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Unsuccessful treatment in pulmonary tuberculosis: factors and a consequent predictive model

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Background: Cure is particularly valuable in pulmonary cases (PTB), as unsuccessful treatment fuels incidence and resistance to antibiotics. This study aims to identify individual factors of PTB unsuccessful treatment in Portugal and to develop a consequent predictive model. **Methods:** Using the Portuguese TB surveillance database (SVIG-TB), PTB cases older than 15 years notified from 2000 to 2012 in Continental Portugal were analyzed. Unsuccessful treatment included the WHO categories (failure, default, death and transferred out). Based on a literature review, predictors involved sociodemographic, behavioral, disease-related and treatment-related factors. Binary logistic regression was used to estimate unsuccessful treatment factors and to develop the predictive risk model. **Results:** The unsuccessful outcome rate in PTB patients was of 11.9%. The predictive model included the following factors: TB/HIV co-infection (OR 4.93), age over 64 years (OR 4.37), IV drugs abuse (OR 2.29), other diseases (excluding HIV and Diabetes, OR 2.09) and retreatment (OR 1.44), displaying a rather good validity. **Conclusion:** The overall treatment unsuccessful treatment rate in PTB patients complies with the 85% WHO success threshold. The predictive model of unsuccessful treatment proved well. *Nomogram* representation allows an early, intuitive identification of PTB patients at increased risk. The model is liable to widespread use as a prognostic tool.

Introduction

Tuberculosis (TB) remains an important Public Health problem globally as one of the top 10 causes of death worldwide in 2015, causing heavy social, familiar and economic dysfunctions. Meanwhile, low burden TB countries face the challenge of re-emergence of the disease in specific population sub-groups, where the control level is reduced. This weakness fosters transmission, a higher number of cases resistant to antituberculous drugs and consequently contributes to increase the unsuccessful treatment rates.[1,2]

Notifications of TB cases provide a good proxy indication of incidence in countries that have both high-performance surveillance systems and an easy access to quality health care, meaning that few cases (or a negligible number) skip diagnosis and notification.[3]

Portugal remains the highest TB incidence in Western Europe,[4] with a recently incidence estimate of 19.2 per 1 00 000 population.[5] Additionally, over the last few years, the disappearance of high incidence municipalities (≥50 cases/1 00 000 population) has been witnessed.

Municipalities such as Oporto (46.3/1 00 000 population), Lisbon (44.0/1 00 000 population), Setubal and Algarve region still present an intermediate incidence (>20 cases/1 00 000 and <50 cases/1 00 000 population). This profile corroborates that Portugal has now an urban TB pattern (Lisbon and Oporto concentrate 68.5% of all new cases and 45% reside in Lisbon metropolitan area).[6–8]

An effective TB program has two main pillars: to detect the disease as early as possible and to ensure that those diagnosed do complete their appropriate treatment course and get cured.[9] It achieves high enough detection and cure rates and a low level of acquired bacillary resistance to antibiotics. Each country must have, then, an intrinsic information system as expressed in the five-point DOTS strategy to monitor these indicators.[10]

Portugal began the implementation of this strategy in 1994 with the compulsory nominative notification of TB cases to both the Notifiable Diseases Program and the TB National Program (TBNP). In 2000 it standardized the outcome definition by adopting the categories issued by WHO.[9]

According to WHO, Portugal has maintained detection and success rates above objectives established for a good control level, at least 70% and 85%, respectively.[6] A high coverage by appropriate treatment is crucial for achieving the End TB Strategy milestones, that preconizes a new TB treatment success rate of ≥90% until 2025.[1]

With this new goal in mind and considering that there is still a small number of studies on this topic and none in Portugal, it proved relevant to focus on risk factors for PTB unsuccessful outcomes; and, if possible, to predict and prevent unsuccessful outcomes for each patient attending clinical services.

This study aimed to identify individual factors associated with unsuccessful treatment outcomes of PTB cases in Continental Portugal and to develop and validate a predictive model to assist physicians with the timely identification of pulmonary cases needing closer, adapted follow-up to prevent unsuccessful treatments.

Methods

Study design, data source and outcome definition

A retrospective cohort study was carried out using the TBNP nationwide surveillance system (SVIG-TB), based on compulsory TB notifications by general practitioners or pulmonary specialists, at their offices, when diagnosis is defined following appropriate criteria. This is an official reliable system, evaluated on a yearly basis according to WHO guidelines. Each notification is complemented and updated during follow-up appointments, by medical specialists.

PTB cases, aged ≥ 15 years notified in SVIG-TB, resident in Continental Portugal (henceforth referred to as Portugal), diagnosed and treated during the period of 2000–2012 were included. Given the study nature, relevant variables according to the literature review for unsuccessful outcomes were studied. Other variables, like Programmed Directly Observed Treatment and Initial Treatment, were not considered, due to equivocal data, leading to a strong possibility of misleading interpretations, only

possible to overcome through direct consultation of the patient's clinical process. Alcohol dependence was based on self-reported, inquired information, including if patients feel guilty or uncomfortable about their own alcohol consumption. Tobacco information is not recorded in SVIG-TB.

In line with WHO criteria, SVIG-TB categorized a six possible and mutually exclusive categories for treatment outcomes, grouped in this study into a binary outcome: (i) Successful outcome—if PTB patients were treated before and declared cured, including both negative smear microscopy at the end of treatment at least one previous follow-up test and in case of not providing sputum samples, cure is declared if treatment completed and absent of disease clinical evidences (categories 1 and 2). (ii) Unsuccessful outcome—if treatment of PTB patients resulted in failure (i.e. remaining smear-positive after 5 months of treatment, cat. 3), default (i.e. patients who interrupted their treatment for two consecutive months or more after registration, cat. 4), death (cat. 5) or were transferred-out (cat. 6).[9]

Data analysis

Frequencies (%) were used to describe patients' characteristics. Relationships between treatment outcomes and potential predictor categorical variables (year of notification, sex, age group, birthplace, occupation, chest X-ray findings, HIV infection, Diabetes (DM), other co-morbidities (excluding HIV and DM), alcohol dependence, intravenous (IV) or other drugs abuse, reclusion, homelessness, community residence and type of case) were assessed using logistic regressions.

Odds ratios (OR) and their 95% confidence intervals (95%CI) were estimated using binary logistic regression, with PTB treatment result as the outcome (event: non-success vs. success).[11] The final multivariate logistic model was developed, including variables that were significant in bivariate analyses, with *forward stepwise* (Likelihood Ratio) method, *logit* function (entry-0.05; removal-0.10).

Data concerning 2000–2012 were regrouped as: (i) 2000–2009 (training-set), to identify the predictors of unsuccessful outcomes, analysed globally (2000–2009) and considering two periods, 2000–2004 and 2005–2009 (based on recently published research results[12] that had identified distinct patterns between these two periods); (ii) fitted models were then applied on data regarding 2010–2012 (test-set, only recently available) to verify the model's ability to predict an unsuccessful case. The Receiver Operating Characteristic (ROC) curve was used as a measure of the model's predictive discrimination[13], as well as the Positive Predictive Value (PPV) and Negative Predictive Value (NPV).[14] Different model variants were considered, taking into account a global one, the sub-division in two time-periods and different stratifications, in particular, by sex, co-infection TB/HIV and type of case. The best performance characteristics and coherence with the literature were crucial for choosing the final model.

Statistical analyses were performed using R and IBM SPSS softwares. A significance level of 0.05 was adopted.

Ethics committee approval and informed consent were not required, as the data were anonymized and based on an official national surveillance system.

Results

A total of 34252 PTB patients were enrolled during the study period (2000–2012). 29 664 were more than 15 years and were categorized for treatment outcomes, 24 950 in 2000–2009 (training-set) and 4714 in 2010–2012 (test-set).

The training-set population showed a predominance of the male sex (69.8%), a mean age of 43.56 ± 17.67 years, a median age of 41 years with the age group 25–44 years being the majority (46.8%).

The unsuccessful outcome rate in PTB patients was 11.9%, categorized in failure (0.2%), default (5.0%), death (6.6%) and transferred-out (0.1%). Higher unsuccessful treatment rates were observed in: residents in the districts of Lisbon (13.3%) and Oporto (12.0%), male sex (13.3%), aged over 64 years (19.2%) and 25–44 years (11.7%), immigrants (13.2%), workers of community residences (28.1%) and prisons (20.7%)—workers of the National Health Service had the lowest unsuccessful treatment (5.1%)—alcohol abusers (15.5%), IV drug abusers (30.4%), other drugs abusers (23.3%), inmates (24.8%), homeless (33.8%), living in community residences (27.8%), TB/HIV co-infected (29.6%), with pathologies other than HIV or DM (19.1%) and with history of previous treatment (19.3%). Patients with DM (10.6%) had a lower unsuccessful treatment rate compared with those who were not diabetic (11.9%). Test-set population showed similar distributions.

Relationships between unsuccessful outcomes and the potentially explanatory factors, globally (2000–2009) and in the two sub-periods (2000–2004 and 2005–2009) are presented in Table 1.

Results show some improvement, as in 2005–2009 a lower unsuccessful treatment rate was achieved. In the overall analysis and by sub-period, significant differences were found in the groups regarding almost all predictors. Only *place of birth* (2005–2009) and the *co-existence of* DM did not evince statistical differences between exposure groups.

Table 2 shows crude and adjusted for age and sex OR. All risk factors showed a significant relationship with unsuccessful outcomes, with the exception of *co-existence of DM* and *no cavitations* on chest X-ray findings (by comparison with normal results).

Considering the different models tested (global, sub-division in two time-periods and different stratifications), the best performance characteristics and coherence with the literature were achieved using the period 2005–2009.

The predictive risk model of unsuccessful treatment (table 3) included the following predictors: TB/HIV co-infection (OR 4.93; 95%CI 3.50–6.96), age over 64 years (OR 4.37; 95%CI 2.64–7.22), IV drugs abusers (OR 2.29; 95%CI 1.50–3.50), other comorbidities (excluding HIV and Diabetes, OR 2.09; 95%CI 1.63–2.68) and retreatment cases (OR 1.44; 95%CI 1.06–1.95).

Predictive model performance characteristics were: Area under receiver operating characteristic curve = 75.9% (95%CI 74.1–77.7), Sensitivity = 71%, Specificity = 73% (both associated with a cut value of 0.07) and an Overall Corrected Percentage of 72.8%. In the validity model, sensitivity and specificity were, respectively, 64.5% and 65.8%, with a positive predictive value of 19.3 and a negative predictive value of 93.6.

Figure 1 (*nomogram*) represents the final predictive model graphically, once shaped for practical application, as an intuitive and useful technique to assist clinical decision-making.

Discussion

The demographic profile identified is consistent with findings in other studies and highlights a TB endemic pattern for Portugal.[2,15–17] The largest number of cases occurred in urban districts, where their focuses converged with poverty and overcrowding,[18] and with other main disease risk groups, as the homeless, IV and other drugs abusers.[19–21] Literature shows these factors as increasing unsuccessful outcomes as well.

Some potential limitations need to be addressed. We focused only PTB patients, as they really drive whole population control results: this is the most relevant and frequent form of TB sustaining undesired community transmission. Sub-notification of PTB cases, it is thought to be rather low and pertaining to cases with milder symptoms, probably with low contagiousness, that may be detected in a later period or cure spontaneously; this phenomenon doesn't affect study results. In Public Health the control-key is to cancel out transmission, being this group the most important to intervene. Also restriction to a more homogeneous group maximizes understanding and acceptance of the proposed predictive model by eventual users.

Table 1 Number (%) of PTB cases unsuccessfully treated by patient characteristics, Continental Portugal, 2000–2009

	Global **No. (%)**	χ^2 ***P***	**2000–2004** **No. (%)**	χ^2 ***P***	**2005–2009** **No. (%)**	χ^2 ***P***
Year of notification						
2000–2004	1795 (**12.7**)	<0.001				
2005–2009	1152 (10.7)					
Sex						
Female	593 (8.2)	<0.001	351 (8.6)	<0.001	242 (7.7)	<0.001
Male	2354 (**13.3**)		1444 (**14.3**)		910 (**12.0**)	
Age group (yrs)						
15–24	166 (6.5)	<0.001	119 (7.4)	<0.001	47 (4.9)	<0.001
25–44	1400 (11.7)		929 (13.4)		471 (9.4)	
45–64	639 (9.7)		339 (9.6)		300 (9.9)	
≥ 65	742 (**19.2**)		408 (**19.2**)		334 (**19.2**)	
Birthplace						
Portugal	2564 (11.6)	0.014	1560 (12.3)	0.001	1004 (10.7)	0.859
Abroad	383 (**13.2**)		235 (**15.3**)		148 (10.8)	
Occupation						
Other	1563 (9.3)	<0.001	947 (9.9)	<0.001	616 (8.4)	<0.001
National Health System	40 (5.1)		26 (6.4)		14 (3.7)	
In Community residence	27 (**28.1**)		14 (**27.5**)		13 (**28.9**)	
Prison	23 (**20.7**)		18 (**25.7**)		5 (12.2)	
Other healthcare	3 (3.5)		1 (2.0)		2 (5.4)	
Chest X-ray findings						
Normal	159 (**13.5**)	<0.001	111 (**14.0**)	<0.001	48 (**12.3**)	<0.001
Cavitations (yes)	1058 (9.5)		620 (10.2)		438 (8.6)	
Cavitations (no)	1348 (12.8)		816 (13.9)		532 (11.3)	
HIV co-infection						
No	904 (6.5)	<0.001	433 (6.9)	<0.001	471 (6.1)	<0.001
Yes	925 (**29.6**)		550 (**32.3**)		375 (**26.4**)	
Diabetes mellitus						
No	2819 (11.9)	0.164	1726 (12.7)	0.184	1093 (10.7)	0.650
Yes	128 (10.6)		69 (10.9)		59 (10.1)	
Other comorbidities[a]						
No	2397 (10.9)	<0.001	1517 (11.9)	<0.001	880 (9.5)	<0.001
Yes	550 (**19.1**)		278 (**20.0**)		272 (**18.2**)	
Alcohol dependence						
No	1782 (9.8)	<0.001	1037 (10.4)	<0.001	745 (9.1)	<0.001
Yes	649 (**15.5**)		402 (**17.3**)		247 (**13.4**)	
IV drug abuse						
No	1773 (8.9)	<0.001	1020 (9.3)	<0.001	753 (8.3)	<0.001
Yes	804 (**30.4**)		531 (**33.8**)		273 (**25.4**)	
Other drugs						
No	1903 (9.5)	<0.001	1128 (10.3)	<0.001	775 (8.6)	<0.001
Yes	513 (**23.3**)		292 (**25.8**)		221 (**20.7**)	
Reclusion						
No	2395 (10.8)	<0.001	1393 (11.5)	<0.001	1002 (10.0)	0.001
Yes	90 (**24.8**)		62 (**29.2**)		28 (**18.5**)	
Homelessness						
No	2344 (10.6)	<0.001	1377 (11.4)	<0.001	967 (9.7)	<0.001
Yes	154 (**33.8**)		86 (**36.9**)		68 (**30.5**)	
Community residence						
No	2257 (10.4)	<0.001	1320 (11.1)	<0.001	937 (9.6)	<0.001
Yes	230 (**27.8**)		137 (**31.4**)		93 (**23.8**)	
Type of case						
New case	2382 (10.8)	<0.001	1450 (11.7)	<0.001	932 (9.7)	<0.001
Retreatment	565 (**19.3**)		345 (**19.7**)		220 (**18.8**)	

a: Excluding HIV and DM.

The main goals of SVIG-TB are population surveillance to support to clinical decision and patient follow up simultaneously. This implies that some specific necessary research information either is unavailable, or does not have the required shape.

The option to perform a case-control analysis after approaching SVIG according to a retrospective cohorts design (which supposes the direct calculation and use of Relative Risk as the association parameter) was based on the possibility and advantage to determine OR. This approach ensures then both the comparability with existing studies (usually using OR) and the achievement of valid precision estimates—unsuccessful outcomes may be rare events in some strata.[11]

To our knowledge, a predictive model for unsuccessful treatment of PTB patients in Portugal has not been created so far. But other researchers have developed models for predicting such outcomes in settings different from the present one, thus corroborating their relevancy and potential for external validity.[14,22,23]

The model was created assuming the theoretical causation basis implied in the known history of the disease.[1] The levels of association of predictors to unsuccessful outcomes were obtained from the empirical ground under focus. The model's prediction capabilities were analysed in the same geodemographic ground, leading to very satisfactory parameter values, ensuring its appropriateness to assist physicians in predicting unsuccessful treatment. Regarding PPV and NPV values it is important to state that both are directly related to the prevalence of the event in the population and in cased of low prevalence's (as in this study), it is expect that PPV will be far higher than NPV.[14] The model chosen presented the highest PPV value found in the different models tested.

Table 2 Odds ratios (OR) for unsuccessful treatment among PTB cases, crude and adjusted for age and sex, Continental Portugal, 2000–2009

	Bivariate analysis			Adjusted for age and sex		
	OR	95%CI	P	OR	95%CI	P
Year of notification						
2000–2004	1.21	1.12–1.31	<0.001	1.22	1.13–1.32	<0.001
2005–2009	1.00			1.00		
Sex						
Female	1.00					
Male	**1.71**	1.56–1.88	<0.001			
Age group (yrs)						
15–24	1.00					
25–44	**1.92**	1.63–2.27	<0.001			
45–64	**1.56**	1.31–1.87	<0.001			
≥65	**3.44**	2.88–4.11	<0.001			
Birthplace						
Portugal	1.00			1.00		
Abroad	1.15	1.03–1.30	0.015	**1.31**	1.16–1.47	<0.001
Occupation						
Other	1.00			1.00		
National Healthcare System	0.53	0.38–0.72	<0.001	0.54	0.39–0.75	<0.001
Community residence	**3.82**	2.44–5.98	<0.001	**3.66**	2.30–5.81	<0.001
Prison	**2.55**	1.61–4.05	<0.001	**2.92**	1.83–4.66	<0.001
Other healthcare	0.35	0.11–1.12	0.077	0.41	0.13–1.30	0.128
Chest X-ray findings						
Normal	1.00			1.00		
Cavitations (yes)	0.67	0.56–0.80	<0.001	0.66	0.55–0.79	<0.001
Cavitations (no)	0.94	0.79–1.12	0.496	0.87	0.73–1.04	0.121
HIV infection						
No	1.00			1.00		
Yes	**6.08**	5.49–6.74	<0.001	**7.27**	6.48–8.15	<0.001
Diabetes						
No	1.00			1.00		
Yes	0.88	0.73–1.06	0.164	0.92	0.76–1.11	0.391
Other comorbidities[a]						
No	1.00			1.00		
Yes	**1.93**	1.74–2.14	<0.001	**1.89**	1.71–2.09	<0.001
Alcohol dependence						
No	1.00			1.00		
Yes	**1.69**	1.53–1.86	<0.001	**1.68**	1.52–1.86	<0.001
IV drug abuse						
No	1.00			1.00		
Yes	**4.48**	4.07–4.93	<0.001	**5.96**	5.33–6.66	<0.001
Other drugs						
No	1.00			1.00		
Yes	**2.88**	2.58–3.22	<0.001	**3.25**	2.89–3.66	<0.001
Reclusion						
No	1.00			1.00		
Yes	**2.72**	2.14–3.46	<0.001	**2.78**	2.18–3.56	<0.001
Homelessness						
No	1.00			1.00		
Yes	**4.29**	3.52–5.24	<0.001	**4.43**	3.62–5.42	<0.001
Community residence						
No	1.00			1.00		
Yes	**3.30**	2.82–3.87	<0.001	**3.17**	2.70–3.72	<0.001
Type of case						
New case	1.00			1.00		
Retreatment	**1.98**	1.79–2.19	<0.001	**1.86**	1.68–2.06	<0.001

a: Excluding HIV and DM.

The predictive model included as PTB unsuccessful treatment independent risk factors: TB/HIV co-infection, age over 64 years, IV drugs abuse, other comorbidities and retreatments. Age over 64 years was also reported as a factor of unsuccessful outcomes by different researchers.[16,17]

The TB/HIV co-infection was the most strongly associated factor with PTB unfavorable outcomes, verified by others, in particular for death only[15,17,24] just default,[19] or with death, default and failure.[25]

In either developed or developing countries, drugs-dependent patients are driving the epidemic, given their difficulties to complete medical evaluation, their higher delay in initiating treatment and their low and irregular adherence.[26] Results of the present study are consistent with such evidence, as IV drugs abuse was a strong predictor of unsuccessful treatment.[14,19]

Hinkin and colleagues[27] analyzed adherence to treatment in HIV patients positively tested for illegal drug use. HIV-positive patients had significantly worse adherence to treatment than HIV-negative, presenting a four times higher risk of failure in treatment adherence.

Researchers in Portugal also reinforced the connection between TB and drug addiction, as major Public Health issues, and the need to improve case identification and cure rates.[28]

As in other countries, non-IV drugs abuse has been also identified as a behavioral determinant for unsuccessful treatment, namely alcohol dependence.[14,19] But in contrast, in our final model, such

Table 3 Factors associated with unsuccessful treatment among PTB cases, Continental Portugal, 2005–2009 (Predictive model)

	Bivariate analysis			Multiple logistic regression		
	OR	**95%CI**	**P**	**OR**	**95%CI**	**P**
Age group (yrs)						
15–24[a]	1.00			1.00		
25–44	2.02	1.49–2.75	<0.001	0.72	0.43–1.21	0.209
45–64	2.13	1.55–6.35	<0.001	1.39	0.83–2.32	0.207
≥65	4.63	3.37–6.35	<0.001	**4.37**	2.64–7.22	<0.001
HIV infection						
No[a]	1.00			1.00		
Yes	5.52	4.75–6.42	<0.001	**4.93**	3.50–6.96	<0.001
Other comorbidities[b]						
No[a]	1.00			1.00		
Yes	2.12	1.83–2.46	<0.001	**2.09**	1.63–2.68	<0.001
IV drug abuse						
No[a]	1.00			1.00		
Yes	3.76	3.21–4.40	<0.001	**2.29**	1.50–3.50	<0.001
Type of case						
New case[a]	1.00			1.00		
Retreatment	2.15	1.83–2.53	<0.001	**1.44**	1.06–1.95	<0.001

a: Reference category.
b: Excluding HIV and Diabetes; OR = odds ratio.
CI = confidence interval.

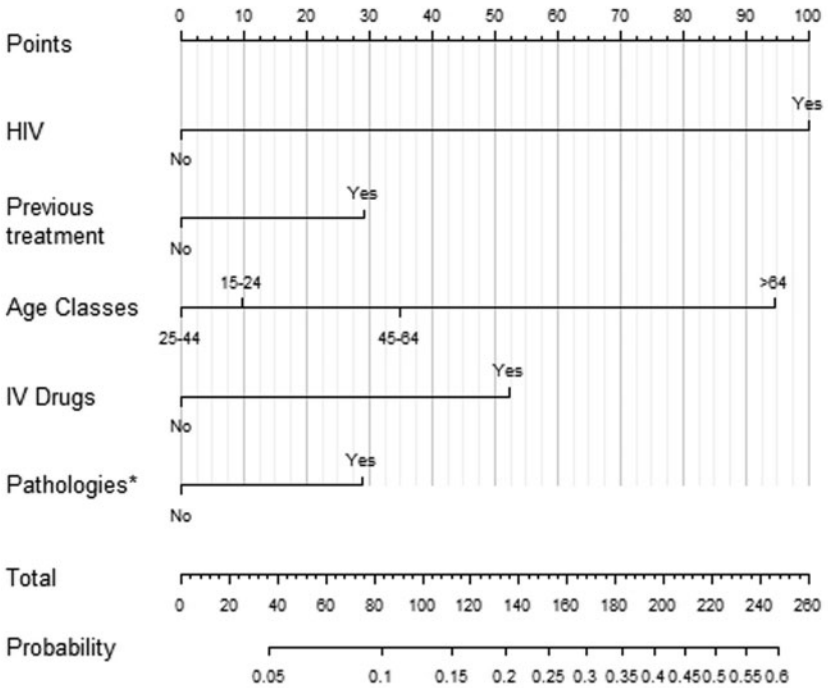

Figure 1 Nomogram for the identification of PTB patients at risk for unsuccessful treatment outcomes, Continental Portugal. Instructions: locate patient status on each of the horizontal axes representing individual information. Draw a straight line up to the 'Points' axis to determine how many points the patient receives for his/her status. Sum up the points for each predictor and locate this sum on the 'Total' axis. Draw a line straight down from the 'Total' axis until it intersects the horizontal line 'Probability', corresponding to the expected probability of unsuccessful treatment outcomes. ∗Other comorbidities, (excluding HIV and Diabetes)

effect was not observed, despite its identification in the bivariate analysis.

Comorbidities excluding HIV and DM were a factor associated with increased unsuccessful outcomes. Indeed, anemia, dyspnea, chronic coronary heart disease,[29] renal insufficiency,[30] other infectious diseases, immunosuppression and neoplasias[29] are recognized as being associated with TB unsuccessful outcomes.

Another important factor found was the history of previous treatment, consistently with different studies,[14,17,21,31] as these patients require longer treatments and at least five first-line antibiotics.[32,33]

Contrary to findings by other researchers, male sex was not identified in the multiple model. This seems to indicate that, in our study, its possible effect was overridden by the weight of other factors that should, these, be a real concern for the TBNP, as they may be preventable and sex, a confounder. This was corroborated by the bivariate analysis, when adjusted for age and sex, which showed an increased risk for unsuccessful treatment in TB/HIV co-infection, IV or other drugs abuse groups.

Similarly, DM was not identified as a risk factor in Portugal. However, several studies indicate that DM patients have a higher risk of developing TB, as well as of having unfavorable treatment

results. Baker and colleagues,[34] in a systematic review, showed the association of DM with treatment failure and death during treatment. This study highlights the attention needed during treatment of DM patients, which may include disease diagnostic tests, improving clinical monitoring and therapy.

In our study one possible explanation to the appearance of DM as a protector, can be the high coverage (84.2%) by medical surveillance in DM patients (with two or more registered medical appointments in 2014), reported by the Portuguese National Diabetes Centre. This reveals a special care in monitoring and controlling this risk group metabolically and an additional positive discrimination by health professionals of a group usually associated with negative TB outcomes.

Furthermore, considering that some unsuccessful predictors also predict TB infection or disease, susceptible of being detected, the probability to detect TB may well be increased by these factors. Persons with DM, HIV positive or socially disadvantaged may have been submitted to a higher TB scrutiny. So, the notified population may have its overall probability of unsuccessful treatment artificially increased, as patients with these factors may be overrepresented. This issue is particularly important when the detection practices vary in time or space, making the analysis of unsuccessful outcomes factors a really complex challenge.

Concluding, the overall level of unsuccessful treatment complied with WHO 85% threshold for successful treatment. However, the heterogeneity of unsuccessful outcomes rates—more severe in identified exposure certain specific groups—show the need for a strong commitment of TBNP to counteract these results. Relevant predictors of unsuccessful treatment for PTB in Portugal were coherently identified, in spite of database limitations. A robust predictive model included several known risk factors: TB/HIV co-infection, age over 64 years, IV drugs abuse, other diseases (excluding HIV and Diabetes) and retreatment. This model was represented through a *nomogram* that can easily identify patients at increased unsuccess risk upon admission, thus orienting physicians to a more adapted approach to selected cases: an appropriate clinical strategy can improve the course of any case with a higher probability of unsuccessful outcomes.

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Conflicts of interest: None declared.

Key points

- Identification of individual factors associated with unsuccessful treatment outcomes of PTB cases in Continental Portugal, in a nationwide retrospective cohort study.
- A robust predictive model including several known risk factors: TB/HIV co-infection, age over 64 years, IV drugs abuse, other diseases (excluding HIV and Diabetes) and retreatment, displaying a rather good validity.
- This model, translated into a nomogram—a user-friendly and intuitive tool, can help physicians to timely identify PTB cases at higher risk of unsuccessful outcomes, who may then undertake close monitoring and other clinical actions to promote success.
- National and international pertinence, considering Tuberculosis, Public Health and methodological perspectives.

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