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Effects of water improvement and defluoridation on fluorosis-endemic areas in China: A meta-analysis☆

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A B S T R A C T

This meta-analysis systematically evaluated the effects of water improvement and defluoridation on fluorosis-endemic areas in North and South China. The study used PubMed, Embase, China National Knowledge Infrastructure, and Wanfang to retrieve relevant research studies published between January 2000 and October 2019. The data included water fluoride levels, dental fluorosis prevalence in children 8−15 years of age, urinary fluoride levels in children and adults, and skeletal fluorosis prevalence in adults. Fixed-effects and random-effects models were used in the meta-analysis. A total of 17 research articles met the inclusion criteria and had an average water improvement period of 15.8 years. With water improvement, water fluoride levels decreased from 2.72 mg/L to 0.54 mg/L (95% confidence intervals: −2.75, −1.58), which was below the standard for drinking water (1.5 mg/L). Additionally, after water improvement, the prevalence of dental fluorosis decreased from 54.5% to 36.2% (95% confidence intervals: 0.12, 0.31) in children, and the prevalence of skeletal fluorosis decreased from 13.7% to 4.2% (95% confidence intervals: 0.16, 0.40) in adults. Urinary fluoride levels decreased from 3.06 mg/L to 1.70 mg/L (OR = −2.03, 95% confidence intervals: −2.77, −1.30) in children and from 2.29 mg/L to 1.72 mg/L (OR = −0.57, 95% confidence intervals: 0.65, −0.49) in adults. The results showed that the prevalence of dental fluorosis and skeletal fluorosis and urinary fluoride levels were significantly reduced by water improvement. This study findings revealed that the effects of water improvement and defluoridation were greater in South China than in North China, and it is obviously related to the time of water improvement and reducing fluoride.

Author statement

WFQ, LY, and LYJ conceived of and designed the study; they had full access to all data in the study, take responsibility for the integrity of the data, the accuracy of the data analysis and wrote the report. TDX, ZJN, YX, LYQ and PFT critically revised the report. WJS, HZX, and SLP performed the statistical analysis. All authors contributed to data acquisition and analysis. All authors reviewed and approved the final version of this manuscript.

1. Introduction

Endemic fluorosis is a worldwide disease that is closely related

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to the abundance of fluoride in the environment. Fluorine is the 13th most abundant element in the Earth's crust, present at 544 ppm. According to the World Health Organization (WHO), fluorosis has become a major health problem. It is a chronic systemic disease that is caused by excessive intake of fluoride via drinking water, food, air, and other means. Long-term high fluoride intake induces damage to the musculoskeletal, endocrine, gastrointestinal, renal, reproductive, and neurological systems (Li et al., 2009; Li and Wang, 2001; Roy and Dass, 2013). At present, more than 50 countries have high fluoride levels in drinking water (Fawell et al., 2006; Fewtrell et al., 2006).

China has one of the most serious endemic fluorosis problems in the world. As well as affecting human health, fluorosis negatively impacts the economy because of medical expenses for patients, the requirement for government funds for prevention and treatment of fluoride-related illness, and high fluoride content in crops which affects the income of farmers (Wang et al., 2012). Drinking-water-borne fluorosis is one of the most important types of endemic fluorosis in China. It is prevalent in 31 provinces, cities, and autonomous regions in the North and South of China, and affects 59.579 million individuals from 80,011 villages and 1049 counties. Among them, Heilongjiang, Jilin and Liaoning (Northeast Three Provinces), Shanxi and Tianjin (North China), Inner Mongolia and Qinghai (Northwest China) have severe drinking-water-borne fluorosis. The main clinical outcomes caused by long-term drinking of high-fluoride water are dental fluorosis and skeletal fluorosis (Sun and Gao (2013); China's key endemic disea, 2004–2010; Sun (2016); O World Health Organiz (2012a); O (World Health Organiz, 2012b). There have been research reports from the late 20th century to the present day that the most effective way to reduce the prevalence of dental fluorosis and skeletal fluorosis is through water improvement and defluoridation (Cheng et al., 2001; Liang, 1998). For more than 40 years, the Chinese government has invested a lot of resources in water improvement and defluoridation projects in fluoride-endemic areas (Zhao and Wang, 2011). Currently, there are several provinces in China that urgently require water improvement and defluoridation, and the government needs to focus on the prevention and control of fluorosis in different regions of South and North China.

To reduce residents' intake of high-fluoride water and prevent the occurrence of fluorosis, water-improvement projects to decrease fluoride in the water supply and a national sanitary standard for drinking water have been applied in China. Due to different implementation periods and management strategies, there are still significant differences in the effects of water improvement and defluoridation projects among various provinces. To evaluate these projects, surveys are performed in one province, city, or region, which provide limiting information. To comprehensively assess the effects of these projects on the prevention and treatment of drinking water-borne endemic fluorosis, a meta-analysis was undertaken. After a systematic and comprehensive literature search, this study determined the inclusion and exclusion criteria and rigorously evaluated the research studies, while minimizing bias and ensuring the objectivity, authenticity, and reliability of the study findings.

2. Methods

2.1. Search strategy

This study evaluated the study content and scope of previously published reports and generated inclusion and exclusion criteria. A list of relevant data from each study was created, including the sample size, study design, publication time, implementation time, and location, among others. The heterogeneity of the research indicators was analyzed to determine whether the indicators could be pooled for analysis. When there was heterogeneity, sensitivity analysis or appropriate statistical methods were used to estimate the effect.

2.2. Inclusion and exclusion criteria

Studies on water improvement and defluoridation performed in China between January 2000 and October 2019 that reported water fluoride levels <1.5 mg/L after defluoridation according to the three-level standard for fluoride content reported in "Standards for Drinking Water for Rural Living" and that provided any of the following information—fluoride content in drinking water (the threshold level of fluoride content in drinking water was >1.5 mg/L before defluoridation and <1.5 mg/L after defluoridation), prevalence of dental fluorosis in children between the ages of 8 and 15 years, prevalence of skeletal fluorosis in adults, and urinary fluoride levels in children and/or adults—were included in the study. The exclusion criteria were studies that did not have water data or data entry formats unsuitable for Revman 5.3 statistical software, studies with repeated research, and studies with fluorosis combined with other diseases.

2.3. Literature retrieval strategy

This study searched PubMed, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang using the following terms in the title, keyword, or abstract, "water improvement", "defluorination", "dental fluorosis", or "skeletal fluorosis". Additionally, we performed a retrospective citation search. The retrieval time range of published literature was 2000–2019.

2.4. Study quality analysis

This study evaluated the quality of each study based on Jianping Liu's systematic evaluation method of non-random research (Liu, 2001a; Liu, 2001b; Liu, 2002). The study quality evaluation included whether the sampling method of the survey area and population was reported, whether there were strict laboratory quality control methods, whether the basic characteristics of the survey respondents were the same, whether the detection methods of water fluoride and urinary fluoride levels and the diagnostic methods of dental fluorosis and skeletal fluorosis were reported, and whether the statistical methods were correct. "Yes" was recorded as 1 point, and "no" was recorded as 0 point. A total of 0–2 points was classified as D level, 3–4 points was classified as C level, 5–6 points was classified as B level, and 7 points was classified as A level.

2.5. Data extraction

Two investigators (Wang FQ and Liu Y) independently performed the data extraction. The data included publication time, type of study, time and place of investigation, duration of water treatment, prevalence of dental fluorosis in children between the ages of 8 and 15 years, prevalence of skeletal fluorosis in adults, fluoride levels in drinking water, and fluoride levels in urine. Revman 5.3 statistical software requires binary variables presented as number of patients/surveys and continuous variables presented as mean ± standard deviation.

2.6. Statistical analysis

This study used Revman 5.3 statistical software provided by the Cochrane Collaboration Network. The chi-square test (χ^2) was used to evaluate heterogeneity among the studies ($P = 0.05$). When heterogeneity had $P > 0.05$, multiple independent studies were considered to be homogeneous. A fixed-effects model was selected to calculate the combined statistics. When heterogeneity had $P \leq 0.05$, multiple studies were considered to be heterogeneous, and heterogeneity treatment methods such as sensitivity analysis or subgroup analysis were used. Sensitivity analysis aimed to determine whether there were differences in the (1) combined statistics when selecting different statistical models, (2) conclusions before and after the removal of low-quality quality studies, (3) conclusions following hierarchical or subgroup analyses of the literature, and (4) conclusions before and after changing the inclusion and exclusion criteria. Odds ratio (OR) was used for binary variables, and weighted mean difference (WMD) was used for continuous variables. Dichotomous variables and continuous variables were expressed using 95% confidence intervals. The corresponding *P*-value was obtained using the Z test for the combined statistics. Statistical significance was set at $P \leq 0.05$.

3. Results

3.1. Search results

From PubMed, Embase, and CNKI obtained 1164 studies, and from Wan fang obtained 583 studies. Therefore, a total of 1747 studies were obtained from all four databases, of which 1140 were duplicates, 581 were included in PubMed, Embase, and CNKI, and 26 were included in Wanfang. Finally, a total of 17 studies were included in the meta-analysis (Fig. 1).

3.2. Basic information and quality evaluation of the studies

The 17 research articles were cross-sectional studies published between 1980 and 2019. The water improvement projects lasted between five and 30 years and covered 17 provinces, cities, and counties. All studies reported the prevalence of dental fluorosis in children, 6 studies reported the degree of dental fluorosis in children, 10 studies reported the prevalence of skeletal fluorosis in adults, 15 studies reported the fluoride levels in drinking water, 5 studies reported the urinary fluoride levels in children, and 2 studies reported the urinary fluoride levels in adults. There were 14 studies that described water sampling methods, 15 studies that reported the detection methods of fluoride in water, 7 studies that reported the detection methods of urinary fluoride, 16 studies described the diagnostic methods of dental fluorosis, and 12 studies described the diagnostic methods of skeletal fluorosis (Table 1 and Fig. 2).

3.3. Effects of water improvement and defluoridation by establishing water improvement projects

Fifteen studies (Ma, 2010; Zheng et al., 2010; Chang et al., 2018; Shu et al., 2013; Wang et al., 2008; Zhao et al., 2012; Liu et al., 2019; Guo et al., 2015; Li et al., 2014; Jian et al., 2013; Guo et al., 2002; Xu, 2005; Pu et al., 2019; Yu et al., 2004; He et al., 2011) reported fluoride levels in drinking water. There were 5149 original water samples and 1876 treated water samples (i.e., following the water improvement project). The results were the following, $Q = 3786.87$, $P < 0.00001$, $I^2 = 100\%$; comprehensive test $Z = 7.24$, $P < 0.00001$; and combined $WMD = -2.17$, 95% confidence intervals (-2.75, -1.58). The difference in water fluoride levels after water improvement was statistically significant ($P \leq 0.05$; Fig. 3). Using subgroup analysis, the studies were divided into two areas of China (South and North). The results were the following, $WMD = -2.22$, 95% confidence intervals (-2.69, -1.75), $P < 0.00001$ for South China, and $WMD = -2.11$, 95% confidence intervals (-2.82, -1.40), $P < 0.00001$ for North China. The differences were statistically significant ($P \leq 0.05$; Supplementary Figure 1).

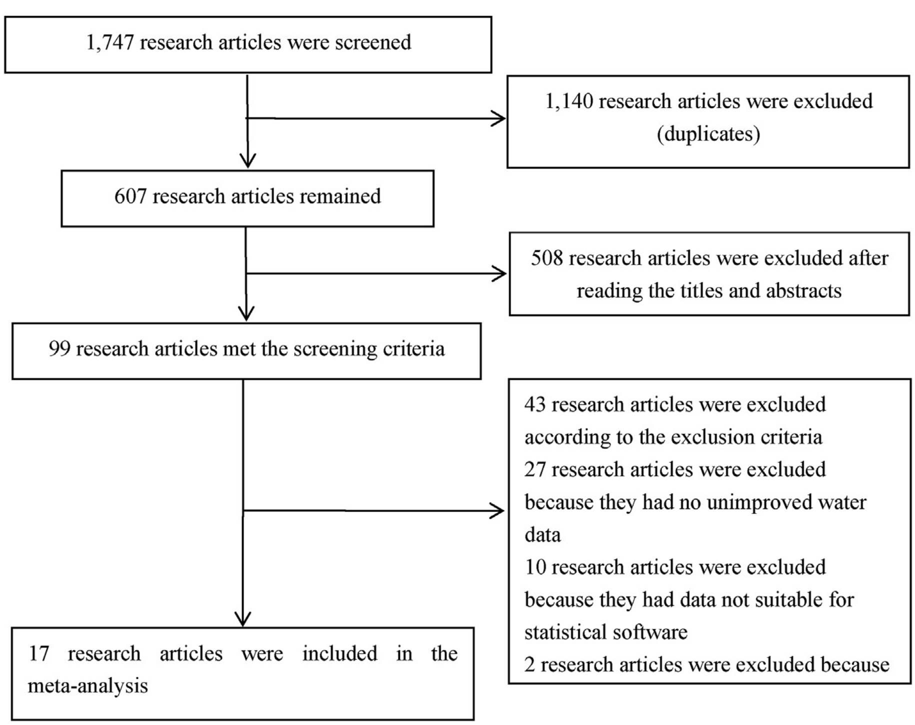

Fig. 1. Research flow chart.

Table 1
Characteristics of the studies.

Name	Publication year	Survey time	Survey place	Fluorosis type	Water collection method		Selected area	Water improving period (year)	NOS score
					Unimproved drinking water (village)	Improved drinking water (village)			
Ma GQ (Ma, 2010)	2010	2009	Henan	Drinking water-type	East, south, west, north, center	Terminal piped water	/	30	4
Kou BZ (Kou, 2015)	2015	2002–2007	Jilin	Drinking water-type	/	/	/	6	4
Zheng ZG (Zheng et al., 2010)	2010	2009	Guangxi	Drinking water-type	East, south, west, north, center	Factory water sample and terminal piped water	3 villages	/	4
Yu QL (Yu et al., 2008)	2008	2004	Gansu	Drinking water-type	/	/	39 villages	14	3
Chang ZL (Chang et al., 2018)	2018	2012–2016	Inner Mongolia	Drinking water-type	East, south, west, north, center	Terminal piped water	11 counties/3 villages	5	6
Shu CL (Shu et al., 2013)	2013	2009	Jiangsu	Drinking water-type	East, south, west, north, center	Factory water sample and terminal piped water	3 cities/8 counties/24 villages	30	6
Wang JH (Wang et al., 2008)	2008	2005–2007	Liaoning	Drinking water-type	East, south, west, north, center	Factory water sample and terminal piped water	13 cities/50 counties	5	6
Zhao YN(Zhao et al., 2012)	2012	2011	Ningxia	Drinking water-type	East, south, west, north, center	Terminal piped water	11 villages	5	5
Liu ZH (Liu et al., 2019)	2019	2016–2017	Tianjin	Drinking water-type	/	/	524 villages	15	4
Guo SH(Guo et al., 2015)	2015	2015	Shaanxi	Drinking water-type	East, south, west, north, center	Terminal piped water	3 villages	29	4
Li PF (Li et al., 2014)	2014	2012–2013	Shanxi	Drinking water-type	East, south, west, north, center	Terminal piped water	6 counties	/	3
Jian HH(Jian et al., 2013)	2013	2012	Anhui	Drinking water-type	East, south, west, north, center	Terminal piped water	2 counties/6 villages	/	4
Guo XC (Guo et al., 2002)	2002	2001	Hunan	Drinking water-type	East, south, west, north, center	Terminal piped water	10 counties/18 villages	15	4
Xu XH (Xu, 2005)	2005	2003	Shandong	Drinking water-type	East, south, west, north, center	Terminal piped water	4 villages	20	2
Pu GL (Pu et al., 2019)	2019	2009–2017	Qinghai	Drinking water-type		Terminal piped water	4 counties/12 villages	8	3
Yu Jiang (Yu et al., 2004)	2004	2002	Guangdong	Drinking water-type	East, south, west, north, center	Terminal piped water	3 cities/24 villages	15	3
He XM(He et al., 2011)	2011	2008–2009	Fujian	Drinking water-type	East, south, west, north, center	Factory water sample and terminal piped water	4 villages	24	3

Name	Publication year	Inclusion criteria			
		Dental fluorosis	Urinary fluoride	Water fluoride	Skeletal fluorosis
Ma GQ (Ma, 2010)	2010	Dean's method	Ion-selective electrode method (WS/T89.1996)	Standard test method for drinking water (GB/T5750.5–2006)	Diagnostic criteria of endemic osteochondrosis (WS192 . 2008)
Kou BZ (Kou, 2015)	2015	Industry standard of the Ministry of health (WS/T208-2011)	Ion-selective electrode method (WS/T89.1996)	/	Diagnostic criteria of endemic osteochondrosis (WS192 . 2008)
Zheng ZG (Zheng et al., 2010)	2010	Dean's method	Ion-selective electrode method (WS/T89.1996)	Standard test method for drinking water (GB/T5750.5–2006)	Diagnostic criteria of endemic osteochondrosis (WS192 . 2008)
Yu QL (Yu et al., 2008)	2008	/	/	Standard test method for drinking water (GB5750-1985)	/
Chang ZL (Chang et al., 2018)	2018	Industry standard of the Ministry of health (WS/T208-2011)	Ion-selective electrode method (WS/T 898–2015)	Standard test method for drinking water (GB/T5750.5–2006)	Diagnostic criteria of endemic osteochondrosis (WS192 . 2008)
Shu CL (Shu et al., 2013)	2013	Dean's method	Ion-selective electrode method (WS/T89.1996)	Standard test method for drinking water (GB/T5750.5–2006)	Diagnostic criteria of endemic osteochondrosis (WS192 . 2008)
Wang JH (Wang et al., 2008)	2008	Dean's method	Ion-selective electrode method (WS/T89.1996)	Standard test method for drinking water (GB/T5750.5–2006)	Clinical grade diagnosis of endemic osteochondrosis (GB163961996)
Zhao YN(Zhao et al., 2012)	2012	Dean's method	/	Standard test method for drinking water (GB/T5750.5–2006)	/
Liu ZH (Liu et al., 2019)	2019	Industry standard of the Ministry of health (WS/T208-2011)	/	Standard test method for drinking water (GB/T5750.5–2006)	/
Guo SH(Guo et al., 2015)	2015	Dean's method	/	Standard test method for drinking water (GB/T5750.5–2006)	X-ray diagnosis of osteochondrosis (WS192-1999)
Li PF (Li et al., 2014)	2014	Dean's method	/	/	/
Jian HH(Jian et al., 2013)	2013	Industry standard of the Ministry of health (WS/T208-2011)	/	Standard test method for drinking water (GB/T5750.5–2006)	/
Guo XC (Guo et al., 2002)	2002	Dean's method	/	Standard test method for drinking water (GB5750-1985)	X-ray diagnosis of osteochondrosis (WS192-1999)
Xu XH (Xu, 2005)	2005	Dean's method	/	Standard test method for drinking water (GB5750-1985)	X-ray diagnosis of osteochondrosis (WS192-1999)
Pu GL (Pu et al., 2019)	2019	Dean's method	/	Standard test method for drinking water (GB/T5750.5–2006)	X-ray diagnosis of osteochondrosis (WS192-1999)
Yu Jiang (Yu et al., 2004)	2004	Dean's method	/	Standard test method for drinking water (GB/T5750.5–2006)	X-ray diagnosis of osteochondrosis (WS192-1999)

Table 1 (*continued*)

Name	Publication year	Inclusion criteria			
		Dental fluorosis	Urinary fluoride	Water fluoride	Skeletal fluorosis
He XM(He et al., 2011)	2011	Dean's method	Ion-selective electrode method (WS/T89.1996)	Standard test method for drinking water (GB/T5750.5–2006)	X-ray diagnosis of osteochondrosis (WS192-1999)

Fig. 2. Dental fluorosis and X-ray results of skeletal fluorosis.

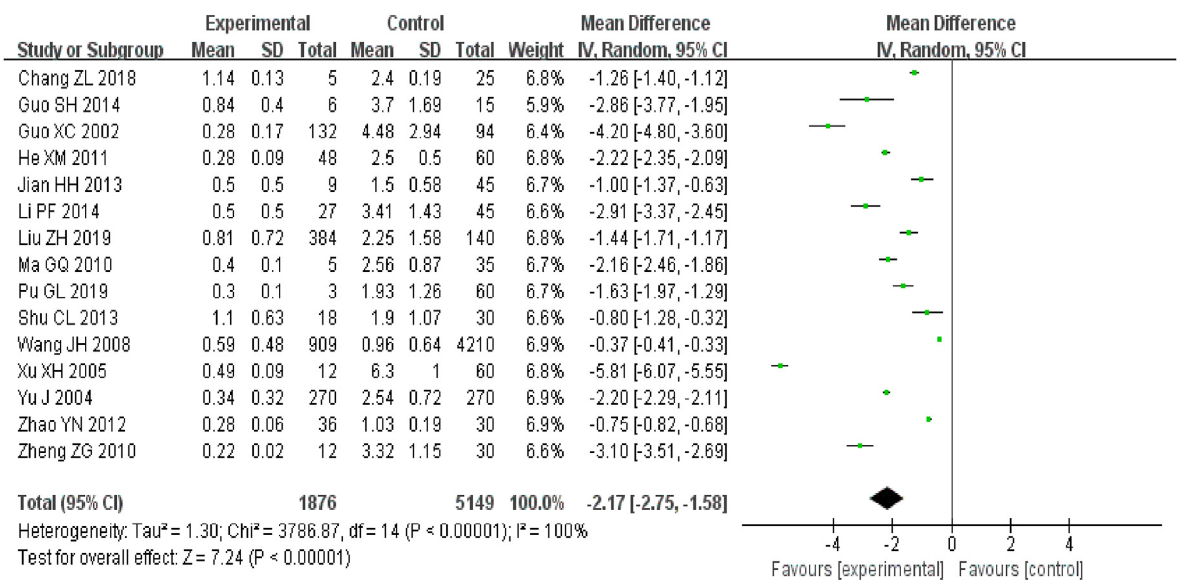

Fig. 3. Water fluoride levels after water improvement and defluoridation.

3.4. Prevalence of dental fluorosis in children 8–15 years of age

Seventeen studies (Ma, 2010; Kou, 2015; Zheng et al., 2010; Yu et al., 2008; Chang et al., 2018; Shu et al., 2013; Wang et al., 2008; Zhao et al., 2012; Liu et al., 2019; Guo et al., 2015; Li et al., 2014; Jian et al., 2013; Guo et al., 2002; Xu, 2005; Pu et al., 2019; Yu et al., 2004; He et al., 2011) provided information on dental fluorosis in children between the ages of 8 and 15 years. The number of children with dental fluorosis before and after water improvement was 53,419 and 51,036 cases, respectively. The results were the following, Q = 2545.39, $P < 0.00001$, $I^2 = 99\%$; comprehensive test Z = 6.72, $P < 0.00001$; and combined OR = 0.19, 95% confidence intervals (0.12, 0.31). There was a significant difference ($P \leq 0.05$) in the prevalence of dental fluorosis in children after water improvement and defluoridation (Fig. 4). Using subgroup analysis, the studies were divided into South and North China. The results were the following, OR = 0.18, 95% confidence intervals (0.11, 0.28), $P < 0.00001$ for South China, and OR = 0.22, 95% confidence intervals (0.12, 0.39), $P < 0.00001$ for North China. The differences were statistically significant ($P \leq 0.05$; Supplementary Figure 2). Fourteen studies reported (Ma, 2010; Kou, 2015; Yu et al., 2008; Chang et al., 2018; Shu et al., 2013; Wang et al., 2008; Zhao et al., 2012; Liu et al., 2019; Guo et al., 2015; Guo et al., 2002; Xu, 2005; Pu et al., 2019; Yu et al., 2004; He et al., 2011) the duration of water improvement. Using subgroup analysis, the studies were divided into three subgroups: 5–10 years, 11–20 years, and 21–30 years. The results showed that the 5–10 years subgroup had OR = 0.41, 95% confidence intervals (0.28, 0.60), $P < 0.00001$; the 11–20 years subgroup had OR = 0.14, 95% confidence intervals (0.05, 0.45), $P < 0.00001$, and the 21–30 years subgroup had OR = 0.10, 95% confidence intervals (0.03, 0.30), $P < 0.00001$. The differences were statistically significant ($P \leq 0.05$; Supplementary Figure 3).

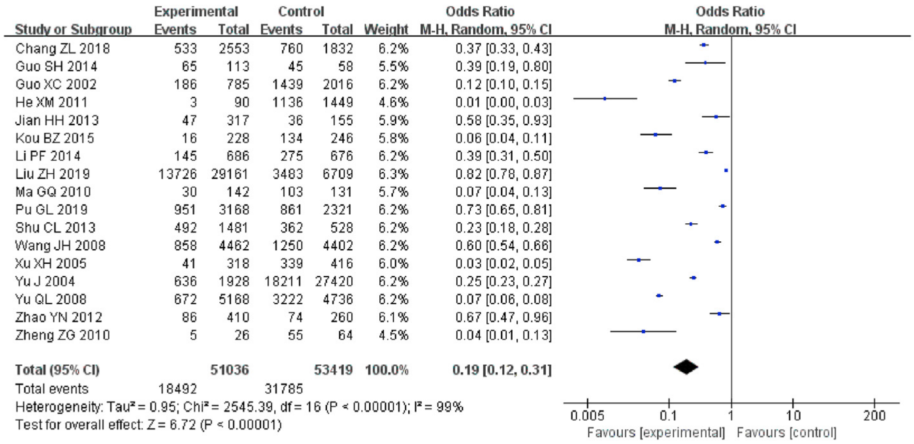

Fig. 4. Prevalence of dental fluorosis in children between the ages of 8 and 15 years.

3.5. Degree of dental fluorosis in children 8–15 years of age

Six studies (Zheng et al., 2010; Shu et al., 2013; Liu et al., 2019; Guo et al., 2015; Li et al., 2014; Jian et al., 2013) reported the degree of dental fluorosis in children between the ages of 8 and 15 years after water improvement and defluoridation. Researchers surveyed children in areas without water improvement (1741 cases). There were 689 children without dental fluorosis, 316 with suspicious dental fluorosis, 296 with extremely mild dental fluorosis, 160 with mild dental fluorosis, 148 with moderate dental fluorosis, and 56 with severe dental fluorosis. A total of 3033 children were surveyed after water improvement: 1598 children had no dental fluorosis, 496 had suspicious dental fluorosis, 458 had extremely mild dental fluorosis, 337 had mild dental fluorosis, 160 had moderate dental fluorosis, and 60 had severe dental fluorosis. According to the degree of dental fluorosis, the results were $Q = 271.25$, $P < 0.00001$, $I^2 = 88\%$; comprehensive test $Z = 0.56$, $P < 0.00001$, and combined $OR = 0.93$, 95% confidence intervals (0.72, 1.20), $P < 0.0001$. There was a statistically significant improvement in the degree of dental fluorosis in children after water improvement ($P \leq 0.05$). Additionally, the results had combined $OR = 2.25$, 95% confidence intervals (1.58, 3.24), $P < 0.0001$ for no dental fluorosis; combined $OR = 0.84$, 95% confidence intervals (0.63, 1.11), $P < 0.03$ for suspicious dental fluorosis; combined $OR = 0.81$, 95% confidence intervals (0.61, 1.06), $P < 0.06$ for extremely mild dental fluorosis; combined $OR = 0.95$, 95% confidence intervals (0.41, 2.22), $P < 0.00001$ for mild dental fluorosis; combined $OR = 0.30$, 95% confidence intervals (0.11, 0.84), $P < 0.0001$ for moderate fluorosis; and combined $OR = 0.13$, 95% confidence intervals (0.01, 2.19), $P < 0.00001$ for severe dental fluorosis. The results showed that there was statistical significance among the subgroups ($P \leq 0.05$; Fig. 5).

3.6. Prevalence of skeletal fluorosis in adults

Eight studies (Ma, 2010; Kou, 2015; Zheng et al., 2010; Chang et al., 2018; Wang et al., 2008; Zhao et al., 2012; Xu, 2005; He et al., 2011) reported the prevalence of skeletal fluorosis in adults. The prevalence of skeletal fluorosis before and after water improvement was 13.7% and 4.2%. The results were $Q = 117.75$, $P < 0.00001$, $I^2 = 94\%$; comprehensive test $Z = 5.86$, $P < 0.00001$; and combined $OR = 0.26$, 95% confidence intervals (0.16, 0.40), $P < 0.0001$. There was a statistically significant decrease in the incidence of skeletal fluorosis after water improvement (Fig. 6). Using subgroup analysis, the studies were divided into South and North China. The results were $OR = 0.35$, 95% confidence intervals (0.13, 0.96), $P < 0.00001$ for South China and $OR = 0.24$, 95% confidence intervals (0.14, 0.40), $P < 0.00001$ for North China. The difference was statistically significant ($P \leq 0.05$; Supplementary Figure 4). Seven studies (Ma, 2010; Kou, 2015; Chang et al., 2018; Wang et al., 2008; Zhao et al., 2012; Xu, 2005; He et al., 2011) reported information on water improvement duration. Using subgroup analysis, we divided the studies into 5–10 years and 20–30 years. The results showed that the 5–10 years subgroup had $OR = 0.26$, 95% confidence intervals (0.11, 0.61), $P < 0.00001$, and the 20–30 years subgroup had $OR = 0.20$, 95% confidence intervals (0.13, 0.31), $P = 0.15$. The difference was statistically significant ($P \leq 0.05$; Supplementary Figure 5).

3.7. Urinary fluoride levels in children 8–15 years of age and adults

Five studies (Ma, 2010; Kou, 2015; Zheng et al., 2010; Shu et al., 2013; Guo et al., 2002) reported urinary fluoride levels in children (8–15 years of age) before (1520 samples) and after (1128 samples) water improvement. The results were $Q = 155.33$, $P < 0.00001$, $I^2 = 97\%$; comprehensive test $Z = 5.41$, $P < 0.00001$; and combined $WMD = -2.03$, 95% confidence intervals (-2.77, -1.30), $P < 0.0001$. There was a statistically significant decrease in urinary fluoride levels in children after water improvement and defluoridation ($P \leq 0.05$; Fig. 7). Two studies (Ma, 2010; Chang et al., 2018) reported urinary fluoride levels in adults (753 samples before water improvement and 826 after). The results were $Q = 0.00$, $P < 0.96$, $I^2 = 0\%$; comprehensive test $Z = 13.74$, $P < 0.00001$; and combined $WMD = -0.57$, 95% confidence intervals (-0.65, -0.49), $P < 0.0001$. The results showed that there was a statistically significant decrease in urinary fluoride in adults after water improvement and defluoridation (Fig. 8).

4. Discussion

Drinking water fluoride levels represent an indicator of the effects of water improvement and defluoridation (Liu et al., 2019; Pu et al., 2019). The average duration of water improvement projects was 15.8 years (5–30 years). Following water improvement, fluoride levels in drinking water decreased from 2.72 mg/L to 0.54 mg/L, which complies with WHO standards (0.5–1.5 mg/L) Reimann and Banks (2004); O (World Health Organiz, 2017). There was a significant reduction in water fluoride levels following water improvement and defluoridation in different provinces in China ($P < 0.00001$). Additionally, there was a significant reduction in

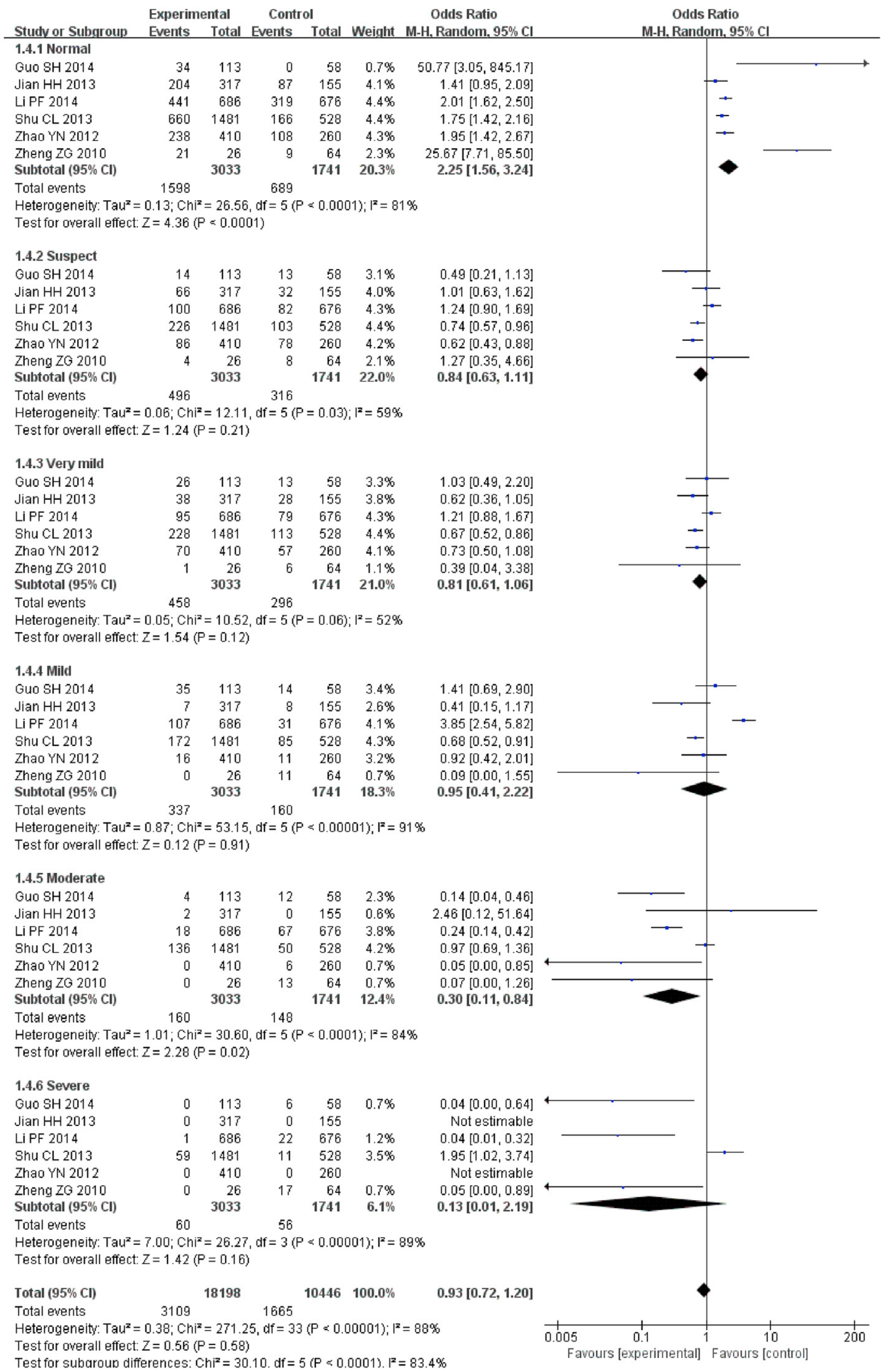

Fig. 5. Degree of dental fluorosis in children between the ages of 8 and 15 years.

water fluoride levels in North and South China ($P < 0.00001$); however, the effects of defluoridation were greater in the Southern provinces than in the Northern provinces, which may be related to the economy, culture, precipitation, and water resources in South China (Lv et al., 2019).

The prevalence of dental fluorosis in children ages 8–15 years is one of the most important indicators for assessing the effects of water improvement and defluoridation (Wang et al., 2004; Zhai et al., 2010). This study showed that the prevalence of dental fluorosis in children after water improvement and defluoridation decreased from 54.5% to 36.2% ($P < 0.00001$). Additionally, the prevalence of dental fluorosis in children decreased from 67.1% to 29.7% in South China and from 48.5% to 36.8% in North China ($P < 0.00001$). Following water improvement and defluoridation, the prevalence of dental fluorosis was comparatively lower in South China.

Based on the duration of the water improvement projects, the studies were divided into three sub-groups: 5–10 years (prevalence of dental fluorosis decreased from 34.0% to 22.6%, OR = 0.41), 11–20 years (prevalence of dental fluorosis decreased from 61.1% to 35.4%, OR = 0.13), and 21–30 years (prevalence of dental fluorosis decreased from 76.0% to 32.3%, OR = 0.10). The prevalence of dental

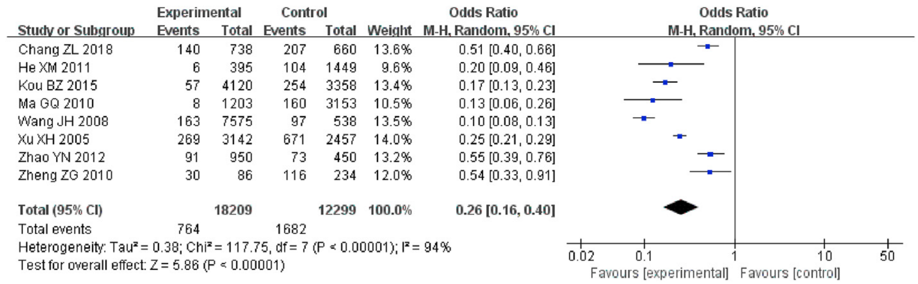

Fig. 6. Prevalence of skeletal fluorosis in adults.

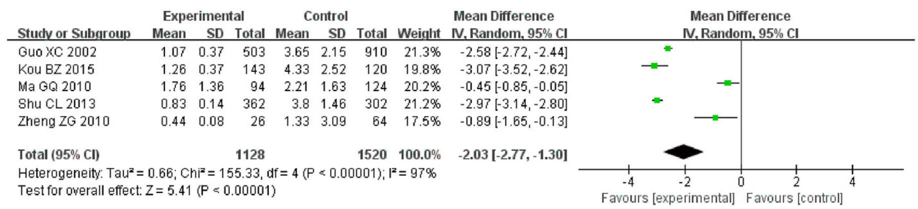

Fig. 7. Urinary fluoride levels in children after water improvement and defluoridation.

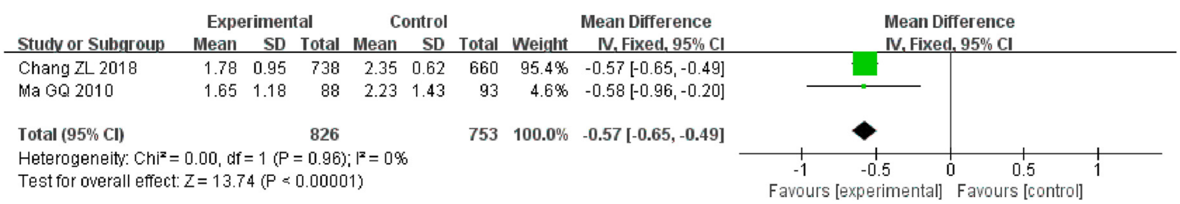

Fig. 8. Urinary fluoride in adults after water improvement and defluoridation.

fluorosis in children declined with the duration of water improvement/defluoridation ($P \le 0.05$). Dental fluorosis in children decreased by more than 30% after 1–20 years and 21–30 years of water improvement and defluoridation. Therefore, the duration of water improvement had a linear negative correlation with the prevalence of dental fluorosis.

Six studies (Zheng et al., 2010; Shu et al., 2013; Liu et al., 2019; Guo et al., 2015; Li et al., 2014; Jian et al., 2013) reported the degree of dental fluorosis in children ages 8–15 years. According to Dean's fluorosis index, dental fluorosis can be classified as normal (39.6% increased to 52.7% after water improvement, OR = 2.25), suspicious (18.2% decreased to 16.4% after water improvement, OR = 0.84), very mild (17.0% decreased to 15.1% after water improvement, OR = 0.81), mild (9.2% increased to 11% after water improvement, OR = 0.95), moderate (8.5% decreased to 5.3% after water improvement, OR = 0.30), and severe (3.2% decreased to 2.0% after water improvement, OR = 0.13). The severity of dental fluorosis in children was significantly reduced following water improvement and defluoridation ($P \le 0.05$).

Eight articles (Ma, 2010; Kou, 2015; Zheng et al., 2010; Chang et al., 2018; Wang et al., 2008; Zhao et al., 2012; Xu, 2005; He et al., 2011) reported the prevalence of skeletal fluorosis in adults after water improvement (8–31 years). The results showed that the prevalence of skeletal fluorosis in adults decreased from 13.7% to 4.2% after water improvement ($P \le 0.05$). The prevalence of skeletal fluorosis decreased from 13.1% to 7.5% in South China after water improvement (OR = 0.35) and from 13.8% to 4.1% in North China after water improvement (OR = 0.24). The results showed that there was a significant difference in the reduction of fluoride levels in water after water improvement in the fluoride-affected areas of North and South China ($P \le 0.05$). The effect on skeletal fluorosis was comparatively greater in North China. This result may be attributed to differences in population/migration habits from the Northern areas (cold) to the Southern areas (warm). Further results showed that the prevalence of skeletal fluorosis in adults decreased by 9.2% (OR = 0.26) and 8.8% (OR = 0.20) after 5–10 years and 21–30 years of water improvement, respectively. Therefore, the prevalence of skeletal fluorosis in adults decreased with the duration of water improvement ($P \le 0.05$).

According to the WHO "Basic Methods for Assessment of Renal Fluoride Excretion in Community Prevention Programmes for Oral Health" (O (World Health Organiz, 2014), urinary fluoride levels represent a reference index for evaluating endemic fluorosis. After water improvement, urinary fluoride levels decreased from 3.06 to 1.70 mg/L (OR = −2.03; $P \le 0.05$) in children and from 2.29 to 1.72 mg/L (OR = −0.57; $P \le 0.05$) in adults.

This study included 17 provinces with drinking water-type fluorosis, and a systematic and comprehensive analysis of the effects of 40 years of water improvement and fluoride reduction in China. The results of the analysis will provide guidance for the prevention and treatment of drinking water-type fluorosis in the future in China and worldwide. The provinces this study have included are relatively large, which results in significant heterogeneity in the analysis results. However, analysis of the non-random effects model shows that the results are reliable.

5. Conclusions

This meta-analysis systematically reviewed the effects of water improvement and defluoridation in different fluorosis-endemic areas in China in the past 40 years. The results revealed that reducing water fluoride levels can effectively control fluorosis. The prevalence of dental fluorosis in children and skeletal fluorosis in adults and the levels of urinary fluoride in children and adults were significantly reduced by defluoridation in the Northern and Southern regions of China.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2020.116227.

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