EXECUTIVE SUMMARY

Germany, home to over 1.5 million asylum seekers, spent 10.3 million euros (EUR) on compulsory medical screenings of new asylum applicants in 2015. The motivation and importance behind these clinical evaluations and infectious disease (ID) screenings is for both the sake of protecting patients/asylum seekers *and* the public at large[1]. However, discrepancies in medical evaluation protocols across the 16 autonomous federal "states" / *länder* (given discretion in pathogen-specific screening) has resulted in excess spending without supportive cost benefit analyses. An economic evaluation of cost differences between states for fiscal year 2015 revealed exorbitant expenses, particularly in states employing comprehensive / "extended" screenings, and researchers are calling for an evidence-based approach[1]. The *weniger ist mehr* "Less is More" policy recommendations make use of documented and contemporary "best practices" in the field of refugee medical screenings (and specifically tuberculosis testing recommendations), and would result in a minimum of 3.1 million euros saved related to improved guidelines for ID screening, with little to no increase in public health risk[1].

BACKGROUND

Refugees & Germany

As the result of regional humanitarian crises, poverty, social deprivation, and most notably the war in Syria, the European Union (EU) has experienced a high influx of asylum-seekers and migrants in recent years[2]. In 2015 the EU received approximately 995,000 asylum applications, (twice as many as the previous year) with Germany receiving the largest portion, around 175,000 (equal to about 18%)[3]. It was also in 2015 that Syrians represented the largest group of asylum seekers in the EU, with nearly 90% of first quarter 2016 applicants registering in Germany[2]. The system used to manage asylum applications known as *Erstverteilung von Asylbegehrenden*, or "Initial Allocation System for Asylum Seekers" (EASY) helps distribute and track applicants[2] quasi-randomly according to algorithms[1, 3] and state quotas[1, 31]. During this first official step in the asylum-seeking process applicants are registered with an identification number[1, 3] but no demographic or socioeconomic information is collected. Only minimal information is required and basic data on receiving state and country of origin are entered into the system. At this point each asylum-seeker need only record his or her intention to formally 'apply' for asylum once he or she receives state placement. The application process happens at local/regional "arrival centers" within each state that serve as branches of the Federal Office for Migration and Refugees (BAMF) within

assigned stated. Upon arrival at the center in addition to recording personal data, completing an application, and an interview, a medical examination is conducted.

Refugees & Communicable Disease

Due to the fragmented contextual factors leading to displacement and their "journey," (often marked by food shortage, lacking medical attention, poor hygiene, overcrowding, exploitation, accidents, violence, and even potential exposure to extreme temperatures), Asylum seekers, like many migrants, are particularly vulnerable populations[4, 5]. In fact, refugee camps are often fertile centers for disease epidemics. Thus, Germany, like many nations, have policies in place for medically screening asylum seekers. And often nations are motivated to allocate funds to particularly screen for IDs that by nature, being communicable, could pose a threat to the public.

And though there is no short supply of infectious diseases of which refugees are particularly susceptible, tuberculosis (TB) has been documented to be the most prevalent infection among asymptomatic immigrants and refugees with a prevalence of 40-71%[4]. Research out of Spain, looking at transmissible diseases among migrants entering Europe found that the most frequent disease was latent tuberculosis (LTBI) lending to the importance of disease screenings of refugees to manage what will surely be a much larger public health problem if unaddressed[1, 7]. In Europe, over a quarter of the tuberculosis cases in are diagnosed from foreign born migrants[8]. And in 2015, after the arrival tens of thousands of Syrian refugees Germany saw an annual incidence increase of over 1,000 new active tuberculosis cases. Since 2015, this incidence rate has remained almost unchanged, at a rate of 7.2 cases per 100,000 population, with foreign born nationals having 19 times higher incidence than German citizens, respectively: 42.6 vs 2.2 cases[9]. For this reason Germany, along with 21 other European nations, has laws around the screening of active or latent tuberculosis among migrants[8].

The German Health Care System

Germany, delineated by specified eligibility, offers universal health care coverage to its residents, citizens, and undocumented migrants. Social security / contribution-based coverage called *gesetziche krankenversicherun* / "sickness funds," accounts for the majority of health care coverage with roughly 10% of the substitutive coverage gap coming from private insurance options[10]. Refugees and undocumented immigrants are intended to be covered by social security only in the instances of acute illness or pregnancy and childbirth.

The Federal Joint Committee (G-BA), through representing the individual associations receiving sickness funds and disbursing services is main avenue for

regulation when it comes to health care in Germany[10]. The health care expenditure comprises 11.2 percent of the national GDP, as of 2014[10].

Germany ranks well, seventh out of 35, with regards to the criteria set forth by the Euro Health Consumer Index looking at outcomes, generosity, and wait times[11]. But with the influx of refugees into the country since fall of 2014 the health care system has faced sudden demands for acute care[12]. The national health care system of Germany now faces a challenge for meeting the needs of these asylum seekers, a population expected to have now hit 1.5 million[13]. What complicates a now strained resource system is the added complexity of providing care to a vulnerable group in which foreign linguistic socio-cultural circumstances factor into the challenges faced in the system, subsequent health outcomes,and quality of provided care[13]. The *Asylbewerberleistungsgesetz* / "Asylum Seekers Benefit Act" (ASBA), helps asylum seekers receive support (in-kind and as cash) for accommodations and heating, food, clothing, personal hygiene, medical services etc. However, there is a great deal of discretion with the provision of these services as enforcement power lies at regional and local levels[14, 15, 16].

Political Bodies, Institutes & Organizations

When it comes to the monitoring, provision, and regulation of health care specifically around infectious disease and migrant populations- a variety of actors at varying levels come into play. Because the 1.5 million asylum seekers[13] receive benefits and limited health care coverage through the Statutory Health Insurance (SHI) system, receiving "sickness funds," the Federal Joint Committee / G-BA, is a critical actor in this policy area[10]. The Federal Joint Committee / G-BA is composed of a group of public health agencies that lead regulatory changes within the health care field in Germany. Though parliament can establish legislation around health care, and the Ministry of Health can issue decrees, the G-BA is seen as the highest decision-making body around physicians, dentists, hospitals, and health insurance funds in Germany; which includes quality assurance of both in and outpatient care[15, 16].

The Federal Joint Committee has 13 voting members, an impartial chair and two impartial members and representatives from the Federal Association of Statutory Health Insurance Funds, the German Hospital Federation, the National Association of Statutory Health Insurance Physicians (and Dentists), as well as five patient representatives[10, 15, 16]. The G-BA has eight working groups around topics such as Pharmaceuticals and Need Related Planning[15, 16]. Typically these working committees will put forward a report and recommendation that will then be evaluated by the Institute for Quality and Efficiency (IQWiG). The IQWiG is a foundation legally charged with supporting the G-BA through evaluating the cost-effectiveness of proposed

directives[15, 16]. The directives of the G-BA are legally binding however, it is ultimately the responsibility of governmental officials and the Ministry of Health to supervise and audit the decisions and guidelines made by the G-BA[15, 16].

Section 62 of the German Asylum Procedure Act requires asylum seeking applicants to undergo a medical examination to assess for infectious disease, which may include chest x-rays, blood work, and stool samples[17,18]. Section 36(4) of the German Law on the Prevention and Control of Infectious Diseases "Infektionsschutzgesetz" (IfSG) specifically requires the evaluation of tuberculosis. The responsibility for carrying out these policies fall to the individual 16 federal states of Germany. All examination costs and required treatment are covered by the state. The results of the compulsory medical examination have no bearing on their application for asylum, however if they refuse treatment for a diagnosis that poses a risk to public health this may result in their expulsion[19]. The Robert Koch Institute (RKI), an agency under the Ministry of Health responsible for maintaining disease registries and controlling infectious diseases, closely monitors positive cases of tuberculosis[9]. RKI also maintain disease registries for specific diseases[9]. The RKI reports that in 2016 there were 5,915 cases of TB[9]. And 74.3% of these cases were detected by active case finding mainly through medical screenings of asylum seekers[9].

In addition to the obvious players of the Federal Joint Committee (and more specifically the committee on Need Related Planning), the Institute for Quality and Efficiency, the Ministry of Health and the Federal Office for Migration and Refugees, due to the nature of the policy issue at hand, and the movement of refugees across international borders, combined with the global impact of infectious disease outbreaks, other relevant entities include the World Health Organization (WHO), the UNHCR, the European Centre for Disease Prevention and Control (ECDC)[1, 20], the TB Advocacy ad-hoc Working Group of the European Respiratory Society (ERS)[8, 21], and local nonprofits working with refugees. Other specific institutions conducting research on infectious disease and seroprevalence of pathogens in Germany include: The Department of Clinical Immunology and Rheumatology, the German Center for Infection Research, the German Center for Lung Research, the Center for Infectious Diseases and Infection Control, and the Institute of Tropical Medicine.

POLICY OPTIONS & RECOMMENDATIONS

All asylum seekers in Germany undergo compulsory medical screening. This is after they are dispersed across the 16 federal states according to an algorithm and quotas. However, each state varies in medical screening protocols, and this

heterogeneity lends to strange and cost-ineffective practices when assessed on a national level. In fact, one study out of the Department of General Practice and Health Services Research at the University Hospital in Heidelberg and the School of Public Health at Bielefeld University monetized the costs relative to expected yields for medical screenings of asylum seekers and analyzed just how costly differences in screening methodology was for Germany[1].

Policy Options:

1. Let present trends continue, allowing each of the 16 states autonomy over screening practices of asylum seekers.
2. Implement policy coordinating more consistent and cost-effective protocols for medical screening of asylum seekers.

Option 1: Present Trends

As mentioned above, currently there is significant differences in screening practices across the 16 federal states of Germany with regards to the medical examinations required for asylum seekers. Outside of general physical and health evaluation, by law- tuberculosis is the only required infectious disease that must be and is consistently screened for across all states, for people ≥16 years[1, 17, 18]. However, for everything else including human immunodeficiency virus (HIV), hepatitis B, syphilis, and enteric pathogens and parasites such as shigella or salmonella, no evidence-based protocol currently (and formerly for that matter) guides medical decisions pertaining to these compulsory medical examinations[1,17, 18]. The result is that thousands of asymptomatic asylum seekers are undergoing likely unnecessary and cost-ineffective screenings[1]. Of the 441,899 asylum seekers in Germany on record for 2015 88% were screened for TB, 22.9% for enteropathogens, 16.9% for hepatitis B, 13.1% for syphilis and 11.3% for HIV. The total cost for these screenings came to 10.3 million euros. The economic analysis conducted by Bozorgmehr et al. categorized the style of screening practices of each state into three categories: A) Exclusive screening for TB in asylum seekers ≥16 years of age (the minimum required by law); B) Extended screening of pregnant women and/or asylum seekers ≤ 16 years of age; and C) Extended screenings for additional infectious diseases other than TB. The main result from this study was that states with Category C extended screening methods had 2.84 times the per capita costs than Category A screening states[1]. This study revealed unnecessarily high costs for screening practices and called for evidence-based approaches, such as those formulated the Canadian Collaboration for Immigrant and Refugee Health, to guide and implement smarter legislation better responding to comparing accrued costs against gained

benefits[1]. With communicable diseases such as enteropathogens, HIV and hepatitis B, the benefits relative to program costs are rather low when compared to the societal benefit of detecting, treating and preventing the more easily airborne spread of tuberculosis[1, 7]. This is especially true given the high prevalence of multi-resistant organisms (MRO) in refugees' country of origin and the very expensive and critical growing concern with multidrug-resistant tuberculosis (MDR-TB)[7, 22].

***Option 2*: Recommendations**

Supported by the highlighted economic analysis[1] and extensive current literature related to ID best practices for refugees- I strongly recommend that the the below outlined and attached "Less is More" / *weniger ist mehr* program/protocol for consideration and review by the Need Related Planning Committee of the Federal Joint committee (G-BA). Naturally the Institute for Quality and Efficiency (IQWiG)[10, 15, 16], will thoroughly vet and corroborate the viability of my recommendations.

The main aspects of revising the current medical screening protocols centers on two main items: 1) consistency across all 16 federal states, and 2) defaulting to category A extended ID screening related to TB only unless otherwise indicated symptomatically or based on increased risk in country of origin. I specifically recommend the continuation of all asylum seekers ≥ 16 years be tested for TB regardless of symptomatology. I furthermore recommend the implementation of proven cost-effective options over traditional tuberculin skin tests (TSTs)[23, 24]. Depending on age and pregnancy status, please see Appendix 1 for diagnostic tools indicated to be most medically appropriate and cost effective.

The main emphasis in this protocol is the use of interferon-gamma release assays (IGRAs), an improved blood sample test that can differentiate antibodies of BGG/TB vaccines and latent infection (LTBI) or active TB disease, drastically increasing its cost-effectiveness over antiquated TST screenings[24], which are also not found to be appropriate for refugees due to time lag in diagnosis and the high mobility of this population[8, 23]. However, IGRAs are not indicated for children < 5 years[25]. Chest X-rays remain a standard in symptomatic diagnosing and are found to be cost-effective. Contact tracing and sputum screening have now been shown to be cost-ineffective and outdated since the introduction of IGRAs[24, 26, 27]. In fact, even though not screening is *always* crudely cheaper than screening, IGRAs are so effective they've proven to be both more cost-effective when compared to traditional options and are extremely cost-effective against not screening at all[27]. Furthermore, IGRAs are said to have strong evidence specifically for high risk groups, such as refugees[24].

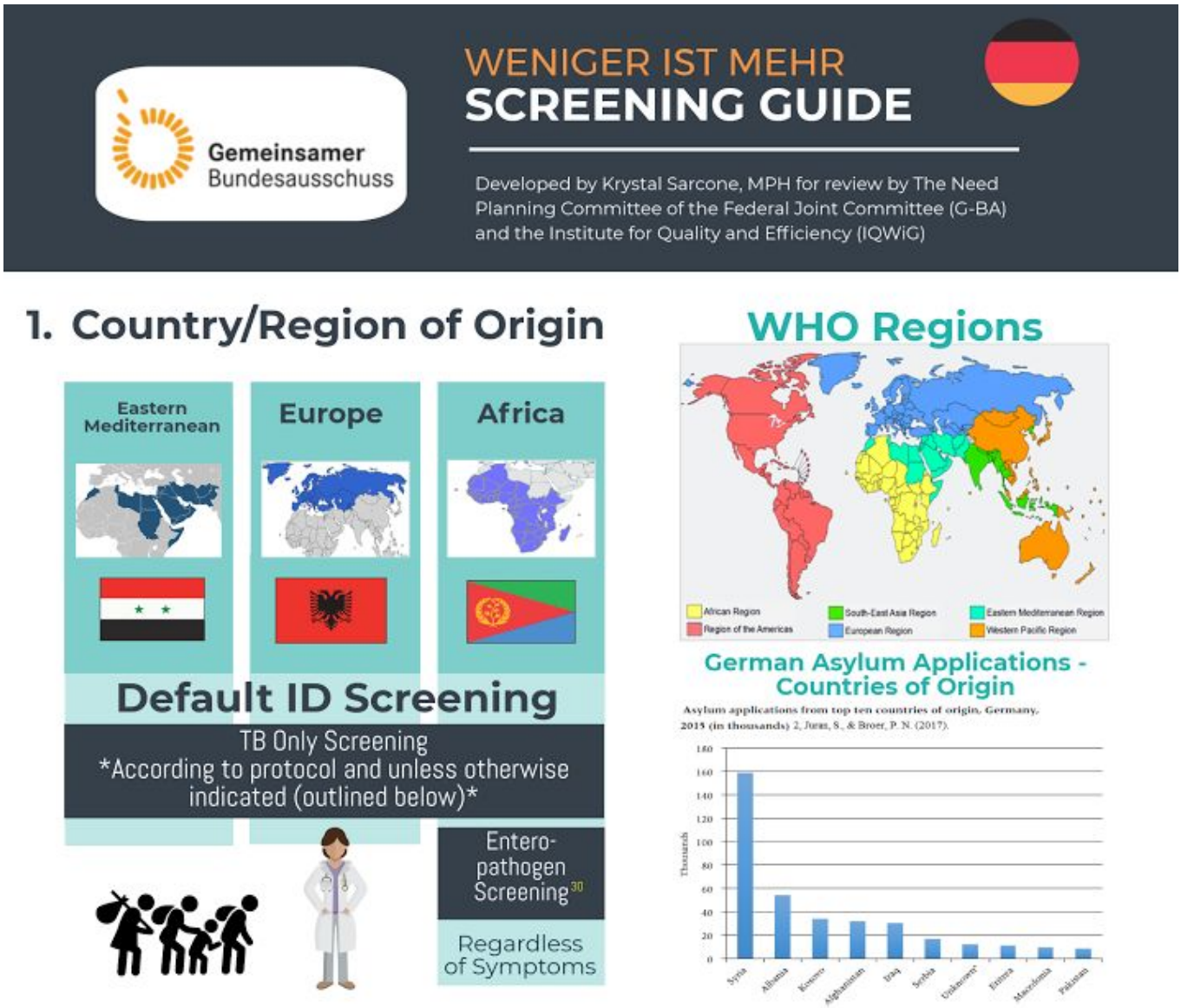
Due to the high prevalence of multi-resistant organisms (MRO) in many the refugees countries of origin, MRO screening or drug susceptibility testing (DST) is highly recommended and thus I include the use of GeneXpert for all positive results of latent and active TB[5, 6, 21]. If patients present with additional symptoms providers retain discretion and the responsibility to screen for enteropathogens and other IDs in accordance with typical diagnostic guidelines. My recommendations includes flexible advice to physicians to to be mindful of current literature supporting seroprevalence and incidence rates among refugees from specific countries of origin. For example: 1) despite a polio outbreak in Syria in 2013, Syrian refugees entering the EU are at very low risk for active polio[1* 22] and other enteropathogens[29], 2) sub-saharan africans are most at risk for enteropathogens such as filariasis[7] and vector-borne malaria[25], 3) adult Syrian refugees are well immunized against Measles Mumps and Rubella (MMR) however only about 68.9% of Syrian refugee children and adolescents have complete immunity[28]. Decisions for screening such other IDs should be made with symptomatic or sound medical rationale and in consideration of true risk and likelihood as demonstrated with the above examples. I also highly recommend asylum seeking patients that have self-reported or been diagnosed with highly correlated comorbid conditions, such as HIV+, be screened as if symptomatic and follow indicated active TB line of testing.

If such changes were made to the compulsory medical screenings of asylum seekers, I estimate the nation would save at least 3.1 euros with little to not added risk to individual mortality or threat to the public's health[1].

[1*] A study assessing analyzing stool samples from 629 Syrian asylum seekers less than three years of age found that 14.8% were positive for enteroviruses. However no wild-type poliovirus was found, only Sabin-like in only nine cases, indicating an OPV (polio vaccination) strain[22]. This indicates that so far there is low risk associated with the influx of Syrian refugees, with regards to spreading active polio[22].

APPENDICES

Appendix 1: Infographic of Proposed Screening Protocol



2. TB Screening Protocol

	Asymptomatic	Symptomatic
 Adults / ≥ 16 Years	CXR	CXR & IGRA
 Pregnant Women	-	IGRA
 Kids < 16 but ≥ 5 Years	-	CXR & IGRA
 Children < 5 Years	-	CXR & TST

- **Treat highly correlated self-reported or diagnosed co-morbid cases, such as HIV+ asymptomatic and follow above guidelines**
- **All positive diagnostic tests should have follow up GeneXpert analysis!**

KEY & SUPPORTIVE DATA

TST = tuberculin skin test and has been used for nearly a century, also known as PPD test. With the onset of IGRA, TST is no longer the preferred diagnostic tool (reactive results from BBG vaccine), is often cost-ineffective in comparison to IGRA and is certainly not idea for refugees due to time lag with diagnosing.
CXR = Chest X-Ray used to detect active pulmonary TB. Is an effective tool for diagnosing active cases and often positive TB cases require both an TST or IGRA with a chest xray.
IGRA = due to advances in .... allows this blood test to detect antibodies, not to be confused with those from the BBG / TB vaccine. IGRA-only strategies are more cost effective than TST-IGRA and all-non IGRA screening options. However, IGRA is not appropriate/indicated for children less than 5 years.
GeneXpert - using a sputum sample, with a turnaround time of 2 hours, GeneXpert is a molecular test analyzing the DNA and gene mutations of TB bacteria and can determine resistance to the drug Rifampicin, a critical detail in predicting drug-resistance TB treatment options.

3. Additional ID Screening Protocol

All additional ID screening should only be done in line with current medical practices and conducted on discretion after reviewing a medical history, physical examination, self reported and observed symptoms, e.g. asylum seekers with origin countries in sub-Saharan Africa should be screened for malaria[25].

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