

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA

PhD THESIS

EPIDEMIOLOGICAL ASPECTS OF TUBERCULOSIS
IN CHILDREN IN THE OLTENIA REGION AND
TYPE OF RESISTANCE TO SPECIFIC THERAPY

Summary

Scientific Coordinator

Professor Florica **POPESCU, MD, PhD.**

PhD fellow: Venera Cristina PÎRVULESCU (DINESCU)

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DEFINITION AND HISTORY

Tuberculosis is an infectious disease that has a chronic course and is caused by *Mycobacterium tuberculosis* (Mt) or Koch bacillus (BK) which belongs to the genus *Mycobacterium* germ.

During the 17th and 18th century, corresponding with the industrial revolution and massive urbanization tuberculosis (TB) gains epidemic proportions in Europe. Despite the efforts and measures implemented, more than ten million new cases of disease are being diagnose annually. Due to the character endemic disease, Romania faced the same problems as most of Europe. Since 2007, Romania is part of the Plan to Stop TB in 18 High Priority Countries of the WHO European Region, 2007-2015, initiated by the WHO Regional Office for Europe. The plan aims to eliminate TB as a public health problem by 2050.

EPIDEMIOLOGY

Mt. is most commonly transmitted from a patient with pulmonary tuberculosis contagious to others through what are aerosolized infectious particles through coughing, sneezing or speaking. Children can be infected by an adult. In the last decade, TB emerged as a major health problem among children who represent a small percentage of all TB cases. As in most European countries, in Romania after the Second World War, endemic tuberculosis showed a downward trend, attributed to the increased wealth and secondary to the introduction of specific antituberculosis chemotherapy.

CLINICAL ASPECTS

The clinical manifestations of TB infection are dependent on the host's immune response, T-cell mediated response and macrophages. Interaction between Mt. – healthy organism remains indifferent in 70 % of cases. Only 30 % of cases are infected. Infection in turn, may evolve differently. Therefore, over 90% of cases remain dormant and only 10% of cases can turn into disease, so it is important not to confuse the term "tuberculosis infection" with that of "tuberculosis disease".

METHODS OF DIAGNOSIS

Recent discoveries have improved the ability to diagnose latent infection and active tuberculosis in children, but establishing the diagnosis of latent infection or active disease in children who are infected with HIV remains a major challenge, especially in countries where HIV-TB co-infection is frequent.

Diagnosis of tuberculosis in children is more difficult than in adults because the clinical signs are nonspecific, radiography can be difficult to interpret and routine laboratory tests are not helpful .

THERAPY OF TUBERCULOSIS IN CHILDREN

Treatment of TB in children follows the same general principles as treatment of adults, but is also showing specific features. From a historical perspective, the indications for treating children with tuberculosis were extrapolated from clinical trials in adults with pulmonary tuberculosis.

Antituberculosis drugs

Anti-tuberculosis drugs used in the treatment of children are the same as those used in adults. Five major drugs are considered first-line agents in the treatment of tuberculosis : isoniazid (INH) , rifampicin (RMP) , pyrazinamide (PZA) , ethambutol (E) and streptomycin (S).

Mechanisms of action

Anti-TB medication is acting exclusively on ongoing multiplication bacilli and is inactive on dormant germs. Tuberculostatic medication is acting differently *in vivo* and *in vitro*, hereby, INH and RMP are bactericide *in vitro* and *in vivo*, PAS is bacteriostatic *in vitro* and *in vivo*; PZA is bactericide *in vivo*, E is bacteriostatic *in vivo* and S is bactericide *in vivo*.

Genomic and transcriptional profile of multidrug -resistant Mycobacterium tuberculosis .

Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to at least two of the best anti-TB drugs, INH and RMP. TB-SDR (Single drug resistance) is defined as the resistance of bK strains in one class of tuberculosis. MDR term was extended to any fluoroquinolone and second-line injectable agent (excluding streptomycin). This particular type of resistance was called extensively drug resistant tuberculosis (XDR TB).

Therapeutic regimens for the treatment of TB in children are identical to those of adults. There have been established codes or symbols that identify recommended drugs regimens. A regimen has two phases: an initial phase (intensive) and a follow-up phase. The number placed before phase represent the duration in months. The number that appears subscribed indicates the number of doses per week.

STUDY OBJECTIVES

Aim of the study

- Identify the frequency of tuberculosis in children under 15 years in the South West region of Romania and identify the main factors involved in achieving these variables.
- Analysis of resistance to anti-TB treatment of BK strains isolated from children.

The specific objectives of the study

- Presenting the evolution of number of cases of TB in children according to the year of detection and evolutionary trend.
- Comparative analysis of the number of cases according to different variables.

- Identify the incidence of tuberculosis in children at regional and county level.
- Analysis of the incidence of tuberculosis in children and determine the risk of tuberculosis among different groups of children.
- Identification bK resistant strains frequency in children.
- Establish associations between drug resistance strains isolated from children bK variables of interest.

MATERIAL AND METHODS

Material

To achieve the proposed objectives were two groups:

Lot 1 - TB frequency analysis was performed on a batch of 627 diagnosed cases of tuberculosis in children under 15 years. The cases were diagnosed during the period 2006-2012 from 5 counties of the South West region.

Lot 2 - To estimate the resistance to treatment was constituted a larger batch that included a total of 4370 cases diagnosed with tuberculosis at national level. Age of inclusion in the study group was 0-17 years; there were included only cases detected in 2010-2012.

Methods

TB frequency was monitored in studied groups and expressing its use both as absolute frequency (number of cases) and relative frequency (percentage). For calculating incidence were accepted formula used for its presentation to report the number of new cases per number of people at risk.

Population at risk considered in the study was the pediatric population whose age at the time of reporting was under 15 years of their residence in the South West region, respectively constituted 5 counties (Dolj , Gorj , Olt, County , Vâlcea) . Population data were taken from the database of the National Institute of Statistics (INS) offered online platform Temo available <https://statistici.insse.ro/shop/?lang=ro>.

RESULTS AND DISCUSSION

I. Epidemiology of tuberculosis in the pediatric population

I.1. Distribution of cases of tuberculosis in children

I.1.1 . Distribution of cases of tuberculosis in children by gender

TB infection was identified with a higher frequency in males, having been found a total of 335 boys, representing 54.03 % of the total number of cases reported with age under 15 years; girls represented 46 % of all cases (285 cases) .

I.1.2 . Distribution of cases of tuberculosis in children by area of origin

Residence in urban areas showed an obvious "masculinization" of TB infection in children under 8 years. The contribution of rural cases behaved differently in two distinct periods. In the first period, 2006-2009 it conveys a decreasing trend, moving towards a balance between the two areas. After 2009 however the percentage of cases in rural areas has grown steadily and has increased so that in 2012 it represents almost 75 % of all reported cases , meaning that in four cases detected three cases came from rural areas .

Other districts have registered a significantly higher number of cases from rural areas a , their share of the total number of cases is over 60 % and over 70 % Vâlcea in this rural county the number of cases being almost 2.5 times higher than in urban areas than the cases (56 rural / urban 23) .

I.1.3 . The distribution of the number of cases of TB in children by age

Cases of infection in young children (aged 0-4 years) accounted for 30 % of pediatric cases being diagnosed in all 5 counties of the South West region a number of 187 cases of tuberculosis in this age group. Cases belonging to the age group 10-14 years accounted for the largest share of pediatric cases (46 %) were identified a number of 279 cases , representing almost half of the cases reported . The lowest percentage was observed in intermediate -age children (age group 5-9 years) with a total of 146 cases , number that represents 24% of total.

I.2 . The incidence of tuberculosis in children in the South- West Oltenia

I.2.1. The annual incidence of tuberculosis in children in the South- West Oltenia and counties surrounding

A particular aspect was observed at the onset of the analyzed period, when there was a clear downward trend in the share of the number of cases in young children, from 37.1% in 2006 to 28.6 in 2007, reaching in 2008 percentage of cases in this age group to reach a minimum of 23.2% .

The highest incidence was observed value for Dolj County with 33.74 cases / 100.000, which is the county which provided most cases of tuberculosis in children. An average incidence of over 30 cases / 100,000 was encountered in Michigan (30.82 cases / 100,000) .

The lowest incidence among counties in the region were noted Vâlcea (19.11 cases / 100,000) , which was the only one that showed an incidence below 20 cases / 100,000 and in Gorj with an incidence of tuberculosis children of this county of 21.78

II.2.2. Analysis incidence of resistance bK depending on the sex

In males the incidence of tuberculosis (28.94 cases / 100,000) was higher than the incidence of tuberculosis in female children (25.5 cases / 100,000) , but the risk was not significantly higher for males (RR = 1.13 , CI95 % 0.96 to 1.33 ; p = 0.14) .

The biggest difference between the incidence of tuberculosis in children male and female was observed in Gorj county , where the incidence of tuberculosis in boys (24.76 cases / 100,000) was 33.12 % higher than TB incidence in girls (18.6 cases / 100,000) . However no identifiable risk higher in men compared to women (RR = 1.29 ; CI95 % 0.85 to 1.96 ; p = 0.23).

1.2.3. Analysis incidence of resistance bK depending on the environment of provenance

Higher frequency of tuberculosis in rural areas was confirmed by finding a higher incidence of 38.45 % children in rural areas of 31.27 cases / 100,000 (95% CI 29.69 to 49.98) compared with those with residence in urban areas (22.61 cases / 100,000 ; IC95 % from 23.24 to 33.22) . The risk of tuberculosis infection in children under 15 years of rural areas in this context was almost 1.5 times higher compared with peers from urban areas (RR = 1.437 ; CI95 % 1.11 to 1.8 ; P = 0.006) .

1.2.4. The annual incidence of tuberculosis in children by age

During the analyzed period only small age groups , 0-4 years and 4-9 years tended to decrease in annual incidence rates of tuberculosis , most expressed trend was observed in the age group 0-4 years, especially in 2006-2010 .

Assessment of the incidence of tuberculosis each year of age from 0-14 years has allowed the TB susceptibility to a profile marked by a higher frequency in children under 1 year (36.5 cases / 100,000) and those aged over 12 years , when the incidence of tuberculosis starts to grow faster , reaching the age of 14 TB rate is over 55 cases / 100,000 .

Children under 1 year were particularly more affected by tuberculosis infection compared to older ages of childhood. He drew particular attention to the high frequency of tuberculosis in 2006 at rural children (113.48 cases / 100,000) and 2012 (89.37 cases / 100,000) was observed tendency resurgence of tuberculosis in infants , increasing the almost 4 times tuberculosis in children under 1 year of 2012 rural is disturbing .

II. BK resistance analysis of tuberculosis cases in children

II.1. General characteristics of the lot

The small number of cases of tuberculosis resistant strains of Mycobacterium tuberculosis treatment and detected in children was established a nationally representative sample that included all cases of tuberculosis reported in children under 18 years in 2010-2012 . Lot tuberculosis cases detected and reported in patients aged under 18 years included a total of 4370 cases.

II.2. Analysis incidence resistant strains antituberculosis

II.2.1. Analysis of the evolution incidence in the period analyzed

Were detected a total number of 43 cases who presented infection tuberculous with strains bK resistant to antituberculosis . The incidence of tuberculosis with the bK -resistant at one or more anti-tuberculosis of the was of 9.84 cases / 1000.

Number of cases detected were relatively well distributed on the years evaluated , being detected 13 cases of tuberculosis with resistance to antituberculosis in 2010 , 15 cases in 2011 respectively 14 cases of strains bK resistant to one or more antituberculosis detected in 2012.

The evolution by year detection revealed tendency increased incidence resistant strains antituberculosis detected among studied cases. This increased from an incidence of 8.48 cases / 1000 in 2010 to a value of 10 cases / 1000 in 2011, to achieve value of 10.48 cases / 1000 in 2012.

II.2.2. Analysis incidence of resistance bK depending on the sex

Cases distribution on sex has highlighted a larger number of cases with tuberculosis infection produced by a resistant strain to one or more specific drugs for female gender. Thus, were detected 29 cases among girls. Cases of tuberculosis with resistant bK detected in girls have represented over two thirds of total number of cases of tuberculosis with resistant bK to specific drugs. In these conditions we could estimate the risk of tuberculosis infection with resistant bK strains as being twice higher in girls than in boys (RR = 2,037; IC95 % 1.07 to 3.84; P = .0281).

II.2.3 . Analysis incidence of resistance bK depending on the environment of provenance

Cases of tuberculosis with bK resistant were almost equally distributed in the two environments of provenance, being detected 22 cases in rural areas and 21 in urban.

II.2.4. Analysis of resistance BK incidence by age

The average age of cases in which resistant strains were isolated BK was higher by almost 5 years compared to cases involving strains susceptible to tuberculosis or to which resistance has not been established .

Thus in cases involving strains resistant BK mean age 15.12 ± 2.59 was years and to the strains bK 10.31 ± 5.82 years sensible difference was highly statistically significant ($p < 0.001$).

Most cases have been identified in children over 14 years. In this age group were identified 31 cases of tuberculosis resistant to isolated bK one or more antituberculosis . They accounted for almost three -quarters of the total strains resistant BK (72.09 %).

II.2.5. Resistant incidence analysis based on the classification of cases.

Most cases of isolated strains were resistant tuberculosis BK was the new cases (N = 36 cases) , their share of all cases of resistant strains being 83.72 %.

Chronic tuberculosis which was the involvement of resistant strains was identified in 3 cases (6.98 %) and three cases were relapses after treatment (6.98 %). One case has been declared as treatment failure, the share of this category of cases in cases with resistant strains of tuberculosis was 2.33 %.

All 3 cases of chronic tuberculosis detected in children nationwide were cases whose etiology involving a strain resistant tuberculosis.

Also , the 7.14 % (3 cases) in the case with a treatment failure (57 cases) were involved bK -resistant strains , and in 1 case out of 15 patients reported that relapse of tuberculosis strains was isolated involvement BK resistant within this category of cases is 5.26 %.

II.2.6. The incidence of resistance according to HIV status BK

Although tested nearly 30 % of cases of tuberculosis in children being tested in a total number of 1196 cases of tuberculosis, confirmation rate was relatively high (2.42 %), 29 cases were confirmed to have associated infection HIV. The rate of tuberculosis among HIV- garment all children with tuberculosis was 0.24 %, however.

Of the 43 cases whose etiology was represented by strains resistant tuberculosis BK almost two thirds (29 cases, representing 67.44 %) were not tested for HIV. A total of 4 cases was confirmed after tests confirmed the presence of human immunodeficiency virus infection. Thus, about 5% (4.9 %) of cases detected tuberculosis resistant tuberculosis in children was objectified garment HIV- tuberculosis, and in 23% of HIV cases has been invalidated.

II.3. The incidence of tuberculosis resistant to more than two anti-tuberculosis (MDR TB)

Total number of cases of children identified as bK strains resistant to more than one tuberculosis (MDR TB) was relatively small, only 10 cases, but their importance in identification is very high. Almost three quarters of the strains were resistant only to one class of anti-tuberculosis (TB SDR), 33 cases and 10 cases were isolated strains resistant to multiple tuberculostatics bK .

Incidence of tuberculosis resistant to multiple tuberculostatics expressed an alarming upward trend among children. It has evolved from a value of 1.31 reported incidence in 2010 to a value of 2.67 cases / 1000 in 2011 to reach 2012 in 3 cases / 1,000 cases of tuberculosis.

In cases resistant to bK only one class of antituberculosis garment HIV risk cases of tuberculosis in children was 15 times higher than the BK -sensitive tuberculosis. (RR = 15.07; IC95 % from 4.784 to 47.485; P < 0.0001).

Recording a number of 3 fatal cases of children with tuberculosis strains resistant tuberculosis BK allowed for a rate of MDR tuberculosis mortality in children under 1% and SDR.

The risk of death was greatest for cases infected with resistant bK more than two classes of tuberculosis (MDR TB) , which is over 12 times higher than in cases of tuberculosis sensitive BK (RR = 12.69 ; IC95 % 1.89 to 84.96 ; p = 0.009) .

CONCLUSIONS

After analyzing the data obtained in this study we could draw the following conclusions:

Analysis of sex ratio identified a higher frequency of cases in boys, aspect that suggest a higher susceptibility them than girls.

We notice a pattern of greater frequency of tuberculosis in children at age of first entry into the community preschool (2-4 years) and entered the community school (6-7 years).

Starting from the fact that the weight of cases of tuberculosis in young children ranged from 23.2% in 2008 and 37.1 % in 2006, we can say that age cannot be use as a criterion with a reasonable level of safety in developing the suspicion of tuberculosis in children. There are many variables that can interfere the distribution of cases by age. The most frequently involved being the demographic phenomenon witch is the main characteristic of the last decade with decrease in the share of small children.

The largest share of cases is given by children from Dolj County , the picture provided by the situation of children in this county is strongly reflected in the evolution of the incidence of tuberculosis in the entire region .

The average of incidence of tuberculosis in Oltenia region was 27.68 cases / 100,000. In most years was observed incidence of tuberculosis decreased compared to 2006, except in 2011 when it was registered a growth of 10.8% in the incidence and 2010 with an increase of 7.1% respectively.

Evaluation of TB incidence for each year of age from 0 to 14 years allowed the profiling of tuberculosis susceptibility marked by a higher frequency in children under 1 year of age and those over 12 years, especially in rural areas. The risk of tuberculosis in children under 1 year from rural areas was almost 3 times higher than those of the same age but with residence in urban areas.

Differences between the two residence areas in the incidence by age in children have been linked to the existence of a peak incidence in children from rural areas who emerged earlier (age 2 years) and in children from urban areas at 4 years.

The incidence of resistant strains was 9.84 cases/1000 cases of tuberculosis and its evolution showed increasing trend in the incidence of tuberculosis resistant strains.

The average age of cases in which BK resistant strains were isolated was higher by almost 5 years compared to cases involving strains susceptible to anti-tuberculosis drugs or resistance has not been established, aspect due on one hand because of high number of cases of tuberculosis in adolescence, but especially by the difficulty of isolating bacillus in small children. The MDR TB was more frequently detected in female cases.

Most cases from witch have been isolated antituberculous resistant BK strains was the new cases. Chronic Tuberculosis and therapeutic relapses accounted together for about 15%.

Incidence of tuberculosis resistant to multiple tuberculostatics expressed an alarming upward trend among children, being observed increase more than 2.5 times the weight of BK MDR strains, nearly half of the cases detected in 2012 was cases cases with MDR. This finding is consistent with current data showing an increase in MDR TB in certain regions of Eastern Europe, Central Asia and in parts of Africa.

The risk of death was greatest for cases infected with MDR bK , which is over 12 times higher than in cases of tuberculosis sensitive BK (RR = 12.69 ; CI95 % 1.89 to 84.96 ; p = 0.009).

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CURRICULUM VITAE

Nume: DINESCU (PÎRVULESCU)

Prenume: VENERA CRISTINA

Data și locul nașterii: 26.12.1973, Craiova, Dolj

Cetățenie: româna

Adresa: Bld. Dacia, Bl. E1, Sc.1, Ap. 14; Craiova, județul Dolj

Telefon: 004 0740492161

Email: veneradi@yahoo.com

Stare civilă: căsătorită

Studii:

1988-1992 Liceul Sanitar Craiova

1992-1998 -UMF Craiova - Facultatea de Medicină, UMF Craiova, media de
absolvire 9,90

2007 – 2009 Masterat - Managementul Unităților Sanitare, UMF Craiova

2005 – medic specialist Igienă;

2013 – medic specialist Medicina muncii;

Locuri de muncă anterioare

2007-2008 – Medic specialist igienă, ASP Olt, Departamentul Prevenție;

2008 – 2014 – Asistent universitar Disciplina Igienă. Sănătatea Mediului;

2014 – prezent - Asistent universitar Disciplina Medicina Muncii. Boli profesionale;

Locul de muncă actual și funcția

2014 – UMF Craiova, Facultatea de Medicină, Departamentul 4, Disciplina
Medicina Muncii, Boli profesionale, Asistent universitar;

LISTĂ REALIZĂRI ȘTIINȚIFICE

Cercetare – Granturi = 1

1. Colaborator în grantul «CANCREGOLT» - Organizarea registrului de cancer Oltenia nr. 41016/2007 din cadrul Programului PARTENERIATE IN DOMENIILE PRIORITARE ;

Articole publicate in extenso în reviste indexate BDI = 9

1. **Dinescu Venera**, Madan Marinela, Prejbeanu Ileana, Petrisor D., Dinescu SN, Melinte V., Dragomir Manuela. Romanian Journal of Hygiene and Public Health , **2008**; 58(1):125-131;
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4. Sorin Dinescu, Venera Dinescu, Elena Catalina Bica, Florin Pietrariu, Marinela Madan. THE FREQUENCY OF METHEMOGLOBINEMIA IN CHILDREN AND THE CONTEXT OF ITS OCURRENCE ISEE, Barcelona 13-16 septembrie **2011**, P-1090
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10. Nina Ionovici, Rahela Iulia Marcu, **Venera Dinescu**, Maria Magdalena Mateică: Incidența și evoluția cazurilor de silicoză în clinica de Medicina Muncii din Craiova în ultimii trei ani; Sănătate Publică, Economie și Management în Medicină, Chișinău, Rep. Moldova, 3 (54) 2014, 45-47; ISSN 1729-8687

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5. Dinescu Venera, Prejbeanu Ileana, Madan Marinela, Dragomir Iuliana Manuela. Incidența intoxicațiilor cu nitriți în județul Olt; Zilele UMF Craiova ediția a XXXVIII-a, 6-7 iunie 2008, Abstr. p342;
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20. Dinescu Venera, Bădulescu Adriana, Schenker Michael. ALIMENTAȚIA ȘI ACTIVITATEA FIZICĂ – FACTORI DE RISC MODIFICABILI ÎN CANCERUL COLULUI UTERIN, Zilele UMF din Craiova 5 -6 iunie 2010;
21. Dinescu S.N., Bădulescu F., Dinescu Venera, Schenker M., Melinte V. STUDIU PRIVIND MORTALITATEA PRIN CANCER AL COLULUI UTERIN ÎN JUDEȚUL DOLJ; Zilele UMF din Craiova 5 -6 iunie 2010
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26. Hurezeanu Adriana, Dinescu Venera. ASPECTE ALE RELAȚIEI DINTRE DEZVOLTAREA NEUROPSIHICĂ ȘI COMPORTAMENT LA PUBERI ȘI ELEVII, Zilele UMF din Craiova 8 -9 iunie 2012; Hurezeanu Adriana, Dinescu Venera. IMPLICAȚIILE UNOR COMPORTAMENTE CU RISC ÎN STAREA DE SĂNĂTATE LA ELEVII, Zilele UMF din Craiova 8 -9 iunie 2012;
27. Dinescu Venera, Hurezeanu Adriana, Dinescu S.N., Vasile Ramona. FUMATUL ȘI CONSUMUL DE ALCOOL LA ADOLESCENȚI, Zilele UMF din Craiova 8 -9 iunie 2012;
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29. PULMONARY TUBERCULOSIS WHEEZING IN EARLY CHILDHOOD, Dumitra G., Bobârnac Ana, **Dinescu Venera**, Bulucea D. A 5-a Conferință a Doctoranzilor și a 2-a Conferință a Postdoctoranzilor în Medicină și Farmacie; Tirgu Mureș; 4-6 iulie; 2012;
30. Dinescu Venera, Dinescu S.N., Vasile Ramona. Influența anturajului în adoptarea obiceiului de a fuma la adolescenți. Zilele UMF din Craiova, 7 -8 iunie 2013;
31. Dinescu V, Dinescu S, Ionovici N, Balseanu A. The impact of nearest community environment in acquiring by teenagers of unhealthy behaviours: smoking and alcohol consumption; New face of function and dysfunction current progress in biomedical science and medical education, Iași; 09.05-10.05.2013;
32. **Dinescu Venera**, Ionovici Nina, Bica Elena Catalina. „Aprecierea influenței factorilor de microclimat asupra stării de confort termic într-o colectivitate de copii prescolari”. Zilele UMF din Craiova a XLIV-a editie, iunie 2014, ISSN 1843-2441

Manifestari stiintifice internationale = 3

1. The 25th International Congress of Pediatrics, august 2007, Athens, Grece;
2. ISEE, Barcelona, 13-16 septembrie 2011
3. 31st Annual Meeting of the European Society for Pediatric Infectious Diseases, Milan, may 28 – june 01, 2013

Manifestari stiintifice nationale = 16

1. Al XII-lea Congres Național de Medicina Muncii, 23-25 septembrie 2004;
2. Simpozionul Național de Patologie Infecțioasă, Iași, 28-30 septembrie 2006;
3. Al IV-lea Congres Național Privind Infecția HIV/SIDA în România, București 12-14 octombrie 2006;
4. Zilele UMF Craiova -Simpozion: Actualitati in oncologie, Craiova, 8-9 iunie 2007;
5. Al X-lea Congres Național de Igienă, Craiova 8-10 mai 2008;
6. Zilele UMF Craiova ediția a XXXVIII-a, Masa rotundă – Cancerul de sân în Oltenia – Frecvență și factori de risc, Craiova, 6 iunie 2008;
7. Zilele UMF Craiova ediția a XXXVIII-a, Simoziion Provocari în sănătatea comunitară, Craiova, 6-7iunie 2008;
8. A VI-a Conferință a Societății Romîne de Oncologie Medicală, București, 8-10 septembrie 2008;
9. Zilele UMF Craiova, 2009
10. Zilele UMF Craiova, 2010
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12. Zilele UMF Craiova, 2012
13. A 5-a Conferință a Doctoranzilor și a 2-a Conferință a Postdoctoranzilor în Medicină și Farmacie; Tirgu Mureș; 4-6 iulie; 2012
14. Zilele UMF Craiova, 2013
15. Zilele UMF Craiova, 2014
16. New face of function and dysfunction current progress in biomedical science and medical education, Iași; 09.05-10.05.2013;

Organizare manifestări științifice

1. Zilele UMF Craiova ediția a XXXVIII-a, Simoziion Provocari în sănătatea comunitară, Craiova, 6-7 iunie 2008 - secretar științific