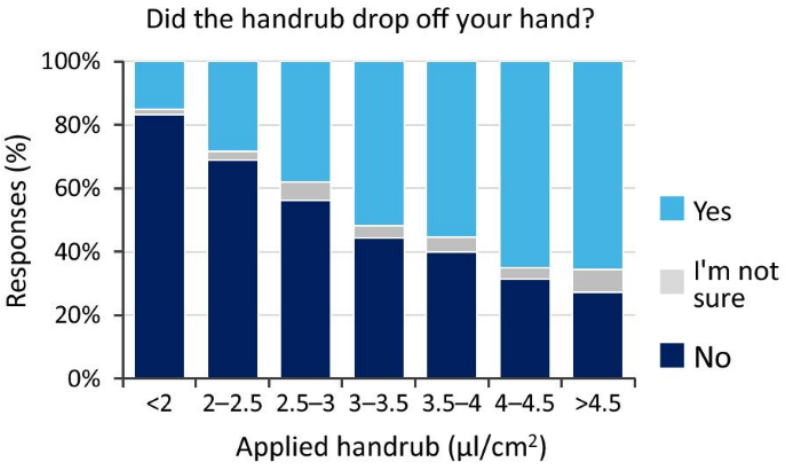

Figure 13. Handrub dripping (spillage) during a hand hygiene event. Note: 1.5 ml and 3 ml ABHR volumes on an average sized hand derives to 2.51 and 4.01 µl/cm^2 relative dose, respectively [2].

4.5.2.1. Quantification of spillage

Figure 14 presents the dripping results from a study, in which the spilled volume of ABHR was quantitatively measured [49]. Participants (n = 24) performed hand hygiene

using either an absolute dose of 3 ml ABHR or relative doses of 3, 4 and 5 µl/cm². When 3 ml of ABHR was applied, the mean spillage was 0.84 ± 0.39 ml, corresponding to 28.2 % of the total dose (Figure 14A). Thus, only 2.15 ± 0.39 ml remained on the hands for performing hand hygiene. Substantial inter-individual variation in spillage was observed, ranging from 6.6 % to 50.8 %.

The average hand surface area of participants in this study was 340.8 cm², which was slightly smaller than that reported in the previous study [2]. Accordingly, the application of 3 ml from handrub corresponded to an average relative volume of 4.49 µl/cm².

Taking hand size into consideration, when participants were provided with a different relative amount of handrub (3, 4, or 5 µl/cm²), the average spillage rates were 12.7 %, 20.4 %, and 23.9 %, respectively (Figure 14B) [49].

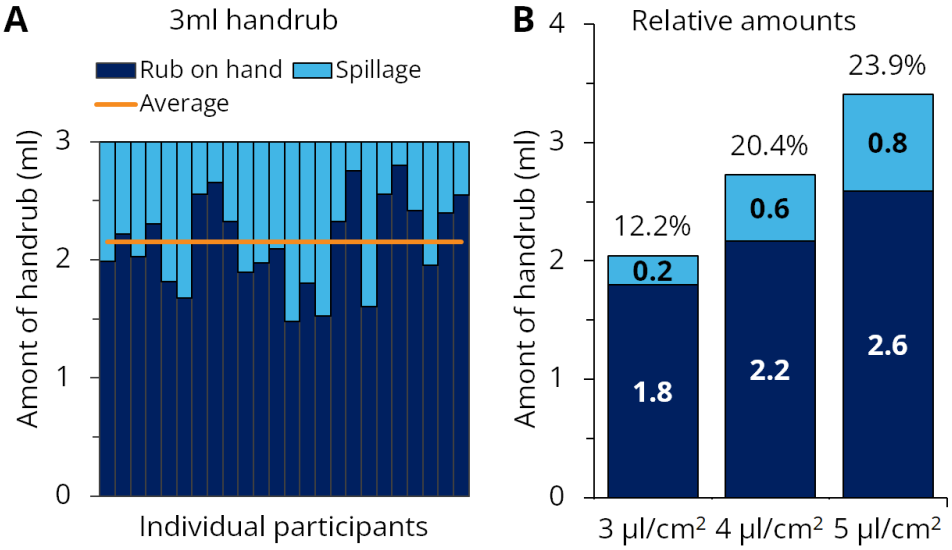

Figure 14. Spillage of handrub during hand hygiene. A) Individual measurements when 3 ml of handrub was provided to participants. B) Average spillage at different relative ABHR amounts [49].

4.5.2.2. Spillage at different relative ABHR amounts

To further analyze spillage and drying times, an additional dataset was collected from twelve participants. Six different relative doses of handrub (ranging from 1 to 6 µl/cm²) were tested. Each measurement was repeated twice to improve reliability. Hand coverage was not assessed in this setting, and no soap-and-water handwashing was performed between Hand rubbing events. Each participant carried out 12 hand hygiene events using only ABHR.

Figure 15A presents the average drying times. Even at doses of only 2 µl/cm², the average drying time exceeded the WHO-recommended 30 seconds. Spillage also increased continuously with higher doses, ranging from 8 % of the total applied volume at 1 µl/cm² to 24 % at 6 µl/cm² (Figure 15B). Note that drying time did not increase linearly with applied dose; instead, a saturation-like effect was observed. This pattern is likely explained by the corresponding spillage, as an increasing proportion of the applied volume was lost through dripping. Consequently, the amount of ABHR remaining on the hands did not increase in linearly with the increased dispensed volumes [49].

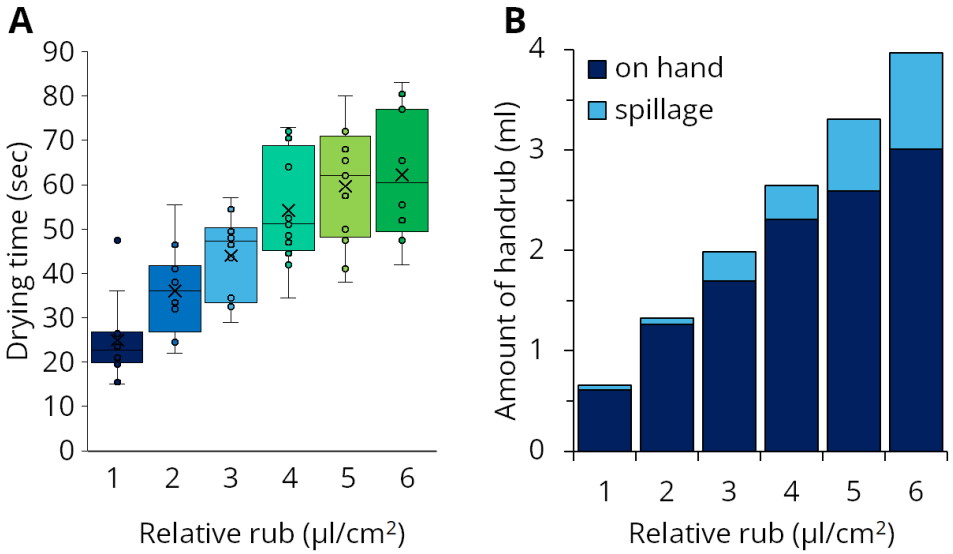

Figure 15. A) Drying times at six different relative amounts of handrub; B) and the corresponding spillage [49].

4.5.2.3. Individual differences in spillage

The dropped amount also varied individually across the different relative volumes. Figure 16 illustrates two representative cases. Participant #16 consistently dropped less than 10 % of the provided handrub at all relative volumes; thus, increasing the applied volume resulted in progressively more handrub remaining on the hands (Figure 16A). In this case, increasing the volume appeared to be a rational choice. In contrast, in the case of Participant #24, spillage increased dramatically (from 3.2 % to 32.8 % at 3 and 5 µl/cm², respectively, Figure 16B). As a result, the actual amount of handrub retained on the hands remained nearly constant: 2.3, 2.6, and 2.7 ml for 3, 4, and 5 µl/cm², respectively. At this

individual, increasing the provided volume offered little benefit, yet generated waste. Individual differences are likely the results of variations in hand hygiene technique [49].

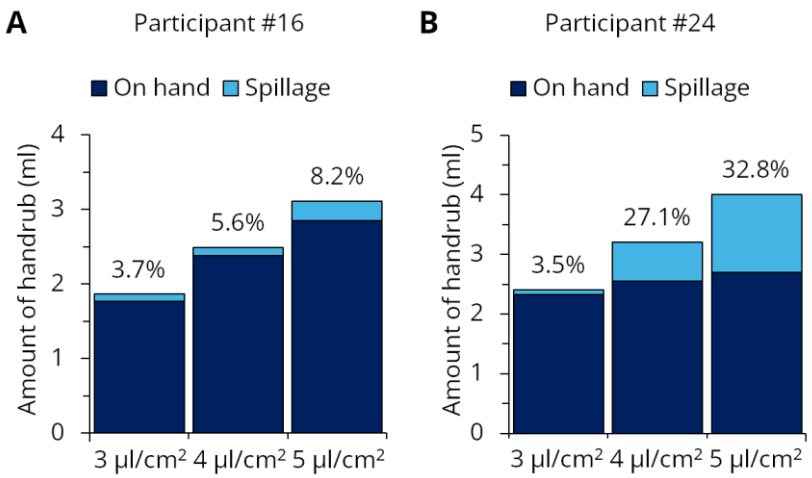

Figure 16. Individual differences in dropped handrub volume at different relative application amounts, highlighting the importance of training [49].

4.5.3. Volume-awareness

By promoting informed hand hygiene behavior, awareness-based approaches support more sustainable improvements in practice and help bridge the gap between formal compliance and actual effectiveness. Hand hygiene awareness fosters an understanding how hand hygiene should be performed, more specifically whether individuals are able to judge the adequate volume of handrub.

Participants were asked how they felt about the applied ABHR volume, whether they considered it sufficient. Participants were not informed about the actual volumes provided. While increases in the applied volumes were generally perceived, the results clearly showed that participants were unable to accurately assess the exact amount (Figure 17). For example, when a relative dose of 4–4.5 µl/cm² was applied (corresponding to approximately 3 ml for an average-sized hand), 27 % of students reported that the volume was insufficient, whereas 26 % felt it was too much. These findings indicate that individuals cannot reliably judge the adequacy of the applied ABHR volumes [2].

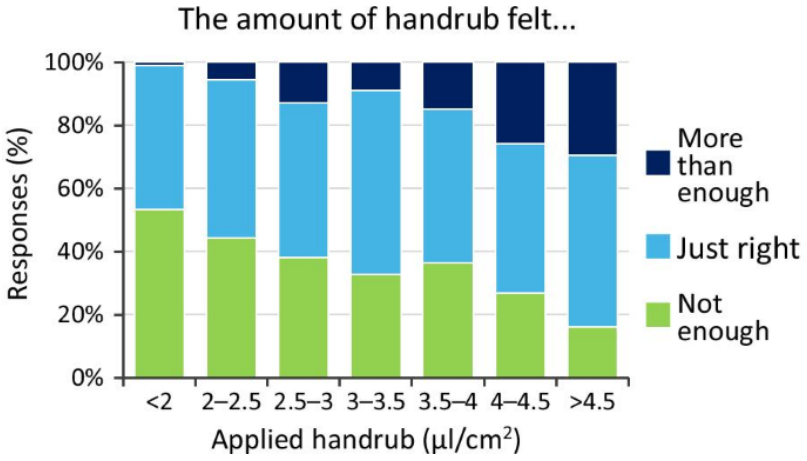

Figure 17. Volume awareness – the ability of the participants to assess the ABHR volume given to them. Note: 3 ml ABHR volumes on an average sized hand resulted in 4.02 µl/cm^2 relative amount [2].

4.6. Gel format handrubs

Some healthcare workers prefer ABHR formulations that easier remain on the hand and less likely drip [32, 52]. Gel format ABHRs are similar in composition to liquid ABHRs but contain a gelling agent (e.g., hydroxy methylcellulose), which increases the viscosity [33]. The following section summarizes how this higher viscosity influences the parameters investigated during hand hygiene.

4.6.1. Gels and coverage

Gel and liquid format ABHRs were compared in a large-scale study [33]. In total, 641 hand hygiene events were recorded and analyzed. Each participant used both gel and liquid ABHRs at absolute volumes of 1.5 and 3 ml, making hand size irrelevant for this comparison. At 1.5 ml, both formats resulted in missed surface areas exceeding 5 %. When the dose was increased to 3 ml, the total missed area decreased to 2.0 % at the gel, and 1.1 % at the liquid ABHRs (Figure 18). Statistical analysis confirmed that the reduction in missed areas between 1.5 ml and 3 ml was significant at both formats ($p < 0.001$). Significant difference was found between the two formats: liquid ABHR consistently outperformed gel ABHR, with smaller average missed areas (5.8 ± 1.0 and 7.0 ± 0.7 at 1.5 ml, and 1.1 ± 0.2 and 2.0 ± 0.4 at 3 ml, respectively). This difference was significant at both the linear mixed-effects model ($p = 0.002$) and the generalized mixed-effects model ($p = 0.004$).

The relative handrub amount was also calculated at the individual level by incorporating hand size. As shown in Figure 19, increasing the relative amount of gel ABHR resulted in an almost linear increase in hand coverage within the investigated volume range. In contrast, liquid ABHR reached a plateau at 3–4 µl/cm². In other words, the plateau occurred at a lower relative amount at liquid ABHR than at gel [33].

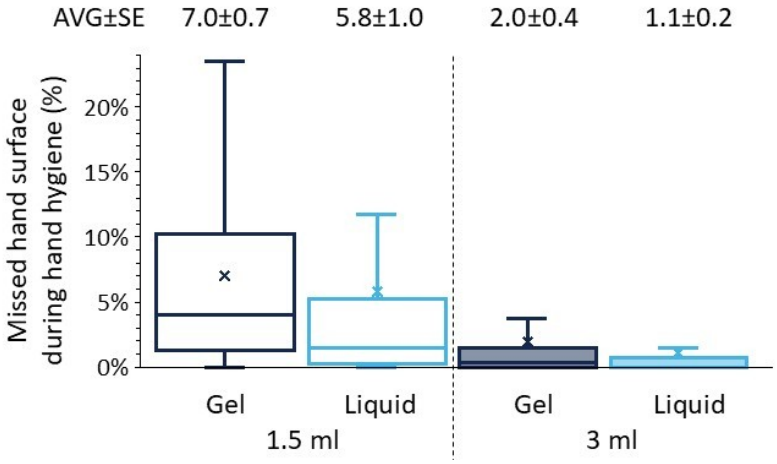

Figure 18. Hand coverage: missed hand surface area with liquid and gel format ABHRs, using 1.5 and 3 ml volumes of each ABHR formats [33].

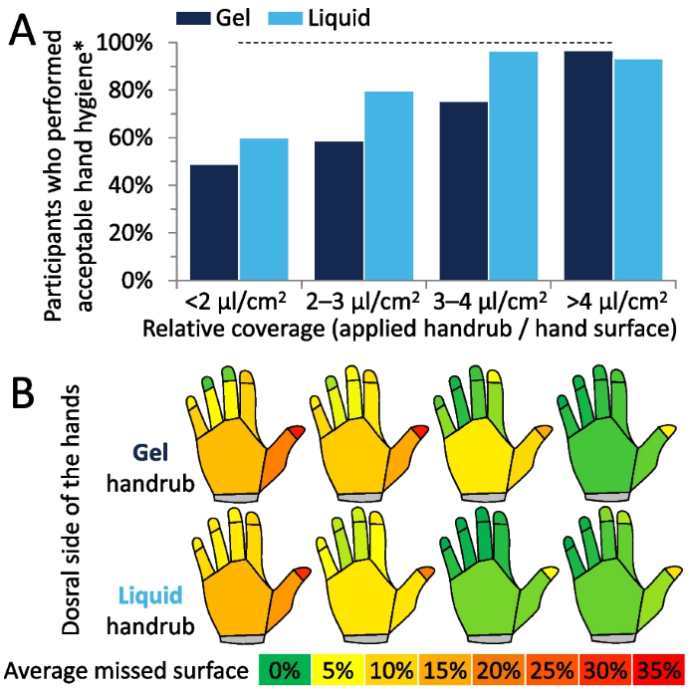

Figure 19. A) Percentage of participants who performed acceptable hand coverage in the case of different relative ABHR amounts (acceptable hand coverage here means that the participants covered at least 95 % of their hands' surfaces). B) Most frequently missed regions on the dorsal side of the hands in case of different relative coverage values [33].

4.6.2. Gels and drying times

When 3 ml of handrub was applied, drying times exceeded the WHO-recommended 20–30 seconds, averaging 40 seconds at gel and 42 seconds at liquid formulations (Figure 20). At 1.5 ml, drying times were close to 30 seconds (30 seconds at gel and 32 seconds at liquid). Statistical analysis showed that both formulation types (gel vs. liquid) and applied volumes (1.5 vs. 3 ml) had significant effects on drying times ($p = 0.007$ and $p < 0.001$, respectively; Marginal R^2/Conditional R^2: 0.157/0.395). Although the difference between the different formats is significant, however, it was small enough to say it has no practical significance in the clinical settings [33]. Considerable inter-individual variability in drying times was also observed, consistent with the patterns described in earlier measurements.

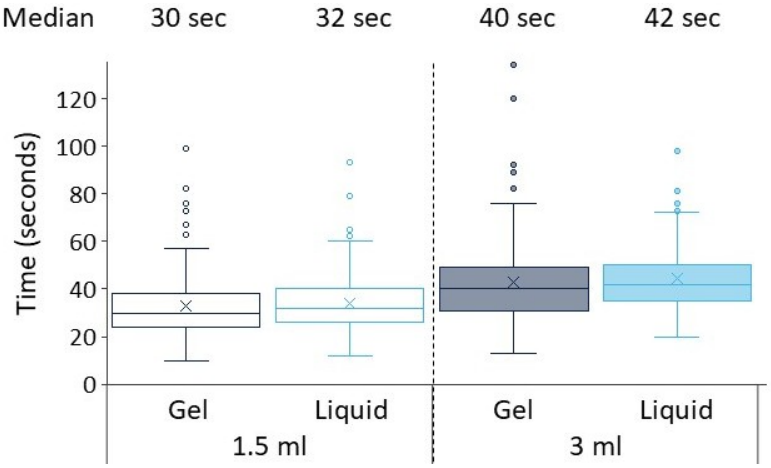

Figure 20. Drying times at gel and liquid format ABHR applications [33].

4.6.3. Gels and spillage

To semi-quantitatively document ABHR spillage, the paper-based method was applied (see Section 3.4.2). A limitation of this method is that an equal volume of gel leaves a smaller fluorescent mark on the paper compared to liquid ABHR. Despite this limitation, the results clearly indicated that increasing the applied volume from 1.5 ml to 3 ml led to greater spillage at both liquid and gel handrubs (Figure 21). A common assumption is that gel ABHRs are better, because in that case there is no spillage. Our findings demonstrate that this is not accurate, spillage does occur with gels and spillage increases with the applied volume. Although it would be valuable to determine the exact spilled volumes for the two formulations, this method is not suitable for such quantification [33].

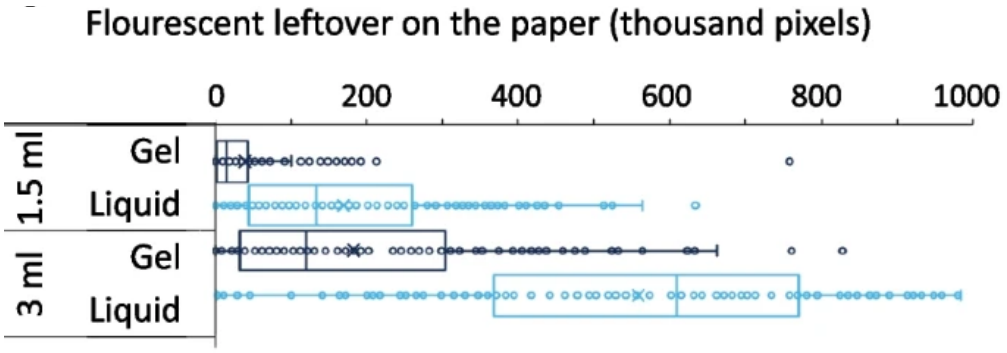

Figure 21. Spillage at different ABHR volumes measured by the semi-quantitative method [33].

4.6.4. Gels and volume awareness

At liquid ABHR, volume awareness was similar to that observed in the previous study. As shown in Figure 22, 60 % of the participants considered 1.5 ml of liquid to be sufficient, compared to 40 % for the same volume of gel. In both cases, participants tended to perceive the same amount of gel as being more than the equivalent amount of liquid. Notably, the responses for 1.5 ml from liquid were comparable to those for 3 ml from gel. Since germicidal capacity depends solely on the applied volume and not on the formulation, the fact that participants' perceptions varied with formats further supports the conclusion that on subjective judgment of ABHR volume's sufficiency cannot be relied upon [33].

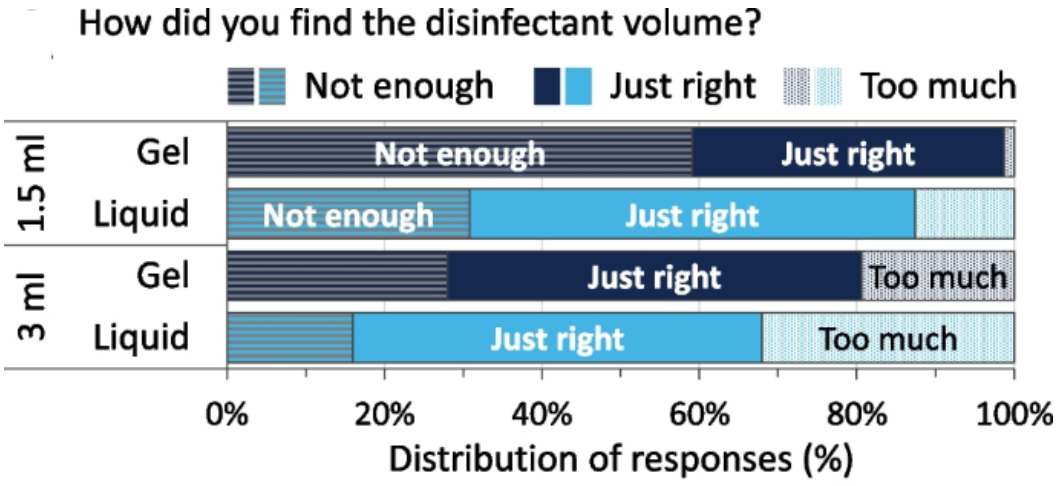

Figure 22. Participants' responses regarding volume awareness [33].

4.7. Foam format handrubs

Foam handrubs are stored as low viscosity liquids in refill containers and then turn into foam during dosing as the liquid ABHR moves through the pump mechanism and air is added. Over time, the foam collapses and reverts to its liquid state, as illustrated in Figure 23. For comparison with other formulations, the volume of foam ABHR is always expressed as the liquid-equivalent volume [47].

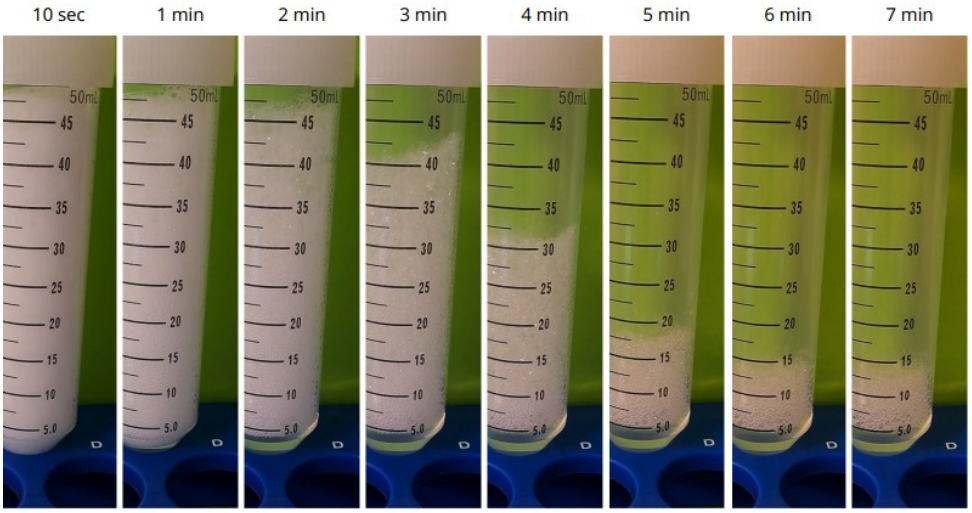

Figure 23. Foam format handrub transforms back to liquid form over time. In this picture, 3 doses were collected in 50 ml centrifuge tubes [47].

4.7.1. Foams and coverage

Our results indicate that hand coverage critically depends on the volume. At 1.5 ml, the average missed hand surface was 5.6 %, 3.1 %, and 2.1 % with liquid, gel, and foam, respectively, while at 3 ml the uncovered surface decreased to 3.1 %, 1.5 %, and 1.0 % (Figure 24A). At 1.5 ml, 36 %, 18 %, and 9 % of participants failed to achieve 95 % coverage when using liquid, gel, and foam, respectively. To put this into perspective, the median hand surface area in this study was 350 cm^2; thus, 5 % uncovered area corresponds to approximately 14 cm^2, roughly the surface area of a thumb. At 3 ml, coverage improved substantially, the failure rates reduced to 13 %, 4 %, and 4 % with liquid, gel, and foam, respectively (Figure 24B). The reduction in missed surface area between 1.5 ml and 3 ml was statistically significant ($p < 0.001$), independently from the format [46].

When comparing the formats, foam performed best overall, while both gel and foam significantly outperformed liquid ($p < 0.001$). Interestingly, this finding contrasts with

results from a previous study [33; see Section 4.6.1], where liquid outperformed gel. The liquid ABHR results were consistent in the two studies; for instance, at 1.5 ml ABHR dose the average missed surface area was 5.8 % [33] compared to 5.6 % [46]. In contrast, gel performance differed in the average missed areas 7.0 % [33] and 3.1 % [46]. We attribute this discrepancy to environmental conditions: the earlier study was conducted in cold temperatures (November), whereas the present study took place in warm conditions (spring and summer). Temperature changes affected not only the room temperature, which varied between 23 °C and 27 °C, but also participants' skin temperatures. Since measurements were carried out immediately after students arrived to the building, their hand skin temperatures were lower during colder outdoor conditions. Gel viscosity is temperature-dependent; as temperature increases, gels become more fluid-like, and easier to distribute. The poorer coverage values observed in the cold can thus be explained by the reduced spreadability of gel under those conditions.

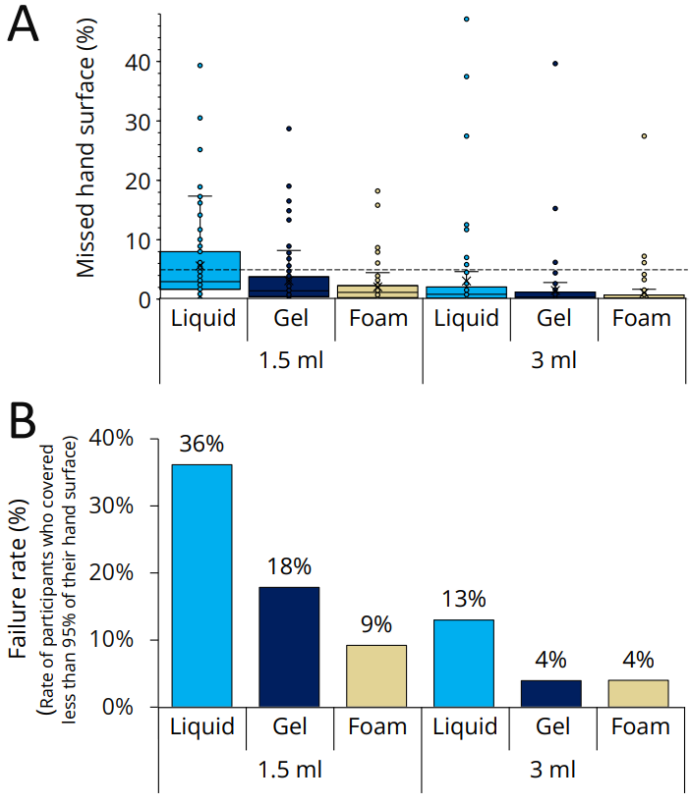

Figure 24. Hand coverage: A) missed hand surface areas with liquid, gel and foam format ABHRs, using 1.5, and 3 ml volumes of each ABHR format, and B) the corresponding failure rates [46].

4.7.2. Foams and drying time

As mentioned earlier, foam pumps have a specific design, typically making it impossible to adjust the dispensed volume. To compare different volumes, three different handrub dispensers were tested, of which participants received either single or double doses [47]. The dispensers were coded as ‘Blue’, ‘Yellow’, and ‘Green’ to maintain anonymity. On average, the ‘Blue’ dispenser provided 0.68 ± 0.11 ml ABHR, while the ‘Yellow’, and ‘Green’ dispensers provided 0.80 ± 0.07 ml, and 1.28 ± 0.08 ml, respectively (in liquid-equivalent volume) (Figure 25A).

Hand coverage by the handrub strongly correlated with the volume applied. When 1 dose of ABHR was applied, the missed hand surface was 10.1 %, 12.1 %, and 1.2 % with the ‘Blue’, ‘Yellow’, and ‘Green’ dispensers, respectively (Figure 25B). Missed areas were reduced to 1.5 %, 3.9 %, and 0.6 %, respectively, when double dose was applied. The difference in coverage between the different dispensers was significant when one dose was applied ($p < 0.01$) but was not significant with two doses. Notably, one dose from the ‘Green’ dispenser provided almost the same volume as two doses from the ‘Blue’ dispenser (1.28 ml, and 1.36 ml), and the missed areas were also similar (1.2 % and 1.5 %). This suggests that the applied volume of handrub is the main factor that determines the quality of hand hygiene by the coverage achieved. In the two cases where less than 1 ml of ABHR were applied, participants missed more than 10 % of their hands. This clearly shows that any volume under 1 ml is not sufficient [47].

There was significant difference in drying times when different dispensers were used, applying both one and two doses ($p < 0.01$ in both cases). Drying time also strongly depended on the applied ABHR volumes (Figure 25C). The single doses from the 'Blue' and 'Yellow' dispensers (dispensed volume <1 ml, >10 % of the hand surface was missed) required 17.3 and 18.1 seconds to dry, which almost complies with the suggested minimum rubbing time of 20 seconds [47].

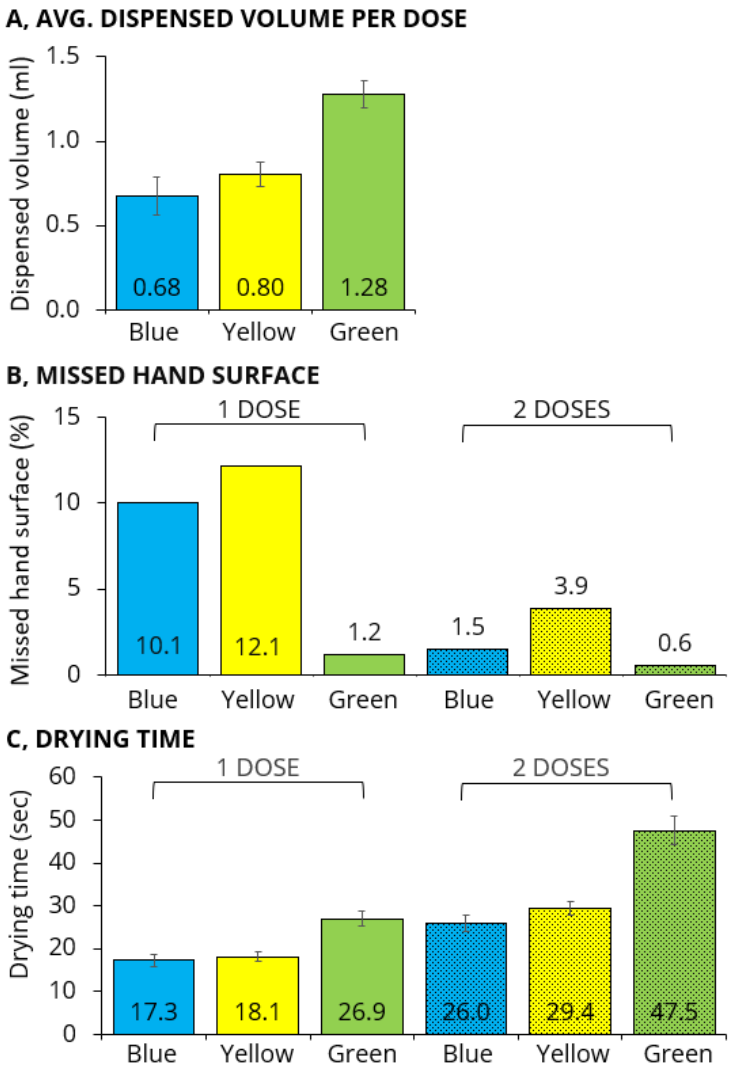

Figure 25. A) Volume dispensed by one dose from each dispenser. B) Average missed hand surfaces when one or two doses were applied. C) Average drying times, as self-reported by the participants [47].

4.7.3. Foams and spillage

Figure 26 shows spillage, measured by the fluorescent spots left after hand hygiene. Note that the same volume of different ABHR formats produces drops of varying sizes, so the fluorescence cannot be directly compared between formats. Spillage was higher for all formats when 3 ml from handrub was used compared to 1.5 ml. Similar to our earlier conclusion regarding gels [33], we can conclude here that spillage occurred with foam ABHR, and that this spillage increased as the provided volume increased [46].

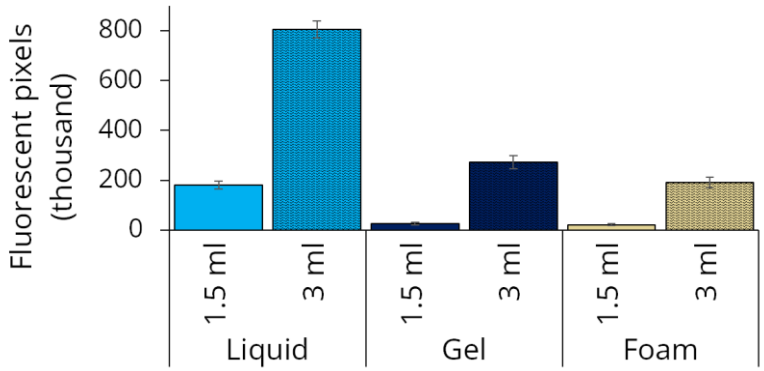

Figure 26. Spillage of different ABHR formats measured by the semi-quantitative method. Based on [46].

4.7.4. Foam and volume awareness

It was mentioned earlier that participants tended to perceive the same amount of gel as being more than the equivalent amount of liquid [33]. In this study, we observed the same pattern, with foam being perceived similarly to gel [46]. Participants felt that the same amount of foam and gel was greater than the liquid format of ABHR (Figure 27).

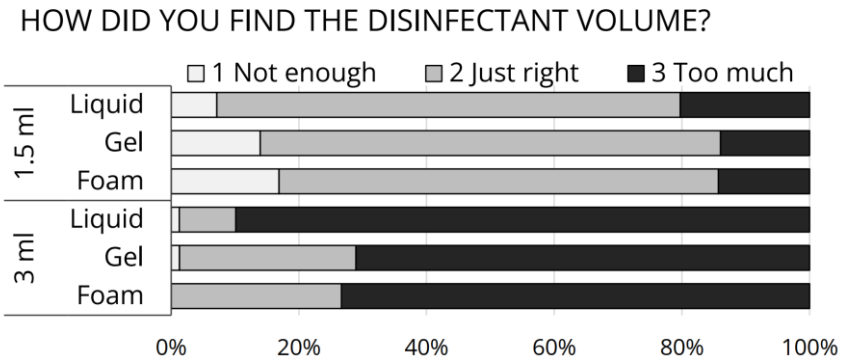

Figure 27. Participants' responses regarding volume awareness [46].

4.8. Other important factors

Our studies identified additional factors that influenced hand hygiene performance, which have been under-studied in the literature.

4.8.1. Skin temperature

The failure rate (the proportion of participants who could not achieve at least 95 % coverage) decreased as participants' hand temperature increased when using liquid

ABHR (Figure 28A). The median hand temperature during the study was 36.2 °C, which divided participants into two equal-sized groups. When liquid ABHR was used and participants' skin temperature was below 36.2 °C, the failure rate was above 34 %. At temperatures above 36.2 °C, the failure rate decreased to approximately 11 %.

In contrast, the opposite trend was observed with gel ABHR: failure rates increased from 9 % to almost 13 % as temperature rose. Foam followed a similar pattern to gel, although the difference was smaller (6 % vs. 7 %, respectively) [46].

Hand temperature also affected drying time, most likely through its impact on the evaporation rate of the handrub (Figure 28B). At higher temperatures, evaporation occurred more quickly, resulting in shorter drying times for all formats. Accordingly, drying times decreased with increasing hand temperature in every format [46].

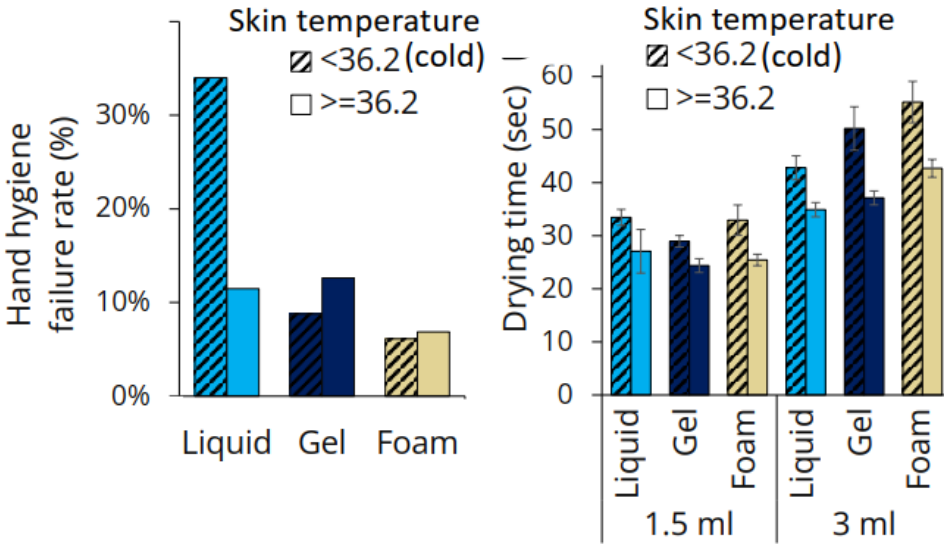

Figure 28. Effect of skin temperature on coverage and drying time [46].

4.8.2. Skin hydration

Hydration had a significant effect on failure rate (coverage) regardless of the formulation (Figure 29). A hydration level above 40 (indicating well-hydrated skin) resulted in better coverage. In the same experiment, skin oil content was also measured, but it showed no significant impact on hand coverage. Hydration did not have a large effect on drying time [46].

Alcohol not only evaporates from the hand surface but is also absorbed [53–54]. We hypothesized that dehydrated hands would absorb more of the handrub. In theory, if the

stratum corneum contains less water, it becomes more permeable [55–57]. This hypothesis was subsequently supported by the hydration measurements [33].

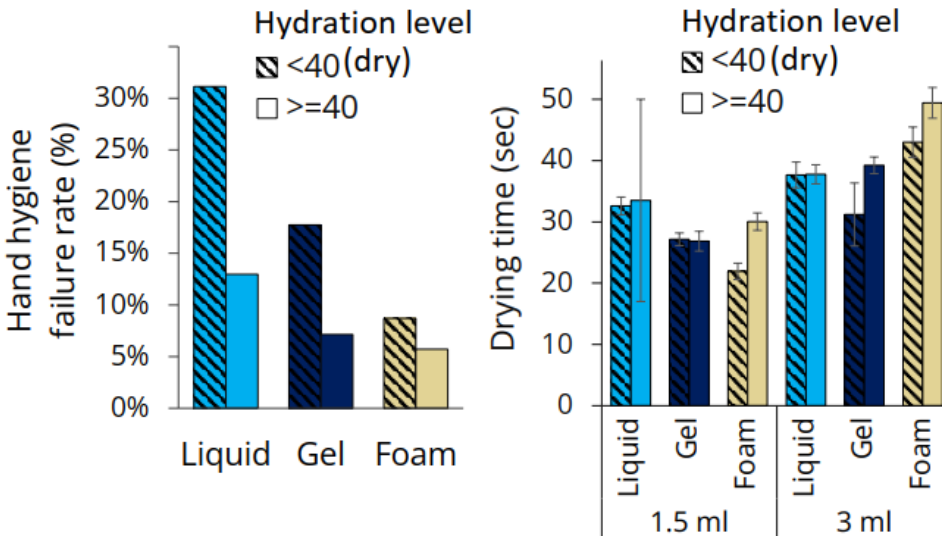

Figure 29. Effect of skin hydration on coverage and drying time [46].

4.8.3. Individual differences in drying time caused by an unknown skin parameter

An interesting observation was made in that study, where different relative amounts of liquid ABHR were applied [49]. The doses were administered in ascending order from 1 to 6 µl/cm², and then in descending order from 6 to 1 µl/cm². Thus, the first and the twelfth measurements were performed with the same 1 µl/cm² relative doses, yet in some cases the drying times differed markedly (Figure 30). Participants also noticed this difference, one of them noted that her skin felt 'full of handrub and could not take more'. Although further research is needed to address this phenomenon, we suspect that the emollient in the handrub altered skin hydration, thereby prolonging drying time. Previous data have also suggested that, in addition to the applied amount, hand size, and spillage, another factor influences drying time. This observation suggests that the missing factor may be skin dryness. Alternatively, the emollient component (e.g., glycerin) may accumulate within the skin and subsequently redissolve upon repeated applications, thereby altering the drying time. Further investigations are required to determine the validity of these hypotheses. Nonetheless, the phenomenon is consistently observed and given the frequency of handrub use in clinical practice, it is highly likely that this effect is also relevant in healthcare settings. According to the WHO guidelines, numerous hand

hygiene events may be required subsequently while performing e.g., aseptic procedures on a patient.

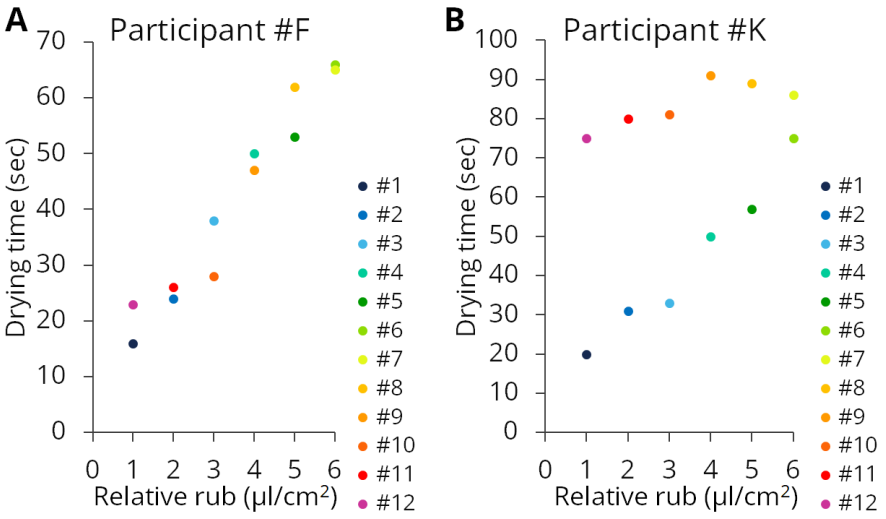

Figure 30. Changes in drying times for two participants. A) For Participant #F, drying time did not change during the experiment, B) for Participant #K, drying time continuously increased. At 1 µl/cm² (applied as both the 1st and 12th doses), drying times were 20 seconds and 75 seconds, respectively [49].

4.9. Microbial validation

The six different relative amounts of liquid handrub were tested *in vitro* using an *E. coli* suspension (Figure 31). Colony counts decreased progressively with increasing handrub amounts; however, the reduction became smaller with each additional 1 µl/cm² of handrub applied.

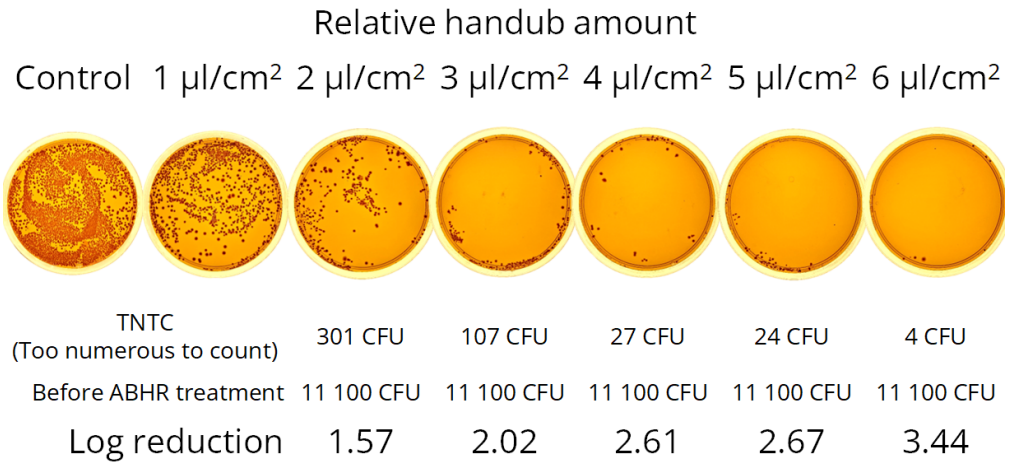

Figure 31. Effect of different amounts of handrub on *E. coli* suspension and the corresponding calculated log reduction factors [49].

5. DISCUSSION

Our results indicated that a volume of 1.5 ml is inadequate, as it left on average 4 % of the total hand surface uncovered by disinfectant [2]. In the same experiment, 3 ml of ABHR resulted in only 1.02 % of the hand surface being missed. In another study, results were similar; 1.5 ml ABHR volume was insufficient of either formulations, as the uncovered areas exceeded 5 % of the total hand surface [33]. In contrast, with 3 ml, the uncovered areas decreased to 2 % with the gel and 1.1 % with the liquid ABHRs.

Volume of 3 ml is a reasonable approximation for medium-sized hands; however, optimizing the volume for each individual seems to be the best approach [36, 49]. Simply increasing the applied volume may not be beneficial, as it can lead to excessive spillage and unnecessary waste of disinfectants, particularly at smaller hands [2].

The areas most frequently missed during hand hygiene (thumbs and fingertips) were consistent across our studies and were independent from the ABHR formats [2, 32, 46]. Several previous studies have also identified thumbs and fingertips as the most commonly missed areas [11, 14, 58, 59].

Providing participants with a volume adjusted to their hand sizes can have three positive effects:

1. it increases coverage for individuals with larger hands,
2. reduces spillage and material waste,
3. and may also improve compliance, as previous reports indicate that healthcare workers prefer shorter rubbing times [32, 33, 60].

There is a major discrepancy in the literature regarding drying time. Even with 1.5 ml volume, application times often exceeded the 20–30 seconds recommended by the WHO Guideline, regardless of formulation. In contrast, 3 ml volume – reported by several studies as the amount required for adequate coverage – showed an average drying time of around 40 seconds [33] (with typical ethanol concentration below 80%). Volumes that dry in under 30 seconds are typically equal to or below 1.5 ml, which generally does not provide complete hand coverage [2]. Similar conclusions have been reported by other studies [61–62].

Further analysis of our results revealed that even when drying time was corrected with hand size, considerable variation remained. This suggests that other intrinsic factors, such as skin temperature and hydration may influence drying time [2].

Completing hand rubbing too quickly with an inadequate ABHR volume can be problematic, as it may give healthcare workers a false sense of safety, leading them to believe they are complying with guidelines [27, 47, 63]. Furthermore, compliance has been reported to decrease with higher applied volumes, as healthcare workers tend to skip hand hygiene to avoid longer application times [32, 60]. Several studies have reported that in clinical settings, mean drying times were less than 15 seconds [26]. One study found that the median drying time on the ward was only 5–12 seconds [64]. Other studies reported drying times of 6–11 seconds [65], 7.6 seconds [66], or 13 seconds [67]. Stahmeyer et al. also estimated that in the case nurses had bene fully compliant, (meaning 100 % hand hygiene compliance and 30 seconds of hand rubbing per occasion) then they would spend 1.5–2 hours per patient day performing hand hygiene.

In routine clinical practice, neither coverage nor microbial reduction is typically assessed, so healthcare workers often estimate the adequacy of handrub volume based on drying time. In the case the drying time reaches around 50 seconds - as was observed on average with 3 ml of handrub – this may create the false impression that too much handrub was used [49].

Surprisingly, evidence-based literature on the practical differences among ABHR formulations remains very limited [33]. Current evidence is insufficient/inconclusive to definitively determine whether one ABHR format is more effective than another [52]. Product preference among users appears to be strongly influenced by familiarity; participants tended to prefer the format they routinely used at work. Those accustomed to foam preferred foams while those accustomed to gels preferred gels [32].

The acceptability of ABHR products is determined not only by their format (liquid, gel, or foam) but also by their formulation (ethanol- or isopropanol-based) and the presence of various additives such as super fatting or relipidizing agents [68].

According to my results, the difference in surface coverage between liquid and gel formulations was significant; however, this finding may be specific to the conditions of our study. Likely due to their higher viscosity, gels tend to spill less, allowing healthcare workers to handle larger applied volumes more effectively, regardless of the hand size. Both extrinsic factors (ambient temperature and humidity) and intrinsic factors (hand temperature, skin type, and hydration level) may also have influenced the results.

Nevertheless, our findings suggest that coverage is primarily determined by the applied ABHR volumes and, to a lesser extent, by the ABHR formats [2, 33].

Volume awareness - how accurately participants could judge whether the applied ABHR volume was sufficient for complete hand coverage - was low during all experimental settings. Participants frequently underestimated the amount needed. Even at a volume of 1.5 ml, 7 % of students reported that the amount felt 'too much.' Furthermore, 25 % of those who believed the applied volume was adequate ('just right') made technical errors during hand hygiene, leaving more than 5 % of their hands' surface uncovered [33].

In conclusion, determining the appropriate ABHR volume is an extremely complex issue. Factors such as format, chemical composition, evaporation rate, hand size, application time, spillage, room temperature, skin temperature, and skin hydration all play important roles [46]. These elements together factors in, and determines whether hand hygiene is successful or not. Since people are generally poor at judging the correct volume, tools or systems that assist in calculating the proper amount of handrub are needed.

5.1. Limitations

The method initially developed to measure spillage was not perfect in quantity estimation. While most of the dropped volume was collected in the bowl and could be measured, in some cases, drops landed on the floor, suggesting that the amount of spillage in this study may be underestimated [49].

A key factor in compliance is formulation preference – with an overwhelming dominance of compatibility (i.e., skin intolerance overrides all other preferences). There are several studies examining the past and current preferences of healthcare workers. This study is also directed towards manufacturers, as in the future, products should better comply with the individualized needs of healthcare workers. Less application time, friendlier composition etc., are factors without a handrub will not be used regardless of its application or antimicrobial efficiency [46].

Defining an exact application volume for a real-life clinical setting is rather complicated. As someone starts rubbing their hand and the disinfectant is being spread, the relative ABHR volume ($\mu l/cm^2$) is not constant. The ratio changes during the hand rubbing process as the handrub is simultaneously being spread and absorbed while also

evaporating. To further complicate the equation, the evaporation rate is influenced by volume, and chemical composition (e.g., alcohol concentration) therefore, this dynamic relationship can only be estimated. *In vitro* environment application time (time required for the disinfectant to take effect and reach the standardized microbial reduction) cannot be identical with the practical *in vivo* application time (contact time) [2].

6. CONCLUSIONS

My research experiments answered the following research questions:

1) What is the primary factor determining hand hygiene performance? Hand hygiene performance is primarily determined by the amount of handrub applied, the volume of ABHR plays a crucial role in the quality of hand hygiene. The proportion of the hand surface covered with ABHR was strongly dependent on the applied volume. When only 1 ml of handrub was used, participants failed to cover an average of 7.1 % of their hands. The commonly recommended 3 ml is a reasonable approximation for medium-sized hands; however, individual hand size should be taken into account. The same absolute volume may feel excessive for individuals with small hands, while it may be just sufficient for persons with larger hands. Therefore, adjusting the dosage to the hand size could improve overall compliance to the protocol. It is recommended to foster adjustable dosing, based on the introduction of relative handrub volume; defined as the applied disinfectant volume divided by the hand surface area.

2) What practical limitations are associated with the application of larger volumes of handrub in routine clinical practice?

Applying large amounts of handrub has practical limitations. A valid argument against using higher volumes of ABHR is the extended drying time required. Drying times for 3 ml volume – regardless of the formulation – were much longer than the recommended times. Unrealistically long drying times may reduce compliance, as healthcare workers might be inclined to skip hand hygiene altogether. Developing faster-drying handrubs that still maintain high antimicrobial efficacy would help address this issue. Moreover, increasing the application volume was not shown always beneficial, as it resulted in significantly greater spillage without improving hand surface coverage.

3) Does the optimal volume of handrub differ between formats (liquid, gel, and foam)?

Results suggest that the optimized volumes may vary for ABHR formats. For gel, and foam formulations, the optimal relative amount could differ from that of liquid ABHR, mainly because of their different spillage characteristics. It should also be noted that for

gel handrubs, temperature plays an important role in consistency: at lower temperatures these can be rubbed in harder, whereas at higher temperatures these become almost fluid. Thus, the optimal dose may vary at winter and summer. For liquid handrubs, this temperature dependency is not relevant.

4) Can a personalized, hand size–dependent handrub volume provide a feasible and effective solution for optimizing hand hygiene performance?

The implementation of a personalized, hand size–based volume can help to achieve the goals of maximizing coverage while minimizing spillage and drying time. Based on the current data, it appears that for liquid handrubs, applying approximately 4 µl/cm² provides sufficient coverage, ensures effective microbial reduction, and reduces spillage, thereby potentially contributes to increased compliance. This is consistent with the current literature, as 3 ml from handrub applied to an average-sized hand corresponds to a relative volume of approximately 4 µl/cm².

The next step in validating this concept would be a large-scale clinical study that also includes different ABHR formats. For this, dispensers capable of providing personalized amounts of handrub would be required. While such technology does not yet exist, all of its components are already available on the market. We have demonstrated that hand size can be easily measured with the current techniques. Hand hygiene compliance monitoring systems are increasingly common in hospitals. These systems typically identify users with RFID cards, and dispensers can already record who is the user to generate compliance statistics. With minor technological innovation, it would be feasible to store individual hand size data on personal RFID cards, enabling ‘smart’ dispensers to deliver personalized doses of handrub.

We strongly believe this represents the future of hand hygiene, and we are happy to share all our data with anyone interested in developing such a system. This approach could reduce costs by minimizing spillage, improve performance by ensuring complete coverage, and enhance compliance by rationalizing drying time.

7. SUMMARY

Hand hygiene is the most effective measure to prevent healthcare-associated infections. Although the use of alcohol-based handrubs has become the global standard, the optimal application volume has not yet been clearly defined. Current guidelines recommend application a “palmful” of product, acknowledging that the required volume varies with hand size. The aim of this work was to estimate the optimal ABHR volume for effective hand hygiene and to identify the factors influencing it.

Our studies demonstrated that ABHR volume plays a crucial role in hand hygiene performance. Using only 1 ml product left approximately 7 % of hand surfaces uncovered, while 3 ml reduced the uncovered area to around 1 %. However, increasing the volume caused excessive spillage and prolonged drying times, often exceeding 40 seconds, which may discourage compliance. Hand size was found to significantly affect both coverage and drying time. Therefore, to determine optimal dose for any individual, I propose using the concept relative ABHR volume, calculated as the applied volume divided by the total hand surface area. For medium-sized hands 3 ml corresponds to approximately 4 µl/cm², which appears to be an optimal balance between efficacy, spillage, and drying time, ultimately supporting better compliance and reducing product waste. Skin temperature, hydration level, and ABHR formats (liquid, gel, or foam) also influenced both coverage and drying time.

Applying personalized, relative ABHR dosages in the clinical practice would undoubtedly be beneficial. This could be achieved through smart dispensers capable of identifying users (e.g., via RFID) and delivering customized volumes. Such technology represents a promising step toward the personalized, data-driven hand hygiene of the future.

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9. BIBLIOGRAPHY OF PUBLICATIONS

Publications related to the thesis:

Bansaghi S, Voniatis C, Heck R, Milassin M, Szijárto A, Haidegger T. (*under submission*) Evidence-Based Hand Hygiene: What is the Optimal Handrub Volume to Apply.

Voniatis C, Bansaghi S, Darbha M, Szerémy P, Szijártó A, Haidegger T. (*under submission*) Evidence-based hand hygiene: Neglected parameters that matter. A Quality Improvement Study.

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