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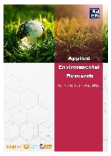

Research Article

Assessing the Short- and Long-Term Health Effects of Nitrogen Dioxide in Agadir, Morocco: A WHO AirQ+ Model Application

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Abstract

Epidemiological studies have revealed that exposure to atmospheric nitrogen dioxide (NO_2) increases the risk of acute and chronic diseases. This study used the WHO AirQ model to assess both the short- and long-term impacts of NO_2 on human health in the city of Agadir in Morocco. The mean NO_2 values were obtained from measurements taken at two locations. This study assessed the long- term health effects of NO_2 on natural all-cause mortality (LT-ACM), mortality due to respiratory diseases (LT-RD), and morbidity due to chronic obstructive pulmo-nary disease (LT-COPD), as well as the short-term health impacts of NO_2 on natural all-cause mortality (ST-ACM), mortality due to respiratory diseases (ST-RD), and asthma hospitalizations and emergency admissions (ST-A). The attributable proportion (AP) per 10 μg m^{-3} in adults aged 30 and over in LT-ACM, LT-RD, and LT-CPOD was estimated to be 16.42%, 23.49%, and 23.49%, respectively; the number of attributable cases (NAP) was estimated to be 323, 17, and 11, respectively; and the RRs were estimated to be 1.20 (95% CI: 1.09–1.43), 1.31 (95% CI: 1.09–1.56), and 1.31 (95% CI: 1.09–1.43), respectively. In addition, the AP at 25 μg m^{-3} for all ages in ST-ACM, ST-RD, and ST-A was estimated to be 17.15%, 9.25%, and 21.45%, respectively, and the NAP was estimated to be 12, 182, and 15, respectively. A significant number of deaths and serious cases of asthma and COPD can be avoided if the NO_2 concentrations are below the WHO exposure limits. The findings of this study match those of previous studies on the impact of air pollution on humans. Reducing NO_2 emissions from various sources, especially car exhaust, and enhancing monitoring systems are two methods that may significantly mitigate adverse health effects in the population.

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Introduction

Air pollution is recognized as the most serious environmental danger to human health because it contributes significantly to disease burden. Furthermore, evidence showing that air pollution has a wide-ranging impact on health has increased significantly [1]. Furthermore, estimates from the World Health Organization (WHO) suggest that 99% of the world's population breathe air that exceeds WHO-recommended limits and contains high amounts of pollutants, with low- and middle-income countries experiencing the highest exposure [2]. Additionally, the WHO Air Quality Guidelines (AQGs)

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for particulate matter (PM), ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) have been updated since their last publication in 2005 [3]. Following a rigorous evaluation of the collected evidence, the WHO decreased the prevalence of practically all AQGs, starting in 2021. WHO AQG 2021 proposed a yearly average NO_2 concentration of no more than 10 μg m^{-3}. In comparison, the WHO AQG 2005 value for NO_2 is 40 μg m^{-3}. Although these AQGs are not mandatory for countries, the WHO has established four interim target values (IT) that countries can use, depending on their circumstances.

There are many chemical species of NO_x, but the most common air pollutant of interest from a human health perspective is NO_2. Indeed, 4 million new cases of pediatric asthma are estimated to be attributable to NO_2 pollution each year worldwide, 64% of which occur in urban centers, representing 13% of the global incidence [4]. NO_2 is a secondary pollutant produced mostly by the combustion of fossil fuels, and traffic emissions account for up to 80% of the ambient NO_2 in European cities [5–6]. NO_2 was shown to be associated with nonaccidental and cause-specific mortality [7], to have adverse effects on respiratory function, hospital admissions and premature death [8] and to be associated with asthma exacerbation and incidence [9–11]. However, the associations between NO_2 and total mortality and respiratory diseases are causal [12–13].

In many nations, ambient air quality is monitored using a network of fixed stations. Moreover, Morocco's network is not well-developed, with only 29 stations in 15 cities. As a result, the restricted number of stations in the Agadir makes it difficult to accurately describe the general population's exposure, which symbolizes the important relationship between ambient air pollution levels and the resulting consequences for human health. These stations provide an overview of pollution levels in cities and regions, but they do not detect local effects such as air pollutants recently produced by local sources [14–15]. According to estimates, the economic cost of air pollution in Morocco in 2020 is expected to be between 0.6% and 1.4% of the country's GDP [16].

To our knowledge, no study has used the WHO AirQ+ model to assess the health impact of NO_2 on the Moroccan population has been carried out. However, recent studies using this method have focused on ozone [17], and PM [18]. The aim of this study was to quantify the long-term mortality and short-term morbidity associated with NO_2 exposure.

Materials and methods

1) Study area

Agadir is a city in southwest Morocco on the Atlantic coast located at 30°25′12″ north latitude and 9°35′53″ west longitude, 31 m above sea level (Figure 1). The main economic activity is agro-agriculture in addition to tourism. According to the latest census in 2014, the city has 420,288 inhabitants. The Agadir region is divided between arid and semiarid bioclimatic zones, with eight dry months per year. The average annual rainfall was approximately 260 mm. There are more than 340 sunshine days annually. Temperatures are strongly influenced by the year-round trade wind front, and vary little between winter and summer. The average temperature ranges from 14 to 16°C in January to 19–22°C in July. In 2019, the average maximum and minimum temperatures were 26.9°C (August) and 12.7°C (January), respectively, with relative humidities between 32% and 85%. Winds were predominantly from the west or northwest, with moderate average speeds. In winter, northerly and north-western winds cause precipitation and humidity. The south and southeast winds (Chergui) caused heat and dryness. However, the region experiences occasional upwelling of Saharan air, which can exceptionally increase temperatures above 40°C for a few days.

2) NO_2 exposure estimates and population health data

A single mobile station serves as the primary air quality monitoring network in the Agadir. Air pollutants were analyzed at two locations from April 2016 to April 2017. Hourly, daily, monthly, and annual average NO_2 concentrations were measured throughout this period to assess the short-term and long-term exposure of Agadir city residents. The data were derived from the 2016 and 2017 monthly reports of the Air Quality Monitoring Committee for the Souss-Massa Region located in Agadir. The missing values for each measurement were replaced with the median values.

The latest 2014 national report of the General Census of Population and Housing (GCPH2014), generated by the government organization's High Planning Commission, provided data on the average number of exposed people.

The long-term impact of NO_2 on human health was assessed in adults aged 30 years and older in relation to all-cause mortality (natural), mortality due to respiratory diseases, and hospital admissions for COPD. In addition, the short-term human health impact of NO_2 was assessed for all ages in relation to all-cause mortality (natural), mortality due to respiratory diseases, hospital admissions, and emergency room admissions for asthma. We considered the admissions and deaths reported at the Souss-Massa Regional Hospital (SMRH) (hospital mortality) in Agadir to be in line with the requirements for using the AirQ+ tool.

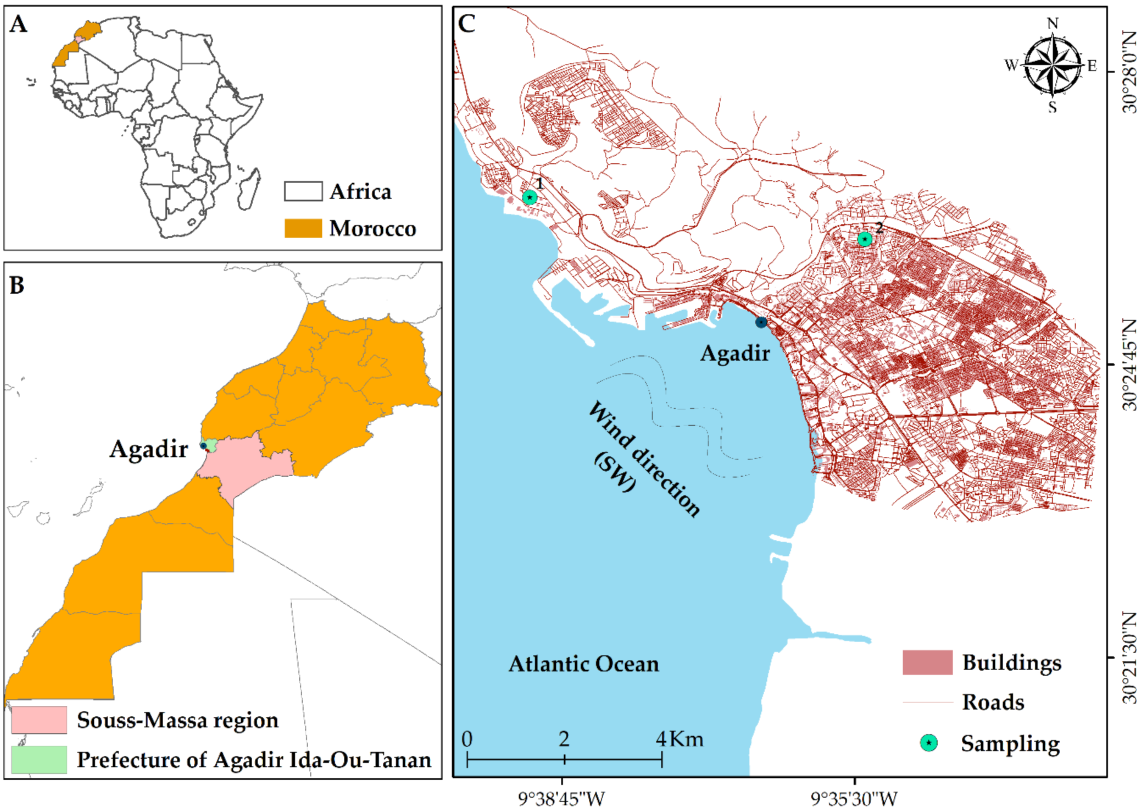

Figure 1 Location map of the study area. Morocco in Africa (A), study area in Agadir Ida Ou Tanan Prefecture (B), and locations of the mobile air pollution measuring station in 2016–2017 (green circles) numbered 1 and 2.

3) WHO AirQ+ software for health impact assessment

AirQ+, version August 2022, is a software tool developed by the WHO Regional Office for Europe to assess the disease burden caused by air pollution and its impact. AirQ+ includes methods for determining the impact of both short- and long-term exposures to ambient air pollution. Primary approaches rely on scientific data derived from epidemiological cohort studies, which demonstrate established associations between average concentration levels found in polluted air over time and mortality rates in exposed populations [19].

The results of AirQ+ are based on the use of concentration–response functions, which link pollutant exposure levels to a variety of health events across the study area and time period. These functions represent the relative health risks associated with a specific change in exposure level. These findings are based on epidemiological studies and can be used when the association is accepted as causal. Table 1 displays the health effects and the suggested relative risks (RRs) used in this study.

To quantify long-term and short-term effects, WHO AirQ+ requires the following data: annual mean NO_2 concentrations for long-term and short-term exposure effects, population at risk (adults aged 30 and up or total population), hospital admissions or deaths, WHO AQG threshold (X0) NO_2 values recommended by WHO 2005 and 2021 (Table 2), and relative risk values (RRs) (Table 1).

For AirQ+, the RR due to air pollution is usually modeled with a log-linear function [22] according to the formula $RR = \exp^{\beta \times (X-X_0)}$, where X denotes the pollutant concentration in µg m^{-3} and X_0 denotes the threshold or counterfactual value. In the log-linear model, β indicates the change in RR for a one-unit change in concentration X. The attributable proportion (AP) is the attributed fraction of the health effect due to exposure in a given population at a specified time interval. This fraction can be calculated by $AP = 1 - (1/RR)$, where RR is the relative risk for the health effect of NO_2 exposure.

For each baseline incidence (I) of the selected health effect in an exposed population, the number of cases per population unit (IE) can be calculated by $IE = I \times AP$. For a population of a given size N, the number of attributable cases (NAP) can be estimated by $NAP = N \times AP$ [23].

In this study, the main results provided by the WHO AirQ+ were presented, such as AP, NAP and RR (95% CI) for long-term annual mean NO_2 exposure and short-term 24-hour mean NO_2 exposure.

Table 1 Health endpoints and suggested relative risks (RRs)

Exposure	Health endpoint	RR (CI 95%) per 10 μg m^{-3}	Reference
Long-term	Mortality, all causes (natural)	1.02 (1.01–1.04)	[8]
	Respiratory mortality	1.03 (1.01–1.05)	[8]
	COPD	1.03 (1.01–1.04)	[8]
	Asthma [a]	1.014 (1.008–1.020)	[20]
Short-term	Mortality, all causes (natural)	1.0072 (1.0059–1.0085)	[21]
	Respiratory mortality	1.0067 (1.0025–1.0109)	[21]

Note: [a] Hospital and emergency room admissions for asthma.

Table 2 Examples of NO_2 air quality standards for common air pollutants are given in the Moroccan air quality standards and public information thresholds for air quality monitoring, the European Ambient Air Quality Directive (Directive 2008/50/EC), the USA National Ambient Air Quality Standards, and the World Health Organization Air Quality Guidelines (WHO AQG 2005 & 2021) for the protection of human health

Averaging time	Morocco limit 2010 [a]	WHO AQG 2005	EU limit 2008 [b]	NAAQS USA [c]	WHO AQG 2021				
					AQG level	IT 1	IT 2	IT 3	IT 4
Annual	50	40	40	106	10	40	30	20	–
24-h	–	–	–	–	25	120	50	–	–
1-h	200	200	200	200	200	200	200	200	200

Note: [a] Morocco health protection limit value 2010 (Decree No. 2-09-286 of December 8, 2009, fixing air quality standards and air monitoring procedures), [b] EU limit value 2008 (Directive 2008/50/EC) and [c] National Ambient Air Quality Standards.

Results and discussion

Over the study period, the annual average hourly NO_2 concentration was 100.57 μg m^{-3}. This concentration was 2.51 times higher than that of the WHO AQG 2005 (40 μg m^{-3}). Whereas the annual average daily NO_2 concentration was 160.33 μg m^{-3}, this concentration was below the 2005 WHO recommended value (200 μg m^{-3}).

Table 3 shows the long-term health effects of NO_2 (natural all-cause mortality, respiratory disease mortality, and COPD morbidity) and the short-term health effects of NO_2 (natural all-cause mortality, respiratory disease mortality, and morbidity due to asthma hospitalizations and emergency room admissions). In fact, the cumulative annual incidences of natural all-cause mortality, respiratory disease mortality, and COPD per 100,000 people in adults aged 30 years and older were 968.48, 34.98, and 13.79, respectively. However, the cumulative annual incidences of all-cause mortality, respiratory disease mortality, asthma hospitalization, and emergency admission per 100,000 people for all ages were 467.77, 16.89, and 16.18, respectively.

The WHO reported deaths attributed to ambient air pollution as age-standardized for both sexes per 100,000 people as 59.16 (40.83–76.86) for Morocco, 48.25 (32.55–63.62) for Algeria, 54.74 (39.56–69.72) for Libya, 54.74 (39.56–69.72) for Tunisia, 104.5 (79.08–129.5) for Egypt, and 62.45 (38.64–87.11) for Mauritania in 2019 [24]. Attributable to ambient air pollution, disability adjusted life years (DALYs) per 100000 for both sexes were reported to be 1,292 (901.2–1,674) for Morocco, 931.8 (1,239–6,374) for Algeria, 1,263 (834.4–1,671) for Libya, 1,113 (814.3–1,413) for Tunisia, 2,499 (1,909–3,108) for Egypt, and 1,543 (934.4–2,182) for Mauritania. According to the Global Burden of Disease 2019 study, 11.80% of all deaths and 8.41% of all DALYs worldwide, 12.81% of all deaths and 8.18% of all DALYs in Morocco are caused by air pollution [25].

1) Long-term NO_2 health impact assessment

Table 4 shows both the long- and short-term health impacts of exposure to NO_2 threshold concentrations. There is strong epidemiological evidence of the effects of NO_2 on human health. Indeed, Huangfu and Atkinson's systematic review and meta-analysis [8] identified several cohort studies that showed positive associations between NO_2 and mortality, with random effects summary RRs of 1.02 (95% CI: 1.01–1.04), 1.03 (1.00–1.05), 1.03 (1.01–1.04), and 1.06 (1.02–1.10) per 10 μg m^{-3} for all-cause (24 cohorts), respiratory (15 cohorts), COPD (9 cohorts), and ALRI (5 cohorts) mortality, respectively.

This systematic review and meta-analysis included cohort studies on human populations exposed to long-term NO_2 and O_3 levels. All-cause, respiratory, COPD, and ALRI mortalities were all included as health outcome indicators. A risk of bias tool was used to examine the studies included in the meta-analysis. The study findings are shown as forest plots, and random-effects models were used for the quantitative meta-analyses. The certainty of evidence for each pollutant/outcome pair was assessed using a novel (Grading of Recommendations Assessment, Development, and Evaluation (GRADE) adaption.

Table 3 Health data population characteristics, Agadir city, Morocco, 2016

Exposure	Health endpoint	Age (years)	Population at risk [a]	Hospital admissions or deaths [b]	Incidence (per 100,000 population at risk per year)
Long-term	Mortality, all causes (natural)	30	202,999	1,966 deaths	968.48
	Respiratory mortality			71 deaths	34.98
	COPD			28 admissions	13.79
Short-term	Mortality, all causes (natural)	All	420,288	1,966 deaths	467.77
	Respiratory mortality			71 deaths	16.89
	Ashma [c]			68 admissions	16.18

Note: [a] Data from the GCPH2014 dataset, [b] Only data from the cardiology and pneumology departments were considered and [c] Hospital and emergency room admissions for asthma.

1.1) Long-term impact of NO_2 on natural all-cause mortality

The AirQ+'s default RR for all-cause natural mortality was estimated to be 1.02 (95% CI: 1.01–1.04). The WHO AirQ+ results (Table 4) indicate that for a mean annual NO_2 concentration of 100.57 µg m^{-3}, 222 deaths caused by long-term exposure to NO_2 would be potentially avoidable out of the 1,966 deaths in adults aged 30 and older; thus, the AP represented 11.3% if the mean annual NO_2 concentration did not exceed 40 µg m^{-3}, which is the threshold recommended in WHO AQG 2005. The RR calculated for this situation was 1.13 (95% CI: 1.06–1.27). For example, if the annual mean NO_2 concentration did not exceed 30, 20, or 10 µg m^{-3}, the APs were 13.04, 14.75, and 16.42%, respectively, which are the second and third interim target values and the WHO AQG level recommended for 2021. The NAP significantly moves from IT1 to the AQG.

The RR was calculated using ecoepidemiological and time-series research to represent the increased risk induced by pollutant exposure. The daily association between air pollution and the resulting health impacts, such as mortality from respiratory disorders, COPD, or hospital and emergency room admissions for asthma, was investigated. The study showed that increasing the NO_2 concentration by 10 µg m^{-3} resulted in a 0.13%–0.20% increase in total mortality. The increase in the RR for each 10 µg m^{-3} decrease in NO_2 suggested that increasing the NO_2 concentration influences natural all-cause mortality.

Figure 2 presents a complex picture of the long-term impact of NO_2 on all-cause mortality, with variations in reported risks across countries and study years. While most studies suggest a positive association between long-term NO_2 exposure and mortality, the magnitude of the effect is generally modest. This study from Morocco reports a RR of 1.130 (95% CI: 1.060-1.270), indicating a 13% increase in mortality risk for each 10 µg m^{-3} increase in long-term NO_2 exposure. Compared to other studies, this study presents a moderately elevated risk, falling within the range observed in studies from various countries. For instance, Yorifuji & Kashima (2020) in Japan found a similar RR of 1.060 (95% CI: 1.020–1.110) [26]. However, this study stands out for its narrower confidence interval compared to studies reporting similar RRs, such as Desikan et al. (2016) in Canada (RR = 0.940, 95% CI: 0.760–1.170) [27]. This suggests greater certainty in the risk estimate provided by this study.

Several US-based studies [28–35] reported RRs close to 1, indicating small to moderate increases in mortality risk. Similar findings were observed in Canada [36–37] and Europe [38–46].

However, certain studies, like Jerrett et al. (2009) in Canada (RR 1.230, 95% CI: 1.000–1.510) and Filleul et al. (2005) in France (RR = 1.140, 95% CI: 1.030–1.260), reported more substantial risk elevations. Interestingly, some studies, particularly Chen et al. (2016) in China [47], reported RRs below 1, suggesting a potential protective effect of NO_2, though these findings require cautious interpretation. This variability in risk estimates across studies could be attributed to differences in study populations, exposure levels, methodologies, and the influence of confounding factors.

The wide range of reported confidence intervals highlights the inherent uncertainty in quantifying the precise magnitude of the risk. This study with its relatively narrow confidence interval, contributes to a more precise understanding of the NO_2-mortality relationship. However, further research, including meta-analyses and investigations into potential dose-response relationships, is crucial for refining our understanding of this complex issue.

Subsequently, this study adds to the growing body of evidence demonstrating a positive association between long-term NO_2 exposure and all-cause mortality. Its relatively precise risk estimate, in comparison to other studies with wider confidence intervals, reinforces the importance of prioritizing NO_2 mitigation strategies. Further research is needed to clarify the magnitude of the risk, understand the contributing factors, and inform the development of effective air quality guidelines to protect public health.

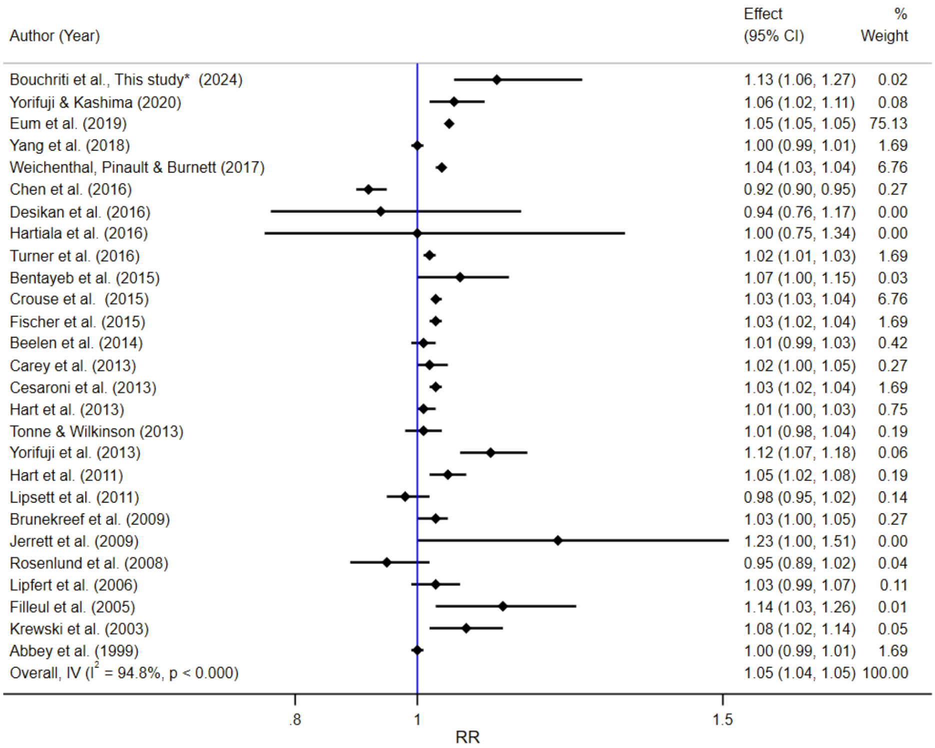

Figure 2 Forest plot of study-specific estimates of long-term relative risk of mortality, all causes (natural) relevant to a 40 µg m^{-3} increase in NO_2 exposure stratified by years.

1.2) Assessment of the impact of NO_2 on long-term health and respiratory mortality

The AirQ+'s default RR for respiratory disease mortality was estimated to be 1.03 (95% CI: 1.01–1.05). The WHO AirQ+ results (Table 4) indicate that for a mean annual NO_2 concentration of 100.57 µg m^{-3}, 12 deaths caused by long-term exposure to NO_2 are potentially avoidable out of 71 deaths in adults aged 30 and older; thus, the AP represents 16.39% if the mean annual NO_2 concentration does not exceed 40 µg m^{-3}, which is the threshold recommended in WHO AQG 2005. The RR calculated for this situation was 1.20 (95% CI: 1.06–1.34).

AP concentrations were 18.83, 21.19 and 23.49% if the annual mean NO_2 concentration did not exceed 30, 20 and 10 µg m^{-3}, respectively, which are the second and third interim target values and the AQG level recommended by the WHO in 2021. The NAP significantly moves from IT1 to the AQG, so the number of potentially avoidable deaths rose from 13 to 17. Furthermore, for each 10 µg m^{-3} increase in the NO_2 concentration, the RR for the increase in total mortality ranged from 0.20 to 0.31%. Given the increase in the RR for each 10 µg m^{-3} decrease in NO_2, we can conclude that increasing the concentration of NO_2 had an effect on mortality due to respiratory diseases.

Figure 3 shows that this study reported a significantly higher RR of 1,200 (95% CI: 1,060–1,340) for respiratory diseases associated with NO_2 exposure than most other studies. This finding suggests a stronger association between NO_2 exposure and respiratory health issues in Morocco than in the other countries.

This study aligns with the findings of several other studies that also showed a relatively high risk. Yorifuji & Kashima (2020, Japan) [8] reported an RR of 1,290 (95% CI: 0,920–1,810), suggesting a similar magnitude of risk, although the confidence interval was wider, indicating more uncertainty. Hvidtfeldt et al. (2019, Denmark) reported an RR of 1,220 (95% CI: 1,150–1,290), suggesting a strong association, with a narrower confidence interval supporting the findings of this study. Carey et al. (2013, UK) reported an RR of 1,220 (95% CI: 1,160–1,270), suggesting a strong association with a slightly lower risk compared with Morocco. Yorifuji et al. (2013, Japan) [48] reported an RR of 1,190 (95% CI: 1,060–1,340) with a similar confidence interval to this study, further suggesting a similar magnitude of risk.

However, this study contrasts with the findings of the majority of studies in Figure 3 that report RRs closer to 1, indicating a weaker association between NO_2 exposure and respiratory diseases. These studies included those conducted by Eum et al. (2019, US) with an RR of 1,050 (95% CI: 1,044–1,056), Yang et al. (2018, Hong Kong) with RRs of 0,990 (95% CI: 0,940–1,040) [49], Weichenthal, Pinault & Burnett (2017, Canada) with an RR of 1,060 (95% CI: 1,040–1,080), Turner et al. (2014, US) with an RR of 1,020 (95% CI: 1,000–1,040), Crouse et al. (2015, Canada), with an RR of 1,020 (95% CI: 1,010–1,040), Fischer et al. (2015, Netherlands) with an RRs of 1,020 (95% CI: 1,010–1,030), Dimakopoulou et al. (2014, EU) with an RR of 0,970 (95% CI: 0,890–1,040) [50], Carey et al. (2013, England), with an RR of 1,080 (95% CI: 1,040–1,130), Cesaroni et al. (2013, Italy) with an RR of 1,030 (95% CI: 1,000–1,060), Hart et al. (2011, US), with an RR of 1,040 (95% CI: 0,950–1,140), Katanoda et al. (2011, Japan), with an RR of 1,070 (95% CI: 1,030–1,120) [51], Lipsett et al. (2011, US), with an RR of 0,960 (95% CI: 0,860–1,080), Brunekreef et al. (2009, Netherlands) with an RR of 1,110 (95% CI: 1,000–1,230), Jerrett et al. (2009, Canada), with an RR of 1,080 (95% CI: 0,640–1,840), Abbey et al. (1999, US) with an RR of 0,990 (95% CI: 0,980–1,010). These studies generally had confidence intervals that did not overlap with those of this study.

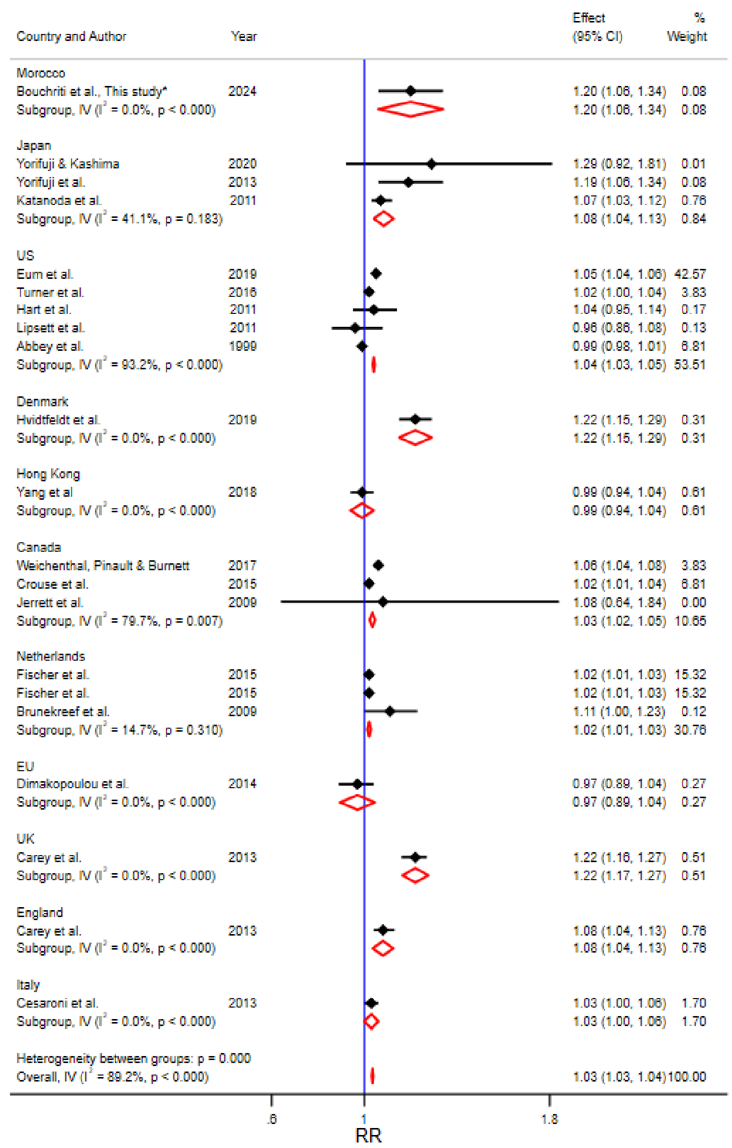

Figure 3 Forest plot of study-specific estimates of long-term relative risk of respiratory mortality relevant to a 40 µg m^{-3} increase in NO_2 exposure stratified by countries.

The high RR found in Morocco aligns with previous studies in other countries, such as Japan, the UK, and Denmark, confirming the potential for a significant impact of NO_2 exposure on respiratory health. The higher RR in Morocco than in other studies suggests that specific environmental or population characteristics may contribute to increased vulnerability to NO_2-induced respiratory problems. Further investigation is required to identify the specific factors involved. This elevated risk highlights the need for effective NO_2 mitigation strategies in Morocco to protect public health and reduce the burden of respiratory diseases.

It is crucial to consider the different methodologies employed by each study (e.g., study design, population characteristics, and exposure assessment methods) to ensure a fair comparison. Differences in air quality regulations, population density, and other contextual factors across countries can influence the association between NO_2 exposure and respiratory health.

This study provides valuable evidence for a strong association between NO_2 exposure and respiratory diseases in Morocco. This higher risk compared to other studies warrants further research to understand the underlying factors and develop targeted interventions to improve air quality and protect public health.

1.3) Long-term health impact assessment of NO_2 on COPD morbidity

The AirQ+'s default RR for COPD mortality was estimated to be 1.03 (95% CI: 1.01–1.04). The WHO AirQ+ results (Table 4) indicate that for a mean annual NO_2 concentration of 100.57 µg m^{-3}, 5 cases caused by long-term exposure to NO_2 would be potentially avoidable out of 28 COPD admissions in adults aged 30 and older; thus, the AP represented 16.39% if the mean annual NO_2 concentration did not exceed 40 µg m^{-3}, which is the threshold recommended in WHO AQG 2005. The RR calculated for this situation was 1.20 (95% CI: 1.06–1.34).

AP concentrations were 18.83, 21.19 and 23.49% if the annual mean NO_2 concentration did not exceed 30, 20 and 10 µg m^{-3}, respectively, which are the second and third interim target values and the AQG level recommended by the WHO in 2021. The NAP significantly moves from the IT1 to the AQG level, so the number of potentially avoidable deaths increases from 5 to 7. Furthermore, for each 10 µg m^{-3} increase in the NO_2 concentration, the RR for the increase in total mortality ranged from 0.20 to 0.31%. Given the increase in the RR for each 10 µg m^{-3} decrease in NO_2, we can conclude that increasing the concentration of NO_2 had an effect on COPD mortality.

Figure 4 presents a global overview of the long-term impact of NO_2 on COPD, revealing a consistent trend of increased risk, albeit with variations in magnitude across studies and countries. This study reports a RR of 1.200 (95% CI: 1.060–1.340) in Morocco, indicating a 20% increase in COPD risk for each 10 µg m^{-3} increase in long-term NO_2 exposure. This finding aligns with other studies demonstrating elevated risks, such as Lindgren et al. (2009) in Sweden (RR = 1.269, 95% CI: 1.026–1.561) [52], Næss et al. (2007) in Norway (RR = 1.210, 95% CI: 1.050–1.390) [53], and Schikowski et al. (2005) in Germany (RR 1.229, 95% CI: 1.121–1.357) [54].

However, this study distinguishes itself with a relatively narrow confidence interval compared to studies reporting similar RRs, like Yorifuji et al. (2010) in Japan (RR = 1.11, 95% CI: 0.78–1.56) [55], suggesting greater certainty in the risk estimate provided by this study. This strengthens the argument for a robust association between long-term NO_2 exposure and COPD risk in the Moroccan context.

Other studies, including those conducted in China [56–58], England [59], Italy [60–61], Denmark [62], Hong Kong [63], Iran [64] and the Netherlands [65], generally reported more modest increases in COPD risk associated with long-term NO_2 exposure. The variability in risk estimates across studies could be attributed to differences in population characteristics, NO_2 exposure levels, study methodologies, and the influence of other environmental and lifestyle factors.

This study with its relatively precise risk estimates and alignment with findings from other countries, contributes valuable data to the global understanding of the long-term health impact of NO_2 on COPD. While further research, including meta-analyses and dose-response analyses, is crucial to refine this understanding, the available evidence strongly suggests that long-term NO_2 exposure poses a significant risk factor for COPD development. This underscores the urgent need for public health interventions aimed at reducing NO_2 emissions, promoting sustainable transportation, and implementing effective air quality standards to protect respiratory health on a global scale.

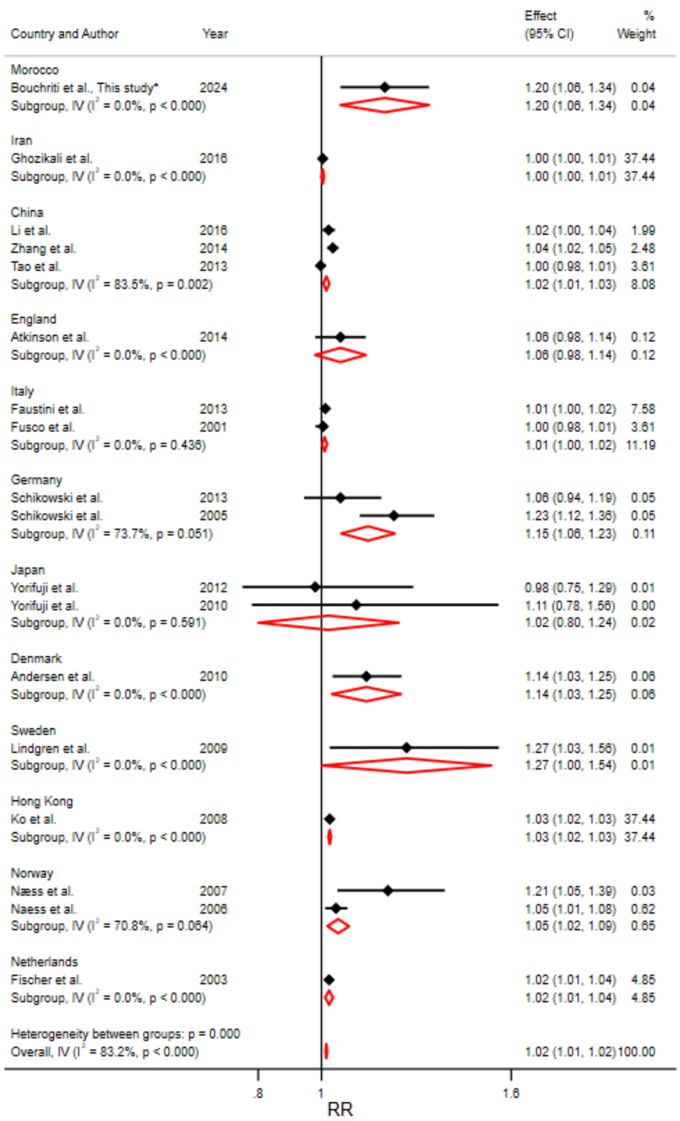

Figure 4 Forest plot of study-specific estimates of long-term relative risk of COPD relevant to a 10 μg m^{-3} increase in NO_2 exposure stratified by countries.

2) NO_2 short-term health impact assessment

The effects of short-term exposure are not offered as an alternative to assessing long-term exposure but rather as a guideline. Furthermore, the impacts of short-term exposure are heavily included in estimations of long-term effects. Short-term impacts are minor in comparison to long-term effects, as one would expect.

2.1) NO_2 short-term health impact assessment on natural all-cause mortality

We wanted to determine the number of non-accidental deaths caused by short-term NO_2 exposure over the WHO AQG 2005 recommended daily hourly mean concentration (200 μg m^{-3}). The default RR value used by AirQ+ for all-cause natural mortality was estimated at 1.0072 (95% CI: 1.0059–1.0085). Calculations were performed for all-cause mortality, with an average yearly NO_2 exposure of 160.33 μg m^{-3} across the research period, using threshold values of IT1, IT2, and AQG (Table 4).

The results indicate that excess deaths are potentially avoidable if the WHO-recommended values for NO_2 are respected. The results in Table 4 indicate that for an annual mean NO_2 concentration of 160.33 μg m^{-3}, 56 deaths caused by short-term exposure to NO_2 would potentially be avoidable from the 1,966 deaths at all ages if the NO_2 concentration did not exceed 120 μg m^{-3}, which represents WHO AQG 2021 IT1. The AP was estimated to be 2.85%, with an estimated RR of 1.03 (95% CI: 1.02–1.04). These findings were consistent with those reported by Miri et al. in Iran. (2015) (AP = 2.08%) and Karimi et al. (2019) (AP = 1.34%) [66–67]. For the IT2 and AQG levels, the AP was estimated to be 7.61 and 9.25%, respectively. For each 25 μg m^{-3} increase in the NO_2 concentration, the RR for the increase in total mortality ranged from 0.02 to 0.10%.

Table 4 Long- and short-term health impact assessment of NO_2 in Agadir city, 2016–2017

Exposure	Health endpoint	Age (years)	X_0 ($\mu g\ m^{-3}$) [a]	RR (CI 95%) [b]	AP (%) [c]	NAP [d]
Long-term	Mortality, all causes (natural)	30	40 [e]	1.13 (1.06-1.27)	11.30 (5.85-21.15)	222 (115-416)
			30 [f]	1.15 (1.07-1.32)	13.04 (6.78-24.18)	256 (133-475)
			20 [g]	1.17 (1.08-1.37)	14.75 (7.7-27.09)	290 (151-533)
			10 [h]	1.20 (1.09-1.43)	16.42 (8.62-29.9)	323 (169-588)
	Respiratory mortality		40 [e]	1.20 (1.06-1.34)	16.39 (5.85-25.59)	12 (4-18)
			30 [f]	1.23 (1.07-1.41)	18.83 (6.78-29.13)	13 (5-21)
			20 [g]	1.27 (1.08-1.48)	21.19 (7.7-32.5)	15 (5-23)
			10 [h]	1.31 (1.09-1.56)	23.49 (8.62-35.72)	17 (6-25)
	COPD		40 [e]	1.20 (1.06-1.27)	16.39 (5.85-21.15)	5 (2-6)
			30 [f]	1.23 (1.07-1.32)	18.83 (6.78-24.18)	5 (2-7)
			20 [g]	1.27 (1.08-1.37)	21.19 (7.7-27.09)	6 (2-8)
			10 [h]	1.31 (1.09-1.43)	23.49 (8.62-29.9)	7 (2-8)
Short-term	Asthma	All	120 [i]	1.06 (1.03-1.08)	5.45 (3.16-7.68)	4 (2-5)
			50 [j]	1.17 (1.09-1.24)	14.22 (8.42-19.63)	10 (6-13)
			25 [k]	1.21 (1.11-1.31)	17.15 (10.22-23.51)	12 (7-16)
	Mortality, all causes (natural)		120 [i]	1.03 (1.02-1.04)	2.85 (2.34-3.36)	56 (46-66)
			50 [j]	1.08 (1.07-1.10)	7.61 (6.28-8.92)	150 (124-175)
			25 [k]	1.10 (1.08-1.12)	9.25 (7.65-10.82)	182 (150-213)
	Respiratory mortality		120 [i]	1.07 (1.05-1.10)	6.94 (4.51-9.3)	5 (3-7)
			50 [j]	1.22 (1.13-1.31)	17.87 (11.85-23.44)	13 (8-17)
			25 [k]	1.27 (1.17-1.39)	21.45 (14.34-27.93)	15 (10-20)

Note: [a] Cutoff value (annual mean), [b] Relative risk with its 95% confidence interval for a cutoff value X0 (annual mean). Log-linear computation method, RR (X) = eβ (X -Xo), where β = 0.001980262729617973 (0.0009950330853168092- 0.003922071315328133), [c] Estimated attributable proportion (%), [d] Estimated number of attributable cases, [e] WHO AQG 2021 IT1 (annual), [f] WHO AQG 2021 IT2 (annual), [g] WHO AQG 2021 IT3 (annual), [h] WHO AQG 2021 (annual), [i] WHO AQG 2021 IT1 (24-h), [j] WHO AQG 2021 IT2 (24-h), [k] WHO AQG 2021 (24-h) and AQG: Air quality guidelines, IT: Interim target.

2.2) Short-term health impact assessment of NO_2 on respiratory disease mortality

We are interested in calculating the number of deaths due to respiratory diseases attributable to short-term daily exposure to NO_2 exceeding the daily hourly mean concentration recommended by the WHO AQG 2005 (200 $\mu g\ m^{-3}$). The default RR value taken by AirQ+ for mortality due to respiratory diseases was estimated at 1.0067 (95% CI: 1.0025–1.0109). Calculations were carried out for all-age mortality, with a mean annual NO2 exposure of 160.33 $\mu g\ m^{-3}$ over the study period for threshold values of IT1, IT2 and AQG (Table 4).

The results in Table 4 indicate that for an annual mean NO_2 concentration of 160.33 $\mu g\ m^{-3}$, 5 deaths caused by short-term NO_2 exposure could be avoided from the 71 deaths at all ages if the NO2 concentration did not exceed 120 $\mu g\ m^{-3}$, which represents WHO AQG 2021 IT1. The PA concentration was estimated to be 6.94%, with an estimated RR of 1.07 (95% CI: 1.05–1.10). For the IT2 and AQG levels, the AP was estimated to be 17.87 and 21.45%, respectively. For each 25 $\mu g\ m^{-3}$ increase in the NO_2 concentration, the RR for the increase in total mortality ranged from 0.07 to 0.27%.

2.3) NO_2 short-term health impact assessment on asthma hospitalizations and emergency admissions

NO_2 induces asthma in children [42] and causes asthma attacks in children and adults [68]. We are interested in calculating the number of cases due to asthma hospitalizations and emergency room admissions attributable to short-term daily NO_2 exposure exceeding the daily hourly mean concentration recommended by the WHO AQG 2005 (200 $\mu g\ m^{-3}$). The default RR value taken by AirQ+ for natural all-cause mortality was estimated at 1.014 (95% CI: 1.008–1.020). Calculations were performed for patients of all ages, with a mean annual NO_2 exposure of 160.33 $\mu g\ m^{-3}$ over the study period for threshold values of IT1, IT2 and AQG (Table 4).

The results indicate that excess cases would potentially be avoidable if the WHO recommended values for NO_2 were respected. The results in Table 4 indicate that for an annual mean NO_2 concentration of 160.33 $\mu g\ m^{-3}$, 4 cases caused by short-term exposure to NO_2 could be avoided from the 68 admissions at all ages if the NO_2 concentration did not exceed 120 $\mu g\ m^{-3}$, which represents WHO AQG 2021 IT1. The PA concentration was estimated to be 5.45%, with an estimated RR of 1.06 (95% CI: 1.03–1.08). Fischer et al. (2015) found similar results (RR = 1.02, 95% CI: 1.01–1.03). For the IT2 and AQG levels, the APs were estimated at 14.22

and 17.15%, respectively. For each 25 μg m^{-3} increase in the NO_2 concentration, the RR for the increase in total mortality ranged from 0.06 to 0.21%.

Conclusion

Studies from around the world have consistently demonstrated a clear link between long- and short-term exposure to NO_2 and increased risks of all-cause mortality, respiratory mortality, and COPD. While the magnitude of this risk varies, the overall trend raises serious concerns for public health, especially in rapidly developing nations, such as Morocco. Research conducted in the city of Agadir, Morocco, specifically highlights a strong association between long-term NO_2 exposure and adverse respiratory health outcomes. However, this finding must be interpreted with caution because of the acknowledged limitations of health data and air quality monitoring in the region.

The AirQ model is a useful tool for estimating air pollution's health impacts, but it has limitations. It relies on simplified representations of complex atmospheric processes and human behaviors, which can lead to inaccuracies in predicting actual pollutant concentrations. The model assumes uniform population distributions and exposure patterns, which may not reflect diverse urban environments. The accuracy of AirQ's predictions depends on input data quality and availability, which can be affected by inaccuracies or gaps in data. It also focuses on population-level impacts, neglecting individual susceptibility and behavioral factors. Therefore, researchers and policymakers should consider these limitations when interpreting research on NO_2 and respiratory health and continuously update concentration-response functions with diverse data.

To address these challenges and protect the health of its citizens, Agadir City needs to prioritize improving data collection and implementing targeted interventions. Agadir City must invest in a robust and reliable air quality monitoring network, specifically within the city, to ensure regular and accurate measurement of NO_2 and other key pollutants. Simultaneously, it is crucial to enhance health data collection and reporting systems, particularly by improving access to healthcare and diagnostic facilities to ensure a more accurate understanding of the true burden of respiratory illnesses.

Furthermore, Agadir City should enforce stricter vehicle emission standards to curb NO_2 emissions from a primary source, encourage the adoption of cleaner vehicle technologies, and phase out older polluting vehicles. Investing in a comprehensive and efficient public transportation system is vital, along with creating dedicated cycling lanes and pedestrian-friendly urban spaces, to reduce reliance on private vehicles and promote active, healthy modes of transportation. The integration of green spaces and urban forestry into city planning will not only enhance Agadir's aesthetic appeal, but also serve as a natural air purification system, creating a healthier and more breathable environment for its residents. Finally, targeted public awareness campaigns in Agadir City are crucial to educate citizens about the health risks of NO_2 pollution, empower them to make informed choices to minimize their exposure, and advocate cleaner air policies.

By directly addressing both the data limitations and sources of NO_2 pollution, Agadir City can effectively mitigate the health risks associated with this harmful pollutant and create a healthier and more sustainable future for its residents.

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Conflict of interest

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