The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our National Health Library and Knowledge Service Summary of Evidence Protocol.

YOUR QUESTION

What is the efficacy of 60% alcohol-based hand gel vs non-alcohol-based hand gel for both COVID-19 and non-COVID-19 scenarios?

IN A NUTSHELL

ECDC notes that alcohol-based disinfectants have been shown to significantly reduce infectivity of enveloped viruses such as SARS-CoV-2 in concentrations of 70%-80% with one-minute exposure time[2]. CDC recommends that unless hands are visibly soiled, an alcohol-based hand rub is preferred over soap and water in most clinical scenarios due to evidence of better compliance compared to soap and water[3]. Hand rubs are generally less irritating to hands and are effective in the absence of a sink. CDC does not have a recommended alternative to hand rub products with greater than 60% ethanol or 70% isopropanol as active ingredients. Benzalkonium chloride along with both ethanol and isopropanol is deemed eligible by FDA for use in the formulation of hand rubs for use in healthcare settings. However, available evidence indicates that benzalkonium chloride has less reliable activity against certain bacteria and viruses than either of the alcohols.

BMJ Best practice refers to CDC and WHO guidance, and cites the need to wash hands often with soap and water for at least 20 seconds, or with an alcohol-based hand sanitiser that contains at least 60% alcohol[4].

Berardi et al[5] note that disinfectant effectiveness in alcohol-based hand rubs depends on: type of alcohol; concentrations; quantity applied on hands; and time of exposure. Isopropanol, ethanol, n-propanol or combinations of these alcohols are most commonly used in hand rubs. As distinct from other antiseptics, these alcohols do not have the potential for acquired bacterial resistance and none are effective against bacterial spores. When used at the

same concentration, ethanol seems to have a lower bactericidal activity than propanols. However, ethanol has superior viricidal activity than propanols against non-enveloped viruses. Also, skin tolerance is better with ethanol compared to n-propanol or isopropanol. Thus, ethanol is often the alcohol of choice in alcohol-based hand rub preparations. Ethanol concentrations of 60% to 95% (v/v) are deemed safe and effective for disinfection by the United States Food and Drug Administration, CDC and the WHO, including for use against SARS-CoV-2. The choice for formulation rather than the concentration of alcohol is also an important consideration. The authors conclude that despite all of the products on the market ethanol content in alcohol-based hand rubs should be between 60% and 95%[5].

Kratzel et al[14] found that SARS-CoV-2 was efficiently inactivated by WHO-recommended formulations, supporting their use in healthcare systems and viral outbreaks.

The residual effect of hand sanitisers is discussed by Wilson et al[17], concluding that residual antinoroviral hand sanitizers may reduce infection risks for up to 4 hours.

Appelgrein et al[18] studied ozonated water compared with propanol-based hand rubs and found ozone to be inferior to propan-1-ol 60% hand rub for hand asepsis. However, Breideblik et al recommend ozonised water as an alternative that is viable especially for people with skin problems which alcohol-based products may adversely affect[19].

IRISH AND INTERNATIONAL GUIDANCE

What does the World Health Organization say?

Water, sanitation, hygiene, and waste management for SARS-CoV-2, the virus that causes COVID-19. Interim guidance 29 July 2020[1]

Functional hand hygiene facilities should be available for all health-care workers at all points of care, in areas where PPE is put on or taken off, and where health-care waste is handled. In addition, functional hand hygiene facilities should be available for all patients, family members, caregivers and any other visitors, and should be available within 5 metres of the toilets, as well as at the entry/exit of the facility, in waiting and dining rooms and in other public areas. An effective alcohol-based hand rub product should contain between 60% and 80% of alcohol and its efficacy should be proven according to the European Norm 1500 or the standards of the ASTM International known as ASTM E-1174. These products can be purchased on the market, but can also be produced locally in pharmacies using the formula and instructions provided by WHO.

What does the European Centre for Disease Prevention and Control say?

European Centre for Disease Prevention and Control (2020) Disinfection of environments in healthcare and non healthcare settings potentially contaminated with SARS COV-2[2]

There is no specific document providing advice; however, reference is made to the fact that in general, alcohol-based disinfectants [ethanol, propan-2-ol, propan1-ol] have been shown to significantly reduce infectivity of enveloped viruses such as SARS-CoV-2, in concentrations of 70%-80% with one minute exposure time.

What do the Centers for Disease Control and Prevention (United States) say?

CDC (2020) Hand Hygiene Recommendations: Guidance for Healthcare Providers about Hand Hygiene and COVID-19[3]

CDC recommends using alcohol-based hand rubs with 60%-95% alcohol in healthcare settings. Unless hands are visibly soiled, an alcohol-based hand rub is preferred over soap and water in most clinical situations due to evidence of better compliance compared to soap and water. Hand rubs are

generally less irritating to hands and are effective in the absence of a sink. CDC does not have a recommended alternative to hand rub products with greater than 60% ethanol or 70% isopropanol as active ingredients. Benzalkonium chloride along with both ethanol and isopropanol is deemed eligible by FDA external for use in the formulation of healthcare personnel hand rubs. However, available evidence indicates benzalkonium chloride has less reliable activity against certain bacteria and viruses than either of the alcohols.

POINT-OF-CARE TOOLS

What does BMJ Best Practice say?

Coronavirus Disease 2019 (COVID-19). Prevention[4]

BMJ Best practice refers to CDC and WHO guidance. Reference is made of the need to wash hands often with soap and water for at least 20 seconds, or with an alcohol-based hand sanitiser that contains at least 60% alcohol.

INTERNATIONAL LITERATURE

What does the international literature say?

ALCOHOL BASED HAND GELS

BERARDI, A et al (2020) Hand sanitisers amid CoViD-19: A critical review of alcohol-based products on the market and formulation approaches to respond to increasing demand [5]

The world is facing a medical crisis amid the COVID-19 pandemic and the role of adequate hygiene and hand sanitisers is inevitable in controlling the spread of infection in public places and healthcare institutions. There has been a great surge in demand for hand sanitisation products leading to shortages in their supply. A consequent increase of substandard products in the market has raised safety concerns. This article, therefore, presents a critical review of hand sanitation approaches and products available on the market in light of the scientific evidence available to date. This review also provides a range of hand sanitisation product formulations and

manufacturing instructions to allow for extemporaneous preparations at the community and hospital pharmacies during this urgent crisis. In addition, this emergent situation is expected to continue; hence hand sanitisers will be in demand for an extended time, and the availability and purchase of substandard products on the market create an ongoing safety concern. Therefore, this article also provides various commercial organisations interested in stepping forward the production and marketing of hand sanitisers with a guide on the development of products of standardised ingredients and formulations.
Disinfectant effectiveness in alcohol-based hand rubs depends on 1 type of alcohol; 2 concentrations; 3 quantity applied on hands; 4 time of exposure. Isopropanol, ethanol, n-propanol, or combinations of these alcohols are most commonly used in hand rubs. As distinct from other antiseptics, these alcohols do not have the potential for acquired bacterial resistance. None of these alcohols is effective against bacterial spores. When used at the same concentration, ethanol seems to have a lower bactericidal activity than propanols. However, ethanol has superior viricidal activity than propanols against non-enveloped viruses. Also, skin tolerance is better with ethanol compared to n-propanol or isopropanol; thus ethanol is often the alcohol of choice in the ABHR preparations.
Ethanol concentrations of 60% to 95% (v/v) are deemed safe and effective for disinfection by the United States Food and Drug Administration (US FDA), CDC and the WHO, including for use against SARS-CoV-2. Interestingly, Edmonds et al suggested that the antimicrobial activity of the ABHRs is highly dependent on the choice of formulation rather than on the concentration of alcohol. They also suggested that the liquid, gel and foam-based products can all be equally effective if the ethanol content used was within the 60%–95% standard range. However, increasing ethanolic concentrations of hand rubs from 80% to 85% can reduce the contact time necessary to achieve an efficient bactericidal activity. Despite this, the WHO, US FDA and CDC still maintain their recommendations of 60%–95% ethanol content in ABHRs.

DESHPANDE, A et al (2018) Comparative antimicrobial efficacy of two hand-hygiene products in intensive care units: a randomized controlled trial[6]

OBJECTIVE Contaminated hands of healthcare workers (HCWs) are an important source of transmission of healthcare-associated infections. Alcohol-based hand sanitizers, while effective, do not provide sustained

antimicrobial activity. The objective of this study was to compare the immediate and persistent activity of 2 hand hygiene products (ethanol [61% w/v] plus chlorhexidine gluconate [CHG; 1.0% solution] and ethanol only [70% v/v]) when used in an intensive care unit (ICU). DESIGN Prospective, randomized, double-blinded, crossover study SETTING Three ICUs at a large teaching hospital PARTICIPANTS In total, 51 HCWs involved in direct patient care were enrolled in and completed the study. METHODS All HCWs were randomized 1:1 to either product. Hand prints were obtained immediately after the product was applied and again after spending 4-7 minutes in the ICU common areas prior to entering a patient room or leaving the area. The numbers of aerobic colony-forming units (CFU) were compared for the 2 groups after log transformation. Each participant tested the alternative product after a 3-day washout period. RESULTS On bare hands, use of ethanol plus CHG was associated with significantly lower recovery of aerobic CFU, both immediately after use (0.27 ± 0.05 and 0.88 ± 0.08 log10 CFU; P = .035) and after spending time in ICU common areas (1.81 ± 0.07 and 2.17 ± 0.05 log10 CFU; P<.0001). Both the antiseptics were well tolerated by HCWs. CONCLUSIONS In comparison to the ethanol-only product, the ethanol plus CHG sanitizer was associated with significantly lower aerobic bacterial counts on hands of HCWs, both immediately after use and after spending time in ICU common areas.

DEV KUMAR, G et al (2020) Biocides and Novel Antimicrobial Agents for the Mitigation of Coronaviruses[7]

The aim of this review is to provide information, primarily to the food industry, regarding a range of biocides effective in eliminating or reducing the presence of coronaviruses from fomites, skin, oral/nasal mucosa, air, and food contact surfaces. As several EPA approved sanitizers against SARS-CoV-2 are commonly used by food processors, these compounds are primarily discussed as much of the industry already has them on site and is familiar with their application and use. Specifically, we focused on the effects of alcohols, povidone iodine, quaternary ammonium compounds, hydrogen peroxide, sodium hypochlorite (NaOCl), peroxyacetic acid (PAA), chlorine dioxide, ozone, ultraviolet light, metals, and plant-based antimicrobials. This review highlights the differences in the resistance or susceptibility of different strains of coronaviruses, or similar viruses, to these antimicrobial agents.

GOLD, NA et al (2020) Alcohol Sanitizer[8]

Maintaining hand hygiene has been established as crucial for reducing the colonization and incidence of infectious diseases in all populations. Compliance with hand hygiene recommendations is believed to play a significant role in decreasing the risk of gastroenteric and respiratory infections. Strict hand hygiene is even more important for health-care workers (HCW) as unclean hands may aid in the transmission of microorganisms from patient to patient, leading to increased morbidity, mortality and costs associated with healthcare-associated infections (HCAIs). In 2002, HCAIs were a cause of 99,000 deaths in the United States of America, and the 2004 annual economic impact of HCAIs was estimated to be US$6.5 billion. Evidence suggests that hand sanitization significantly reduces the transmission of healthcare-associated pathogens and the incidence of HCAIs. Despite the emphasis on the importance of hand hygiene, recent studies show poor hand hygiene compliance in medical settings. According to the Center for Disease Control and Prevention (CDC), hand hygiene encompasses the cleansing of your hands using soap and water, antiseptic hand washes, alcohol-based hand sanitizers (ABHS), or surgical hand antiseptics. These days, alcohol-based hand sanitizers are increasingly being used instead of soap and water for hand hygiene in healthcare settings. Their ease of use, increased availability and proven effectiveness are some of the reasons why alcohol-based hand sanitizers are gaining popularity. In one study, a hospital-wide hand hygiene campaign with special emphasis on bedside alcohol-based hand disinfection resulted in sustained improvement in hand-hygiene compliance, coinciding with a reduction of nosocomial infections and MRSA transmission. A systematic review also demonstrated with moderate certainty that having bedside alcohol-based solutions increased compliance with hand hygiene among HCWs. It is, however, important to keep in mind that the efficacy of alcohol hand sanitizers is dependent upon the type of alcohol, the quantity applied, the technique used and the consistency of use. There are also situations where these products are not ideal, for example, in preventing the spread of certain alcohol-resistant infections or when hands are significantly soiled and the bacterial load is too high.

The World Health Organization defines an alcohol-based hand rub as "an alcohol-containing preparation (liquid, gel or foam) designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Such preparations may contain one or more types of alcohol, other active ingredients with excipients, and humectants." Alcohol-based hand

antiseptics mostly contain isopropanol, ethanol, n-propanol, or a mixture of these as their active ingredients. The antimicrobial activity of alcohols is attributed to their ability to denature and coagulate proteins. This causes microbes to lose their protective coatings and become non-functional. The Center for Disease Control and Prevention recommends formulations containing 80% [percent volume/volume] ethanol or 75% isopropyl alcohol; however, generally speaking, sanitizers containing 60% to 95% alcohol are acceptable. The recommended percentages of ethanol and isopropyl alcohol are kept as 80% and 75% because these values lie in the middle of the acceptable range. Notably, higher than recommended concentrations are also paradoxically less potent because proteins are not denatured easily without the presence of water. Alcohol concentrations in antiseptic hand rubs are often expressed as percent by volume and rarely as percent by weight. A study conducted on 85% [weight/weight] ethanol, showed that a 15 seconds contact time was enough to reduce gram-positive and negative bacteria by greater than 5 log10 steps. Research suggests that alcohols are swiftly germicidal when applied to skin, but have no noticeable persistent residual activity. However, it has been documented that the regrowth of bacteria does occur slowly after its use. This may be because of the sublethal effect alcohol may have had on the residual bacteria. Adding chlorhexidine, octenidine, or triclosan to alcohol-based hand rubs may result in somewhat persistent protection as well. 4% chlorhexidine has shown persistent bactericidal activity against methicillin-resistant Staphylococcus aureus for up to 4 hours from application. Ethanol, the most common alcohol ingredient, appears to be the most effective alcohol against viruses; whereas, propanol is considered to be a better bactericidal alcohol. The combination of alcohols may also have a synergistic effect. The concentration of alcohol in hand sanitizers also changes its efficacy, with one study demonstrating that a hand rub with 85% ethanol content was significantly better at reducing bacterial populations compared to preparations of 60% to 62% ethanol. ABHS also often contain humectants, such as glycerin, which help prevent skin dryness, and emollients or moisturizers, such as aloe vera, which help replace some of the water that is stripped off during use. None of the above-mentioned alcohols have shown a potential for acquired bacterial resistance, and are therefore considered highly effective for repeated use in medical settings.

GOLIN, AP et al (2020) Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses[9]

Background: The emergence of the novel virus, SARS-CoV-2, has posed unprecedented challenges to public health around the world. Currently, strategies to deal with COVID-19 are purely supportive and preventative, aimed at reducing transmission. An effective and simple method for reducing transmission of infections in public or healthcare settings is hand hygiene. Unfortunately, little is known regarding the efficacy of hand sanitizers against SARS-CoV-2.
Methods: In this review, an extensive literature search was performed to succinctly summarize the primary active ingredients and mechanisms of action of hand sanitizers, compare the effectiveness and compliance of gel and foam sanitizers, and predict whether alcohol and non-alcohol hand sanitizers would be effective against SARS-CoV-2.
Results: Most alcohol-based hand sanitizers are effective at inactivating enveloped viruses, including coronaviruses. With what is currently known in the literature, one may not confidently suggest one mode of hand sanitizing delivery over the other. When hand washing with soap and water is unavailable, a sufficient volume of sanitizer is necessary to ensure complete hand coverage, and compliance is critical for appropriate hand hygiene.
Conclusions: By extrapolating effectiveness of hand sanitizers on viruses of similar structure to SARS-CoV-2, this virus should be effectively inactivated with current hand hygiene products, though future research should attempt to determine this directly.

IONIDIS, G et al (2016) Development and virucidal activity of a novel alcohol-based hand disinfectant supplemented with urea and citric acid[10]

Background: Hand disinfectants are important for the prevention of virus transmission in the health care system and environment. The development of broad antiviral spectrum hand disinfectants with activity against enveloped and non-enveloped viruses is limited due to a small number of permissible active ingredients able to inactivate viruses.
Methods: A new hand disinfectant was developed based upon 69.39% w/w ethanol and 3.69% w/w 2-propanol. Different amounts of citric acid and urea were added in order to create a virucidal claim against poliovirus (PV), adenovirus type 5 (AdV) and polyomavirus SV40 (SV40) as non-enveloped test viruses in the presence of fetal calf serum (FCS) as soil load. The exposure time was fixed to 60 s.

Results: With the addition of 2.0% citric acid and 2.0% urea an activity against the three test viruses was achieved demonstrating a four log10 reduction of viral titers. Furthermore, this formulation was able to inactivate PV, AdV, SV40 and murine norovirus (MNV) in quantitative suspension assays according to German and European Guidelines within 60 s creating a virucidal claim. For inactivation of vaccinia virus and bovine viral diarrhea virus 15 s exposure time were needed to demonstrate a 4 log10 reduction resulting in a claim against enveloped viruses. Additionally, it is the first hand disinfectant passing a carrier test with AdV and MNV.
Conclusions: This new formulation with a low alcohol content, citric acid and urea is capable of inactivating all enveloped and non-enveloped viruses as indicated in current guidelines and thereby contributing as valuable addition to the hand disinfection portfolio.

IWASAWA, A et al (2012) Virucidal activity of alcohol-based hand rub disinfectants[11]

We investigated the virucidal activity of commercially available alcohol-based hand rub products against coxsackievirus A7, B5, feline calicivirus F9, and human adenovirus type 3, type 7, type 8 using susceptible cell lines, Vero cells, CRFK cells, and A549 cells. Fifteen tested hand rub products were ethanol (EtOH) for disinfection, two EtOH-based products, one povidone iode-containing product, one alkyldiaminoethylglycine hydrochloride-containing product, six benzalkonium chloride (BAK)-containing products, and four chlorohexidine gluconate (CHG)-containing products. Some active ingredients [BAK, benzetonium chloride, and CHG] were diluted with EtOH to make 0.5% and 0.2% solutions. Virus inactivation rates were calculated after contact with each hand rub product for 10 or 60 seconds. Of the hand rub products tested, only the povidone iode-based product showed antiviral activity superior to that of EtOH against all the strains. EtOH solutions of active ingredients (0.2% and 0.5%) also showed decreased antiviral activity. In conclusion, antiviral activity of all the commercially available alcohol-based hand rub products except that containing povidone idode was dependent on their active ingredients. The povidone idode-containing hand rub product kept its effectiveness even after the dilution with EtOH. Although alcohol-based hand rub products are convenient and suitable for the control of some microbes, they are not generally recommended for the control of viral infections.

JING, JLJ et al (2020) Hand Sanitizers: A Review on Formulation Aspects, Adverse Effects, and Regulations[12]

Hand hygiene is of utmost importance as it may be contaminated easily from direct contact with airborne microorganism droplets from coughs and sneezes. Particularly in situations such as pandemic outbreak, it is crucial to interrupt the transmission chain of the virus by the practice of proper hand sanitization. It can be achieved with contact isolation and strict infection control tool like maintaining good hand hygiene in hospital settings and in public. The success of the hand sanitization solely depends on the use of effective hand disinfecting agents formulated in various types and forms such as antimicrobial soaps, water-based or alcohol-based hand sanitizer, with the latter being widely used in hospital settings. To date, most of the effective hand sanitizer products are alcohol-based formulations containing 62%-95% of alcohol as it can denature the proteins of microbes and the ability to inactivate viruses. This systematic review correlated with the data available in PubMed, and it will investigate the range of available hand sanitizers and their effectiveness as well as the formulation aspects, adverse effects, and recommendations to enhance the formulation efficiency and safety. Further, this article highlights the efficacy of alcohol-based hand sanitizer against the coronavirus.

Kampf, G et al (2018) Efficacy of ethanol against viruses in hand disinfection[13]

Ethanol is used worldwide in healthcare facilities for hand rubbing. It has been reported to have a stronger and broader virucidal activity compared with propanols. The aim of this review was to describe the spectrum of virucidal activity of ethanol in solution or as commercially available products. A systematic search was conducted. Studies were selected when they contained original data on reduction of viral infectivity from suspension tests (49 studies) and contaminated hands (17 studies). Ethanol at 80% was highly effective against all 21 tested, enveloped viruses within 30 s. Murine norovirus and adenovirus type 5 are usually inactivated by ethanol between 70% and 90% in 30 s whereas poliovirus type 1 was often found to be too resistant except for ethanol at 95%. Ethanol at 80% is unlikely to be sufficiently effective against poliovirus, calicivirus (FCV), polyomavirus, hepatitis A virus (HAV) and foot-and-mouth disease virus (FMDV). The spectrum of virucidal activity of ethanol at 95%, however, covers the majority of clinically relevant viruses. Additional acids can substantially improve the virucidal activity of ethanol at lower concentrations against eg

poliovirus, FCV, polyomavirus and FMDV although selected viruses such as HAV may still be too resistant. The selection of a suitable virucidal hand rub should be based on the viruses most prevalent in a unit and on the user acceptability of the product under frequent-use conditions.

KRATZEL, A et al (2020) Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols[14]

We found that SARS-CoV-2 was efficiently inactivated by WHO-recommended formulations, supporting their use in healthcare systems and viral outbreaks. Of note, both the original and modified formulations were able to reduce viral titers to background level within 30 s. In addition, ethanol and 2-propanol were efficient in inactivating the virus in 30 s at a concentration of >30% [vol/vol]. Alcohol constitutes the basis for many hand rubs routinely used in healthcare settings. One caveat of this study is the defined inactivation time of exactly 30 s, which is the time recommended but not routinely performed in practice. Our findings are crucial to minimize viral transmission and maximize virus inactivation in the current SARS-CoV-2 outbreak.

PRADHAN, D et al (2020) A Review of Current Interventions for COVID-19 Prevention[15]

COVID-19 infection is a pandemic, surface to surface communicable disease with a case fatality rate of 3.4% as estimated by WHO up to March 3, 2020. Unfortunately, the current unavailability of an effective antiviral drug and approved vaccine make the situation more critical. Implementation of an effective preventive measure is the only option left to counteract CoVID-19. Further, a retrospective analysis provides evidence that contemplates the decisive role of preventive measures in controlling severe acute respiratory syndrome (SARS) outbreak in 2003. A statistical surveillance report of WHO showed that maintaining coherent infection, prevention and control guidelines resulted in a 30% reduction in healthcare-associated infections. The effectiveness of preventive measures completely relies on the strength of surface disinfectants, the composition of hand sanitizer, and [availability of] adequate resources for the manufacture of personal protective equipment (PPE). This review considers various preventive measures such as selection of surface disinfectants, appropriate hand sanitization, and PPE as a potential intervention to fight against COVID-19.

SUCHOMEL, M et al (2020) Evaluation of World Health Organization-Recommended Hand Hygiene Formulations[16]

As a result of the coronavirus disease pandemic, commercial hand hygiene products have become scarce and World Health Organization (WHO) alcohol-based hand rub formulations containing ethanol or isopropanol are being produced for hospitals worldwide. Neither WHO formulation meets European Norm 12791, the basis for approval as a surgical hand preparation, nor satisfies European Norm 1500, the basis for approval as a hygienic hand rub. We evaluated the efficacy of modified formulations with alcohol concentrations in mass instead of volume percentage and glycerol concentrations of 0.5% instead of 1.45%. Both modified formulations met standard requirements for a 3-minute surgical hand preparation, the usual duration of surgical hand treatment in most hospitals in Europe. Contrary to the originally proposed WHO hand rub formulations, both modified formulations are appropriate for surgical hand preparation after 3 minutes when alcohol concentrations of 80% wt/wt ethanol or 75% wt/wt isopropanol along with reduced glycerol concentration (0.5%) are used.

WILSON, AM et al (2020) Comparison of estimated norovirus infection risk reductions for a single fomite contact scenario with residual and nonresidual hand sanitizers[17]

Background: The purpose of this study was to relate experimentally measured log10 human norovirus reductions for a nonresidual [60% ethanol] and a residual hand sanitizer to infection risk reductions.
Methods: Human norovirus log10 reductions on hands for both sanitizers were experimentally measured using the ASTM International Standard E1838-10 method, with modification. Scenarios included product application to: 1. inoculated fingerpads with 30- and 60-second contact times; and 2. hands followed by inoculation with human norovirus immediately and 4 hours later. Hand sanitizer efficacies were used in a mathematical model estimating norovirus infection risk from a single hand-to-fomite contact under low and high environmental contamination conditions.
Results: The largest log10 reductions for the residual and nonresidual hand sanitizers were for a 60-second contact time, reducing infection risk by approximately 99% and 85%, respectively. Four hours after application, the residual hand sanitizer reduced infection risks by 78.5% under high contamination conditions, whereas the nonresidual hand sanitizer offered no reduction.

Discussion: Log10 virus and infection risk reductions were consistently greater for the residual hand sanitizer under all scenarios. Further data describing residual hand sanitizer efficacy with additional contamination or tactile events are needed.
Conclusions: Residual antinoroviral hand sanitizers may reduce infection risks for up to 4 hours.

NON-ALCOHOL BASED HAND GELS

APPELGREIN, C et al (2016) Ozonated water is inferior to propanol-based hand rubs for disinfecting hands[18]

Ozone is a strong oxidizing biocide that has broad-spectrum antimicrobial properties. The aim of the study was to compare the efficacy of ozone to a propanol-based hand rub for hand disinfection. Twenty subjects were enrolled in an in-vivo cross-over trial. The investigation indicated that ozone is inferior to propan-1-ol 60% hand rub for hand asepsis.

BREIDEBLIK, HJ et al (2019) Ozonized water as an alternative to alcohol-based hand disinfection[19]

Background: Hand hygiene plays a vital role in the prevention of transmission of micro-organisms. Ozone (03) is a highly reactive gas with a broad spectrum of antimicrobial effects on bacteria, viruses, and protozoa. It can easily be produced locally in small generators, and dissolved in tap water, and quickly transmits into ordinary 02 in the surrounding air. Aim: To compare ozonized tap water and alcohol rub in decontamination of bacterially contaminated hands. Methods: A cross-over study among 30 nursing students. Hands were artificially contaminated with Escherichia coli (ATCC 25922), then sanitized with ozonized tap water (0.8 or 4 ppm) or 3 mL standard alcohol- based rub (Antibac 85%). The transient microbes from fingers were cultivated and colony-forming units (cfu)/mL were counted. The test procedure was modified from European Standard EN 1500:2013.
Findings: All contaminated hands before disinfection showed cfu >30,000/mL. The mean (SD) bacterial counts in (cfu/mL) on both hands combined were 1017 (1391) after using ozonized water, and 2337 (4664) after alcohol hand disinfection. The median (range) values were 500 (0–6700) and 250 (0–16,000) respectively (non- significant difference). Twenty per cent of participants reported adverse skin effects (burning/dryness) from alcohol disinfection compared with no adverse sensations with ozone. Conclusion:

Ozonized tap water is an effective decontaminant of E. coli, and it could be an alternative to traditional alcohol- fluid hand disinfectants both in healthcare institutions and public places. Ozonized water may be especially valuable for individuals with skin problems.

BONDURANT, S W et al (2019) Demonstrating the persistent antibacterial efficacy of a hand sanitizer containing benzalkonium chloride on human skin at 1, 2, and 4 hours after application[20]

Background: Use of hand sanitizers has become a cornerstone in clinical practice for the prevention of disease transmission between practitioners and patients. Traditionally, these preparations have relied on ethanol (60%-70%) for bactericidal action.
Methods: This study was conducted to measure the persistence of antibacterial activity of 2 preparations. One was a non-alcohol-based formulation using benzalkonium chloride (BK) (0.12%) and the other was an ethanol-based formulation (63%) (comparator product). The persistence of antibacterial activity was measured against Staphylococcus aureus using a technique modification prescribed in American Society for Testing and Materials protocol E2752-10 at up to 4 hours after application.
Results: The test product (BK) produced a marked reduction in colony-forming units at each of the 3 time points tested (3.75-4.16-log10 reductions), whereas the comparator produced less than 1-log10 reduction over the same time. The differences were highly significant.
Discussion: In the course of patient care or examination, there are instances where opportunities exist for the practitioner's hands to become contaminated: eg keyboards and tables. Persistent antibacterial activity would reduce the chances of transfer to the patient.
Conclusions: These results show a major improvement in persistent antibacterial activity for the BK formulation compared to the comparator ethanol-based formulation.

HSU, S (2015) Compounds Derived from Epigallocatechin-3-Gallate (EGCG) as a Novel Approach to the Prevention of Viral Infections[21]

Pathogenic viral infections pose major health risks to humans and livestock due to viral infection-associated illnesses such as chronic or acute inflammation in crucial organs and systems, malignant and benign lesions. These lead to large number of illnesses and deaths worldwide each year. Outbreaks of emerging lethal viruses, such as Ebola virus, severe acute respiratory syndrome (SARS) virus and Middle East respiratory syndrome

(MERS) virus, could lead to epidemics or even pandemics if they are not effectively controlled. Current strategies to prevent viral entry into the human body are focused on cleansing the surface of the skin that covers hands and fingers. Surface protection and disinfection against microorganisms, including viruses, is performed by sanitization of the skin surface through hand washing with soap and water, surface disinfectants, and hand sanitizers, particularly alcohol-based hand sanitizers. However, concerns about the overall ineffectiveness, toxicity of certain ingredients of disinfectants, pollution of the environment, and the short duration of antimicrobial activity of alcohol have not been addressed, and the epidemiology of certain major viral infections are not correlated inversely with the current measures of viral prevention. In addition to a short duration on the skin surface, alcohol is ineffective against certain viruses such as norovirus, rabies virus, and polio virus. There is a need for a novel approach to protect humans and livestock from infections of pathogenic viruses that is broadly effective, long-lasting, non-toxic, and environment-friendly. A strong candidate is a group of unique compounds found in Camellia sinensis (tea plant): the green tea polyphenols, in particular epigallocatechin-3-gallate (EGCG) and its lipophilic derivatives. This review discussed the weaknesses of current hand sanitizers, gathered published results from many studies on the antiviral activities of EGCG and its lipophilic derivatives, and the potential use of these compounds as a novel strategy for disease prevention, especially against pathogenic viruses.

LaFleur, P (2017) Non-alcohol based hand rubs: a review of clinical effectiveness and guidelines[22]

Antisepsis that uses running water and an aqueous solution is usually referred to as a 'scrub'. Scrubs are commonly used by surgical staff for hand antisepsis during pre-surgical preparation, and contain agents such as chlorhexidine gluconate or povidone iodine. Scrubbing involves wetting the hands and forearms with water, systematically applying the scrub solution using hands or sponges and rinsing under running water. This process typically takes up to six minutes. The term 'rub' usually refers to hand antisepsis procedures and products that do not require running water. The most commonly used rub products contain at least 60% alcohol. Alcohol-based rubs have a well-established role in infection control strategy in healthcare settings for routine hand sanitization, including hospitals, outpatient clinics, laboratory settings, community settings and for hand sanitization in surgical contexts. The ubiquitous usage of alcohol-based rubs

is based on evidence for reduced infectious transmission, low cost, and their high acceptability and tolerability relative to other methods of sanitization. Nevertheless, there have been some concerns associated with the usage of alcohol-based hand sanitizers, such as religious objections, abuse potential, and flammability. These concerns, combined with a desire to optimize infection control and user acceptability, has led to the development of several non-alcohol based hand rub products. These products use antimicrobial agents such as triclosan, chlorhexidine, iodophors or quaternary ammonium compounds; various combinations and formulations have been developed: eg water-based, foams, gels, nanocapsules. The purpose of this report is to review the evidence regarding the effectiveness of non-alcohol based hand sanitizer for reducing infection rates and infection transmission in the healthcare setting for both healthcare workers and non-healthcare personnel. Another objective of this report is to summarize evidence-based guidelines regarding the use of non-alcohol based hand rubs.

SCHRANK, CL et al (2020) Are Quaternary Ammonium Compounds, the Workhorse Disinfectants, Effective against Severe Acute Respiratory Syndrome-Coronavirus-2?[23]

Due to the high infectivity rate, SARS-CoV-2 is difficult to contain, making disinfectant protocols vital, especially for essential, highly trafficked areas such as hospitals, grocery stores, and delivery centers. According to the Centers for Disease Control and Prevention, best practices to slow the spread rely on good hand hygiene, including proper handwashing practices as well as the use of alcohol-based hand sanitizers. However, they provide warning against sanitizing products containing benzalkonium chloride (BAC), which has sparked concern in both the scientific community as well as the general public as BAC, a common quaternary ammonium compound (QAC), is ubiquitous in soaps and cleaning wipes as well as hospital sanitation kits. This viewpoint aims to highlight the outdated and incongruous data in the evaluation of BAC against the family of known coronaviruses and points to the need for further evaluation of the efficacy of QACs against coronaviruses.

CHLOSTRIDIUM DIFFICILE

NERANDZIC, M M et al (2015) Unlocking the Sporicidal Potential of Ethanol: Induced Sporicidal Activity of Ethanol against Clostridium difficile and Bacillus Spores under Altered Physical and Chemical Conditions[24]

Background: Due to their efficacy and convenience, alcohol-based hand sanitizers have been widely adopted as the primary method of hand hygiene in healthcare settings. However, alcohols lack activity against bacterial spores produced by pathogens such as Clostridium difficile and Bacillus anthracis. We hypothesized that sporicidal activity could be induced in alcohols through alteration of physical or chemical conditions that have been shown to degrade or allow penetration of spore coats.
Principal findings: Acidification, alkalinization, and heating of ethanol induced rapid sporicidal activity against C. difficile, and to a lesser extent Bacillus thuringiensis and Bacillus subtilis. The sporicidal activity of acidified ethanol was enhanced by increasing ionic strength and mild elevations in temperature. On skin, sporicidal ethanol formulations were as effective as soap and water hand washing in reducing levels of C. difficile spores.
Conclusions: These findings demonstrate that novel ethanol-based sporicidal hand hygiene formulations can be developed through alteration of physical and chemical conditions.

EBOLA VIRUS

EGGERS, M et al (2015) Povidone-iodine hand wash and hand rub products demonstrated excellent in vitro virucidal efficacy against Ebola virus and modified vaccinia virus Ankara, the new European test virus for enveloped viruses[25]

Background: The recent Ebola virus (EBOV) epidemic highlights the need for efficacious virucidal products to help prevent infection and limit the spread of Ebola virus disease. However, there is limited data on the efficacy of virucidal products against EBOV, because the virus has a high biosafety level and is only available in a few laboratories worldwide. The virucidal efficacy of antiseptics and disinfectants can be determined using the European Standard EN14476:2013/FprA1:2015. Modified vaccinia virus Ankara (MVA) was introduced in 2014 as a reference virus for the claim “virucidal active

against enveloped viruses for hygienic hand rub and hand wash." For EBOV, also an enveloped virus, the suitability of MVA as a surrogate needs to be proven. The aim of this study was to test the in vitro efficacy of four povidone iodine (PVP-I) formulations against EBOV: 4% PVP-I skin cleanser; 7.5% PVP-I surgical scrub; 10% PVP-I solution; and 3.2% PVP-I and 78% alcohol solution. The formulations were tested with MVA to define the test conditions, and as a secondary objective the suitability of MVA as a surrogate for enveloped viruses such as EBOV was assessed.
Methods: According to EN14476, a standard suspension test was used for MVA. Large-volume plating was used for EBOV to increase test sensitivity and exclude potential after-effects. All products were tested under clean (0.3 g/L BSA) and dirty (3.0 g/L BSA + 3.0 mL/L erythrocytes) conditions with MVA for 15, 30, and 60 s. The concentration-contact time values obtained with MVA were verified for EBOV.
Results: Viral titres of MVA and EBOV were reduced by >99.99% to >99.999% under clean and dirty conditions after application of the test products for 15 seconds.
Conclusions: All products showed excellent virucidal efficacy against EBOV, demonstrating the important role PVP-I can play in helping to prevent and limit the spread of Ebola virus disease. The efficacy against both test viruses after 15 s is helpful information for the implementation of guidance for people potentially exposed to EBOV, and confirms the excellent virucidal efficacy of PVP-I against enveloped viruses. MVA was found to be a suitable surrogate for enveloped viruses such as EBOV.

H1N1

GRAYSON, M L et al (2009) Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers[26]

Background: Although pandemic and avian influenza are known to be transmitted via human hands, there are minimal data regarding the effectiveness of routine hand hygiene (HH) protocols against pandemic and avian influenza.
Methods: Twenty vaccinated, antibody-positive health care workers had their hands contaminated with 1 mL of 10(7) tissue culture infectious dose (TCID)(50)/0.1 mL live human influenza A virus (H1N1; A/New Caledonia/20/99) before undertaking 1 of 5 HH protocols (no HH [control], soap and water hand washing [SW], or use of 1 of 3 alcohol-based hand rubs [61.5% ethanol gel,

70% ethanol plus 0.5% chlorhexidine solution, or 70% isopropanol plus 0.5% chlorhexidine solution]). H1N1 concentrations were assessed before and after each intervention by viral culture and real-time reverse-transcriptase polymerase chain reaction (PCR). The natural viability of H1N1 on hands for >60 min without HH was also assessed.
Results: There was an immediate reduction in culture-detectable and PCR-detectable H1N1 after brief cutaneous air drying—14 of 20 health care workers had H1N1 detected by means of culture (mean reduction, 10(3-4) TCID(50)/0.1 mL), whereas 6 of 20 had no viable H1N1 recovered; all 20 health care workers had similar changes in PCR test results. Marked antiviral efficacy was noted for all 4 HH protocols, on the basis of culture results: 14 of 14 had no culturable H1N1; (P< .002) and PCR results (P< .001; cycle threshold value range, 33.3-39.4), with SW statistically superior (P< .001) to all 3 alcohol-based hand rubs, although the actual difference was only 1-100 virus copies/microL. There was minimal reduction in H1N1 after 60 min without HH.
Conclusions: HH with SW or alcohol-based hand rub is highly effective in reducing influenza A virus on human hands, although SW is the most effective intervention. Appropriate HH may be an important public health initiative to reduce pandemic and avian influenza transmission.

NOROVIRUS

HSU, S et al (2018) Persistent virucidal activity in novel alcohol-based hand sanitizer formulation for potential use against norovirus outbreaks[27]

Background: Norovirus outbreaks are responsible for 19-21 million cases of acute gastroenteritis in the United States. Currently available alcohol-based hand sanitizers are not recommended by the CDC for norovirus outbreak prevention in healthcare settings due to the ineffectiveness of alcohol against nonenveloped viruses. Objectives: This study aimed to evaluate the virucidal activity and persistency of a novel alcohol-based hand sanitizer formulation, P1.1, containing lipophilic epigallocatechin-3-gallate (EGCG), against a human norovirus surrogate.
Methods: A standard 50% Tissue Culture Infective Dose (TCID50) suspension assay was used to determine the virucidal capacity of P1.1 against feline calicivirus (FCV), a surrogate for human norovirus required by the Environmental Protection Agency. Separately, residual virucidal activities

after a single application on clean surfaces were determined at 1, 2, 4 and 12 hours. Controls included the formulation without lipophilic EGCG (P0.0), commercially available alcohol-containing sanitizers, and antibacterial liquid hand soap (LHS). One-way ANOVA and Tukey's multiple comparisons test (alpha=0.05) were applied for statistical analysis.
Results: Results: The 60 second suspension test results demonstrate that P1.1 reduced viral infectivity greater than log10 4. In addition, the residue virucidal effect of P1.1 remained strong (reduction of infectivity by >log10 3) beyond 12 hours after a single application on a clean surface. In comparison, commercially available alcohol-based sanitizers and the P0.0 formulation failed to reduce infectivity by more than log10 3. LHS did not show virucidal activity or prolonged activity if not washed three times with water. These results demonstrated that P1.1 with lipophilic EGCG effectively inactivates FCV with prolonged residue activity on clean surfaces.
Conclusions: Conclusion: To the best of our knowledge, this is the first report of a non-toxic hand sanitizer/surface disinfectant possessing effective and prolonged virucidal activities against nonenveloped viruses such as norovirus. Therefore, P1.1 containing lipophilic EGCG is potentially a novel and effective approach to prevent norovirus outbreaks.

TULADHAR, E et al (2015) Reducing viral contamination from finger pads: Handwashing is more effective than alcohol-based hand disinfectants[28]
Background: Hand hygiene is important for interrupting transmission of viruses through hands. Effectiveness of alcohol-based hand disinfectant has been shown for bacteria but their effectiveness in reducing transmission of viruses is ambiguous.
Aim: To test efficacy of alcohol hand disinfectant against human enteric and respiratory viruses and to compare efficacy of an alcohol-based hand disinfectant and handwashing with soap and water against norovirus.
Methods: Efficacies of a propanol and an ethanol-based hand disinfectant against human enteric and respiratory viruses were tested in carrier tests. Efficacy of an alcohol-based hand disinfectant and handwashing with soap and water against noroviruses GI.4, GII.4, and MNV1 were tested using finger pad tests.
Findings: The alcohol-based hand disinfectant reduced the infectivity of rotavirus and influenza A virus completely within 30s whereas poliovirus Sabin 1, adenovirus type 5, parechovirus 1, and MNV1 infectivity were reduced <3 log10 within 3 min. MNV1 infectivity reduction by washing hands with soap and water for 30s (>3.0 ± 0.4 log10) was significantly higher than

treating hands with alcohol (2.8 ± 1.5 log10). Washing with soap and water for 30s removed genomic copies of MNV1 (>5 log10), noroviruses GI.4 (>6 log10), and GII.4 (4 log10) completely from all finger pads. Treating hands with propanol-based hand disinfectant showed little or no reduction to complete reduction with mean genomic copy reduction of noroviruses GI.4, GII.4, and MNV1 being >2.6, >3.3, and >1.2 log10 polymerase chain reaction units respectively.
Conclusions: Washing hands with soap and water is better than using alcohol-based hand disinfectants in removing noroviruses from hands.

ZIKA VIRUS

DE NARDO, E et al (2017) Efficacy of Alcohol Based Hand Rubs Against Zika Virus[29]

BACKGROUND: In February 2016 the World Health Organization designated the Zika virus epidemic as a Public Health Emergency of International Concern. This virus has spread rapidly in several continents, including many regions of the United States. Although Zika virus is primarily transmitted through the bites of infected mosquitoes, other transmission pathways are of concern, including that of healthcare worker occupational exposure from patients infected with Zika. The CDC and OSHA have provided guidance for preventing occupational exposure that has been endorsed by National Nurses United. Part of these recommendations is hand hygiene, including the use alcohol-based hand rub (ABHR) containing at least 60% alcohol. To date there have been no studies evaluating effectiveness of ABHR against Zika. The objective of this study was to evaluate the efficacy of two unique ABHR formulations against Zika virus.
METHODS: Test products were a commercially available 70% ethanol gel and foam. Test products were evaluated for efficacy against Zika virus (ZeptoMetrix Corp # 0810092CF) with an in vitro time kill method (ASTM E1052-11). The percent and log 10 reductions of virus particles were determined following exposure to the test product for 15 and 30 seconds.
RESULTS: ABHRs gel and foam tested against Zika virus achieved complete reduction, ≥4.25 log10 (≥99.99%) at 15 and 30 seconds exposure time.
CONCLUSIONS: The two unique gel and foam ABHRs tested effectively reduced Zika virus in vitro, indicating ABHR may be an effective intervention for reducing Zika virus on hands. This data supports official guidance for the use of ABHR, when hands are not visible soiled, for preventing Zika virus exposure when treating Zika infected patients.

Produced by the members of the National Health Library and Knowledge Service Evidence Team†. Current as at 4 August 2020. This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:

Population P person location condition/patient characteristic	COVID -19 OR OTHER VIRUS OR BACTERIA
Intervention I length location type	ALCOHOL-BASED HAND GEL
Comparison C another intervention no intervention location of the intervention	NON-ALCOHOL BASED HAND GEL
Outcome O	INACTIVATION OF VIIRUS

The following search strategy was used:

S1	alcohol based hand N1 (sanitiser or sanitizer or gel or rub or disinfectant)
S2	alcohol based handrub
S3	(MM "Hand Sanitizers")
S4	S1 OR S2 OR S3
S5	virus or bacteria or norovirus or C-diff or Clostridium difficile or c-difficile or enveloped or non-enveloped
S6	COVID-19 or coronavirus or corona virus or Wuhan N2 virus or "2019 n-cov" or "2019 ncov" or "severe acute resiratory syndrome coronavirus 2" or "severe acute respiratory syndrome coronavirus 2" OR SARS-CoV-2 or (2019 and (new or novel) and coronavirus)
S7	(MH "Coronavirus+")
S8	S6 OR S7
S9	S5 OR S8
S10	S4 AND S9
S11	Limit from 2015 to date

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