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## RESEARCH ARTICLE



# Assessment of osteoarticular morbidity in regions with different boron concentrations in deep drinking water of the Republic of Moldova

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## ABSTRACT

**Introduction.** Even if boron is not yet recognized as an essential element for the human body, its insufficient intake is considered harmful, especially for the osteoarticular system. A daily intake of at least 3 mg of boron can fortify bone mass and prevent the onset of osteoarthritis, rheumatoid arthritis, and osteoporosis. This research aims to assess the morbidity caused by rheumatoid arthritis and inflammatory polyarthropathies in the population from regions with different boron concentrations in deep drinking water of the Republic of Moldova.

**Material and methods.** Two full-length descriptive observational studies were conducted: one on osteoarticular morbidity caused by rheumatoid arthritis and inflammatory polyarthropathies (incidence and prevalence), and one on boron concentrations in deep drinking water (public wells and artesian wells). Following national regulations, the Republic of Moldova was divided into three distinct boron-related areas, and in each of them, the boron trend overlapped with the morbidity trend.

**Results.** In the below-the-limit boron area, the research hypothesis was confirmed in two out of three districts, by overlapping osteoarticular morbidity with boron concentrations in deep drinking water and their trendlines. In the limit-level boron area, boron concentrations in drinking water do not appear to influence the studied osteoarticular morbidity in either district. In the above-the-limit boron area, unlike in previous research, trends for boron concentrations in public wells and artesian wells were opposite to those of the incidence and prevalence of rheumatoid arthritis and inflammatory polyarthropathies, confirming the research hypothesis.

**Conclusions.** Out of the three studied areas, the expected phenomenon of low morbidity and high boron concentrations, and vice versa, was observed in two below-the-limit boron districts and two above-the-limit boron districts. The results can be expanded upon in further research in the field.

**Keywords:** boron, osteoarticular diseases, deep drinking water, osteoarthritis, rheumatoid arthritis.

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## Key messages

### What is not yet known about the issue addressed in the submitted manuscript

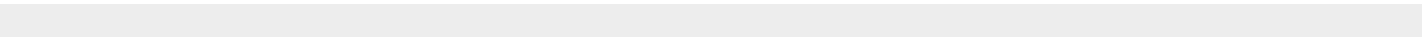
No study has been conducted to link specific osteoarticular morbidity with the boron concentrations in deep drinking water from the Republic of Moldova. Moreover, in previous national reports on boron concentrations in drinking water, this trace element was addressed as a contaminant that should be reduced in the water consumed. This paper examines boron from the perspective of a bone and joint health enhancer.

**The research hypothesis**

Periods of higher boron consumption through deep drinking water by the population, showing a positive trendline, are accompanied by a lower incidence and prevalence of rheumatoid arthritis and inflammatory polyarthropathies, which show a negative trendline—and vice versa.

**The novelty added by the manuscript to the already published scientific literature**

The study offers a new perspective on how boron could be addressed in national regulations concerning drinking water and recommends raising its permissible limit to align with the EU standard for the benefit of the population. The characterization of regions with different boron concentrations in deep drinking water can be used to estimate the impact of this mineral on other body systems in future research.



**Introduction**

Boron is a trace element that has not yet been recognized as essential for the human body. The World Health Organization (WHO) highlights that insufficient boron intake can impair the body’s biological functions, potentially causing long-term harm [1]. The WHO recommends drinking water as the primary source of this element and prioritizing natural springs rich in boron [2].

A minimum intake of 0.4 mg of boron per day can contribute to the strengthening of bone mass, with the regulated boron concentration in drinking water providing the body with basic essential benefits [2, 3]. Moreover, an adequate boron intake can reduce calcium and magnesium loss through urine [4, 5], promote osteogenesis [3, 6], decrease inflammatory joint processes [7, 8], reduce articular discomfort, and improve mobility [4, 9]. Osteoarticular diseases that can be prevented by a boron-rich diet include osteoarthritis, rheumatoid arthritis, and osteoporosis [10-12]. Recent research shows positive effects of boron on bone mass when the daily intake is 3 mg or more [5, 13, 14].

Population studies conducted more than three decades ago revealed that the incidence of arthritis was negatively associated with boron concentrations in soil and foods. Thus, in areas where the population’s daily boron intake was below 1 mg/day, the arthritis incidence ranged from 20 to 70%, while in regions where it was 3-10 mg/day, the incidence of this pathology was between 0 and 10% [4]. Since those findings, no other population study of comparable scale has been conducted.

Following the previous national report, in the southern region of the Republic of Moldova, in Administrative Territorial Unit Gagauzia, drinking water is richest in boron, with concentrations reaching up to 3 mg/l. These results have not yet been linked with the population’s health status [15]. Considering the lack of research on boron’s impact on public health in our country, and the fact that osteoarticular diseases are the most studied in relation to daily boron intake, this association was chosen for our study.

Even though European regulations have set a limit of 1,5 mg/L of boron in drinking water and mention that this parameter can be raised to 2.4 mg/L in boron-rich areas [16], in our country, the maximum allowable boron concentration in drinking water is 1 mg/L [17]. Another justification for this research is to provide arguments for aligning national

regulations on boron concentrations in drinking water with European standards.

This study aims to assess the morbidity caused by rheumatoid arthritis and inflammatory polyarthropathies in the population from regions with different boron concentrations in deep drinking water (public wells and artesian wells) of the Republic of Moldova.

**Material and methods**

To achieve the intended purpose, two full-length descriptive observational studies were conducted: one on osteoarticular morbidity and one on boron concentrations in deep drinking water.

*The first step* involved conducting a full-length descriptive observational study on osteoarticular morbidity (incidence and prevalence) caused by rheumatoid arthritis and inflammatory polyarthropathies during the period 2016-2020 (Table 1).

The results were analyzed and presented for the group of rheumatoid arthritis and inflammatory polyarthropathies as a whole. According to the International Statistical Classification of Diseases and Related Health Problems, Eleventh Revision (ICD-11), the group includes nine diseases, their codes being included between FA20 and FA27 and FA2Z.

**Table 1.** A brief description of the first full-length descriptive observational study on osteoarticular morbidity

Criteria	Description
Object of study	Adult morbidity due to rheumatoid arthritis and inflammatory polyarthropathies
Source of information	Data from the Health Data Management Department of the National Agency for Public Health
Collection method	Data processing, calculation of multiannual averages
Volume	A comprehensive study covering the period 2016-2020
Place of performance	National Agency for Public Health

During *the second step*, a full-length descriptive observational study on boron concentrations in deep drinking water—from public wells and artesian wells—covering the 2015-2022 period was conducted (Table 2).

The main argument of including water from public wells into our study was that this water source is frequently used by the rural population, which according to the National Bu-

reau of Statistics in 2017 constitutes 57.1% of the country's population and is a representative part of this research.

**Table 2.** A brief description of the second full-length descriptive observational study on boron concentrations in deep drinking water

Criteria	Description
Object of study	Boron concentrations in water from public wells and artesian wells across the territory of the Republic of Moldova
Source of information	Data from territorial Public Health Centers (2015-2020)
Collection method	Data processing, calculation of annual and multiannual averages
Volume	A comprehensive study for the period 2015-2020, with 2,706 samples investigated
Place of performance	National Agency for Public Health

Of the 2706 samples investigated, 480 were public well water and 2226 were artesian well water. The results were taken from the registers of territorial public health centers for the period 2015-2020. All available results from both sources were analyzed. Most samples were collected during the late summer-autumn period (August-November) or during spring (March-April). For artesian well water, for each locality, at least one sample from each artesian well has been collected per year, and the majority of them were analyzed for boron concentrations. For public well water, samples were collected less often, with an average periodicity of 1-3 samples analyzed for boron concentrations in 6 years, and not for all researched localities.

Given the national regulations restrict the boron concentrations in deep drinking water to 1 mg/L, the territory of the Republic of Moldova was divided into three distinct areas:

- *Below the limit* – boron concentrations between 0 and 0.8 mg/L;
- *Limit* – boron concentrations between 0.9 and 1.2 mg/L;
- *Above the limit* – boron concentrations above 1.2 mg/L.

From the available data, the most representative districts for each area were selected – for below the limit districts – districts with average values close to the lower limit, for districts in the limit area – average values close to the limit of 1 mg boron/l and for above the limit districts - maximum average values recorded in the country. Both public wells and artesian wells values were taken into consideration, but one of the two values for each district was the basis for the selection.

Following these criteria, selected districts for each boron-related area are:

- *Below the limit area*:
  - Călărași: 0.2 mg B/L in public wells;
  - Briceni: 0.25 mg B/L in artesian wells;
  - Drochia: 0.3 mg B/L in public wells.
- *Limit area*:
  - Cahul: 0.9 mg B/L in artesian wells;
  - Vulcănești: 1.1 mg B/L in artesian wells.

- *Above the limit area*:

- Ceadir-Lunga: 1.8 mg B/L in public wells;
- Comrat: 1.43 mg B/L in artesian wells.

In the *final stage*, boron concentrations in deep drinking water and adult morbidity due to rheumatoid arthritis and inflammatory polyarthropathies were graphically overlaid for each selected district, and trendlines for both boron concentrations and osteoarticular morbidity were calculated using Microsoft Excel 2021.

*Statistical data processing*: For the prevalence data of adults with rheumatoid arthritis and inflammatory polyarthropathies, the average prevalence for the research period was calculated. Boron concentration data in deep drinking water were organized into two separate databases: one for public wells and another for artesian wells. Average boron concentrations were calculated separately for each village and district, including the Administrative Territorial Unit Gagauzia, on a yearly basis. Subsequently the total average concentration for the analyzed period was determined for each district. Microsoft Excel 2021 was used for database creation and calculations of all averages.

The study protocol was approved by the Research Ethics Committee of *Nicolae Testemițanu* State University of Medicine and Pharmacy (Minutes No 1 of 07.09.2020).

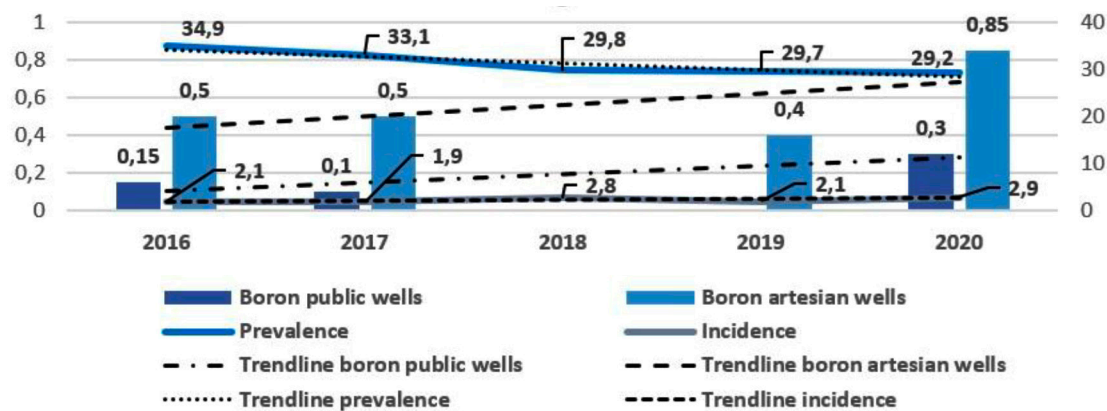
## Results

### *The below-the-limit boron in deep drinking water refers to multiannual averages of boron concentration between 0 and 0.8 mg/L.*

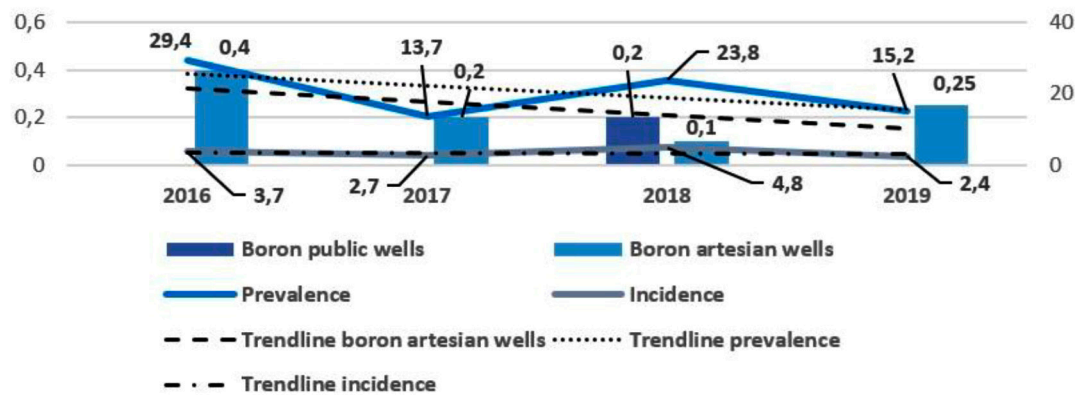
In the Călărași district, in 2020, when the boron concentrations in public wells and artesian wells reached their highest levels during the research period, the prevalence of rheumatoid arthritis and inflammatory polyarthropathies recorded its lowest values. The upward trend in boron concentrations in deep drinking water ( $y = 0.06x + 0.3825$  for artesian wells water and  $y = 0.0442x + 0.0654$  for public wells water) overlapped with a downward trend in the prevalence of rheumatoid arthritis and inflammatory polyarthropathies among adults during the 2016-2020 period ( $y = -1.48x + 35.78$ ) which supports the research hypothesis (Figure 1).

In Briceni, in 2018, both the prevalence and incidence of adults with rheumatoid arthritis and inflammatory polyarthropathies increased against the background of a decrease in boron concentrations in water from public and artesian wells. The trends for boron concentrations in artesian wells ( $y = -3.25x + 28.65$ ), as well as for the incidence ( $y = -0.18x + 3.85$ ) and prevalence ( $y = -0.055x + 0.375$ ) of rheumatoid arthritis and inflammatory polyarthropathies in adults, were all decreasing (Figure 2). Although the trendlines for boron concentrations in deep drinking water and adult morbidity do not support the research hypothesis, the increase in prevalence and incidence coincides with the decrease in boron concentrations in artesian wells.

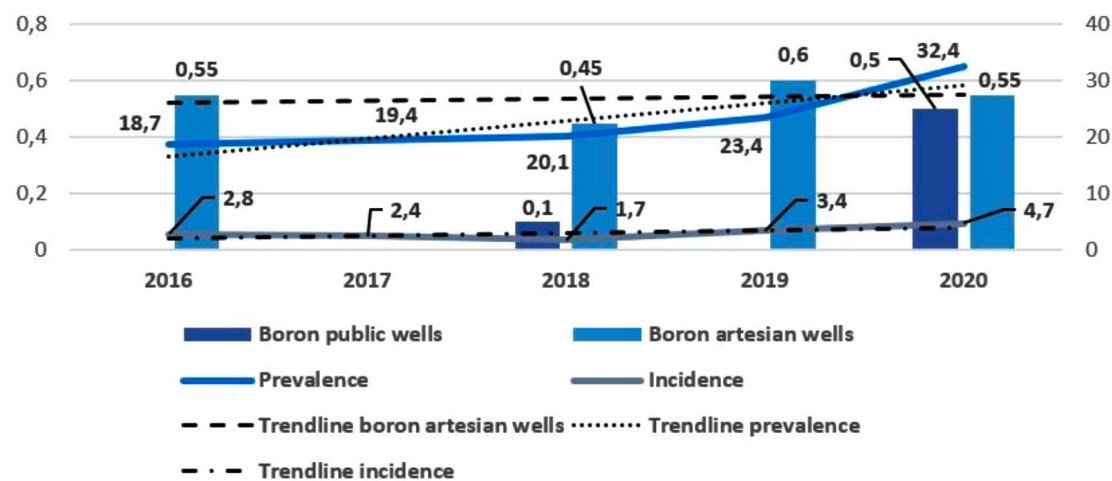
In the Drochia district, in 2020, boron concentrations in deep drinking water, as well as osteoarticular morbidity, reached their maximum values for the analyzed period. Additionally, the trends for boron concentrations in arte-



**Fig. 1** Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Călărași district, 2016-2020



**Fig. 2** Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Briceni district, 2016-2019



**Fig. 3** Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Drochia district, 2016-2020



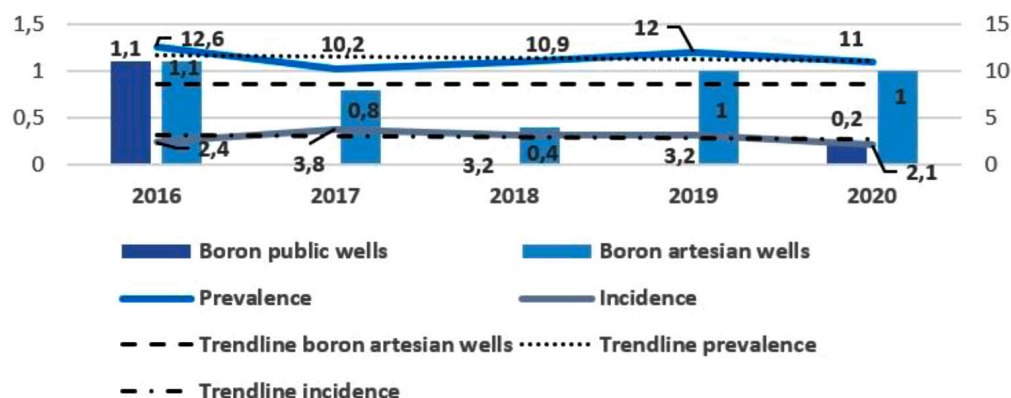


Fig. 4 Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Cahul district, 2016-2020

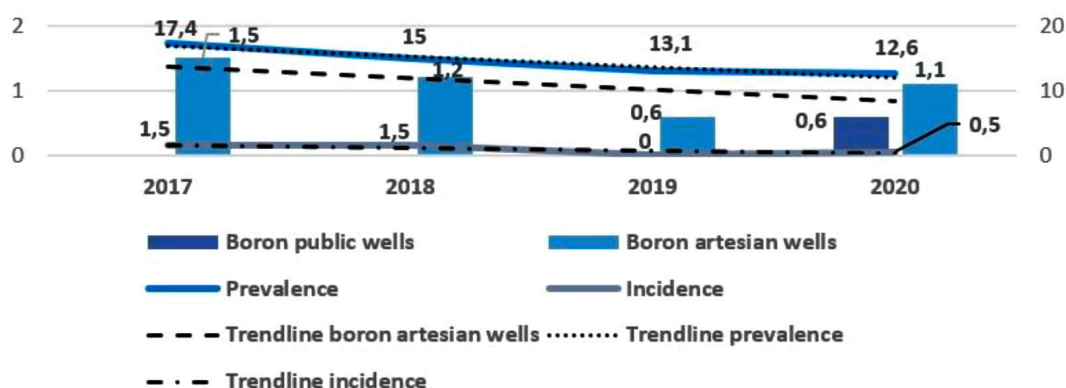


Fig. 5 Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Vulcănești district, 2017-2020

sian well water ( $y = 0.0071x + 0.5143$ ) and prevalence from rheumatoid arthritis and inflammatory polyarthropathies ( $y = 3.14x + 13.38$ ) were both positive (Figure 3). Neither the trendlines for boron concentrations in deep drinking water and osteoarticular morbidity nor of the year-by-year overlap between boron concentrations and incidence/prevalence support the research hypothesis.

**Limit-boron in the deep drinking water area (multiannual averages of boron in deep drinking water between 0.9 and 1.2 mg/L)**

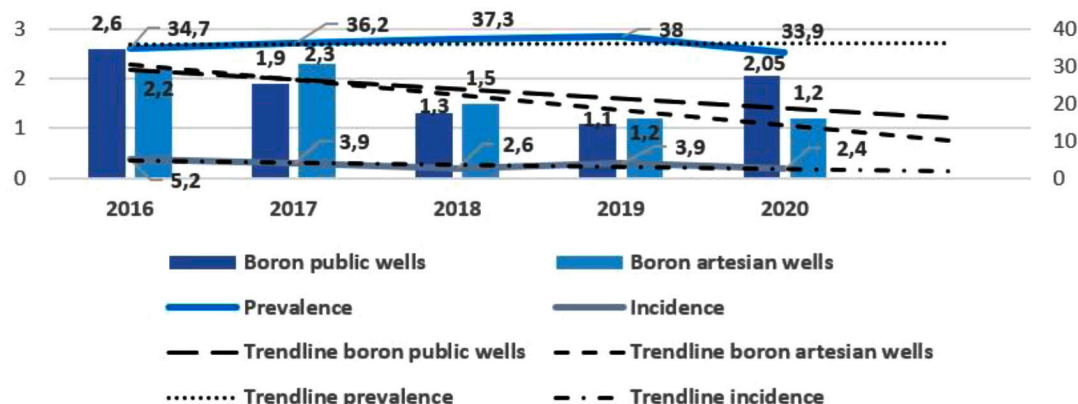
In the Cahul district, in 2016, when the boron concentration in water from public wells and artesian wells reached its highest levels, the prevalence of adults with rheumatoid arthritis and inflammatory polyarthropathies also reached a maximum, while the incidence was at its lowest for the 2016-2020 period. Trendlines for boron concentrations in deep drinking water ( $y = -3E-16x + 0.86$  for boron concentrations in artesian wells) and osteoarticular morbidity ( $-0.14x + 11.76$  for the prevalence and  $y = -0.12x + 3.3$  for the incidence) were both negative (Figure 4). The overlap of high boron concentrations in public and artesian wells with the incidence values matches the

research hypothesis, while the trendlines for boron and morbidity do not.

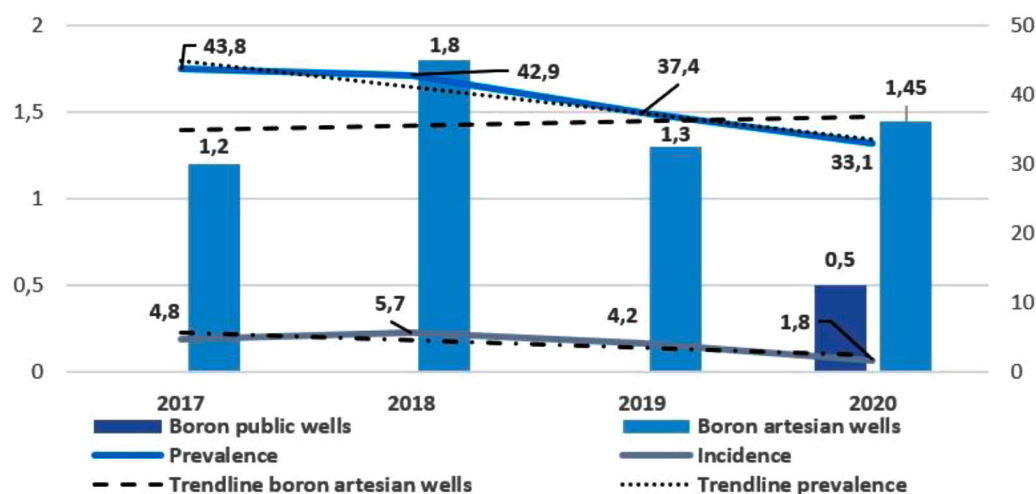
In the second district with limited boron concentration in deep drinking water, Vulcănești, during the years with the highest boron concentrations in public well water (2017-2018), both the prevalence and the incidence of adults with osteoarticular pathologies were at their highest. Additionally, the trends for boron concentrations in artesian wells ( $y = -0.18x + 1.55$ ) and morbidity values ( $y = -1.63x + 18.6$  for the prevalence and  $y = -0.45x + 2$  for the incidence) were negative (Figure 5). The overlapping of boron concentrations in artesian wells and annual osteoarticular morbidity, as indicated by the trendlines equations, is opposite to the research hypothesis.

**Above-the-limit boron in deep drinking water area (multiannual averages of boron in deep drinking water above 1.2 mg/L)**

Boron concentrations in deep drinking water and morbidity indicators in the Ceadr-Lunga district show that prevalence values for rheumatoid arthritis and inflammatory polyarthropathies increased during the period when boron concentration in deep waters was decreasing (2018-



**Fig. 6** Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Ceadr-Lunga district, 2016-2020



**Fig. 7** Boron concentrations in deep drinking water (mg/L) and adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies (per 10,000 inhabitants), Comrat district, 2017-2020

2019). Trends in boron concentrations were negative ( $y = -0.19x + 2.36$  for public wells water and  $y = -0.31x + 2.61$  for artesian wells water), while prevalence of rheumatoid arthritis and inflammatory polyarthropathies showed positive trends ( $y = 0.02x + 35.96$ ) (Figure 6).

In the second selected above-the-limit district, Comrat, increasing boron concentrations in artesian wells water trendline ( $y = 0.025x + 1.375$ ) coincided with decreasing trends in osteoarticular morbidity ( $y = -3.76x + 48.7$  for the prevalence and  $y = -1.05x + 6.7$  for the incidence) (Figure 7). Although osteoarticular morbidity remains high during periods of elevated boron concentrations in artesian wells, the opposing trendlines for incidence and prevalence compared to boron concentrations support the research hypothesis.

### Discussion

During this research, we compared the annual averages of boron concentrations in deep drinking water (from public and artesian wells) with annual averages of incidence and

prevalence of rheumatoid arthritis and inflammatory polyarthropathies in selected districts from each boron-related area, using periods when all relevant data were available. Additionally, we calculated trends for all four indicators – boron concentrations in public well water and artesian wells water; and incidence and prevalence of rheumatoid arthritis and inflammatory polyarthropathies. The aim of this study was to assess whether boron concentrations in deep drinking water can influence osteoarticular morbidity in specific regions, based on existing literature [2-14].

In the below-the-limit boron area of deep drinking water, the Călărași district showed fluctuations in boron concentrations from public and artesian wells that corresponded with the prevalence of adults with rheumatoid arthritis and inflammatory polyarthropathies, consistent with the research hypothesis. This is further supported by the increasing boron and decreasing morbidity trends. Similarly, in the Briceni district, the hypothesis is confirmed by the

overlap of boron concentrations in deep drinking water and the osteoarticular morbidity indicators in adults, along with matching trends across the four indicators. However, in the Drochia district, the research hypothesis was not confirmed.

In the limit-boron area of deep drinking water, the research hypothesis was only partially confirmed in the Cahul district, and only by the incidence of the studied diseases in a single year of the study period; however, the overall trendlines did not align with the hypothesis. In Vulcănești, neither the boron concentrations in deep drinking water nor the morbidity of adults with the studied osteoarticular pathologies corresponded with the research hypothesis, and the trendlines for the three indicators also failed to match it.

In the above-the-limit boron area of deep drinking water, the research hypothesis was largely confirmed in the Ceadâr-Lunga and Comrat districts, where the boron concentrations and their trendlines overlapped with the annual averages and trendlines of morbidity, demonstrating the expected relationship.

The described results complement previously published findings, which showed that in the above-the-limit boron area of deep drinking water in the southern region of the Republic of Moldova, the multiannual averages of rheumatoid arthritis and inflammatory polyarthropathies prevalence were the highest in the country [18]. However, analyzing annual averages instead of multiannual ones, and calculating trends for both boron concentrations and osteoarticular morbidity, revealed mixed results and provided a different perspective on the boron-rich areas.

The limitations of this research include incomplete data on boron concentrations in deep drinking water, particularly for public wells, which were not available for every year. Additionally, morbidity data were only available up to 2020, resulting in differences in the analyzed periods between districts. Furthermore, it was not possible to separate rheumatoid arthritis from other inflammatory polyarthropathies, as the Health Data Management Department provided combined data. Consequently, some results may be influenced by the inclusion of various inflammatory pathologies in the statistics. For the same reason, studying the association with osteoarthritis was not feasible, as it was grouped with other chondropathies.

Taking these aspects into consideration, we believe that future investigations focusing specifically on the association between boron concentrations in deep drinking water and the separate conditions of rheumatoid arthritis and osteoarthritis could be a valuable direction.

## Conclusions

The overlap of trends in boron concentrations in deep drinking water and trends in adult morbidity from rheumatoid arthritis and inflammatory polyarthropathies confirmed the research hypothesis in the above-the-limit boron area (Ceadâr-Lunga and Comrat districts) and partially in the below-the-limit boron area (Călărași and Briceni districts). These results provide a foundation for future research on the impact of boron on public health.

## Competing interests

None declared.

## Authors' contributions

MVR conceived the study and drafted the manuscript, IP participated in the study design and data analysis, EC helped draft the manuscript and contributed to the study design, and LMN performed statistical analysis of clinical data. All authors have read and approved the final version of the manuscript.

## Ethics approval

The study was approved by the Research Ethics Committee of *Nicolae Testemițanu* State University of Medicine and Pharmacy (Minutes No 1 of 07.09.2020).

## Patient consent

Obtained.

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