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Original Article

Optimized Case Finding of tuberculosis among key populations in Ukraine. A follow up study

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Abstract

Introduction: In 2021, there were 4 million tuberculosis (TB) cases that were not detected by health systems, globally. Many of those cases are among hard-to-reach populations or key population groups. An Optimized Case Finding (OCF) strategy was introduced in Ukraine to enhance case detection and identify those "missing" cases. OCF included screening of up to eight referred household and social network contacts of an index TB case. Following the OCF project implementation, TB detection and characteristics of index cases and contacts were assessed.
Methodology: A cohort study using project data (July 2018 – April 2022) was conducted.
Results: In total 7,976 close contacts were engaged in the project from 1,028 index TB cases. Among the contacts, 507 were diagnosed with TB. The TB case detection was 6,356/100,000 and the number needed to investigate was 16. Multiple factors were identified as associated with TB detection including smoking, HIV, poverty, etc. About 90% of cases were identified at the initial screening of the contacts. OCF was proven to be 5.8 times more effective than the standard active case finding using household surveys and 106 times more effective than passive case finding in the general public.
Conclusions: Our study demonstrated the effectiveness of OCF in detecting cases among key population groups and their social networks. We encourage adaptation and use of OCF by civil society organizations that already work with key vulnerable populations around the globe.

Key words: Key populations; optimized case finding; tuberculosis; Ukraine; operational research.

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Introduction

In 2021, global tuberculosis (TB) incidence was near 10 million, with 1.5 million deaths, and 4 million active TB cases that were not detected/notified by health systems [1].

As demonstrated by the literature, these undetected TB cases are disproportionally concentrated among vulnerable and key population groups, who usually have health system access restrictions [2–5]. Key vulnerable populations include socially marginalized individuals including people who use drugs, displaced, homeless, Roma, and former prisoners. Many of them are HIV positive, use drugs, and live in cramped conditions with poor ventilation. These factors heighten the risk of TB acquisition and transmission [6].

The COVID-19 pandemic only worsened the situation by creating additional barriers to health services due to lockdowns and restrictions. As demonstrated by recent data, case detection was hindered throughout the globe and it can be speculated that the vulnerable populations, who already have difficulties accessing the health systems, have suffered the most [1].

To attain the World Health Organization (WHO) End TB targets of a 95% reduction in TB deaths and an 80% reduction in TB incidence by 2030, a focus on vulnerable groups is urgently needed. Two of the three targets in the End TB strategy involve key populations. One of these targets aims to ensure that TB diagnostic and treatment services reach at least 90% of key populations, while the other target aims for a minimum of 90% treatment success [7].

Ukraine is one of the high-burden countries for multidrug-resistant TB. In 2021 estimated TB incidence was 71 per 100k population and the case detection rate was only 59% [1]. As elsewhere, missed TB cases are likely to be concentrated in vulnerable and key populations [4].

TB case finding in the country has mostly relied on a "passive" approach with patients expected to self-present to health facilities. However, vulnerable population groups who are often criminalized and/or

socially marginalized are less likely to self-present and less able to navigate and access the health system. It is thus important to think of "active" and outreach case finding for this group.

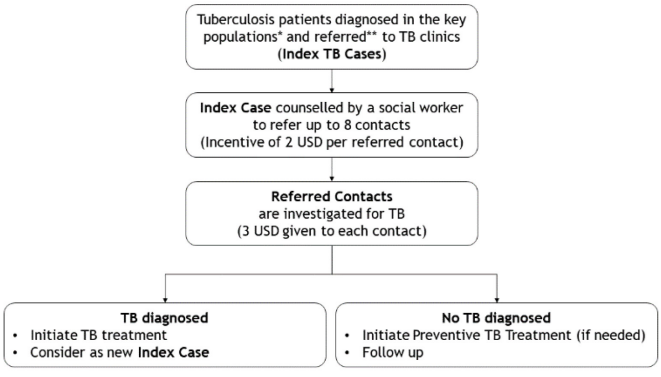
Based on experience from Optimized Case Finding (OCF) showing its effectiveness for HIV detection among key populations, the Alliance for Public Health in Ukraine, which works with key and vulnerable populations, adapted a similar active strategy for TB case finding [8,9].

Fundamentally, the OCF strategy empowers the index TB case to refer up to eight close contacts for TB investigations (Figure 1). Its unique aspect is that the onus is placed on the TB case to decide on the closest contacts within his/her social network. This starkly contrasts with the usual contact tracing strategy which is limited in practice to immediate household contacts.

As demonstrated earlier, this approach was proved to be 3.6 times more effective than active case finding in households and 66 times more effective than passive case finding in the general population [10]. Improving the detection of TB among key populations is important and aligns well with the Sustainable Development Goal of achieving Universal Health Coverage for TB and the WHO Flagship Initiative "Find.Treat.All. #EndTB" [11].

In this follow-up study, we aimed to further describe the strategy of Optimized TB case Finding among key populations and the resulting TB yield in five regions of Ukraine and describe characteristics of index cases that link to the largest number of TB cases. Specifically, among contacts of index TB cases referred for TB investigations using an optimized case-finding strategy, we have aimed to determine: i) total numbers of contacts referred for TB investigations and their socio-demographic characteristics stratified by TB detection, ii) numbers with TB stratified by the time of diagnosis after initial screening, iii) Number Needed to Investigate (NNI) to detect one case iv) numbers started on TB treatment and also v) socio-demographic characteristics of index cases and their association with linkage to TB cases.

Figure 1. Optimized Case Finding for tuberculosis among key population groups in Ukraine.



* Includes people who inject drugs, persons who were in prison up to 2 years prior to TB diagnosis, homeless, the Roma population and internally displaced persons; ** Referred by harm reduction programs and from medical facilities.

Methodology

Study design

This was a retrospective cohort study using routine program data.

General Settings

Ukraine is the largest country in Eastern Europe with a population of 42 million people. There are an estimated 550,000 people from key population groups, 324,300 being people who inject drugs (PWID) [12,13]. The TB incidence rate is 80 (52-115) per 100,000 [1].

The Alliance for Public Health (APH) in Ukraine is a prime recipient (out of 3 recipients in the country) of the Global Fund and PEPFAR country grants. APH along with Center for Public Health (which is a department of the Ministry of Health of Ukraine) coordinates, supervises and monitors HIV prevention and care activities including TB care and harm reduction services for key populations. These services are conducted by over 100 partnering NGOs in the country who work in close collaboration with the Public Health Services of Ukraine.

Specific settings

Tuberculosis management

Since 2018, Ukraine has been transforming the health care system, to provide citizens with equal access to quality medical services, as a result of changes to orient the system so that the patient is at the center of the process. Medical services for the diagnosis and treatment of tuberculosis are included in the program of medical guarantees; a list of services that the state guarantees to the patient which is provided via packages at all levels of medical care. For each of them, a specific list of diagnostic procedures in this area is defined.

The management (diagnosis and treatment) of TB is, according to national and World Health Organization guidelines. Both drug sensitive and drug resistant (DR) TB are managed at TB clinics in primary, secondary, and tertiary/specialized TB facilities (hospitals, dispensaries). Diagnosis is carried out at the TB health facilities. Both drug sensitive and drug-resistant TB

treatment and inpatient care are provided at the specialized TB clinics at the oblast level. Additionally, outpatient/ambulatory care is provided by the network of primary health care units. The "Center for Public Health of the Ministry of Health of Ukraine" provides organizational and technical guidance for the implementation of TB care. Recording and reporting is done using a national electronic database of TB which was introduced in 2012 (TB Register).

Optimized Case Finding for tuberculosis

The OCF strategy is illustrated in Figure 1. Index TB Cases are the patients diagnosed with TB originating from key population groups and referred from health facilities or from TB and harm reduction programs of NGOs. Key population groups include persons who were in prison up to 2 years prior to enrollment, PWID, homeless, the Roma population and internally displaced persons. Index cases were identified by a social worker who provided information on how, and where to refer up to eight contacts for TB investigation. The time period for contact was up to three months prior to the start of the treatment of the index case.

Contacts were broadly classified into four groups:

1. Family contacts: family members of the index cases with whom the patient had interacted on a periodic or regular basis.
2. Household contacts: persons residing with the index case in a common room (including shelters), in an apartment, hostel, house, social welfare institution, children's institution.
3. Occupational contacts: persons working with the patient and staying in the same room for more than 8 hours for at least 1 day.
4. Risky interaction contacts: persons who have had close verbal interactions with the index case in crowded places such as religious gatherings, pub, in public transport, drug-taking point, during inpatient treatment and temporary detention centers.

These contact persons are referred for TB investigations within a maximum of one month from the referral date. The index case receives a monetary incentive of 2 USD for each referred contact. Each contact receives 3 USD for transportation.

The contacts underwent a range of investigations as per medical recommendations/examining doctor's discretion, including clinical examination, X-ray examination (fluorography / radiography / computed tomography) and sputum examination (microscopy, GeneXpert diagnostics). Demographic and risk behavior data including belonging to key population groups data were also collected at the time of screening.

Those diagnosed with active TB were offered TB treatment. Once TB was excluded, the patient was offered Isoniazid Preventive Treatment, and followed up for repeat TB investigations semi-annually for up to 12 months. Those who were diagnosed with TB were identified as an index-cases and bring up to 8 of their own contacts.

Study population and Period

The study sites included 8 TB clinics providing services in the Odessa, Kharkov, Zakarpatya, Dnipropetrovsk and Rivne regions of Ukraine. The study population include contacts of index TB patients originating from key population groups including: people who inject drugs, persons who were in prison up to 2 years prior to enrollment, homeless, the Roma population and internally displaced persons. The study period was from July 2018 to April 2022.

Data collection and analysis

The source of the data was the SyrEx database available at the Alliance and TB Registers/National TB patients register eTB-manager. SyrEx is a database management system developed by the Alliance for Public Health in Ukraine used for monitoring and recording information on clients reached and services provided in community-based prevention programs.

Data of all available contacts and linked cases in the SyrEx database was used in the study. Study data was extracted from sources. Full datasets of the project were used in this study. It was imported into EpiData software and analyzed (version 2.2.2.186, EpiData Association, Odense, Denmark). Data in the database is quality controlled. Additionally, checks were made with program personnel in case of inconsistencies and missing data to ensure data quality. Missing data was not imputed and was excluded from the analysis.

We have summarized the results using descriptive statistics (numbers, proportions). Numbers needed to investigate (NNI) to detect one TB case were calculated. The TB yield was standardized to a 100,000 population. Differences between groups were assessed using the Chi-square test with the level of significance set at $p < 0.05$. Collected data variables included socio demographic and clinical characteristics (all variables are summarized in the Supplementary Tables 1 and 2).

Ethical considerations

An ethical review was conducted and approval was provided by the Institutional Review Board,

International Charitable Foundation "Alliance for Public Health" (approval meeting No 16, dated 08.07.2022). No compensation was provided to subjects as this was a retrospective analysis of already collected data. Compensation for the original inclusion in the project is discussed above.

Results

Indexes, contacts, diagnosis of TB, and linkage to care

There were 1028 index TB cases among key populations. They referred 7976 contacts for TB investigations in health facilities. Data on TB diagnosis was not available for 85 of the contacts. Of the remaining 7891 contacts, about 274 were lost to follow-up after the initial screening having moved, died, or refused participation. TB was detected in 507 contacts (Table 1). The majority (316) of cases (87%) were detected at the initial screening, while only about 13% were detected in subsequent screenings (38, 10.5% during 1 – 6 months and 7, 2% during 7 – 12 months). For 146 cases, the month of TB detection was missing. Using the OCF strategy, the NNI was 16. Of 507 TB patients, 490 (97%) were linked to care and initiated TB treatment. Among all engaged contacts 958 (12%) have received preventive therapy for TB and 27 (2.8%) of those were diagnosed with TB later (only one of those was reported to have drug resistant TB/DR-TB). 161 TB patients were HIV-positive of whom 150 (93%) were also receiving antiretroviral treatment.

Characteristics of study participants

Supplementary Table 1 shows all characteristics of the 7890 participants from key populations where 7384 had no TB and 506 were diagnosed with TB (for one contact with a confirmed diagnosis, data on demographic and clinical characteristics was not available). About 70% of participants were male, 83% had no family, 90% had no permanent job/profession and 25% were homeless. Proportions of four types of contacts recruited through the project were the following: Family – 14%, Household – 33%, Occupational – 6%, and Risk interaction contacts – 47%. HIV was present in about 10% of participants. The most frequent primary key population group was the "injectable drug user" group (36%) followed by the "homeless" group (25%).

Some of the characteristics were significantly associated with TB detection. A full list of comparisons is included in the Supplementary Table 1. Male participants had 1.35 times higher odds ($p < 0.01$) of being diagnosed with TB in the OCF. Being in the age groups of 39 – 49 and 50 + led to increasing odds of having TB compared to the age group of 0 – 17 by 3.8 ($p < 0.01$) and 3.4 ($p < 0.05$) times respectively. The odds of having TB detected in household contacts were 1.5 ($p < 0.05$) times higher than for Family contacts. For risk interaction contacts the odds were 1.4 ($p < 0.05$) times higher than for family contacts. Among Family contacts, those living in kinship had less chance of being diagnosed with TB (odds ratio [OR] 0.1, $p < 0.01$) compared to contacts of relatives of lateral affinity. Among household contacts, those living in apartments had 2 ($p < 0.01$) times higher odds and those sharing a room had 2.4 ($p < 0.01$) times higher odds of being diagnosed with TB, compared to those who lived/resided in social security institutions. There was less chance of being diagnosed with TB for contacts from religious events (OR 0.32, $p < 0.05$) while contacts from drug use venues had 1.27 times higher odds ($p < 0.05$). As expected, smoking was also associated with TB detection (OR 1.62, $p < 0.001$). Smoking a smaller number of cigarettes was protective compared to those smoking higher numbers (OR 0.7, $p < 0.01$). Higher frequency contacts had a higher chance of being diagnosed with TB (OR 2 – 2.8, $p < 0.01$) compared to those with infrequent contacts. The longest time of one-time contact also increased the risk of TB (OR 2 – 3.3, $p < 0.05$). HIV (OR 1.88, $p < 0.001$), chronic occupational diseases (OR 1.45, $p < 0.05$), and exhaustion (OR 1.46, $p < 0.01$) were associated with a higher chance of TB detection. Poverty-related characteristics such as debt (OR 1.26, $p < 0.05$), inability to pay for heating (OR 1.38, $p < 0.01$), and inability to eat meals with meat each day (OR 1.44, $p < 0.001$) as well as spending > 60% of income on food

Table 1. Tuberculosis (TB) detection, number needed to investigate to detect one TB case and linkage to treatment using an Optimized Case Finding strategy in key populations in Ukraine (2018 –2022).

Characteristics	n (%)
Index TB cases among key populations [a]	1028
Contacts of index cases referred for TB investigation	7976
Diagnosed with TB [b]	507 (6.4)
Diagnosed with TB at month 0	316 (87.5)
Diagnosed with TB at months 1 – 6	38 (10.5)
Diagnosed with TB at months 7 – 12	7 (2)
Contacts who received preventive therapy for TB	958 (12)
Diagnosed with TB among those receiving preventive therapy	27 (2.8)
NNI [c]	16
Started on TB treatment [d]	490 (96.7)

[a] Key population groups include: People who inject drugs, partners of people who inject drugs, homeless, Roma people, sex workers and ex-prisoners; [b] For 146 TB patients month of TB diagnosis after screening is missing; [c] Number Needed to Investigate (NNI) to detect one TB case; [d] Percentage calculated using number of diagnosed TB patients as denominator.

(OR 0.75, $p < 0.01$) were associated with TB detection. Compared to those with higher education, participants with lower education had higher odds of being diagnosed with TB (OR 2, $p < 0.05$). Poverty was associated with TB detection and odds of detection were higher by 1.37 times ($p < 0.05$).

TB detection rates

The TB case detection rate using OCF was 6,356/100,000 (Table 2). Compared to case detection used in households of index cases within the general population (1,090/100,000), OCF was 5.8 times more effective. Similarly, comparing OCF to passive case detection in the general population (60/100,000), OCF was 106 times more effective [12].

Characteristics of index cases and relation to linkage to TB case

The characteristics of 433 index cases (for remaining cases as well as for the seed data on characteristics was not available) are summarized in the supplementary table 2. The majority of them (76%) were male, and 91% were above the age of 29. About 80% had no family, 94% had no permanent job/profession and 38% were homeless. HIV was present in about 17% of them. The most frequent primary key population group was the "homeless" group (38%) followed by the "injectable drug user" group (33%). Only 40% of the index cases were linked to contact with TB. The only parameters that were associated with linking to contact with TB were the inability to pay for heating (poverty-related parameter) and being a household contact with someone from a shelter. Those with the inability to pay for heating had 1.93 ($p < 0.01$) times higher odds of referring contacts with TB. Household contacts from shelters had lesser odds (OR 0.3, $p < 0.05$) for referring a contact with TB compared to household contacts from social security institutions.

Table 2. Increase in detection of tuberculosis (TB) through Optimized Case Finding (OCF) in key populations[a] compared to other TB screening strategies in the general population of Ukraine (2018 –2022).

Characteristics	n
Contacts of index cases referred for TB investigation through OCF	7976
Diagnosed with TB	507
TB detection using OCF	
TB /100,000 contacts using OCF in key populations [b]	**6356**
TB detection using active household screening	
TB /100,000 contacts using routine household contact screening [12]	**1090**
Times in increase of detection using OCF strategy for TB case finding [c]	**5.8**
TB detection using passive case finding	
TB per 100,000 people in the general population [12]	**60.1**
Times in increase of detection using an OCF strategy for TB case finding [d]	**66**

[a] Key population groups include: People who inject drugs, partners of people who inject drugs, homeless, Roma people, sex workers and ex-prisoners; [b] 507 / 7976 × 100,000; [c] 6356 / 1090; [d] 6356 / 60.1.

Discussion

This is a follow-up study assessing the overall effectiveness of OCF for TB detection among key populations in Ukraine which can be adapted and implemented in similar settings across the world with prevalent key populations. Our study demonstrates the effectiveness of the OCF strategy in vulnerable populations which implies investigation of referred contacts in both the family and social network of the TB index. Previous studies that assessed the interim effectiveness of the OCF have already proven that lower numbers of contacts are needed to be investigated to detect TB. It showed that OCF is 3.6 times more effective compared to the active case finding in households [12]. The current study using full datasets of the project showed that effectiveness was even higher (5.8 times more effective than active case findings in household contacts). It is 66 times more effective than passive case finding in the general population [12]. The ambitious goals of "Find.Treat.All. #EndTB" would be attainable only if a considerable reduction in "missed TB cases" is achieved among key populations. With the potential identification of one person with TB after the screening of 16 people, the OCF seems to be a viable option that would allow such reduction and would improve case detection, especially among vulnerable populations, and would make the STOP-TB target of reaching at least 90% of key populations attainable [7,11]. This is in line with the UN Sustainable Development Goals which strives to ensure equity and to "leave none behind" [5,14].

Identification of the factors that are associated with TB detection under OCF presented in the results section allows some adjustment of the strategy to increase its effectiveness in case of availability of limited resources and focus on the most vulnerable groups (i.e., people in poverty, those from drug use venues, etc.). Another interesting finding was that about 90% of detected TB cases were identified at the initial screening. This finding demonstrates that in a limited-resource setting, the OCF can be optimized and available resources can be spent on the initial screening. Even in this case, the OCF detection rates would still be remarkable. However, it is important to note that the increase in such

effectiveness will result in a lack of screening in less but still vulnerable populations and "missed cases", so this less rigorous approach is not advisable when resources are available. Analysis of data of the index cases demonstrated that only about 40% of them were referring contacts with TB and they were different from the rest of the indexes in terms of poverty level and household contact type. This demonstrates that there may still be ways to improve outcomes from the project and there may be other factors that would determine "successful" index cases who would refer contacts with TB and call for further investigation.

One strength of the study is the inclusion of five geographic regions of Ukraine which reflects the operational realities of front-line workers. We had detailed data from a large cohort of index TB cases and almost 8000 contacts. Quality control of the APH databases suggests that study data is accurate and reliable. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used for the reporting of findings in our study [15]. The main limitation of the study is that due to the war in Ukraine project faced operational difficulties and some services were interrupted in 2022. Results obtained by Chi-square tests may potentially be confounded and further larger-scale studies will need to be conducted to address this issue. Another limitation was the lack of data on reasons why preventive treatment failed in some of the contacts who ended up getting TB even when they received the prevention. Finally, we have not explored transmission routes and dynamics to identify primary sources of the infection and to explore possible strategies to cut transmission in key populations and the general public. Further studies would be required to answer these questions.

The study findings have several important implications for policy and practice. First, the OCF approach for TB case finding that mimics HIV detection strategies in key populations was successfully implemented by APH in Ukraine [8,9]. The remarkable effectiveness of the simple OCF strategy should be easily replicated in any setting with prevalent key populations with the expectation of having the same level of success. This once again proves the importance of civil society organizations in making health systems accessible especially for vulnerable groups. Scaling-up of the OCF in Ukraine and other countries with low case detection rates with the presence of key populations is an important and realistic approach to reach the WHO targets for TB elimination. Second, in limited-resource settings implementation of the OCF can be adjusted to focus on indexes and contacts that are expected to yield higher number of TB cases. Similarly, follow-up screenings may be disregarded if there are not enough funds and workers to implement them. Finally, this operational research demonstrates the importance of similar studies that show (or in some cases disprove) the effectiveness of "real life" projects, and showcase innovative models that can strengthen healthcare systems and adapt those to be more patient-centric and finally achieve Universal Health Coverage [16–18].

Conclusions

This study once again demonstrated the effectiveness of the OCF among key populations in detecting TB cases. Recruitment of contacts in risk social networks can be implemented easily by civil society organizations that already work with key vulnerable populations. We encourage such initiatives and scaling up of such programs around the globe.

Acknowledgements

To address the problem among missing TB cases Alliance for public health developed and started pilot intervention "Optimized TB case finding and social support of contact persons". The intervention is aimed at screening for TB of contact persons (social, household, family contacts etc.) of vulnerable groups' representatives. The intervention including the conduct of this research is implemented in the framework of the Global fund to fight AIDS, tuberculosis and malaria grant for 2021-2023.

Authors' Contributions

LM: Study conception; protocol design; data extraction, transformation, analysis, and interpretation; drafting manuscript; revising it and giving approval for the final version to be published. EG: designing the protocol; data collection; writing first draft of the paper; critically reviewing the paper and giving approval for the final version to be published. ZI: protocol design; critically reviewing the paper and giving approval for the final version to be published. HD: Study conception; protocol design; data analysis and interpretation; critically reviewing the paper and giving approval for the final version to be published.

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Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Table 1. Socio-demographic-characteristics of TB contacts with, and without TB, Ukraine, 2018 – 2020.

Variable	Total N = 7890		TB diagnosis				Odds Ratio	*p* value
			Yes N = 506		No N = 7384			
	n	%	n	%	n	%		
Sex								
Male	5533	70.1	383	6.9	5150	93.1	1.35	**0.005**
Female	2357	29.9	123	5.2	2234	94.8	1	-
Age (years)								
0 - 17	158	2.0	3	1.9	155	98.1	1	-
18 - 29	927	11.7	46	5.0	881	95.0	2.7	0.098
30 - 49	4974	63.0	341	6.9	4633	93.1	3.8	**0.009**
50+	1831	23.2	116	6.3	1715	93.7	3.4	**0.022**
Contact Type								
Family	1081	13.7	53	4.9	1028	95.1	1	-
Household	2641	33.5	186	7.0	2455	93.0	1.5	**0.016**
Industrial	477	6.0	17	3.6	460	96.4	0.7	0.240
Risk interactions	3691	46.8	250	6.8	3441	93.2	1.4	**0.027**
Family Contact Type								
Not a Family contact	6809	86.3	453	6.7	6356	93.3	-	-
Relatives of lateral affinity of the third degree (uncle, aunt, nephew, niece)	309	3.9	22	7.1	287	92.9	1	-
Kinship (kinship by marriage / cohabitation, between spouses)	135	1.7	1	0.7	134	99.3	0.1	**0.004**
Relatives of lateral kinship of IV degree (cousin, sister, grandfather, grandmother, grandson, granddaughter)	257	3.3	13	5.1	244	94.9	1.44	0.311
Relatives of lateral kinship of the second degree (sibling)	131	1.7	10	7.6	121	92.4	0.93	0.849
Relatives of the first degree of direct affinity (father, mother, son, daughter, spouse, cohabitant)	215	2.7	7	3.3	208	96.7	2.28	0.057
Relatives of the second degree of direct affinity (grandfather, grandmother, grandson, granddaughter)	34	0.4	0	0.0	34	100.0	-	-
Household								
Not a Household contact	5249	66.5	320	6.1	4929	93.9	-	-
Social security institution	1479	18.7	93	6.3	1386	93.7	1	-
Apartment	165	2.1	20	12.1	145	87.9	2	**0.005**
Bed and Breakfast	256	3.2	9	3.5	247	96.5	0.5	0.082
Hostel	47	0.6	2	4.3	45	95.7	0.7	0.765
Rehab Center	14	0.2	0	0.0	14	100.0	-	-
Shelter	286	3.6	22	7.7	264	92.3	1.2	0.378
House	309	3.9	28	9.1	281	90.9	1.5	0.078
Room	85	1.1	12	14.1	73	85.9	2.4	**0.005**
Industrial Contact Type								
Not an Industrial contact	7413	94.0	489	6.6	6924	93.4	-	-
Working specialties, production	284	3.6	11	3.9	273	96.1	1	-
Agriculture, agribusiness	6	0.1	0	0.0	6	100.0	-	-
Beauty, fitness, sports	4	0.1	0	0.0	4	100.0	-	-
Construction, architecture	70	0.9	2	2.9	68	97.1	1.37	1
Educational institution	16	0.2	0	0.0	16	100.0	-	-
IT, computers, internet	1	0.0	0	0.0	1	100.0	-	-
Jurisprudence	4	0.1	0	0.0	4	100.0	-	-
Logistics, marketing	2	0.0	0	0.0	2	100.0	-	-
Medicine, pharmaceutics	16	0.2	0	0.0	16	100.0	-	-
Retail	22	0.3	1	4.5	21	95.5	1.2	0.598
Sale, purchase	15	0.2	2	13.3	13	86.7	3.8	0.133
Security, security	2	0.0	1	50.0	1	50.0	25	0.082
Service area	32	0.4	0	0.0	32	100.0	-	-
Transport, car business	3	0.0	0	0.0	3	100.0	-	-
Other - contacts	2498	31.7	2370	94.9	128	5.1	1	-
Vulnerable group/Key population								
Former prisoners	70	0.9	58	82.9	12	17.1	0.26	**< 0.001**
Homeless	2006	25.4	1834	91.4	172	8.6	0.58	**< 0.001**
IDU	2869	36.4	2700	94.1	169	5.9	0.86	0.221
IDU partners	110	1.4	104	94.5	6	5.5	0.94	0.878
Non-injection drug users	29	0.4	29	100.0	0	0.0	-	0.399
Partners of SW	11	0.1	8	72.7	3	27.3	0.14	0.017
SW	37	0.5	34	91.9	3	8.1	0.61	0.437
Roma population	239	3.0	238	99.6	1	0.4	12.85	**< 0.001**
Forced migrants	20	0.3	8	40.0	12	60.0	0.04	**< 0.001**
MSM	1	0.0	1	100.0	0	0.0	-	1
No additional group	7392	93.7	6916	93.6	476	6.4	-	-
Alcohol consumers	17	0.2	14	82.4	3	17.6	-	-
Additional Vulnerable group/key population								
Forced migrants	45	0.6	38	84.4	7	15.6	-	-
Former prisoners	237	3.0	228	96.2	9	3.8	-	-
Homeless	127	1.6	121	95.3	6	4.7	-	-
IDU	32	0.4	28	87.5	4	12.5	-	-
IDU partners	12	0.2	12	100.0	0	0.0	-	-
Non-injection drug users	2	0.0	2	100.0	0	0.0	-	-
Partners of SW	6	0.1	6	100.0	0	0.0	-	-
Roma population	8	0.1	7	87.5	1	12.5	-	-
SW	12	0.2	12	100.0	0	0.0	-	-

Supplementary Table 2. Social-demographic and clinical characteristics of Index TB cases with high and low number of linked TB cases in Ukraine (2018 –2020).

Variable	Total N = 433		Linked to contacts with TB diagnosis				Odds Ratio	*p* value
			Yes N = 174		No N = 259			
	n	%	n	%	n	%		
Sex								
Female	105	24.2	47	44.8	58	55.2	1.3	0.272
Male	328	75.8	127	38.7	201	61.3	1	-
Age (years)								
0 - 17	1	0.2	1	100.0	0	0.0	-	-
18 - 29	40	9.2	14	35.0	26	65.0	1	-
30 - 49	292	67.4	120	41.1	172	58.9	1.3	0.460
50+	100	23.1	39	39.0	61	61.0	1.2	0.660
Contact Type								
Family	44	10.2	17	38.6	27	61.4	1	-
Household	167	38.6	69	41.3	98	58.7	1.1	0.747
Industrial	12	2.8	6	50.0	6	50.0	1.6	0.478
Risk interactions	210	48.5	82	39.0	128	61.0	1	0.959
Family								
Not a Family contact	389	89.8	157	40.4	232	59.6	-	-
Relatives of lateral affinity of the third degree (uncle, aunt, nephew, niece)	17	3.9	7	41.2	10	58.8	1	-
Kinship (kinship by marriage / cohabitation, between spouses)	1	0.2	0	0.0	1	100.0	-	-
Relatives of lateral kinship of IV degree (cousin, sister, grandfather, grandmother, grandson, granddaughter)	12	2.8	5	41.7	7	58.3	1	1
Relatives of lateral kinship of the second degree (sibling)	8	1.8	3	37.5	5	62.5	0.9	1
Relatives of the first degree of direct affinity (father, mother, son, daughter, spouse, cohabitant)	6	1.4	2	33.3	4	66.7	0.7	1
Household								
Not a Household contact	266	61.4	105	39.5	161	60.5	-	-
Social security institution	87	20.1	41	47.1	46	52.9	1	-
Apartment	13	3.0	6	46.2	7	53.8	1	0.948
Bed and Breakfast	9	2.1	4	44.4	5	55.6	0.9	1
Hostel	2	0.5	1	50.0	1	50.0	1.1	1
Shelter	20	4.6	4	20.0	16	80.0	0.3	**0.043**
House	24	5.5	8	33.3	16	66.7	0.6	0.228
Room	12	2.8	5	41.7	7	58.3	0.8	0.767
Industrial Contact Type								
Not an Industrial contact	421	97.2	168	39.9	253	60.1	-	-
Working specialties, production	8	1.8	2	25.0	6	75.0	1	-
Construction, architecture	1	0.2	1	100.0	0	0.0	-	-
Retail	1	0.2	1	100.0	0	0.0	-	-
Sale, purchase	2	0.5	2	100.0	0	0.0	-	-
Other - contacts	91	21.0	30	33.0	61	67.0	1	-
Vulnerable group/Key population								
Former prisoners	11	2.5	4	36.4	7	63.6	1.2	1
Homeless	165	38.1	73	44.2	92	55.8	1.6	0.078
IDU	145	33.5	60	41.4	85	58.6	1.4	0.195
IDU partners	4	0.9	2	50.0	2	50.0	2	0.601
Partners of SW	2	0.5	0	0.0	2	100.0	-	1
SW	3	0.7	0	0.0	3	100.0	-	0.549
Roma population	1	0.2	0	0.0	1	100.0	-	1
Forced migrants	11	2.5	5	45.5	6	54.5	1.7	0.505
No additional group	407	94.0	164	40.3	243	59.7	-	-
Additional Vulnerable group/key population								
Alcohol consumers	3	0.7	0	0.0	3	100.0	-	-
Forced migrants	6	1.4	3	50.0	3	50.0	-	-
Former prisoners	7	1.6	4	57.1	3	42.9	-	-
Homeless	6	1.4	2	33.3	4	66.7	-	-
IDU	2	0.5	1	50.0	1	50.0	-	-
IDU partners	1	0.2	0	0.0	1	100.0	-	-
Roma population	1	0.2	0	0.0	1	100.0	-	-
Risk contact type / Inpatient (non TB)								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	388	89.6	155	39.9	233	60.1	-	-
Yes	1	0.2	1	100.0	0	0.0	-	-
Risk contact type / Place of joint alcohol drinking								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	320	73.9	133	41.6	187	58.4	1	-
Yes	69	15.9	23	33.3	46	66.7	0.7	0.206
Risk contact type / Religious events								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	388	89.6	156	40.2	232	59.8	-	-
Yes	1	0.2	0	0.0	1	100.0	-	-
Risk contact type / Drug use venue								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	298	68.8	118	39.6	180	60.4	1	-
Yes	91	21.0	38	41.8	53	58.2	1.09	0.713
Risk contact type / Temporary detention facility								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	389	89.8	156	40.1	233	59.9	-	-

Variable	Total N = 433		Linked to contacts with TB diagnosis				Odds Ratio	*p* value
			Yes N = 174		No N = 259			
	n	%	n	%	n	%		
Risk contact type / Sexual relationship								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	387	89.4	154	39.8	233	60.2	-	-
Yes	2	0.5	2	100.0	0	0.0	-	-
Risk contact type / Travel								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	387	89.4	155	40.1	232	59.9	-	-
Yes	2	0.5	1	50.0	1	50.0	-	-
Risk contact type / Vagrancy								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	376	86.8	153	40.7	223	59.3	1	-
Yes	13	3.0	3	23.1	10	76.9	0.44	0.258
Risk contact type / Hangout								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	383	88.5	153	39.9	230	60.1	1	-
Yes	6	1.4	3	50.0	3	50.0	1.5	0.687
Smoking during last 3 months								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	59	13.6	28	47.5	31	52.5	1	-
Yes	330	76.2	128	38.8	202	61.2	0.7	0.211
Smokers / Hookah								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	384	88.7	155	40.4	229	59.6	1	-
Yes	5	1.2	1	20.0	4	80.0	0.37	0.652
Smokers / Cigarettes								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	59	13.6	28	47.5	31	52.5	1	-
Yes	330	76.2	128	38.8	202	61.2	0.7	0.211
Smokers / Number of cigarettes per day								
Missing	103	23.8	46	44.7	57	55.3	-	-
10 to 20	217	50.1	87	40.1	130	59.9	1	-
20 to 40	66	15.2	25	37.9	41	62.1	0.9	0.747
5 to 10	38	8.8	14	36.8	24	63.2	0.9	0.706
Up to 5	9	2.1	2	22.2	7	77.8	0.4	0.488
HIV								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	316	73.0	129	40.8	187	59.2	1	-
Yes	73	16.9	27	37.0	46	63.0	0.85	0.547
Chronic occupational lung disease								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	361	83.4	143	39.6	218	60.4	1	-
Yes	28	6.5	13	46.4	15	53.6	1.32	0.478
Oncological diseases								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	387	89.4	156	40.3	231	59.7	-	-
Yes	2	0.5	0	0.0	2	100.0	-	-
Diseases of gastrointestinal tract								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	229	52.9	94	41.0	135	59.0	1	-
Yes	160	37.0	62	38.8	98	61.3	0.91	0.649
Use of immunosuppressives								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	384	88.7	155	40.4	229	59.6	1	-
Yes	5	1.2	1	20.0	4	80.0	0.37	0.652
Stress								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	357	82.4	141	39.5	216	60.5	1	-
Yes	32	7.4	15	46.9	17	53.1	1.35	0.415
Psychiatry disorders								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	378	87.3	151	39.9	227	60.1	1	-
Yes	11	2.5	5	45.5	6	54.5	1.25	0.761
Diabetes mellitus								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	380	87.8	147	38.7	233	61.3	-	-
Yes	9	2.1	9	100.0	0	0.0	-	-
Exhaustion								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	315	72.7	125	39.7	190	60.3	1	-
Yes	74	17.1	31	41.9	43	58.1	1.1	0.727
Organ transplants								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	388	89.6	156	40.2	232	59.8	-	-
Yes	1	0.2	0	0.0	1	100.0	-	-
Others diseases								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	241	55.7	92	38.2	149	61.8	1	-
Yes	148	34.2	64	43.2	84	56.8	1.23	0.322

Variable	Total N = 433		Linked to contacts with TB diagnosis				Odds Ratio	*p* value
			Yes N = 174		No N = 259			
	n	%	n	%	n	%		
Debt in the household								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	218	50.3	80	36.7	138	63.3	1	-
Yes	171	39.5	76	44.4	95	55.6	1.38	0.122
Inability of the household to pay for a one-week annual leave								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	18	4.2	8	44.4	10	55.6	1	-
Yes	371	85.7	148	39.9	223	60.1	0.83	0.700
Inability to pay for heating/conditioning								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	133	30.7	40	30.1	93	69.9	1	-
Yes	256	59.1	116	45.3	140	54.7	1.93	**0.004**
Inability to pay for meals with meat (chicken, fish or vegetarian equivalent) every other day								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	131	30.3	44	33.6	87	66.4	1	-
Yes	258	59.6	112	43.4	146	56.6	1.52	0.062
Inability to pay for unexpected financial expenses								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	43	9.9	15	34.9	28	65.1	1	-
Yes	346	79.9	141	40.8	205	59.2	1.28	0.459
Inability to afford a phone								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	206	47.6	79	38.3	127	61.7	1	-
Yes	183	42.3	77	42.1	106	57.9	1.17	0.454
Inability to afford color TV								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	170	39.3	72	42.4	98	57.6	1	-
Yes	219	50.6	84	38.4	135	61.6	0.85	0.425
Inability to afford a washing machine								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	158	36.5	62	39.2	96	60.8	1	-
Yes	231	53.3	94	40.7	137	59.3	1.06	0.774
Inability to afford a car								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	23	5.3	7	30.4	16	69.6	1	-
Yes	366	84.5	149	40.7	217	59.3	1.57	0.329
Spend more than 60% of income on food								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	122	28.2	51	41.8	71	58.2	1	-
Yes	267	61.7	105	39.3	162	60.7	0.9	0.644
Remains less than 10% after spending on food and utility								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	123	28.4	46	37.4	77	62.6	1	-
Yes	266	61.4	110	41.4	156	58.6	1.18	0.459
Living cost per day is below 5.05 USD equivalent								
Missing	44	10.2	18	40.9	26	59.1	-	-
No	119	27.5	50	42.0	69	58.0	1	-
Yes	270	62.4	106	39.3	164	60.7	0.89	0.609
Poverty								
No	63	14.5	24	38.1	39	61.9	1	-
Yes	370	85.5	150	40.5	220	59.5	1.11	0.714
Education								
Missing	15	3.5	5	33.3	10	66.7	-	-
Higher	9	2.1	4	44.4	5	55.6	1	-
Incomplete	29	6.7	7	24.1	22	75.9	0.4	0.401
Incomplete higher	13	3.0	8	61.5	5	38.5	1.9	0.666
Secondary	231	53.3	92	39.8	139	60.2	0.8	1
Secondary specialization	136	31.4	58	42.6	78	57.4	0.9	1
Registration in a drug use dispensary								
Missing	258	59.6	105	40.7	153	59.3	-	-
No	166	38.3	65	39.2	101	60.8	1	-
Yes	9	2.1	4	44.4	5	55.6	1.24	0.316
Employment								
Missing	17	3.9	8	47.1	9	52.9	-	-
Unemployed	246	56.8	96	39.0	150	61.0	0	0.524
Commercial sex	2	0.5	0	0.0	2	100.0	-	-
Other	13	3.0	3	23.1	10	76.9	0.5	1
Permanent job	24	5.5	10	41.7	14	58.3	1.1	0.508
Student	3	0.7	2	66.7	1	33.3	3.1	0.400
Temporary work	128	29.6	55	43.0	73	57.0	1.2	0.508
Legal problems								
Missing	22	5.1	8	36.4	14	63.6	-	-
Conditionally sentenced	29	6.7	14	48.3	15	51.7	1	-
Unconvicted	294	67.9	118	40.1	176	59.9	0.7	0.395
Was detained	88	20.3	34	38.6	54	61.4	0.7	0.360