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# **RESEARCH ARTICLE**

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# Illegal gold miners in French Guiana: a neglected population with poor health

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# Abstract

**Background:** In French Guiana, a French overseas territory in South America, 6 to 10 thousands undocumented persons work illegally in gold mining sites in the Amazonian forest. Precarious life conditions lead to poor health but few data exist on the health status of illegal gold miners in French Guiana. The objective of this article was to describe the sociodemographic and health status of this vulnerable population.

**Method:** A prospective cross-sectional survey was conducted in 2015 on gold mine supply sites at the border between French Guiana and Suriname. Health status was assessed through medical examination, past medical history, haemoglobin concentration, and HIV and malaria testing. A questionnaire was used to collect data about the migration itinerary and life conditions on mining sites.

**Results:** Among the 421 adults included in the study, 93.8% (395/421) were Brazilian, mainly from Maranhão (55.7%, 220/395), the poorest Brazilian state. The sex ratio was 2.4. Overall, 48% of persons never went to school or beyond the primary level. The median time spent in gold mining was quite long (10 years), with a high turn-over. One third of the surveyed population (37.1%, 156/421) had high blood pressure, and only two had a medical follow-up. Most persons had experienced malaria (89.3%, 376/421). They declared frequent arboviroses and digestive disorders. Active leishmaniasis was observed in 8.3% of gold miners. Among women, 28.5% were anemic. Concerning HIV, 36.6% (154/421) of persons, mainly men, never got tested before and 6 were tested positive, which represented an HIV prevalence of 1.43% (95%CI =0.29–2.5).

**Conclusion:** These findings support the hypothesis that mining in remote areas is linked to several specific illnesses. Theoretically, gold miners would be presumed to start their economical migration to French Guiana as a healthy group. However, their strenuous working and living conditions there lead to poor health caused by infectious and non infectious diseases. This description of their health status is precious for health policy planners in French Guiana given the importance of controlling communicable disease, and the severity and range of specific illnesses acquired by this neglected population.

**Trial registration:** Clinical trial registration PRS N° NCT02903706. Retrospectively registered 09/13/2016.

Keywords: Gold mining, French Guiana, Neglected population, Global health, Transborder, Hypertension, HIV, Malaria

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# Background

French Guiana (FG) is a French overseas territory located in South America between Suriname and North of Brazil. Although the gross domestic product (GDP) is half that in mainland France (Insee), FG has a higher living standard than neighboring countries. The population of 250,000 inhabitants is composed of Creoles, Maroons, Amerindians, "metropolitan" from mainland France, and immigrants mainly from Caribbean and South America. Most live on the coastal area of this vast territory covered at 90% by Amazonian forest. About 20% of the population lives along the rivers inside the territory. Economical activity is lead by the European Space Center based in Kourou, then fishing, forest exploitation and gold mining activity. The gold richness of the soil was discovered in the middle of the nineteenth century [1]. Initially, exploitation was non industrial and varied according to gold prices. The soaring gold prices in the 1980's and the development of new technologies were followed in the 1990's by a boom of gold mining activity [2]. Alongside the legal activity, illegal gold mining increased drastically, attracting poor workers from neighboring countries. It is estimated that each year 10 tons of gold were extracted illegally while only 1 to 2 tons were extracted legally [3]. It is also estimated that there are about 6 to 10,000 illegal miners working in approximately 600 gold mining sites in the French Amazonian forest [4]. The two gold extraction types, alluvionnary or wells, are destructive for the environment with deforestation, mercury (used for gold particles recovery) pollution and river contamination [1, 5]. Local populations pay a heavy toll, especially Amerindians [6, 7]. A military response was implemented in 2002 with the"Anaconda" operations then "Harpie" operation in 2008 aiming to destroy the logistical chain and supplies [8, 9]. But the borders, represented by rivers and the vast Amazonian forest do not facilitate illegal gold mining control in FG. Illegal gold miners, also called "garimpeiros", are mainly Brazilian [10]. They live deep in the Amazonian forest, with exhausting work and poor hygiene conditions [11]. Access to emergency care is free in French Guiana, in the three hospitals in the main coastal cities as well as in health centers spread along the rivers where the population lives. But the remoteness of the mining sites, the boat costs and the fear of law enforcement hamper effective accessto care. Several outbreaks have been documented in this specific population in French Guiana: influenza A, shigellosis, beriberi, with a high morbimortality rate reflecting the poor health of this population [11, 12]. Malaria also mainly affects gold miners in French Guiana, as in others countries of the Region [13–16]. Throughout the world, many studies have shown the impact of gold mining activities on health [17–21] but to date, there is no exploratory study on global health status of this specific population in FG.

A study was set up in 2015 to assess the malaria epidemiology in illegal gold miners working in French Guiana [10]. Living far from the health care system in the Amazonian forest, this precarious population is not easy to access because of logistical, administrative and security issues. Capitalizing on human resources and funding for the malaria study, further secondary objectives were added in order to assess the global health of this neglected population.

The aim of this paper was to describe the population of illegal gold miners working in French Guiana, their way of life, and identify challenges to their health care.

# Methods

#### Study design

The study was cross-sectional, multicentric and observational. It was conducted between January and June 2015 at resting sites along the Suriname-French Guiana border.

#### Settings

Because of logistical limitations, legal issues and security concerns, recruitment was made at "resting sites" which are spread along the borders. These sites are structured as wooden shacks that are built around bars or shops. *Garimpeiros* use these places to rest and to fulfill their needs for supplies, medical care or leisure.

#### Study size

Designed for malaria assessment, the needed sample size was 387 for an expected *Plasmodium* prevalence of 50%.

# Participants

The inclusion criteria were being over 18 years of age, working in illegal gold mining in FG, being at the resting site for less than 7 days, and accepting to participate in the study. Recruitment was made using the snow-ball effect [22]. After recording the informed consent, a blood sample was taken for malaria diagnosis, haemoglobin measure and an HIV test.

#### Variables

A structured questionnaire was administered by a nurse with an interpreter to collect sociodemographic data, and data concerning the way of life on the mining site, movements, health problems and medical history. Medical examination recorded blood pressure (after a minimum of 15 min of rest and lying down), heart auscultation, presence of diarrhea, splenomegaly, oedema and active leishmaniasis lesions. Hemoglobin was measured with the HemoCue<sup>®</sup> system which was calibrated

World every week. According to the Health Organization (WHO), anemia was defined as haemoglobin below 130 g/l for men, below 120 g/l for women and below 110 g/l for pregnant women [23]. Blood pressure (BP) was measured twice with a wrist monitor after resting. It was classified according to European recommendations [24]: normal (systolic BP (SBP) <140 mmHg, diastolic BP (DBP) < 90 mmHg), grade 1 (140 < SBP < 160, 90 < DBP < 100), grade 2 (160 < SBP < 180, 100 < DBP < 110), and grade 3 (180 < SBP, 110 < DBP). Diarrhea was defined as currently passing three or more stools per day. Two dry blood spots (DBS) on filter paper were sent to the virology department of Bichat Hospital in Paris, France, for HIV testing. After DBS elution, HIV serodiagnosis was performed with a 4th generation ELISA assay (Architect HIV Ag/Ac Combo, Abbott Diagnostics, IL, USA). Positive samples were confirmed with an HIV-1 Western Blot assay (New LAV Blot 1, Biorad, Marnes-la-Coquette, France). We performed Immunocomb II HIV1/ 2 BiSpot test (Alere, Jouy-en-Josas, France) to discriminate between HIV-1 and HIV-2. An appointment at a French health center was given to all participants to get the results, as well as a mosquito-net and condoms.

#### Statistical methods

Descriptive data analyses were carried out using Stata12 software (College Station, Texas, USA). Bivariate analysis used the Chi-Squaretest, t-Student or Kruskall-Wallis tests depending on the type of variable. All statistical analyses used a 5% significance level. Data were mapped with QGIS software. GDP data come from the World Bank online.

#### Ethical and regulatory approvals

As the recruitment took place on the Surinamese border, a partnership with the National Malaria Program of Suriname was implemented and authorizations obtained. In France, the study was approved by the Comitéd' Evaluation Ethique de l'Inserm, an Ethics Committee on Research: Process n° 14–187 (IRB00003888 FWA00005831). The authorization of importation of human biological samples was obtained from the French Ministry of Education and Research, Process N° IE-2014-758. The database was anonymized and declared to the Commission Nationale Informatiqueet Libertés.

#### Results

## Sociodemographic profile of illegal gold miners in French Guiana

During the study, 421 persons were included. The sex ratio was 2.4. Among the 124 women, seven were pregnant (5.6%). The median age was 37 years [interquartile range (IQR) = 30-45], without difference between sexes.

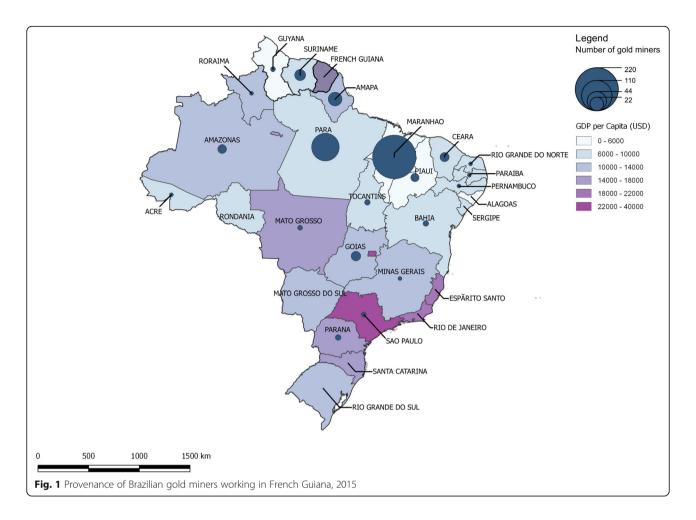
Most of them were born in Brazil (93.8%, 395/421). Other persons were born in Suriname (3.6%, 15/421), in France (1.7%, 7/421), in Guyana (0.5%, 2/421), in Venezuela (0.2%, 1/421) and in Peru (0.2%, 1/421). In Brazil, states of birth were mainly Maranhão (55.7%, 220/395), Para (23.8%, 94/395) and Amapa (6.1%, 24/395) (Fig. 1). Almost all (99%) spoke Portuguese, 96.9% fluently (408/421) and 2.1% (9/421) a little. Only 9% (38/421) spoke French, fluently or a little. Other languages were Sranan-tongo (Maroons language) (18.8%), English (8.0%), Spanish (7.1%) and Dutch (6.9%).

Half of illegal gold miners (48%) never went to school or only had a primary school level. Women had significantly higher education than men: 72.6% had a secondary school level versus 43.4% of men (p < 0.001). Only 13 workers (3.1%) had French social security, one of which was born in France, 3 in Suriname, 9 in Brazil; 7 were women, and 2 were pregnant.

#### Gold mining activity

Garimpeiros had been working for a median 10 years in gold mining [IQR = 5-15], with a minimum of 2 weeks and a maximum of 40 years. This differed between sexes: median duration was 7 years for women versus 10 years for men (p < 0.001). The surveyed persons currently worked in 68 different mining sites, which were grouped in 10 zones according to their proximity and river basin. There was no difference of sex ratio or duration of gold mining activity between those zones, but people were younger in Sophia, Papaïchton and Beiman areas than in others mining areas (p = 0.002). Place of birth (country and state in Brazil) also differed between zones (p < 0.001). Twenty-seven persons were included directly on mining sites in French Guiana. For people included at resting sites, the distance between the resting site and the mining site was one day or more for 63.7% (251/ 394). Modes of transport were boat (99.5%), foot (37.8%), quad (12.8%) and car (1.7%). During the last three years, gold miners had worked in a median number of three different mining sites [IQR = 2-4], ranging from 1 to 25 sites. The majority worked only in FG (67.5%, 284/421). Other persons worked also in Suriname (29.2%), in Brazil (3.6%), in Guyana (2.8%) or in Venezuela (1.2%). Fifteen (3.6%) worked in three or more countries. They had been on the current mining site for a median of six months [IQR = 3-18 months]. The gold extraction was alluvial for 48.5% (204/421) of gold miners, wells for 8.1% (34/421) and both for 39.2% (165/421). Other extraction modes were "moinho" (rock crushing) (9/421) or "pioupiou" (metal detector) (3/421). Six did not answer this question.

Type of work in mining sites differed statistically by sex and 25 persons declared having two jobs. Women were mainly cookers or housewifes (53.2%) or travelling



sellers (40.3%); 9.3% declared sex work activity. Among men, 68% were gold miners, 12.1% travelling sellers, 7.7% transporters, 5.7% machine operators (Fig. 2). Most of them (78.8%) worked only during day-time but 21.2% declared working day and night.

During the last six months, interviewed persons reported having left the mining site a median number of two times [IQR = 1-4] mainly for supplies (44.4%), rest (37%), medical care (25.6%) or family visit (16.4%).

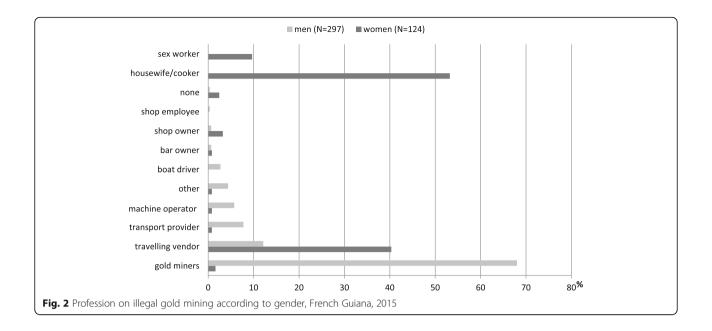
During the past year, 68.2% (287/421) of people declared having moved in a city of the Guiana Shield, a median number of three times [IQR = 1–6]. Most of them went to Paramaribo (49.4%), then Saint Laurent du Maroni (20.1%), Belem (19%), Oiapoque (13%), Macapa (9.5%), Cayenne (8%) and Kourou (2.6%) (Fig. 3). A quarter of Brazilian persons had been to Brazil during the past year (100/395, 25.3%).

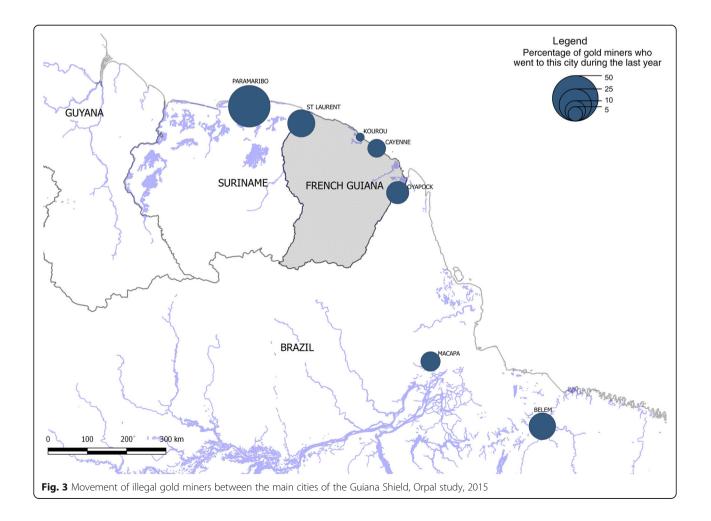
#### Health status of illegal gold miners

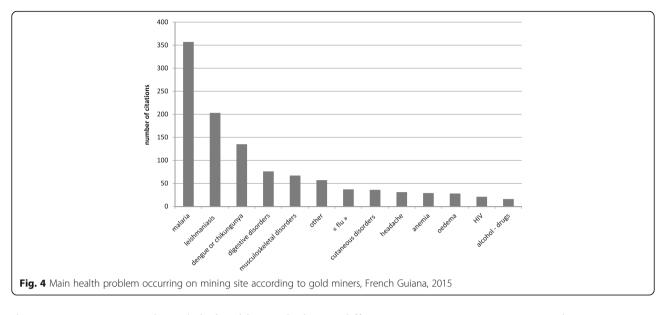
When questioned about the three main problems occurring at the mining site, 357 persons cited malaria, then leishmaniasis (203), dengue or chikungunya (135), digestive disorders (76), and musculoskeletal disorders (67) (Fig. 4).

More than a third (37.1%, 95%CI =32.4–41.7) of gold miners suffered from high blood pressure (HBP), mainly men (42.1% versus 25%, p = 0.001): 93 (22.1%) at grade 1, 47 (11.2%) at grade 2, and 16 (3.8%) at grade 3. Among the ten persons reporting a past history of HBP, two had a medical follow up at the health center of Maripasoula and 2 had erratic treatment use. Concerning cardiac disorders, 7 (1.7%) persons declared having had a myocardial infarction and 14 (3.3%) suffering from cardiac rhythm disorder. Cardiac auscultation found two heart murmurs and four rhythm disorders but not in any of the gold miners with cardiac past history. Two had edema of the lower limbs.

Twenty two percent of included persons had anemia (95%CI =18–25.9), mainly women (28.5% versus 19.3%, p = 0.038), none with hemoglobin below 8 g/dl. Anemia was not related with pregnancy among women. Twenty three persons declared currently having diarrhea (5.5%, 23/421). Thirty five persons (8.3%) had active leishmaniasis. Most of them (65.7%, 23/35) had only one lesion, but twelve (34.3%) had several lesions, up to 5. During







the past year, 57 persons (13.5%) declared having had an anti-leishmanial treatment. Among them, 18 (31.6%) still had active leishmaniasis at inclusion time. Almost all (89.3%) declared a past malaria history, of which 66.2% declared more than 7 prior malaria attacks. Plasmodium spp. prevalence was very high, 22.3% (CI95% = 18.3-26.3) of the study population [10]. Five persons (1.2%) had a splenomegaly, among which 3 had a PCR-Plasmodium spp. positive. Concerning HIV, 36.6% (154/421) had never been tested for HIV. This proportion differed between sexes: 17.7% of women versus 44.4% of men (p < 0.001). Six samples were found positive with the ELISA assay which is a prevalence of 1.43% (95%CI =0.29–2.56). They all presented Western blot profiles of chronic HIV infection and were positive only for HIV-1 with Immunocomb<sup>®</sup>. One was already known to be HIV positive and received care atthe health center of Maripasoula. The 6 HIV positive individuals were aged between 29 to 47 years with a sex ratio of 2:1. The two women declared to be a housewife and cooks, and did not mention sex work. The men were: a shop employee [1], a travelling vendor [1] and gold miners [2]. Only three of the people tested positive retrieved their results.

# Discussion

# Illegal gold miners: mainly poor Brazilian people

Illegal gold miners working in FG were mainly Brazilian, from the poorest states of Brazil, although without direct borders with FG. Actually Maranhão and Para have the highest poverty and unemployment rates in Brazil (Instituto Brasileiro de Geografia e Estatística). Often illiterate, the motive of migration of these persons for gold mining is thus mainly economic as shown in other qualitative reports among miners [25–28]. The provenance of gold miners statistically differed between the different mining zones, suggesting that recruitment could be favored by entourage or people who already experimented gold mining around them [25]. The "forest language" was thus Portuguese, with 99% of people speaking this language at least a little, as observed in Suriname [29]. As in others studies [29, 30], women represented one third of included persons. They had been working in gold mining areas for a shorter time than men, they had the same age but had higher educational level. They often worked in mining sites to support their family financially in Brazil [25, 28]. Profession on the mining site were varied, from mining to support activities thus constituting a micro-society in the Amazonian rainforest as described in Suriname [29]. Sex work activity was probably under-declared due to the attached stigmatization; but it could also be that, contrary to the popular opinion, the majority of women did not engage in sex work on mining camps.

The majority of the surveyed population reported having only worked in French Guiana during the last three years. Actually, in Brazil, illegal gold mining is severely repressed and in Suriname, corruption and concurrence with local persons make it difficult to work for one's own account [9, 25]. Since 2010, more and more wells are being used to extract secondary gold because they are more productive and more difficult to locate by helicopter [9]. Work conditions are known harsh in both: mud and sun in alluvionnary, groundfalls and stuffiness in wells [17]. A fifth of *garimpeiros* worked day and night, testifying of their exhausting work.

## Health problems on mining sites

Malaria was the first health problem cited by interviewed people. Although it might have been influenced by the main topic of the study, almost all declared past malaria history and Plasmodium spp. prevalence was very high [10, 30]. More surprisingly, arboviroses, dengue and chikungunya, were mentioned in second although Aedes aegypti, the main vector in French Guiana, usually lays in clean still water in urban areas.In fact, A. aegypti larvae were found in Bromeliad plants in the rainforest, suggesting that those viral outbreaks can emerge at mining sites [31]. In Australia, in a very different ecological context, gold miners also suffered from dengue and A. aegypti larvae were found in flooded disused mine shafts and wells [17, 32]. Other explanation is the presence of other arbovirus, as Mayaro virus, responsible for sporadic infections or small outbreak in the Amazon region, usually limited to forest areas because of the presence of the vector [33-35]. Mayaro virus infections are probably under-diagnosed because of confusion with other mosquito-borne virus infections, especially dengue fever which is endemic to the same areas [35]. The recent emergence of zika and chikungunya virus had further added to this confusion, especially because of extended arthralgia reported with both infections (chikungunya and Mayaro virus).

Digestive disorders also appeared as an important health problem, linked to the lack of latrines and drinking water [25]. High prevalence of hookworm disease was also previously described on this area [11, 36, 37]. This reflects the multifactorial dynamics of waterborne disease in tropical area, including human behavior (water consumption, occupational activity) and malnutrition in precarious conditions of this exposed population [38].

Prevalence of anemia among women in this study was higher than reported by WHO among women of reproductive age in the Americas: 28.5% (95% CI = 20.4-36.5) versus 16.8% (95% CI = 12.6-23.8) [39]. This can be due to multifactorial causes such as recurrent malaria, poor intestinal absorption related to parasitic diseases, blood loss due to hookworm infection and/or poor food with vitamins and nutrients deficiency. Indeed, a large outbreak of thiamine deficiency among this population was described in 2013–2014 [38].

The prevalence of HBP was higher in this study than in Brazil(37.1% versus 22.8%) [40], while this specific population is young, active and with normal weight. Chronic intoxication to heavy metals such as lead and/or mercury could be an explanation even if the link with HBP is not perfectly established [41–43]. Exposure to lead might be due to cassava consumption as suspected in Amerindian population who has an extremely high level of lead poisoning [44]. Chagas disease, endemic in Latin America particularly in rural area, was also previously described as a risk factor for high blood pressure [45]. Up to 30% of chronically infected people develop cardiac alteration [46].

Illegal gold miners are also exposed to cutaneous disorders such as leishmaniasis due to *L.guyanensis* or

*L.brasiliensis* [47]. Transmitted by sandflies, the reservoir in FG is the two-toed sloth mostly present in the rainforest canopy [48]. Thus deforestation increases contacts with this pathogen. As for malaria [49], the high level of self-medication threatens with the risk of emergence of antileismanial resistance.

Gold mines are potential hotspots for HIV transmission. Sex work seems to be very frequent in gold mining and HIV prevalence has been shown to be higher in sex worker populations [50-53]. Given the large confidence interval of HIV prevalence, the estimate should be interpreted with caution because the study was not designed to evaluate this. Although it seems higher than in mainland France (HIV prevalence = 0.2% [54]) or in Brazil (HIV prevalence = 0.39%, [55]), it is close to estimates in FG (1% in pregnant women [56]). In Brazil, while the HIV epidemic is stabilized in southern regions, HIV detection increased by 62.6% in the past decade in the northeastern region, where most of gold miners are from [57]. There is no prevention for HIV among illegal gold miners and condoms are very expensive on mining sites, reaching up to 10 euros per condom. Women had higher HIV-testing status than men probably because of routine testing during pregnancy. Among the seven pregnant women, all declared having already been tested and were negative for HIV. In this mobile population, only half of HIV positive persons went to get their results at the health center.. These findings show low HIV-testing rates, particularly in men and strongly underline the need to focus efforts on rapid testing rather than serology in this setting to ensure that they have their results.

#### Other potential pathologies described in literature

Leprosy cases diagnosed in FG mainly concern gold miners originating from Brazil, the country with the second highest number of leprosy cases in the world [58, 59]. Bat bites occurred frequently on mining sites, with a potential risk of rabies outbreaks [17, 25, 26]. Trauma were frequent and sometimes severe, motivating 41% of emergency phone calls, mainly due to falling tree, quad accident, or weapon wounds [26]. Garimpeiros are also exposed to fauna poisoning (snake, scorpion...). Given the hard life conditions, alcohol and drugs are often used on gold mining sites [26]. The use of mercury despite it being outlawed exposed gold miners to acute and chronic disorders (neurological respiratory and digestive disorders) [17, 18, 60]. Sexually transmitted diseases and respiratory infections as tuberculosis also seem to be more frequent [17, 61].

## Migration route and health care

Migration could hamper access to health care because of the poverty related to their status, the lack of knowledge about health care or geographical isolation. In a recent study, Médecins Sans Frontières (Doctors Without Borders) reported that death and default rates of tuberculosis treatment for migrant workers were higher than the rates for refugees [62]. This study also underlines the findings of other studies done in areas where migration issues impact malaria control [63]. However, our results suggest that there is a regular and frequent border crossing by gold miners to go to resting sites (median of 2 times per 6 months). Although gold miners are a mobile population who frequently change mining areas, the resting sites might be potentially strategic stability sites of medical mediation. An empirical transnational global health framework taking into account gold miners' particularities thus leads to innovative participatory public health models. The boundaries between countries, isolation and migration flows challenge traditional health systems and promote innovative strategies of medical care.

## Public health consequences

These findings support that mining in remote area is strongly related to several specific illness. Theoretically, given the strenuous working conditions, gold miners would be presumed to start their economical migration to French Guiana as a healthy group, which is called the "salmon bias" [64, 65]. However, their living conditions there might lead to poor health caused by infectious and non infectious diseases. Their close contact with the fauna creates good conditions for the emergence of new pathogens or the reemergence of zoonoses like rabies, yellow fever and other arboviroses [66]. International migration of gold miners also causes social disruptions, including residential and conjugal instability, that may generate risky behaviors, in particular for sexually transmitted disease [67].

Other studies in French Guiana, as elsewhere in the world, suggest that undocumented immigrants are most vulnerable with regards to health [68, 69]. Even if emergency care is theoretically free of charge, access to care is not effective for illegal gold miners because of the remoteness of the mines and the fear of law enforcement [49]. Self-medication is thus very common. Many drugs circulate on the black market and the high price pushes miners to reduce the dosage, threatening with the emergence of resistance to antibiotics and antiparasitic drugs [10, 26, 30]. Moving all around the Guiana Shield and Brazil, gold miners could disseminate other pathogens on their way, as already shown with malaria [70]. The transborder context complexifies care for this neglected population with political, economical and demographical issues. Prevention measures such as mosquito nets, condoms or drinking boiled water often seem not to be used and could be promoted [26, 29].

#### Conclusion

The hostile living conditions at mining sites erodes the miners' health and leads to a broad range of serious non communicable and communicable diseases that may spread beyond mining sites and beyond borders. Improving the knowledge on their specific burden of disease is crucial for health policy planners for disease control. An effective response will benefit from multisectoral approaches for dealing with specific diseaserelated risks, behaviors and environmental Amazonian factors. Consequences of inaction could have repercussion far beyond French Guiana.

#### Abbreviations

AIDS: acquired immune deficiency syndrome; CI: confidence interval; DBP: diastolic blood pressure; FG: French Guiana; GDP: gross domestic product; HBP: high blood pressure; HIV: human immunodeficiency virus; IQR: interquartile range; SBP: systolic blood pressure

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#### Availability of data and materials

Data can be requested from the corresponding author.

#### Authors' contributions

MDo, MN, AA and LM designed the study. FC, LH, MD made acquisition of the data. QH, CC, LM and MDe performed biological exams. MDo and MN analyzed the data. MD, MN, QH, CC, LM, MDe and EM wrote the first draft of the manuscript. All authors contributed to subsequent draft and have reviewed and agreed with the content of the final manuscript. All authors read and approved the final manuscript.

#### Authors' information

Dr. Maylis Douine is a medical doctor with an PHD degree at the Clinical Investigation Center in Cayenne. She is working mainly on epidemiological studies assessing infectious diseases as malaria, chikungunya, Buruli ulcer and papillomavirus.

#### Ethics approval and consent to participate

The study was approved by the Comitéd'Evaluation Ethique de l'Inserm, an Ethics Committee on Research: Process n°14–187 (IRB00003888 FWA00005831). All participants gave their written consent.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have not conflict of interest.

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