Environment International 121 (2018) 703–713

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Review article

Human infectious diseases and the changing climate in the Arctic

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ARTICLE INFO

Handling Editor: Robert Letcher

Keywords:
Human infectious disease
Arctic
Climate change
Zoonosis
Vector-borne
One health

ABSTRACT

Climatic factors, especially temperature, precipitation, and humidity play an important role in disease transmission. As the Arctic changes at an unprecedented rate due to climate change, understanding how climatic factors and climate change affect infectious disease rates is important for minimizing human and economic costs. The purpose of this systematic review was to compile recent studies in the field and compare the results to a previously published review. English language searches were conducted in PubMed, ScienceDirect, Scopus, and PLOS One. Russian language searches were conducted in the Scientific Electronic Library “eLibrary.ru”. This systematic review yielded 22 articles (51%) published in English and 21 articles (49%) published in Russian since 2012. Articles about zoonotic and vector-borne diseases accounted for 67% (n = 29) of the review. Tick-borne diseases, tularemia, anthrax, and vibriosis were the most researched diseases likely to be impacted by climatic factors in the Arctic. Increased temperature and precipitation are predicted to have the greatest impact on infectious diseases in the Arctic.

1. Introduction

Evidence shows that the Arctic land surface temperatures have warmed considerably since the mid-twentieth century (Larsen et al., 2014). In some regions, the rate is nearly double the global average (Hassol et al., 2004). By 2040, there is a predicted increase of 2 °C, and by 2100, between 4 and 7 °C (Hassol et al., 2004). Warmer temperatures in the Arctic cause changes in sea ice, snow coverage, permafrost, ocean warming, and precipitation. Additionally, climate change is occurring concurrently with unprecedented globalization in the Arctic. Greater accessibility to remote locations, increases in tourism and industry, and social change bring new health challenges to the Arctic as well, in addition to already complex issues such as health disparities between indigenous and non-indigenous people, high concentrations of environmental contaminants, and rising chronic disease rates (Arctic Council Ministerial, 2009).

As the Arctic warms at an unprecedented pace, understanding how climatic factors affect infectious diseases in the Arctic is essential. Climate change has been predicted to be the most influential factor in the emergence of infectious diseases (Sonne et al., 2017). The changes in the Arctic climate will have both direct and indirect impacts on the health of Arctic residents, especially in relation to infectious diseases (Larsen et al., 2014). Directly, warmer temperatures can accelerate growth rates of pathogens and animals, including insect vectors (Baylis, 2017; Noskov et al., 2017; Yasjukevich et al., 2013). Increased connection and human migration can introduce infectious diseases to previously isolated areas, exposing highly susceptible populations to new pathogens (Dudley et al., 2015). Extreme precipitation may result in flooding and disruption of water/sanitation infrastructure, elevating the risk for waterborne outbreaks. Indirectly, climatic factors affect infectious disease transmission by altering human behavior. For example, warmer temperatures lead to more people using public bathing waters, providing more opportunities for a waterborne outbreak to start (Eze et al., 2014). Similarly, people spend more time outside (i.e. in forests and public places for picnics and other free time activities), increasing the likelihood of contracting a tick-borne disease (Chashchin et al., 2017). Additionally, changes in climatic factors can expand a disease-vector's geographic range, or enlarge its population, for example more vector species and individuals survive though the winter (Bruce et al., 2016; Burmagina et al., 2014; Chashchin et al., 2017; Mesheryakova et al., 2014; Parham et al., 2015; Yastrebov et al., 2016). Increases in public and health personnel education, vaccination programs, and hygiene, however, help combat the spread of disease, potentially reducing infections even though opportunities for infection may increase as a result of climate change.

Infectious disease rates across the Arctic are highly variable depending on country, disease, age, and sex (AMAP, 2009). For example, disease rates for tularemia in the Arkhangelsk region and Khanty-Mansi

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https://doi.org/10.1016/j.envint.2018.09.042
Received 8 June 2018; Received in revised form 20 September 2018; Accepted 23 September 2018

autonomous area (a.a.), are several times higher than averages registered for the Russian Federation in total (Dudarev et al., 2013). From 2005 to 2015, the Russian male population suffered more deaths from infectious and parasitic diseases than females in virtually every region (Federal State Statistics Services of the Russian Federation, 2017). Even though there has been a significant improvement and less respective deaths for males in the European North of Russia, those in the Khanty-Mansi a.a., Yamalo-Nenets, and Chukotka a.a. still experience a general increase in the related mortality (Federal State Statistics Services of the Russian Federation, 2017). There has been a decline in infectious disease rates in Arctic countries due to improved sanitation, medical treatment/vaccination, and education, but the impacts of the changing Arctic climate are predicted to increasingly affect the health and well-being of Arctic residents (AMAP, 2009).

A previous study suggested that there is a strong association between climatic factors and food- and waterborne diseases in the Arctic, while more research needs to be done to confirm the relationship between vector- and rodent-borne diseases with weather and climatic factors (Hedlund et al., 2014). Temperature and precipitation appear to be the most influential climatic factors on infectious disease incidence in the Arctic. The purpose of this review was to find recent publications in the field and compare the results to a previously published review (Hedlund et al., 2014) to find if any trends or gaps in knowledge emerged.

2. Materials and methods

English searches of this systematic review were conducted in PubMed, ScienceDirect, Scopus, and PLOS One. For the PubMed search, a custom date range, 2013/05/01–2018/03/31 to capture articles published after a previous review (Hedlund et al., 2014). Because ScienceDirect, Scopus, and PLOS One had not been used in the previous review, no date restrictions were used.

The following Medical Subject Heading (MeSH) terms were searched in PubMed: bacterial infections and mycoses; parasitic diseases; virus diseases; climatic processes; climate; climatic; weather; temperature; humidity; rain; snow; Scandinavia; Arctic regions; Canada; Alaska; Greenland; Iceland; Sweden; Norway; Finland; Russia; and Siberia. The MeSH terms used were the same as those from a previous review (Hedlund et al., 2014), but additional terms “humidity,” “snow,” “rain,” “Sweden,” and “Norway” were added. MeSH terms were used rather than single keywords, following search term criteria used in previous reviews (Hedlund et al., 2014; Verner et al., 2016). Because MeSH terms we used for the PubMed search, searches contained subsequent phrases in the MeSH hierarchy. For example, the MeSH phrase “virus diseases” included the following terms via the MeSH hierarchy: “dengue, encephalitis, tick-borne diseases, yellow fever, zika virus infection, encephalitis, and zoonoses.” The “disease” phrases used; bacterial infections and mycoses; virus diseases; and parasitic diseases, all include “zoonoses” within their MeSH hierarchy, in addition to specific zoonotic diseases. Because of this, “zoonoses” was not searched as a stand-alone term. Additionally, “arctic region” is a MeSH term and includes the individual search term “arctic.”

For searches in ScienceDirect and PLOS One, the following terms were used: arctic; bacterial infections; mycoses; parasitic diseases; virus diseases; climatic processes; climate; climatic; weather; temperature; and precipitation. These search terms were selected to try and keep the searches across databases as comparable and inclusive to the selection criteria as possible.

Using all of the search terms from the PubMed, ScienceDirect and PLOS One searches in Scopus yielded very few results. Consequently, the only search terms used were “infectious disease,” “climate,” and “arctic.”

The largest Russian domestic database, the Scientific Electronic Library “eLibrary.ru,” was searched to identify publications relevant to this review among the Russian research literature. The database contains over 28.5 million articles, books, dissertations, conference proceeding, scientific patents, and other research materials across all disciplines. It is integrated with the Russian Science Citation Index. The Advance Search engine was used for conducting the search of all the databases compiled in the eLibrary.ru database. The types of the publication to conduct the search were: research journal articles, books, and academic dissertations. The period of the search was limited between 2013/01/01 and 2017/12/31.

One limitation of the eLibrary.ru database is that there is not possible to work with multiple key words at a time. Therefore, only one key word or phrase was used to fill in the query window. The search terms used were: bacterial human infections; viral human infections; zoonotic infections; vector-borne infections; parasitic infections in humans; tularemia; anthrax; leptospirosis; legionnaire's disease; Sindbis fever; tick-borne borreliosis; tick-borne encephalitis; Lyme disease; hantavirus; West Nile virus; brucellosis; toxoplasmosis; Q fever; climate change related diseases; new infections in the Arctic; and exotic infections in Russia. Additional searches were also done using the reference lists from suitable articles, to see if any authors referenced had published relevant articles for our review.

Selected articles needed to meet the following criteria: involved the Arctic or subarctic regions, consider a correlation between human infectious diseases and climatic factors, and are original research. Because of varying definitions of the Arctic and subarctic, articles were selected if the research focused on cases occurring in Alaska (US), Canadian provinces with Arctic or subarctic territory, Greenland (Denmark), Iceland, Norway, Sweden, Finland, and regions in Russia's Arctic zone. Review articles and vaccine studies were excluded. All searches were conducted in March 2018.

The search terms used for each search were recorded as well as the number of results retrieved for each search. Article titles and abstracts were evaluated for their relevance to the inclusion criteria. All articles that appeared to meet the criteria were selected for a full text review. The articles that met the inclusion criteria after the full text review were included in this review. If an article was found in more than one database, it was only counted for the first database it was found in, eliminating duplicates from the selection process. Fig. 1 includes the selection process and number of articles selected at each phase from the databases.

We also searched the phrase “Arctic AND human AND climate AND one health AND zoonosis” in Scopus ($n = 2$), PLOS One ($n = 17$), ScienceDirect ($n = 28$) and PubMed ($n = 3$, search was restricted to 2013/05/01–2018/09/20) to look for articles relevant to our inclusion criteria specifically relating to “one health” and “zoonosis.” Additional searches of Russian literature in eLibrary (covering years 2013–September 2018) used terms “Arctic” (number (n) of articles found, $n = 8655$), “Climate change” ($n = 6227$), “One health” ($n = 80$), “Zoonosis” ($n = 56$) and “Climate change health” ($n = 69$). Limited Russian literature conceptualized their work based on the “One health” concept used in English literature. The phrase “one health” can often be seen but as just as a part of random sentences meaning “a person has only one health to take care of” or “integral health of all body systems,” rather than the integrated approach to evaluating human, animal, and environmental health. Many of the results overlapped between databases and included articles and reviews that have already been included and referenced in our manuscript, therefore no new articles were found. Excluded results were review articles, pertained to wildlife, or did not meet our specific inclusion criteria.

An additional PubMed search was conducted for each United Nations (UN) designated geographic region, using MeSH terms for climatic factors and infectious diseases to see how the number of publications in the Arctic compared with other regions of the world. Because the Arctic is not a UN designated geographic region, the eight countries with Arctic territories were searched together and not included in the search for their initial UN designation. Alaska and Greenland, however, were searched as Arctic territories, while

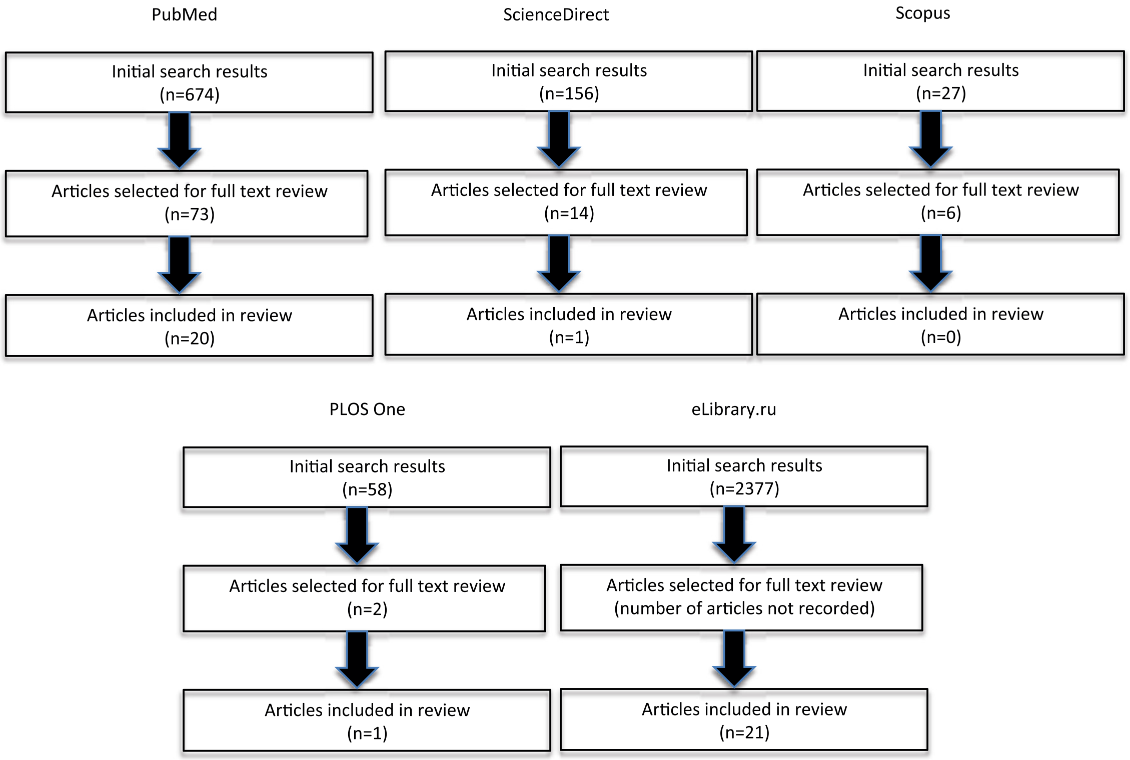

Fig. 1. Systematic review screening process: initial search results, articles selected for a full text review, and articles included in the review.

Denmark and the United States were searched in their UN designated region to avoid inflating the number of Arctic publications. The number of results from each search was used to calculate the percentage of publications coming from each region. The exact number of articles that met criteria investigating the association between climatic factors and climate change and infectious diseases is difficult to know. The results were not reviewed so there are likely a number of articles that do not apply but the percentages likely will be similar across regions, regardless of the exact number of applicable articles. The search terms used were modeled after a previous study done to see where research on climate change and health was being conducted (Verner et al., 2016) and are listed in Table S1.

3. Results

Fig. 1 illustrates the systematic review screening process for the five databases used. The PubMed search revealed 674 records, of which 20 were selected as meeting the criteria. From 156 results in ScienceDirect, one met the criteria to be included in the review. In Scopus, there were 27 results, but none met the inclusion criteria. There were 58 results in PLOS One that were evaluated, and one article met the criteria. Combining the results of all individual searches in the eLibrary.ru, there were 2377 results of which 21 articles met the criteria and selected to be included in this review. Detailed information and main findings for the articles included in this review are available as Table S1.

3.1. Vector-borne diseases and zoonoses

The majority of emerging disease outbreaks in the last 30 years have been either zoonotic or vector-borne (Ruscio et al., 2015). Climatic factors generally affect zoonotic and vector-borne diseases indirectly. The effect on infections results from shifts in the ecosystem or population of the animal or vector, influenced by climatic factors. The mechanisms by which a warming climate disrupt the host-pathogen transmission include changes in host density, increased pathogen survival, vector range expansion, and changes to host susceptibility (Burek et al., 2008). The warming temperature is allowing a northward shift of the boreal forest tree line and the tundra (Parkinson et al., 2014). As a result, animal and insect vectors can move northwards, expanding their range and increasing risk of transmission. Relatively small changes in temperature can make a new environment habitable for an organism, introducing new host-parasite relationships and permitting range expansion (Dudley et al., 2015). A study investigating the range expansion of the *Ixodes ricinus* tick in Sweden found that the range expanded by 10%, with most of the expansion occurring about 60°N, where the range doubled from 12.5% in the early 1990s to 26.8% in 2008 (Jaenson et al., 2012). In the Arctic, infections by *Echinococcus* spp., tularemia, West Nile virus, Hantavirus, tick-borne encephalitis, Lyme disease, and Sindbis fever are predicted to increase as a result of shifts in animal and vector range and population changes (Parkinson et al., 2014). A study in the Khabarovsk Territory, the Amur Region and the Jewish Autonomous Region found that in addition to infections typical for the area, an immune screening found seropositive results for exotic infections, including Sindbis and West Nile virus (Andaev et al., 2014). Warmer temperatures are also predicted to increase the number of rodent and insect vectors surviving over the winter, increasing the transmission of diseases including brucellosis, toxoplasmosis, trichinellosis, Q fever, and Puumala hantavirus (Parkinson et al., 2014).

3.1.1. Tick-borne diseases

Tick-borne diseases are some of the most researched infectious diseases associated with climatic factors and climate change. Temperature and precipitation significantly influence the life cycle and distribution of ticks, and consequently affect the spread of diseases, including tick-borne encephalitis (TBE) and tick-borne borreliosis (TBB) (Semenza and Menne, 2009). Warmer temperature, for example, can accelerate the ticks' development and reproduction, permit range expansion, and expand woodlands and vegetation, resulting in improved habitat conditions. Increased precipitation (severe flooding) however, can negatively affect the tick population and range (Semenza and

Menne, 2009). Socioeconomic factors also affect the exposure to ticks, and consequently tick-borne diseases. Large-scale industrial activities may increase exposure risk, while engaged health authorities may reduce risk (Tokarevich et al., 2017).

Tick-borne encephalitis is caused by the virus family, *Flaviviridae* (Daniel et al., 2018). Ticks in the Ixodidae family serve as a vector and reservoir for the tick-borne encephalitis virus. In Europe and Russia, *Ixodes ricinus* and *Ixodes persulcatus* are responsible for most of the TBE infections, while in North America, *Ixodes scapularis* is the responsible vector (Andersen and Davis, 2017; Daniel et al., 2018; Jaaskelainen et al., 2011). Tick-borne borreliosis (Lyme disease) is caused by the bacteria *Borrelia burgdorferi, Borrelia afzelii* or *Borrelia garinii* (Andersen and Davis, 2017).

The majority of the Russian academic literature on the relationship between infectious diseases and concurrent climatic changes is about tick-borne diseases in the northernmost territories (Burmagina et al., 2014; Chashchin et al., 2017; Kokolova et al., 2014; Popov, 2014; Rudakov et al., 2015; Yasjukevich et al., 2013; Yastrebov et al., 2016). A study investigating epidemiologic changes in TBE incidence in the Russian Federation over twenty years (1997–2006 and 2007–2016) found that the changes are occurring most intensively in Siberia and the Far East (Noskov et al., 2017). In association with the expected warming, the vector range of *I. ricinus* is also predicted to expand northward and eastward. By the end of the 21st century, *I. ricinus* is predicted to settle in the Far East and Kamchatka, where tick-borne encephalitis and borreliosis rarely occur now (Popov, 2014).

The European part of the Russian Arctic (Arkhangelsk, Komi regions) is currently exposed to the increasing TBE and TBB incidence, the northern range expansion of associated ticks, and better survival for tick vectors (Tokarevich et al., 2017), While socioeconomic factors have been considered a cause for the increase in tick-borne disease incidence, the majority of tick-bites occurred during leisure activities (Tokarevich et al., 2017). The annual TBE incidence rates from 2005 to 2015 per 100,000 people were 2–5.4 times higher than compared to the respective rates nation-wide. Epidemiological and climatic data for the Arkhangelsk region suggested that climate warming was a significant factor, responsible for an almost 60 fold increase in morbidity in the period 1980 to 2015. A statistically significant correlation between annual rise in air temperature and TBE cases was found in all districts of the Arkhangelsk region. The TBE cases mostly occur in urban citizens, suggesting an association with urbanization, as well as an increase in temperature (Chashchin et al., 2017).

Vaccination and acaricide treatment reduce TBE mortality. Since 2005, there has been an increase in the use of on-land acaricide treatments funded by governmental programs in the Arkhangelsk region, from 128.2 ha in 2005 to 740.0 ha, coinciding with a decline in TBE incidence (Chashchin et al., 2017). These acaricide treatments are mostly initiated in crowded places; schools, kindergartens, summer camps (particularly children's holiday camps). Private applications are also possible and encouraged among owners of “dacha” (summer houses). Other effective measures to limit tick-borne diseases include strengthening the monitoring of species populations and density of vectors and infection reservoirs, increasing the scale and efficiency of suppression measures, and promoting individual protection from tick-bites (Yasjukevich et al., 2013).

Only one study included in this review about tick-borne diseases was from another country. This study focused on the association between TBE and North Atlantic Oscillation (NAO), mean summer temperatures, and yearly harvested European hare, roe deer, and red fox in Sweden between 1976 and 2011. No significant association was found between TBE cases and NAO index. A relationship between TBE cases and summer temperature was seen, though it is only a minor predictor. From this study TBE cases could best be determined by the number of European hares rather than climatic factors (Palo, 2014).

3.1.2. West Nile virus

Diseases transmitted by mosquito vectors are expected to increase as a result of changes in mosquito populations. Increased temperature permits overwintering of species and can expand the range of the disease causing vectors. West Nile virus is primarily transmitted by the stick of the *Culex* mosquitoes. In a Canadian study investigating the relationship between *Culex* mosquito populations, climate data, and the prevalence of West Nile virus, a strong correlation was identified between the abundance of mosquitos and human cases, and between temperature and infected mosquito pools. In this study, there was not a strong correlation between average precipitation and amount of human cases (Giordano et al., 2017). Additional obstacles to monitoring the relationship between West Nile virus cases and climatic factors include asymptomatic presentation in up to 80% of cases and the delay in symptom onset (between 2 and 12 days after exposure) (Giordano et al., 2017).

3.1.3. Chikungunya virus

Chikungunya virus (CHIKV) is transmitted by the *Aedes* sp. mosquitoes. While not endemic to Canada, the risk of transmission was assessed based on current and projected climate change data. Based on temperature, host ecology, and transmission potential, the current map reveals very low risk for autochthonous CHIKV transmission because there are very few locations with an entire summer month average temperature above 22.8 °C. However, projected models show that there could be an increase in the southern coastal regions where more summers will have suitable climatic conditions for the *Aedes albopictus* mosquito-vector. Overall, there is a very low risk of CHIKV transmission in Canada, but surveillance could be useful because of the high number of travellers returning from CHIKV- endemic countries in the summer (Ng et al., 2017).

3.1.4. Dirofilariosis

Dirofilariosis is a parasitic disease caused by *Dirofilaria immitis* and other *Dirofilaria* species. While the disease usually affects dogs, humans are susceptible to cardiopulmonary dirofilariosis (Morchon et al., 2012). Dirofilariosis is transmitted by mosquito species. The relationship between warming due to climate change and dirofilariosis infections in Russia, Ukraine, and former-Soviet states was investigated retrospectively from 1981 to 2011. Using the results from the retrospective analysis, prediction models for 2030 were developed and the model suggest that warming is associated with the spreading and emergence of human dirofilariosis cases (Kartashev et al., 2014). Human cases are expected to emerge further north, however, there may be a delay in reported cases since most cases appear several years after the conditions for extrinsic incubation are met and the life cycle in dogs has been established (Kartashev et al., 2014).

3.1.5. Tularemia

Tularemia is caused by the bacterium *Francisella tularensis* (Hestvik et al., 2015). Tularemia can be transmitted by contact with infected rodents and hares or by arthropod vectors (deer-fly, horse-fly, mosquitos, and hard ticks) (Petersen et al., 2009). Climatic and ecological factors play a significant role in determining the vector range and population.

About 70% of tularemia cases in Russia occur in the Northwest (Arkhangelsk region) and Siberian federal districts (Khanty-Mansi a.a.). In the former, there is an increase in the number of patients co-infected with tularemia, leptospirosis, and other concurrent infections (Demidova et al., 2016). According to the retrospective, longitudinal study investigating tularemia incidence in the Arkhangelsk region over ten years, the predominant clinical form is bubonic and the outbreak lasted for several years in the 2010s, likely due to ineffective risk elimination in the early years of the epidemic (Burmagina et al., 2014; Meshcheryakova et al., 2014).

In Khanty-Mansi area, the last significant outbreak occurred in 2013 and affected 1005 people. A likely contributor was the expansion of the agent reservoir: northern red-backed voles and common red-toothed shrews to carry the disease in addition to the water vole and blood-sucking insects (Mesheryakova et al., 2014; Ostapenko et al., 2015; Pakhotina et al., 2016). It raised the question on the efficacy of preventive measures against tularemia. A human vaccination with a live tularemia vaccine was concluded to still be the most effective (Demidova et al., 2014, 2016). However, the vaccination level has been decreasing and rather negligible in the affected regions in the last decade, with underfinancing and controversy over the safety of the vaccine excipient among the likely reasons (Burmagina et al., 2014). The hydrographical features of the region might have also attributed the ineffectiveness of prevention as well as relaxed preparedness among public health services due to extended time between outbreaks (Ostapenko et al., 2015).

In addition to preventative measures, a study in Sweden modeled high-risk regions for outbreaks using predicted mosquito abundance and local weather data. Tularemia case data from 1984 to 2012, annual relative mosquito abundance, summer temperature the preceding year, present summer precipitation, and the number of cold days with a thin layer of snow were used. High-risk regions were identified using the model, and a correlation between increased risk for tularemia and high number of cases the previous year, high mosquito abundance, high summer precipitation, and high summer temperatures was established (Desvars-Larrive et al., 2017). However, the model used in this study does not take into account human factors (i.e. time spent outside) and may have overestimated the role mosquitos play in transmission while not accounting for exposure to other infected animals (i.e. voles, as information for regional vole abundance was unavailable) (Desvars-Larrive et al., 2017).

3.1.6. Anthrax

Anthrax is another zoonotic disease seen at increasing occurrences with the permafrost thawing, in particular in the Russian Arctic (Avitisov et al., 2015; Dugarzhapova et al., 2017; Kosilko et al., 2014; Prokudin et al., 2016; Simonova et al., 2017). As the permafrost thaws, exposing buried carcasses of infected animals, ensuing flooding and soil disruption releases thawed anthrax spores (Revich et al., 2012). Humans are mainly infected through contact with infected animals or animal products (mainly cattle), and spores, but can be infected through an insect vector. Both mosquitos (*Aedes aegypti* and *Aedes taeniorhynchus*) and flies (*Stomoxys calcitrans*) can act as a vector for anthrax transmission (Turell and Knudson, 1987). The Siberian and the Far Eastern regions of Russia (mostly effected Yamalo-Nenets a.a. and Sakha Yakutia) contain 7201 registered anthrax hazardous stations (settlements or pastures with previously registered cases of anthrax) and 557 anthrax burial sites (Dugarzhapova et al., 2017). The majority of infected individuals are unvaccinated, residing in rural areas (97.5%), males of working age (77.5%) and infected during slaughtering (90.5%) with meat as the main transmission factor (96.4%) (Dugarzhapova et al., 2017). Low or absent vaccination among these risk groups might be the main risk factor for anthrax infection, rather than climate change, which has been suggested by environmental media (Dugarzhapova et al., 2017).

Some studies explored the abnormally hot summer 2016 in relation to the large outbreak in Yamal (Popova et al., 2016; Simonova et al., 2017). The temperature was 6.7 °C higher than the usual mean in June, and 5.7 °C higher in July. The abnormal air temperatures resulted in warming of the lower soil levels in the areas of anthrax source sites measured on the 15 of July 2016 (10 cm down = more than 20 °C, 40 cm = 12 °C, 100 cm = 5 °C). Additionally, extremely minimal rainfall led to the unusually low air humidity (less than 30%). The outbreak resulted in mass reindeer mortality of 2650 infected animals. Thirty people were also infected out of 266 residents of the outbreak area with one teenage death (Popova et al., 2016; Simonova et al., 2017). The warmed soil conditions became favorable for frozen spores to thaw. The observed meteorological factors contributed to the intense maturation of biting insects, which act as a carrier of the pathogen and the cause of rapid spread of epizootics (Simonova et al., 2017). The immune system of reindeers also weakened due to the difficult heat conditions. The authors also highlighted the challenge of low or absent vaccination against anthrax in the Russian Arctic (Simonova et al., 2017).

A predictive epidemiological model based on the theory of fuzzy sets assessed the risks of epizootic anthrax in animals in the Taimyr Peninsula, neighboring to the Yamalo Nenets a.a. (Prokudin et al., 2016). Predictive calculations showed that with favorable factors for the development of epizootic process (increased land use, poor soil quality, increased summer temperatures) and absence of preventive actions (i.e. animal vaccination), Taimyr's risk of an anthrax outbreak is 81%. With minimal prevention efforts, the risk of an anthrax outbreak decreases by half, to 47%. Preventative actions coupled with factors unfavorable to anthrax development (i.e. minimal land use, normal summer temperatures) reduced the risk further to 24%. The authors conclude that it is necessity to maintain and increase the effectiveness of epidemiological surveillance and prevention for anthrax in animals to prevent a larger spread among humans (Prokudin et al., 2016).

3.1.7. Puumala virus

Puumala virus is a Hantavirus found in Europe and Russia that causes a mild form of hemorrhagic fever and renal syndrome called nephropathia endemica (NE). The virus is carried by bank voles. Climatic factors influence the ecology of the vector, and can be used to predict NE cases. A model in Finland shows that NE cases can be predicted with 34% mean relative prediction error based on bank vole population and air temperature (Haredasht et al., 2013).

3.1.8. Rabies

Rabies virus is transmitted by wild and domestic animals, including dogs, cats, bats, raccoons, and skunks (Plotkin, 2000). In Alaska, the rabies niche was investigated to assess the risk of rabies outbreaks. Vaccination of domestic dogs is the most effective way to reduce risk, but a model was developed using infrastructure and ecological data. Based on the model predictions, the Arctic rabies niche will decay in 2050. However, this model does not take into account host range expansion due to warming or increased human infrastructure, which could increase the risk of rabies (Huettmann et al., 2017). The effect of climate change on fox rabies in Alaska was also investigated, specifically in red and arctic foxes (Kim et al., 2014). Based on a model using climatic factors and passive surveillance of foxes exhibiting symptoms of rabies, reported rabies in red and arctic foxes were found to negatively correlate with temperature and precipitation. Precipitation negatively correlated with rabies cases, suggesting reduced mobility, and subsequently reduced contact risk. While passive surveillance likely results in underreporting, rabid domestic dogs are still the most likely source of human exposure (Kim et al., 2014).

3.2. Airborne diseases (viral and bacterial)

Airborne infection occurs when pathogenic bacteria or viruses are inhaled and penetrate the alveoli (van Leuken et al., 2016). Small, aerosolized droplets can be transmitted through speech, sneezing, and coughing. The droplets, once expelled, are exposed to numerous factors, including wind speed and direction, temperature, and humidity. These factors can influence where and how the infectious particles are traveling, as well as if they will be suspended in one place. However, the abundance of co-factors makes attributing airborne infectious disease shifts in the Arctic as result of climatic factors difficult.

Research suggests airborne diseases (viral and bacterial) have a weak association with climatic factors (Hedlund et al., 2014). Co-factors including human behavior, individual susceptibility and seasonality play an important role in airborne infectious disease transmission. (Hedlund et al., 2014; van Leuken et al., 2016). Prolonged time indoors during the winter increases the risk for direct contact, though basic hygiene and annual influenza vaccination can reduce the risk.

Two viral infections (influenza A and human rhinovirus) were investigated for their association with climatic factors. One study (He et al., 2013) analyzed the spread of influenza A across Canada (October 1999 to August 2012) using temperature and humidity and school terms. Low humidity and low temperature correlated with early emergence and an increase in cases. School closings also played a significant role in reducing the transmission of influenza. Even when accounting for school closings though, climatic factors and the west-to-east spatial pattern of disease spread are still significant predictors for seasonal influenza. One limitation though is age groups were not distinguished. School closing likely would have had a greater impact on school age children (He et al., 2013).

Another study (Ikaheimo et al., 2016) investigated the association between decreased temperature and humidity and human rhinovirus infections (HRV) in Finnish military conscripts. The authors conclude that a decrease in either temperature or humidity correlates with an increase in the risk of HRV three days before an infection. However, at subfreezing temperatures, the risk of HRV infection decreases. This study, however, only included military conscripts (a generally young and healthy population) and conscripts may have delayed treatment due to varying incubation times or mild symptoms (Ikaheimo et al., 2016).

The association between airborne diseases and climatic factors in the Arctic has the lowest number of publications in this review. While there is some evidence suggesting the importance of climatic factors for airborne disease transmission, the abundance of co-factors and low number of publications suggest the need for more research.

3.3. Food- and waterborne diseases

Food- and waterborne diseases can be affected by increased temperature and extreme precipitation. Increased temperature leads to increased pathogen growth and better pathogen survival (Baylis, 2017). Extreme precipitation can result in flooding, which can disrupt and contaminate water and waste treatment facilities (Parkinson et al., 2014). The rapidly warming Arctic and predictions of increased precipitation suggest food- and waterborne diseases will be significantly impacted directly.

It is important to mention though that crowded living conditions and inadequate water and sanitation infrastructure significantly contribute to the spread of food- and waterborne diseases in the Arctic. Close contact in overcrowded houses and the cold climate, keeping people indoors, increases the risk of person-to person transmission of disease (Bruce et al., 2016). Additionally, many homes lack access to a centralized water supply or sewage systems (Dudarev et al., 2013). In rural Alaska, for example, 22% of homes do not have indoor plumbing (Thomas et al., 2016). As a results, residents resort to hauling water into their homes to use for cooking, cleaning, and hygiene. Extreme water rationing may lead to the same basin of water used for multiple washings, increasing the risk of bacterial skin infections (Thomas et al., 2016). Poor sanitation also increases the risk of contamination of food products, increasing the risk of food-borne outbreaks (Dudarev et al., 2013). Additionally, communities without piped-in water may use “self-haul” or “honey buckets” as toilets, where residents haul waste from the home to community sewage lagoons or containers, increasing the risk of diseases spread by fecal-oral transmission (Thomas et al., 2016). Scarce or contaminated water supplies can amplify the number of food- and waterborne diseases, regardless of climatic factors.

3.3.1. Gastroenteritis

Gastroenteritis can be caused by viruses, bacteria, and parasites. Common causes of viral gastroenteritis include norovirus and rotavirus (Barclay et al., 2014). Transmission can occur in food- and waterborne outbreaks and through person-to-person contact. Transmission via the fecal-oral route is possible, and the more likely in Arctic areas with poor sanitation (Bruce et al., 2016).

An outbreak of gastroenteritis occurred in Finland during July and August 2014. Water temperature during the outbreak was several degrees warmer than usual. The exceptionally warm temperatures and long duration of the heat wave are thought to have resulted in more people visiting beaches and possibly more exposure to the infectious viral particles in the water (Kauppinen et al., 2017).

One study investigated the association between heavy precipitation and waterborne outbreaks in Denmark, Norway, Finland, and Sweden from 1992 to 2012. Outbreaks reported to national surveillance system registries and daily precipitation data were compared. An increase in heavy precipitation during the preceding weeks corresponded with an increase in waterborne outbreaks (Guzman Herrador et al., 2016). Many cases of gastroenteritis, however, go unreported, so the actual number is waterborne infections is unknown (Guzman Herrador et al., 2016).

3.3.2. Vibriosis

Vibriosis is caused by *Vibrio* spp. bacteria. In the Arctic, heat waves correlate with more outbreaks of vibriosis, particularly when sea surface temperature is increased. Heat waves in Finland and Sweden in July 2014 positively correlated with abnormal sea surface temperatures and reported cases of vibriosis (Baker-Austin et al., 2016). Despite the sporadic and underreported nature of *Vibrio* infections and lack of detailed “trace-back epidemiologic data”, the reported cases came from coastal medical centers or from patients who had recent exposure to seawater, suggesting a high correlation between disease and exposure to seawater (Baker-Austin et al., 2016). In Canada, similar results were observed with comparing sea surface temperature and cases of *Vibrio parahaemolyticus* (Vp) infection. An increased risk of Vp was observed with sea surface temperatures exceeding 14.3 °C (Konrad et al., 2017).

Another study investigated the relationship between sea surface temperature and *Vibrio* infections around the Baltic Sea in Sweden from 2006 to 2014, and explored how the ECDC (European Centre for Disease Prevention and Control) Vibrio Map Viewer can use environmental data to inform public health. A statistically significant relationship was found between *Vibrio* infections and sea surface temperatures about 16 °C. Based on the data and the ECDC Vibrio Map Viewer, prediction models suggest that there is an increased risk for *Vibrio* infections with climate change, and increasingly warmer seas (Semenza et al., 2017). However, the map does not take into account factors contributing to *Vibrio* ecology apart from sea surface temperature and salinity (i.e. nutrient concentrations, algal blooms) or factors contributing to a person's susceptibility to infection (i.e. immunity, open wounds, travel) (Semenza et al., 2017).

3.3.3. *Escherichia coli* O157

One study investigated the association between weather, livestock density and *E. coli* in Alberta, Canada. *E. coli* O157 cases were found to have a strong correlation with cattle density. Weather variables, including monthly cumulative rainfall, monthly cumulative precipitation, mean temperature, and extreme rain days, were not found to have a significant correlation with *E. coli* O157 cases (Bifolchi et al., 2014).

3.4. Predicting and modeling effects of climatic factors on infectious diseases

In addition to the articles investigating the relationships between climatic factors and specific infectious diseases in the Arctic, several articles investigated the methods for assessing impacts of climatic factors on infectious diseases rates. These articles explored the vulnerability and resilience to changes in infectious disease rates in the Arctic, attempted to predict which infectious diseases would be the most affected, and looked at how infectious disease incidence could be a quantifier for climate related impacts, respectively. As the Arctic

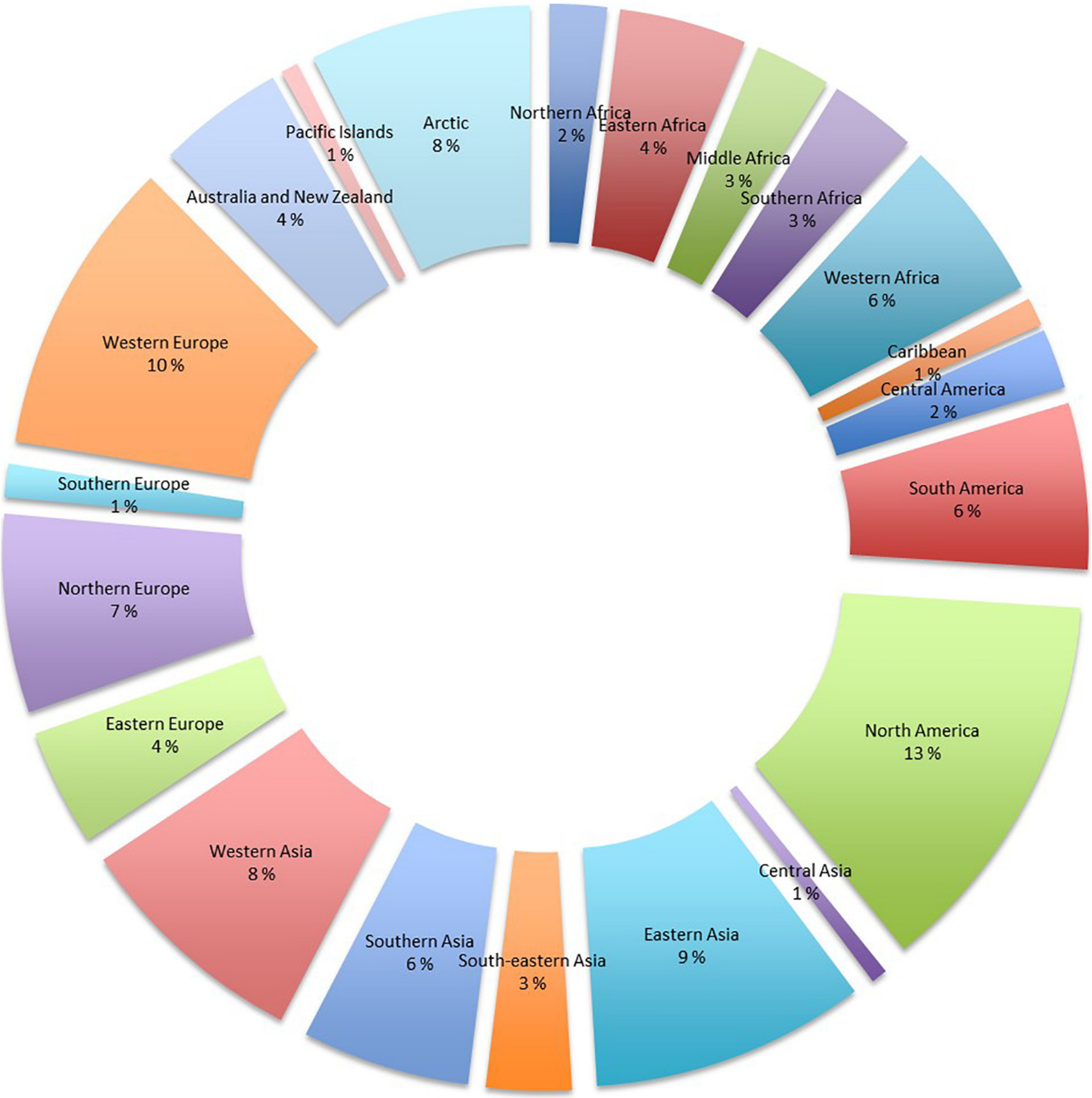

Fig. 2. Percentages of PubMed results from searches about climatic factors and infectious diseases by region. There were a total of 58,563 search results. Search terms for each regional search are available in Supplemental Material List S2: Search terms for Fig. 2.

changes, predicting the effects on human health is important to minimize human and economic costs.

One study established a method for determining European countries' vulnerability to infectious diseases due to climate change using computer modeling. The computer models were based on temperature, precipitation, socioeconomic, and political conditions. The vulnerability and impact of infectious disease transmission resulting from climate change for Scandinavian countries is predicted to be low because of their high adaptive capacity (public health and health care infrastructure, education, distribution of resources, and treatment costs). This suggests that Scandinavian countries will be more resilient and less impacted (Suk et al., 2014). Another study attempted to develop a method for determining which infectious diseases would most likely be affected by climate. Using criteria including: "severity of disease in the human population, human case fatality rate, type of climate that the pathogen can tolerate, and likely incidence of human disease in Canada," experts ranked potential emerging pathogens. Giardiosis, West Nile virus and Chagas disease were ranked highest due to ability to withstand a variety of climates and the number of ways the disease can be transmitted. Coccidiodomycosis and cholera were deemed the least likely to be affected by climate (Cox et al., 2013).

Another study attempted to develop a list of key indicators that could be used to quantify the health impacts of climate change in Canada (Cheng and Berry, 2013). The authors identified eight key indicators but emphasized the need for further development and models. The eight indicators are: "excess daily all-cause mortality due to heat, premature deaths due to air pollution (ozone and particulate matter), preventable deaths from climate change, disability-adjusted life years (DALY's) lost from climate change, daily all-cause mortality (trends associated with heat and air pollution), daily non-accidental mortality (trends associated with heat and air pollution), West Nile virus infection incidence (in humans), and Lyme borreliosis incidence (in humans)" (Cheng and Berry, 2013).

Another study investigated the criteria that can be used to prioritize diseases that will likely emerge or re-emerge in Canada as a result of climate change and assessed the impacts of those diseases. Climatic conditions including annual increase in temperature, summer temperature, winter temperature, summer precipitation, and winter precipitation were evaluated along with determining whether suitable host and vector species are present in Canada. Annual increase in temperature, increase in summer temperature, and increase in summer precipitation are the climatic factors of greatest concern. Based on these evaluations, vector-borne diseases will be the most affected by climatic factors, followed by food- and waterborne diseases. Airborne diseases are not expected to be greatly influenced by the climatic factors (Cox et al., 2012).

Amuakwa-Mensah et al. (2017) analyzed the effect of socioeconomic factors and climate variability on infectious and parasitic disease patients in Sweden from 1998 to 2014. Multiple diseases were assessed in relation to climatic and socioeconomic factors including temperature (winter and summer), average temperature, precipitation, income, education, health personnel, population density, and immigration. Winter temperatures had a non-linear effect on infectious diseases. Precipitation positively correlated with the number of cases. Education and health personnel were negatively correlated with the number of patients. Population density and immigration had a positive effect on the number of patients. The relationship between patients' income and infectious and parasitic diseases followed an inverse "U" shape when mapped in dynamic analysis. There was a high correlation between low income and a high number of patients, but at high incomes, the number of patients decreased (Amuakwa-Mensah et al., 2017).

In the Siberian and Far Eastern Federal Districts, a study on increased tourism since 1997 predicted that human migration and tourism were increasing the risk of exposure for influenza, measles, cholera, poliomyelitis, and Dengue fever in these districts (Noskov et al., 2015).

These articles show that effects of climate change on human health is a growing concern and there is a growing need for research to not just identify associations between infectious diseases and climatic factors, but to use the available data to predict future changes.

3.5. *Global research regarding climatic factors and infectious diseases*

Fig. 2 illustrates the percentages of search results about climatic factors and infectious diseases in various regions. All search terms for each region are available in Supplemental Material List S2: Search terms for Fig. 2. The results suggest that about 7.5% of the research done in this field is from the Arctic.

4. Discussion

The majority ($n = 29$, 67%) of the articles included in this review investigated the relationship between climatic factors and zoonotic/vector-borne diseases in the Arctic, particularly tick-borne diseases, anthrax, and tularemia. The warming climate affects the habitat of the zoonotic animal or vector and subsequently expands or improves its ability to spread disease. In Russia, the habitat for *I. ricinus* is expanding northward and eastward, exposing regions previously inhabitable. Preventative actions including vaccination, acaricide treatments, and education positively reduce risk of tick-borne diseases. Vigilant monitoring of vector populations is also beneficial to predicting potential human cases. While there is also a correlation between warmer temperatures and mosquito survival, the articles selected for this review suggest that most Arctic regions are still mostly inhospitable to spread West Nile Virus or CHIKV because the arctic climate prevents adequate transmission time. The southern regions of Arctic countries, however, are at a higher risk for increased mosquito vector populations and subsequent disease transmission. Outbreaks of tularemia in Russia coincide with expansions in northern red-backed vole, common red-toothed shrew, water-vole, and blood-sucking insects' populations. Models in Sweden successfully used climate data, vector and animal populations to identify high risk-regions for outbreaks. Anthrax outbreaks in the Russian Arctic are coinciding with exposed cattle burial ground due to thawing permafrost and contact with infected animals and animal products. Low vaccination compliance is the greatest risk for anthrax outbreaks though. Studies on Puumala virus and rabies both suggest that the best models for predicting outbreaks utilize population and ecological data. While there is an association between climatic factors, climate change, and disease incidence for vector-borne and zoonotic diseases, the studies included in this review suggest that the climatic factors' effect on the habitat and range are the most influential.

Only two articles (5%) included in this review focused on airborne diseases. Low humidity and low temperature coincided with increased risk of influenza and human rhinovirus, however co-factors like spending more time indoors could have also contributed to the risk. From the studies in this review, there is a weak connection between low temperatures and humidity and airborne disease due to the abundance of co-factors.

Articles about food- and waterborne diseases accounted for 14% ($n = 6$) of the articles included in this study. Warm temperatures contributed to ideal conditions for *Vibrio* spp. to thrive, resulting in elevated numbers of vibriosis case and people spending more time outside. A strong connection between warmer sea surface temperatures and elevated risk for vibriosis emerged from the articles included in this review. However, pre-existing sanitation and water supply issues may also play a significant role in the food- and waterborne illnesses in the Arctic.

Additional articles estimating the impact of climate change on infectious diseases ($n = 6$, 14%) in the Arctic stress the importance of using climate data, vector and zoonoses ecology, socio-economic data, and expert opinion to predict consequences and minimize costs. Using research about the association between climatic factors and infectious diseases, particularly zoonotic, vector-borne, and waterborne, allows for predictions in vulnerability, health impacts, and changes in disease emergence.

4.1. *Publication analysis*

The articles included in this review were compared to articles in a previous review (Hedlund et al., 2014) and analyzed by type of infectious disease, publication year, and country the research focused on to look for trends and gaps in knowledge. There were 29 articles included from the previous study and 43 included in this review (Hedlund et al., 2014). All articles were published between 1970 and 2017.

Collectively, 72 articles (43 from this review, 29 from the previous study) were reviewed to look for trends in the countries being researched and what types of diseases were being studied. Because the previous review was likely the first review in this field (Hedlund et al., 2014), the articles were also analyzed to provide an overview of the research done regarding human infectious diseases and the changing climate in the Arctic. Fig. 3 illustrates how many articles were published about each country and the focus of that research. The majority of the articles published were from Russia (25, 37%) and Canada, (23, 32%), followed by Sweden (10, 14%) Finland (7, 10%), Norway (2, 3%), and Alaska (2, 3%). There were 3 articles published that focused on more than 1 Arctic country (4%). No articles were selected from Greenland or Iceland. Of the articles published by Russian authors, 4 were in English and 21 were in Russian. The majority of research is about zoonotic and vector- borne diseases (56%) and food- and waterborne diseases (25%) in Russia and Canada.

The articles included were published between 1970 and 2017. The majority of the articles were published after 2000, with 16 published from 2000 to 2009 and 53 published from 2010 until 2017. The results of this review reflect an exponential increase in the number of publications about infectious diseases in the Arctic and climatic factors. This trend is consistent with publications about human health and climate change (Verner et al., 2016). The relationship between climate change and health has been investigated since the 1990s (Ebi and Hess, 2017). A study from 2016 conducted a search investigating the volume of research in public health and climate change between 1990 and 2014 (Verner et al., 2016). The yearly number of publications in 1990 was low and remained below 1000 until 2003 (with the exception of 1996) when the number of publications began increasing exponentially

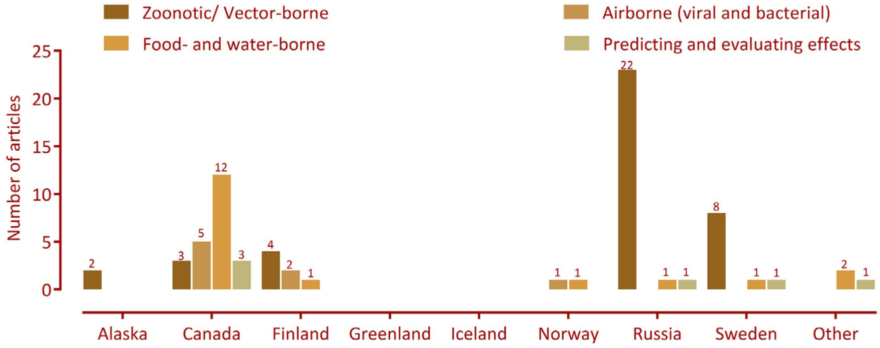

Fig. 3. The main focus of the 72 articles included in this review and a previous review divided by country (Hedlund et al., 2014). There were 43 articles from this study and 29 from a previous study (Hedlund et al., 2014). All articles were published between 1970 and 2017. Articles included in "Other" represent articles that include more than 1 country.

(Verner et al., 2016). In 2014 there were 6079 publications in PubMed related to the health impacts of climate change (Verner et al., 2016). The study revealed a positive trend in the number of publications, however a comparison between climate change and other important sectors (transportation, industry, economy, energy, and health) still shows that research into health is far behind (Verner et al., 2016).

4.2. Likely pathogens affected by climatic factors in the Arctic

A 2014 report, "Climate change and infectious disease in the Arctic: establishment of a circumpolar working group," listed *Brucella* spp., *Toxoplasma gondii*, *Trichinella* spp., *Clostridium botulinum*, *Francisella tularensis*, *Borrelia burgdorferi*, *Bacillus anthracis*, *Echinococcus* spp., *Leptospira* spp., *Giardia* spp., *Cryptosporidium* spp., *Coxiella burnetii*, rabies virus, West Nile virus, Hantaviruses, and tick-borne encephalitis viruses as "potentially climate sensitive pathogens of circumpolar concern" (Parkinson et al., 2014). When comparing the subjects of the 72 reviewed publications from this review and a previous review to the potentially climate-sensitive diseases listed, several trends and gaps emerge (Hedlund et al., 2014; Parkinson et al., 2014). There were 10 articles published about tick-borne encephalitis viruses (Chashchin et al., 2017; Haemig et al., 2011; Kokolova 2014; Lindgren and Gustafson, 2001; Noskov et al., 2015; Palo, 2014; Popov, 2014; Tokarevich et al., 2017; Tokarevich et al., 2011; Yasjukevich et al., 2013; Yastrebov et al., 2016), 9 about tularemia (Burmagina et al., 2014; Demidova et al., 2014, 2016; Desvars-Larrive et al., 2017; Meshcheryakova et al., 2014; Mesheryakova et al., 2014; Ostapenko et al., 2015; Pakhotina et al., 2016; Ryden et al., 2012), 6 about anthrax (Avitisov et al., 2015; Dugarzhapova et al., 2017; Kosilko et al., 2014; Popova et al., 2016; Prokudin et al., 2016; Simonova et al., 2017) 3 about Hantaviruses (Haredasht et al., 2013; Palo, 2009; Pettersson et al., 2008), 1 about West Nile virus (Giordano et al., 2017), 1 about rabies (Huettmann et al., 2017), 1 about *C. burnetii* (Bennet et al., 2006), and 1 about *T. gondii* (Tizard et al., 1976).

When comparing the subjects of previous research and this review, most of the identified pathogens are zoonotic or vector-borne (Hedlund et al., 2014). There were 4 articles about *Vibrio* spp., however *Vibrio* spp. are not included as a "pathogen of circumpolar concern." Studies from Alaska, Canada, Sweden and Finland however suggest that *Vibrio* spp. caused illnesses are associated with increases in sea surface temperature and heat-waves, making *Vibrio* spp. pathogens of "circumpolar concern." There were nine pathogens that were not directly addressed, and most cause gastrointestinal illness, where the causative agent may be difficult to identify.

5. Conclusions

Because the Arctic is warming at an unprecedented rate, research on the potential impacts on infectious diseases is paramount. Climatic factors can directly impact disease transmission, though most of the impacts are indirect, for example, changes in human behavior, vector ecology, or pathogen survival.

Tick-borne diseases, anthrax, and tularemia have a strong association with temperature and precipitation, albeit indirectly. Warmer temperatures have a strong association with increased disease risk because of the resulting changes in vector ecology, potential alterations in human behavior (i.e. more people spending time in the woods), and thawing permafrost exposing cattle burial grounds, increasing the risk that people will come into contact with the infected carcasses or thawed spores. The warming climate can lead to northward expansion of a vector, increasing the range of a vector and greater transport for the pathogen (Sonne et al., 2017). Warmer temperatures also may improve the chances an arthropod vector will survive through the winter and have habitable woodlands and vegetation for reproduction and development. Food- and waterborne diseases, including gastroenteritis and vibriosis are impacted by increased temperature, resulting in more people spending time at public beaches and increased growth of *Vibrio* spp. Although airborne bacterial and viral diseases have a complex relationship with co-factors, there is a link between temperature and humidity that warrants further investigation. Using the data from research about climatic factors and infectious disease rates can help experts predict upcoming outbreaks and estimate the impacts of climate change on health in the Arctic. Exploration into the social and economic factors impacting health in Arctic areas can be used to help predict impacts too. The articles in this review generally support an association between climatic factors (mainly warmer temperatures and increased precipitation) and infectious diseases in the Arctic, particularly for zoonotic and vector-borne diseases. However, preventative actions (i.e. vaccination, access to adequate water and sanitation, and surveillance programs) can reduce infectious disease risk, even if the risk for exposure increases.

From the articles in this review and from previous studies the majority of research appears to come from Russia and Canada, with little coming from Alaska, Norway, Iceland, and Greenland (Hedlund et al., 2014). Most of the articles in this review focus on zoonotic and vector-borne diseases, suggesting they will be the most impacted by the rapidly warming Arctic. The number of articles published in this field has been significantly increasing. The majority of articles published after 2000 suggest a growing interest on the effect climate change could have on infectious diseases in the Arctic and subarctic regions.

There is a growing need to compile available meteorological and health data from across the Arctic to continue to monitor how climate change will affect disease rates. Additionally, the growing number of tourists and immigrants from places where the pathogens of circumpolar concern are endemic adds additional risk. Increased prevention, vaccination, and education will be important in mitigating the effects of climate change on infectious disease rates in the Arctic. Additionally, monitoring and data compilation across the Arctic will help to predict and reduce economic and human costs across the Arctic.

One Health is a cross-disciplinary approach to considering the health of humans, animals, and the environment (Ruscio et al., 2015), which gives a move integrated, and holistic view of Arctic health. While more research is needed to address all of the factors affecting Arctic health, this review contributes to a deeper understanding of the research on human infectious diseases in relation to the changing Arctic climate.

The strengths of this review include using a systematic approach and multiple databases, including the Russian eLibrary.ru. Including the Russian database not only found more articles, but also helped to provide a more comprehensive overview of where research in this field occurs.

The limitations of this review include the language restriction, the rigidity of the inclusion criteria, and the search terms selected. Studies published in a language other than English or Russian were also excluded from this review. Many articles met two out of the three inclusion criteria (i.e. presented research on the Arctic and an infectious disease, but did not focus on the association with climate). The search terms used may have also limited the articles found for the review. Future reviews could use different keywords or perform searches in PubMed using keywords in addition to MeSH terms or expand the searches by using specific key words.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2018.09.042.

Funding

This work was funded by the European Union Horizon 2020 BG-2017-1 (2017–2022)—under Grant Agreement No: 773421-Nunataryuk (Permafrost thaw and the changing Arctic coast, science for socio-economic adaptation) (A.R., K.A.) and by One Arctic – One Health: Animal and human health in the changing climate project funded by Ministry of Foreign Affairs of Finland (Grant Agreement No. HEL7M0674–65) (A.R.; K.A.; A.O.). Additional funding was provided by Fulbright Finland and the Finnish National Agency for Education (A.W.).

Conflicts of interest

The authors declare no conflict of interest.

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