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

Ph.D. thesis
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Introduction

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.

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 2009, the WHO published the Guidelines on Hand Hygiene in Health Care, which remains the most widely followed hand hygiene guideline worldwide. The document provides a description on how to perform hand hygiene, 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. 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.

Large-scale studies measuring actual ABHR usage in clinical settings, the average applied volume ranged from 1 ml to 3.13 ml. The Leapfrog 2022 guidance states that each dispenser activation should deliver at least 1.0 ml product.

1. Objectives

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.

2. Methods

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). Several different foam dispensers were used in our investigations; Cutan Complete Foaming Sanitizer plastic bottle, ES10 (GOJO), Nexa (Ecolab), and Medline (Spectrum) automatic, touch-free dispensers.

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). The system is based on the well-known fluorescent method, and provides immediate, quantitative visual feedback on hand hygiene coverage.

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.

3.4. Disinfectant spillage

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

First, participants were asked whether they noticed any spillage (dripping) of the handrub. 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.

In a further study, semi-quantitative spillage detection was applied. 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. Once the paper dried, it was photographed using a digital camera accessorized with a UV-light. 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.

Finally, we were able to develop a quantitative spillage detection method. 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. 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.

3.5. Hand size determination

A new method, the Automated Area Assessment (AAA) was developed to determine hand size simultaneously with ABHR coverage measurement. This method uses the same Semmelweis System applied to measure handrub coverage. Artificial hand phantom that was fabricated for calibration, a correction factor was calculated, 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.

3.5. Microbial 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.

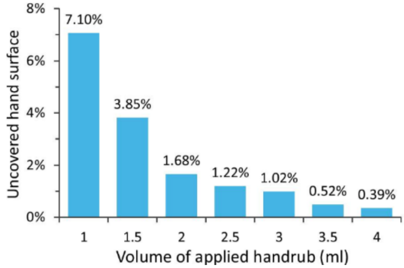
3. Results

4.1 Participants

In my five related publications, the results of 3265 hand hygiene events were summarized. Participants were medical students, surgical residents and laboratory staff members.

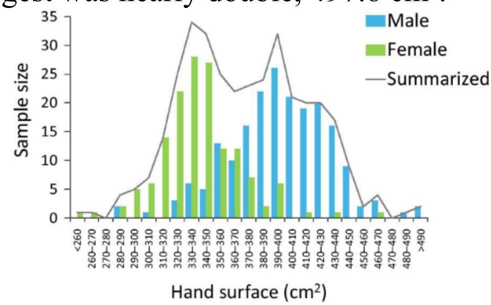
4.2 Effect of ABHR volume on coverage

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.



4.3 Hand size

Digital hand size assessment 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.

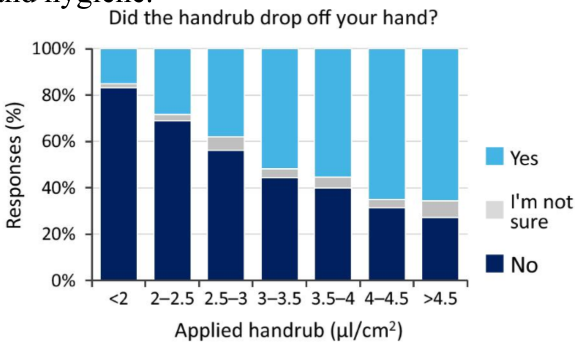


4.4 Relative handrub amount

We introduced the innovative concept of the 'relative handrub amount' to objectively account for individual hand size in hand hygiene. This value is calculated as the applied handrub volume divided by the hand surface area. 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.

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.
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.
In a different settings, 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.
Increasing the ABHR volume may also increase product loss during hand hygiene.



In a follow-up experiment, when 3 ml of ABHR was applied, the mean spillage was 0.84 ± 0.39 ml, corresponding to 28.2 % of the total dose. 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 %.

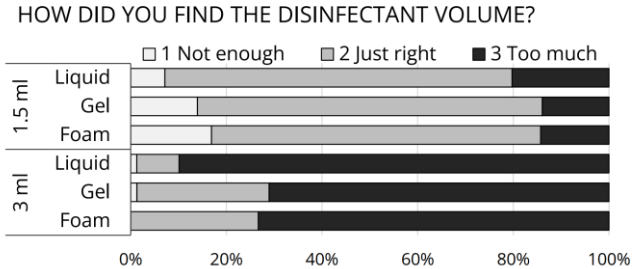
4.6 Gel format handrubs

Gel format ABHRs are similar in composition to liquid ABHRs but contain a gelling agent (e.g., hydroxy methylcellulose), which increases the viscosity.

Gel and liquid format ABHRs were compared in a large-scale study. 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. 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.
A common assumption is that gel ABHRs are better, because in that case there is no spillage. Our 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.

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.
Our results indicate that hand coverage critically depends on the volume. When comparing the formats, foam performed best overall, while both gel and foam significantly outperformed liquid ($p < 0.001$).
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, we can conclude here that spillage occurred with foam ABHR, and that this spillage increased as the provided volume increased.
Participants felt that the same amount of foam and gel was greater than the liquid format of ABHR.



4.8 Other important factors

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

The failure rate decreased as participants' hand temperature increased when using liquid ABHR. 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 %.

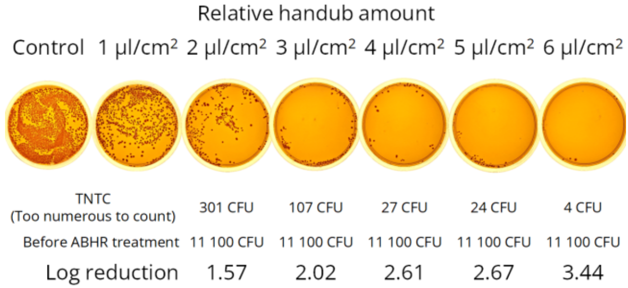
In contrast, the opposite trend was observed with gel ABHR: failure rates increased from 9 % to almost 13 % as temperature rose. Foam followed a similar pattern to gel, although the difference was smaller (6 % vs. 7 %, respectively).

Hand temperature also affected drying time, most likely through its impact on the evaporation rate of the handrub. At higher temperatures, evaporation occurred more quickly, resulting in shorter drying times for all formats.

Hydration had a significant effect on failure rate (coverage) regardless of the formulation; 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.

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.



4. 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 $\mu l/cm^2$ 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 $\mu l/cm^2$.

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.

5. Bibliography of the candidate's publications

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