Spatio-Temporal Distribution of Tuberculosis in an Urban Setting in Germany

A Ten Year Analysis

Räumlich-zeitliche Analyse der Tuberkuloseverteilung in der Stadt Köln 2006 – 2015

Eine 10-Jahres-Analyse

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ABSTRACT

Background Big cities in Europe have the highest incidence rates of TB in otherwise low incidence settings. Understanding of the spatio-temporal patterns of TB incidence can support efforts for TB prevention and control in line with the End-TB Strategy of the WHO in such settings for low incidence settings.

Methods Data from the municipal TB register of Cologne collected between 2006 and 2015 under the infection prevention legislation were retrieved, addresses geographically identified and all notified incident TB cases retrospectively analysed for their spatial and temporal distribution in this large German city using a geographic information system.

Results During the analysed period 1,038 incident cases were reported, equivalent to an incidence rate of 10.03 cases per 100,000 inhabitants. Contagious pulmonary TB contributed 57 % of all cases. Distribution patterns changed over time with decreases in 37 and increases in 22 of the 77 urban sub-districts, three of which showing constant high rates of TB incidence.

Conclusion The study presents a complementary method to monitor the distribution and development of incident TB cases at a disaggregated level of urban sub-districts. Identification of areas with comparatively high incidence can support identification of clusters respectively their prevention and allow better planning for targeted local TB services.

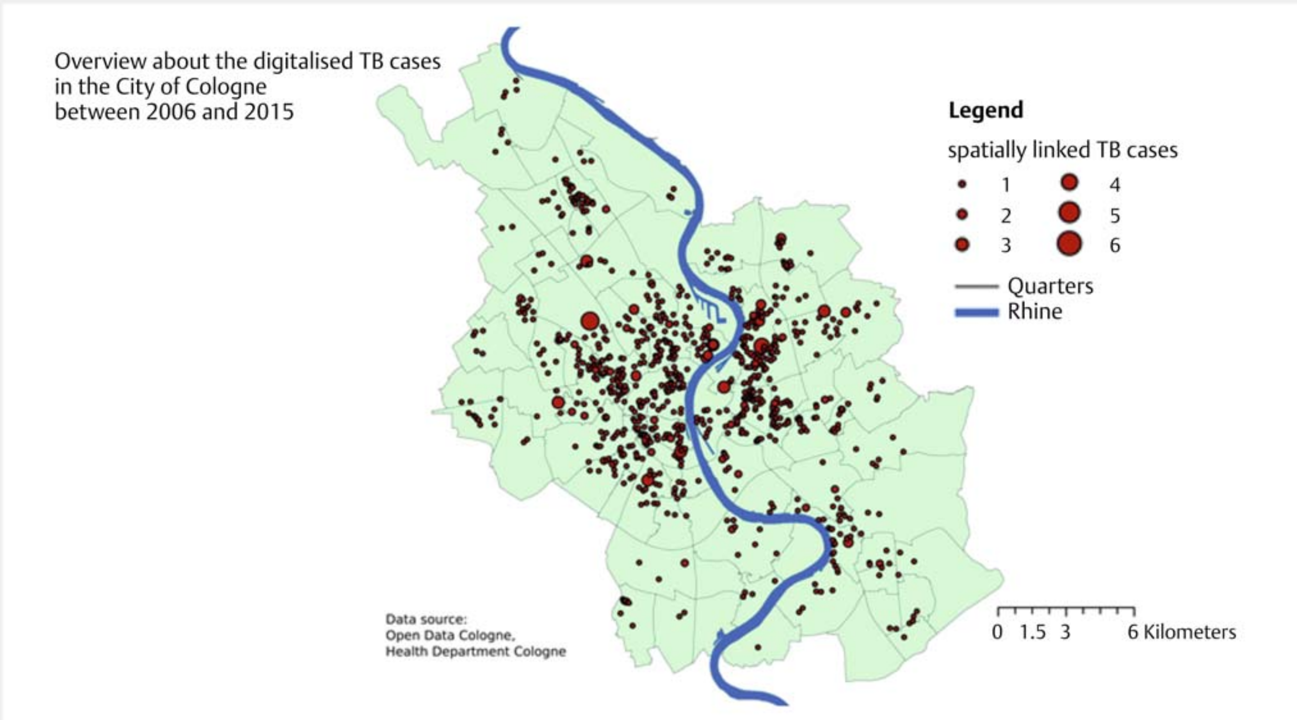
ZUSAMMENFASSUNG

Hintergrund Zu weiten Teilen ist Europa eine Niedriginzidenz-Region für Tuberkulose, innerhalb Europas zeigen jedoch Großstädte deutlich höhere Inzidenzen. Ein genaueres Verständnis der räumlich-zeitlichen Verteilung der inzidenten Fälle kann zur Verbesserung von Prävention und Kontrolle der Tuberkulose in Großstädten führen und einen Beitrag zur Umsetzung der End-TB-Strategie der WHO in Niedriginzidenz-Regionen leisten.

Methoden Daten aller nach Infektionsschutzgesetz in Köln gemeldeten Fälle von Tuberkulose zwischen 2006 und 2015 wurden retrospektiv deskriptiv analysiert. Die Adressen aus dem Register wurden geografisch lokalisiert und mithilfe eines geografischen Informationssystems örtlich-zeitlich über den gewählten Zeitraum analysiert.

Ergebnisse Im Studienzeitraum wurden 1038 inzidente Fälle gemeldet, entsprechend einer Inzidenzrate von 10,03 pro 100 000 Einwohnern. In 56 % der Fälle lag eine pulmonal offene Tuberkulose vor. Die räumliche Verteilung änderte sich im Untersuchungszeitraum. In 37 von 77 Stadtbezirken nahm die Inzidenz ab, während sie in 22 Bezirken zunahm. In 3 Bezirken zeigt sich eine konstant hohe Inzidenz.

Schlussfolgerung Mithilfe eines geografischen Informationssystems lässt sich die Entwicklung der Verteilung von Tuberkulose-Fällen im großstädtischen Raum kleinteilig darstellen. Bezirke mit vergleichsweise hohen Inzidenzen und mögliche Cluster können identifiziert werden. Prävention und Behandlungsmöglichkeiten können gezielter geplant werden.



▶ **Fig. 1** Overview of incident cases.

Introduction

TB remains one of the most relevant infectious diseases globally with around 10 million new infections per year [1].

In Germany there has been a constant decline in incidence until 2014 when a slight reversal in trend occurred in incident cases [2]. Similar to other Western European countries incident cases are unequally distributed in Germany among and within the federal states with highest incidence in the major urban settings [3, 4]. While in the federal state of North Rhine-Westphalia the incidence stood at $6.7/10^5$ the city of Cologne over the last decade had an average 49 % higher incidence of $10.0/10^5$.

In 2014, WHO has launched the "End TB Strategy" with the aim to reduce incident cases in low incidence high resource countries like Germany to 1/100,000 by 2035 and 0.1/100,000 by 2050 [5].

To reach these targets, major steps in reducing incidence would be necessary in these settings. To better understand the situation and to gain information to optimize TB control in Cologne, the 4th largest city in Germany, we analyzed the temporal and spatial distribution of incident TB cases in this city from 2006 to 2015.

In line with the consensus statement for TB control in big cities in the EU [3] and for better planning of the local TB control, this study specifically analyses the pattern of case distribution within the city boundaries, identifies the areas with the highest densities of incident TB cases and changes in distribution over one decade.

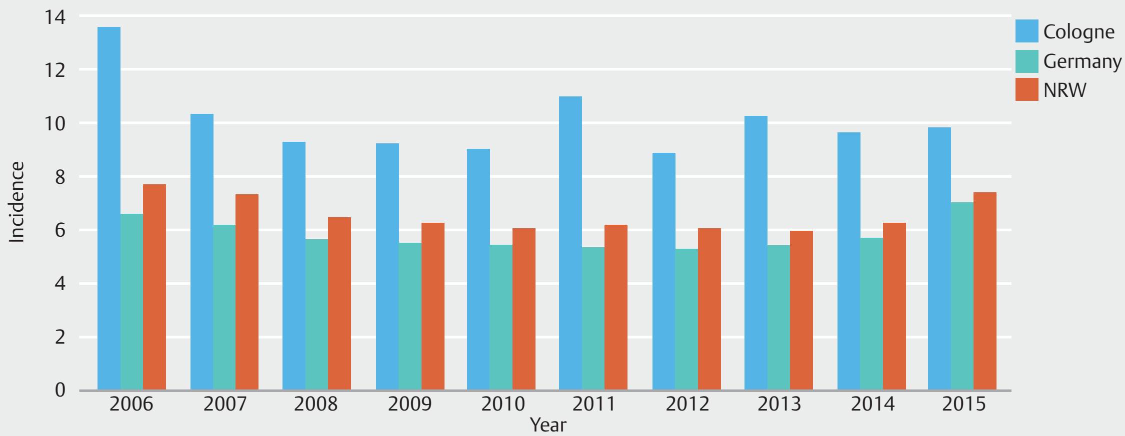
Methods and Setting

Cologne is located in the federal state of North Rhine-Westphalia (NRW) in Germany. This state counts around 1,100 cases of incident TB annually of which around 10 % occur within Cologne [2]. The city as a whole can be seen as a large-scale hotspot of TB incidence in NRW and even in Germany, as already noted by Kistemann et al. (2002) [6].

Data about Cologne such as the number, age and sex distribution of inhabitants were retrieved from open sources of the municipal statistical office, broken down to the administrative sub-units [7, 8]. Population data were directly available for the year 2005 and 2011 – 2014, data for the years 2006 – 2010 were interpolated. Since data for 2015 were not yet available, we used the same numbers as for 2014 [9].

The analysis was based on the local TB register of the municipal health authority of Cologne which captures all notifiable characteristics of incident cases. Comorbidities such as HIV are not part of the notification. All available data of notified incident cases between 2006 and 2015 – collected mandatorily under the federal infection prevention legislation – were retrieved, geographically identified by address and transferred into an Excel® data sheet.

Cologne covers an area of 405 km² and had 1.07 million inhabitants in 2015. Administratively it is subdivided in 9 districts and 86 sub-districts which served as observational units in the analysis. Because of considerable differences in the number of inhabitants very small units were merged with neighboring units to reduce the level of difference.



▶ **Fig. 2** Comparison of TB incidence rates in Cologne, North Rhine-Westphalia and Germany. Data source: Survstat (2016), Amt für Stadtentwicklung und Statistik (2015a) and Municipal Health Authority Cologne.

Following data cleaning and control 1,038 incident TB cases were identified, out of which 967 (93.2 %) could be geographically located using Google Earth Pro (GEP) Version 7.1.5.1557 [10] and thus were available for the spatio-temporal analysis. The distribution over the whole city is depicted in ▶ **Fig. 1**.

Further processing and statistical analysis were done using QGIS 2.8.4 [11], ArcGIS 10.3.1 [12] and R 3.2.3 [13].

As a result, the TB incidences for each sub-district as well as the absolute case numbers were available for analysis and comparison.

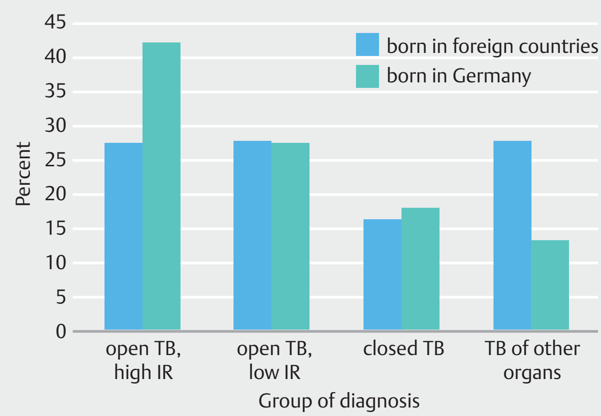
A descriptive analysis was done with regards to age, sex, country of birth and type of tuberculosis. In the spatial analysis differences in incidence between the sub-districts were tested for spatial autocorrelation (global Moran's I) and tested by chi-square test. For further spatial analysis of the distribution of the incident cases we performed optimized hot spot and a cluster-outlier analysis, a tool to identify spatial outliers [14]. We also analyzed temporal differences of incidence density per sub-district (adjusted image differencing) for the whole period as well as separated for the time periods 2006 – 2010 and 2011 – 2015.

Ethical consideration

Only data collected under the German infection prevention and control act was used in a pseudonymized format accessible only for authorized personnel. Personal informed consent therefore was not required. A degree of fuzziness in not ion the geographical figure was applied to avoid direct localisation of addresses.

Results

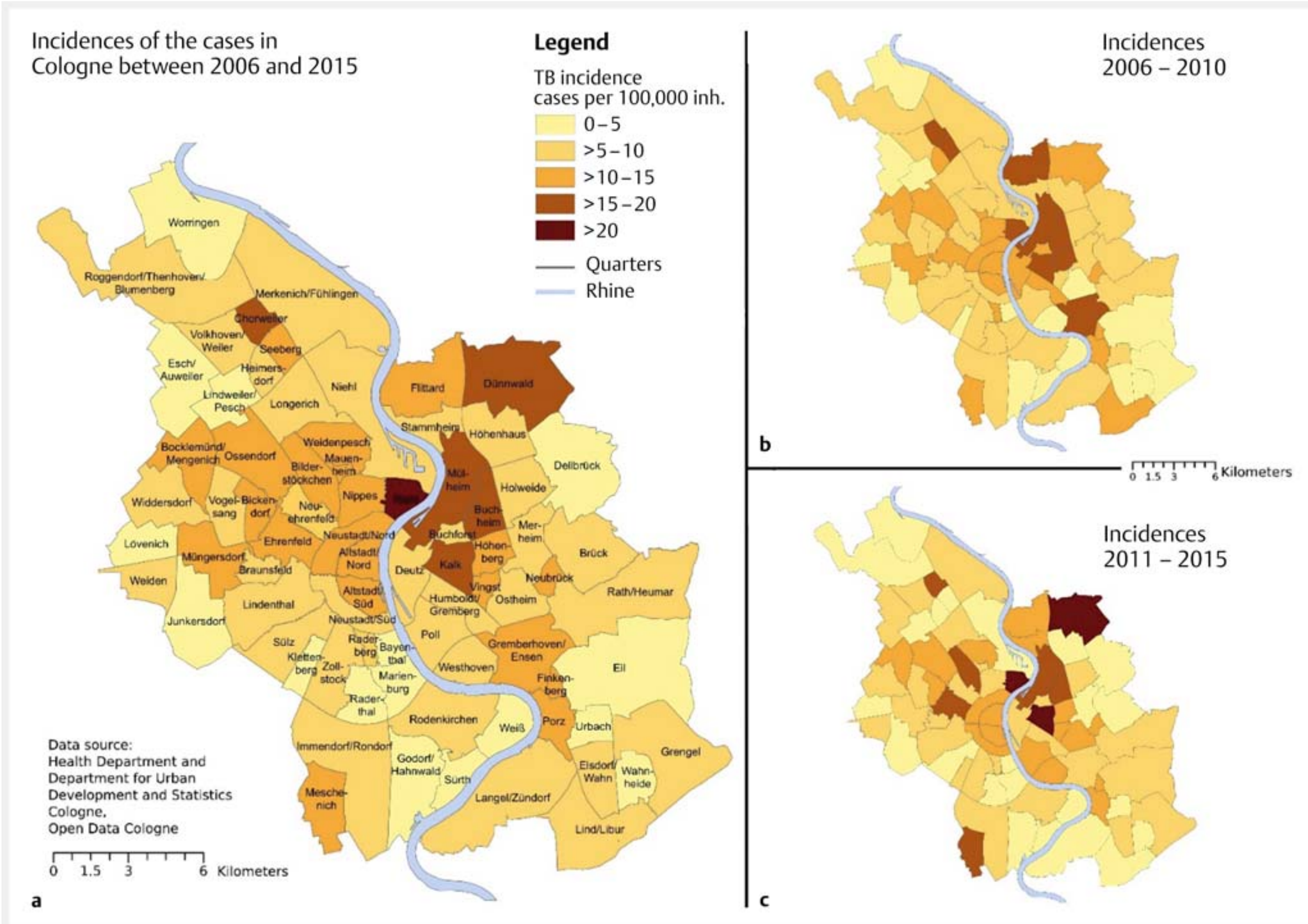
Between 2006 and 2015 a total of 1038 incident cases were notified and 967 (93.2 %) could be geographically located. Among the 71 cases without geographical location 39 were known as homeless. For the others the address was partly incomplete. This number corresponds with an average incidence rate of 10.0 per 100,000 inhabitants and a range over time between



▶ **Fig. 3** Comparison of the group of diagnosis by country of birth. Data source: Municipal Health Authority Cologne (n = 381).

8.80 in the year 2012 and 13.50 in the year 2006 without a clear downward trend after 2006. Meanwhile the national TB incidence slightly decreased from 2006 until 2013 and then rose again in 2014 and 2015 (see ▶ **Fig. 2**).

Of the 1038 incident TB cases notified and registered by the municipal public health authority 63.6 % were males, mean age was 46.3 years (IQR 31 – 61) with more than 45 % of the cases in the age group between 25 and 55 years. Over the whole period 56 % of the incident cases consisted of contagious pulmonary disease (26 % were positive in sputum microscopy and culturally confirmed, 30 % only culturally positive). The remainder were either non-contagious pulmonary cases (11 %) or had extrapulmonary disease (33 %). Resistance testing was done for all cases with culturally confirmed diagnosis (87 %). Any resistance was found in 64 cases (6.2 %) most of which were INH (44) related. MDR-Tb was diagnosed in 11 cases (1 %). No XDR was notified during this period.



▶ **Fig. 4** Incidences of the TB cases in Cologne regarding the years 2006 – 2010 (**a**), 2006 – 2010 (**b**) and 2011 – 2015 (**c**).

The rate of patients born in Germany (40 %) in relation to patients born in foreign countries (60 %) was constant with a slight increase to 68 % in 2015. Foreign born cases originated from 89 different countries with Turkey contributing 14 %. Comparing the type of diagnosed TB under the aspect of the country of birth, it is noticeable that the percentage of contagious (i. e. smear positive and/or culture positive) lung TB is higher among patients born in Germany. Regarding the TB of other organs than the lung, the affected patients were much more often born in a foreign country (▶ **Fig. 3**). Based on individual history, contact data and follow up, the vast majority of cases appear unrelated to each other likely as a result of progression from LTBI to active disease.

The incidence analysis of the sub-districts showed a spatial range from < 5 to > 20 per 100,000. ▶ **Fig. 4** shows the incidence rates of each sub-district for the whole period as well as for the intervals 2006 – 2010 and 2011 – 2015. The distribution is inhomogeneous across the city, but there are no clear trends identifiable. However, some of the sub-districts stand out because of higher or lower incidences.

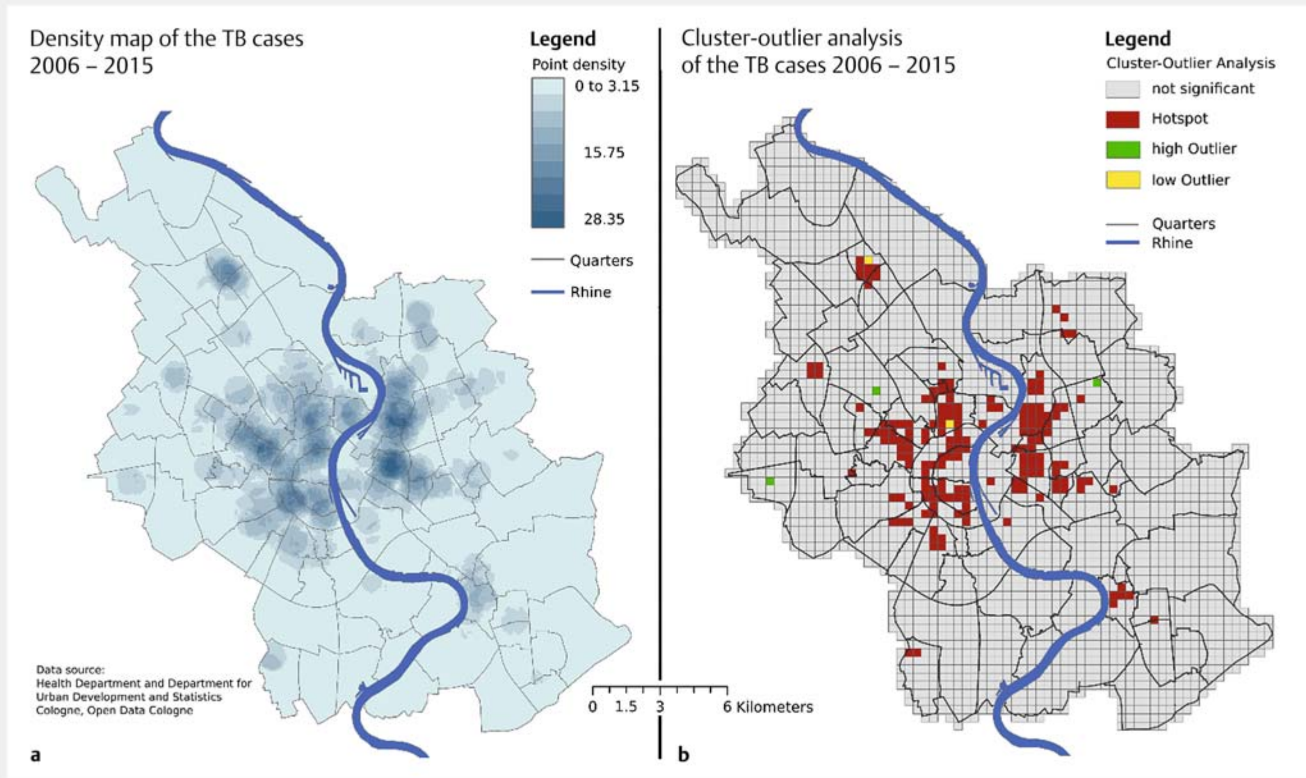
In two city sub-districts (*Godorf/Hahnwald, Weiss*) not a single TB incident case was reported in the period of the study. The highest incidences in contrast were detected in *Riehl* (21.6), *Kalk* (19.5) and *Mülheim* (18.6). They are almost twice as high as the average incidence of the city.

Most of the sub-districts show incidences between 5 and 15, and those with lower incidences more often lie in the outer urban area.

Comparing the two time intervals 2006 – 2010 and 2011 – 2015 some differences can be noted. In general, the incidences in the second interval seem to be more heterogeneous. While during the first years there were 16 sub-districts with an incidence below 5 and none with an incidence above 20, in the second interval there are 23 sub-districts with an incidence below 5 and 3 above 20: *Riehl* (24.83), *Kalk* (21.09) and *Dünnwald* (20.08).

The chi-square test suggests that the incident TB cases are not homogeneously distributed over the city ($p < 0.01$).

The density analysis for absolute numbers of cases and the cluster analysis reveal statistically significant, identifiable hot spots. Global Moran’s I hints towards a middle grade clustering ($p < 0.01$) (▶ **Fig. 5**).



▶ **Fig. 5** Density Map (**a**) and Cluster-Outlier Analysis (**b**) of the incident TB cases in Cologne 2006 – 2015.

Discussion

We analysed the distribution of all notified incident TB cases in one of the largest cities of Germany over a period of 10 years of which 93 % could geographically be located, hence providing a good picture on the spatial and temporal distribution of incident TB in this urban setting. The German infection prevention legislation clearly stipulates the notification process and in line with the RKI reports we assume that notification numbers should be almost equal to the true incidence.

Regarding the spatial dimension of the TB incidence our analysis points towards an inhomogeneous distribution across the sub-districts of the city. As a result, there are areas with TB incidence significantly below the average as well as areas with a TB incidence well above the average. The former are often found at the outskirts of Cologne. This may be caused by the less urbanized environment and a change in housing conditions [15]. Analysing sub-districts not following this pattern could provide additional insights into the local TB dynamics. However, it must be emphasized, that the number of incident TB cases on this scale is low. Under these circumstances a qualitative approach would be preferable for further investigations.

On the other hand, the city sub-districts with the highest TB incidences over time are generally located closer to the city centre. Taking a closer look on the located TB cases it can be observed, that small scale patterns and hotspots occur independent from the sub-districts' borders. The reasons therefore could lie in the urban settlement. The 'Rhine port' in the south-west, as an example for an extremely low population density, can be recognised as a light area on the density map regarding the sub-districts *Deutz* and *Mülheim*. Areas with high TB incidence rates mostly occur in areas with a high population density as to be found in the northern parts of *Mülheim*. However, the sub-districts' inner structure varies and small scale patterns can often explain the inhomogeneity.

One of the sub-districts with the highest TB incidence is *Kalk*. Over time the number of TB cases there remains relatively constant and on the scale of the TB cases there is only little spatial variation within this sub-district. *Kalk* as well as *Mülheim* have been classified as 'Sozialraumgebiet' – a term describing areas with a recognised need to improve general housing and living conditions [16]. Further, *Kalk* is known as an area of the city with high unemployment rates [17]. Without being able to draw causal association from the data here, the observation is in line with the known association between low social status and higher TB incidence.

Riehl on the contrary is not one of the sub-districts with lower social and housing conditions but has an almost equally high TB incidence as *Kalk*. This fact could be linked to certain facilities located in *Riehl*, such as a large retirement home and a refugee accommodation, because both elderly persons and refugees have higher incidences of TB.

The TB incidence in most industrial countries concerns mainly the underprivileged population [18]. While our data for Cologne seem to support that high TB incidences in some parts of the city can partly be related to social economic factors, a much closer inspection of the particular cases is necessary. Our data do not allow drawing a causal association between TB incidence rates to socio-economic variables or vice versa. Considering the low numbers of cases the spatial analysis of the single TB cases on a small scale level including a more detailed assessment of socio-economic conditions is needed for further analysis.

Regarding the increasing numbers of refugees and displaced persons arriving in Europe and in Germany [19], our analysis cannot present any changes echoing that development because of the time period under analysis, but can rather serve as a baseline for follow-up comparative studies looking at the effect of migration.

Analysing the temporal dynamics of TB incidence, a high variation without a clear upward or downward trend can be noticed. In the meantime, TB incidence is slightly rising in the whole of Germany [2]. Compared to NRW or Germany the TB incidence in Cologne is relatively high and can be seen as a hotspot at a large scale.

On the small scale the sub-districts *Mülheim*, *Kalk* and *Riehl* show constantly the highest TB incidences per year and thereby pose local hotspots. Although our data show some clustering, these observations should be considered with caution avoiding the conclusion of simplified causal relations. Such analysis is only possible in larger studies like from the Rotterdam region 1995 – 2006 and is not the focus of our work [20]. Yet in a follow-up study those high incidence sub-districts could be further examined regarding their commonalities and differences. Furthermore, these results suggest the monitoring of high TB areas. Besides they provide an opportunity for the city of Cologne to develop practical approaches to achieve a local reduction of TB incidence rates and adequate provision of services, as suggested by the European Consensus statement and in line with the WHO End TB strategy [3].

Conclusion

The incident TB cases in Cologne between 2006 and 2015 have been digitalised, spatially located and analysed. The resulting maps deliver detailed insights into distribution and development of TB clusters in the city. TB incidence in Cologne and other big cities is higher than in the rest of Germany and inhomogeneously distributed within the city. Urban districts and sub-districts show different patterns of TB incidence with relatively higher rates in the quarters near to the city centre.

As a combined result of analysing the TB incidence rates and the TB cases within sub-districts different TB hotspots could be identified.

This study presents a method to monitor the distribution and development of incident TB cases per administrative units and sub-units of a city, thereby revealing hotspots of TB incidence. The granular presentation of the Tb cases in Cologne allows better understanding of the local TB dynamics and targeted interventions for local prevention and control.

Authors contribution

TK and LMP developed the concept and LMP conducted the main analysis, FN, NF supported the retrieval, analysis and interpretation of the data, LMP wrote the first draft of the manuscript, FN revised the draft with inputs by GAW, NF, TK. All authors read and endorsed the final version,

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Conflict of interest

The authors declare that they have no conflict of interest.

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